MECHANISMS OF STEWARDSHIP IN THE ROMANIAN HEALTH SYSTEM IN THE DECENTRALIZATION CONTEXT

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Keywords: *stewardship, decentralization*

Abstract: *In 2010, on the background of the economical crisis, the Romanian health policy focused on decentralizing hospitals. The present study is based on a literature review and has as aim to present the term of "stewardship" and to the possible influences of the decentralization process on this vital function of the health systems. The stewardship mechanisms are shown by specific field and some considerations are done in relation to the Romanian health system. The decentralization of the hospitals management could have a favorable impact on reaching the consensus and on self-regulating mechanisms, but it raise questions related to the capacity to implement or enforce the regulation, the local planning capacity and the "intelligent" use of information. The monitoring of the inputs, processes and outputs at hospitals' level is necessary in order to insure the equity, the access and the quality of the health services for all the citizens.*

Cuvinte cheie: *stewardship, descentralizare*

Rezumat: *În anul 2010, pe fondul crizei economice, politica de sănătate a avut ca temă predominantă descentralizarea unităţilor spitaliceşti. Studiul de faţă se bazează pe o revizie de literatură şi are ca scop prezentarea sintetică a principalelor mecanisme de stewardship, urmată de analiza critică a posibilelor influenţe ale procesului de descentralizare asupra acestei funcţii esenţiale a sistemelor de sănătate. Descentralizarea managementului unităţilor spitaliceşti în România poate avea un impact favorabil în ceea ce priveşte utilizarea mecanismelor de consens şi respectiv de autoreglare, dar ridică probleme privind capacitatea de implementare a reglementărilor, capacitatea de planificare la nivel local şi capacitatea de utilizare inteligentă a informaţiilor. Este recomandabilă cel puţin monitorizarea indicatorilor de structură, proces şi rezultat la nivelul spitalelor, pentru a asigura echitatea, accesul şi calitatea actului medical în plan naţional.*

INTRODUCTION

The health system in Romania has dealt in the past months with crisis situation that are more and more frequent and sometimes dramatic and unprecedented. These crises are followed by protest movements against the medical staff - both nurses and doctors. Thus, the staff are often on the verge of losing their inner motivation or of choosing a decent working place abroad.

In 2010, on the background of the economical crisis, the health policy focused on decentralizing hospitals. In this context, we consider it appropriate to introduce the reader to the term of "stewardship" and to the possible influences of the decentralization process on this vital function of the health systems.

MATERIAL AND METHOD

The present study is based on a literature review. It synthetically presents the main mechanisms of stewardship and a critical appraisal of the possible challenges of the decentralization process related to these mechanisms.

RESULTS AND DISCUSSIONS

The notion of stewardship was associated with the health systems in The World Health Organization Report from 2000, which conceptually concretized the functional approach of these systems. According to this approach, four essential functions of the health systems are described. These are: delivering health services, creating resources (investing in buildings, equipment and qualified human resources), financing health systems (collecting, pooling and strategic purchasing of health services) and the stewardship, which means running the health system effectively (1). These four universal functions, which must be fulfilled by all health systems, serve to the accomplishment of their goals, of maintaining health, responsiveness to people's (not always medical) expectations and of fair financial contribution.

The same WHO report emphasizes that health is always a national priority. The greatest responsibility in what concerns the effectiveness of the health systems belongs to the government and this should be permanent.

A classical definition of stewardship is that of "function of the governments responsible of the welfare of the population and aiming at the trust and legitimacy with which their actions are received by the citizens." (2). The function of stewardship consists in establishing and respecting the rules of the system and in providing coherent strategies for all the actors in the system, thus being essential for the accomplishment of the other three functions of the health system and for reaching its main goals. The term includes multiple mechanisms, divided by WHO in three main domains (Table 1).

Each of these mechanisms of stewardship can be developed and detailed for each one of the other specific functions of the health system (providing services, resources generation and financing). Table 2 provides examples from the

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Romanian health system.

Table no. 1. Domains and general mechanisms of stewardship

Domain	General Mechanisms
1. Formulation the health policy	1.1. The existence of a vision about the future, concretized in a national health policy
	1.2. Priorisation based on adequate criteria (e.g. the burden of diseases, the financial effectiveness of the interventions)
	1.3. The existence of measurable short- and medium-term development standards
	1.4. Public consultation and reaching consensus
2. Setting the rules and exerting compliance	2.1. Appropriate regulation in relation to the purposes of the health policy
	2.2. Assuring compliance with the regulations
	2.3. Using self-regulation mechanisms
	2.4. Communication and advocacy
3. Collecting information and sharing knowledge	3.1. An informational system that is adequate to the purpose of understanding inputs, processes and outputs of the health system and of the needs derived form these
	3.2. "Intelligent" use of information for strategic, tactical and operational planning

The stewardship mechanisms are multiple and hard to identify for each level of the health system. Table no 2 is far to be exhaustive. Also the governments usually fail in various degrees in exerting the stewardship of the health systems. We will try to specifically present bellow the challenges indices by the hospitals decentralization to some stewardship mechanisms.

a. Having a vision about the future and a national health policy

The current Governance Program contains a chapter specific for health, but there is no a sectoral strategy in the field. The Governance Program mentions the following strategic documents (4):

- A national strategy for health services development for at least eight years;
- A national plan for investments in infrastructure;
- A national plan for hospital bed purchasing;
- A national plan for human resources.

All these documents are very necessary for a coherent and sustainable functioning of the health system. They would have been necessary even before the hospitals decentralization in order to make regulations for the public administrations in line with the Government plans. The Ministry of Health has kept the responsibility of regulating the health services through the approval of the hospitals structure (number of beds per specialty). The ministry has kept also the attribution of controlling all hospitals. However, for drawing up and implementing the plans above, the ministry needs information from the local level concerning the health status, the health determinants and the health services provision and results. The ministry has regulated the information flow and the compulsory reporting from the medical providers. Also the responsible institutions from the central level have been recently reorganized in a unique national institute of public health. But the capacity of the local administration to implement the regulations remains the major challenge of the hospitals decentralization, together with the ministry's capacity to enforce the local government to fulfill the laws.

b. Using consensus-reaching mechanisms

The general law-frame imposes to the central authorities to insure the intersectoral consultation and the transparence of the decisional process during the elaboration of primary and secondary legislation. Those mechanisms are usually implemented and the decentralization is not a threat for this goal. However some local stakeholders may be easier convinced to support some points of view that are more in favor of some interests groups or goals instead of supporting those goals that are in line with the mission or vision of their organization.

The fragility of the civil society mobilization still remains the main problem in reaching the consensus. The civil society representatives are sometimes not very well informed or they support legitimate but not essential goals for public health (e.g. The mobilization for getting a specific treatment in a rare disease could be more powerful than fight against smoking that kills 33000 people per year) (7).

c. Setting regulations that are appropriate for the goals of the health policy and ensuring the compliance with them

The capacity of setting regulations was quite developed in the health field and at least three "waves" of radical changes occurred in the last twenty years of transition. Setting rules is quite a non-expensive process but the capacity to implement and to reinforce the established rules is very important. This capacity is influenced by at least two determinants:

- The rules are too complex or they have shortage in implementation;
- The capacity of applying the rules (given at the end of the day by the number of existing staff that is qualifies and able to identify the deviations in the field) is decreasing. This progressive fall of the control capacity is induces by the lack of specialists' interest for this career, but also by the lack of strategy in the area from the government or ministry side.

d. Self-regulating mechanisms

Table no. 2 (point 2.3) provides some examples of self-regulating mechanisms that are functioning currently within the health system. The decentralization process can induce a better implementation of these mechanisms at the hospital, community or county level. But the central health administration must guarantee the equity, the access and the quality of the health care at national level.

e. a health information system able to provide an understanding of the inputs, processes and outputs of the health system

The health integrated information system was an almost constant objective in each governance program after the '90ies. However the health information flow is still unclear in present. The heath services providers report distinctly both to the national insurance house and to the public health directorate, essential information related to the most common risk factors prevalence or to post-diagnose or post-therapy life expectancy is missing for all noncommunicable diseases. A national health accounts system is not put in place even some international projects with this goal were implemented in Romania. The national health programs' monitoring capacity is limited and no routine for health technology assessment is seen (there is still some political commitment for the future).

Table no. 2. Stewardship mechanisms from the Romanian health system on each specific function

No. (acc. table 1)	Providing services	Resources generation	Financing
1.1.	- an existing strategy for health services development	- a national health workforce plan (for physicians and nurses)	- strategic purchasing of health services or medical equipments
1.2.	- establishing an appropriate package of medical services that could be provided within the social health insurance system	- appropriateness criteria for high technology purchasing	- health technology assessment mechanisms in place
1.3.	- norms for authorization / accreditation	- minimum standards of human resources – number and training - or minimal standards in terms of equipments or facilities per number of population	- plans for purchasing of health services
1.4.	- public consultation related to the basic package of services or to the drugs list - practical guidelines	- involving the communities or the other economic sectors in strategic planning related to health	- public or interministerial consultation related to financing issues like national health programs
2.1.	- the framework contract for medical assistance within the health insurance system - regulations for placing on the market for medical devices or drugs	- licensing the medical staff - norms concerning the minimum number of staff/facilities for 1000 inhabitants	- payment mechanisms - incentives for providing the most important services in a more efficient manner (e.g. Payment per service of the family doctors for immunization)
2.2.	-monitoring the providers' behavior - market surveillance for drugs or medical devices	- contracting services exclusively from accredited providers - assuring sufficient number of qualified staff for control	- a good capacity of collecting funds
2.3.	- surveillance of medical practice by the professional organizations	- free competition - public information regarding the possible access to medical services	- transparence of public spending for health services within a hospital, within a county and among counties
3.1.	- a registry of medical providers - registering the capacity of health services provision	- a national registry for physicians and nurses	- a national health accounts system - measuring the expectations of the population - measuring the risk factors distribution
3.2.	- plans of health services development at county level	- establishing the necessary number of physicians by specialty	- budgeting the national health programs

Probably some lesson were learnt from the past (not to focus on IT purchasing, but on making the information system operational, to maintain the trained staff, to insure the continuity of the strategies between the governments from different political sides). For the further development of the health information system at least some changes are necessaries:

- To collect useful information and from all of the counties;
- To minimize the resources – time and human resources – spent by the health providers for the compulsory reporting.

The decentralization raise the problem of local capacity to collect and analyze the information flow, but also the problem of receiving the necessary information from all the counties at national level.

f. Using the information flow for strategic and tactic planning

The "intelligent" use of the information flow still remains a challenge for the health system both at local and national level. It involves the collection of reliable information, but also appropriate analysis of it and strategic planning based on evidence. The "intelligent" information use is of course much limited at local level, but its development needs to be foreseen also at the central level.

CONCLUSIONS

The stewardship function is essential for achieving the goals of the health system and the way of exerting the stewardship is also influencing the health services provision, the resources generation and the financing of the health system. The stewardship mechanisms are multiples and it is very difficult to make an inventory of all of them. The decentralization of the hospitals management could have a favorable impact on reaching the consensus and on self-regulating mechanisms. But this process raise questions related to the capacity to implement or enforce the regulation, the local planning capacity and the "intelligent" use of information. According to the literature there is difficult to measure the decentralization process, but we recommend the monitoring of the inputs, processes and outputs at hospitals' level, in order to insure the equity, the access and the quality of the health services for all the citizens.

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THE SYNERGY BETWEEN HEALTH EXPENDITURE AND ECONOMY

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Keywords: *health, expenditure, GDP*

Abstract: *Although health indicators in Romania have seen a steady improvement in the last decade, the effects of recent economic crisis have led to a profound imbalance of the Health Care Services. With an aging population, a much lower number of employees and retirees and a institutional reform discrepancy favorable to hospital care, the current government response, the massive amputation of the public expenditure would entail the collapse of the Health System.With a public expenditure share in GDP less than half of EU average and that of health expenditure by 9 times lower than the EU average, Romania occupies for the last two decades the last place in Europe regarding the health expenditure and the last but one place regarding the public expenditure. In this context, it is expected to increase public spending on Health sector. At the same time, Romania must change the structure of Health expenditure and to increase its cost effectiveness for Health Care.*

Cuvinte cheie: *sănătate, cheltuieli, PIB*

Rezumat: *Deşi indicatorii de sănătate în România au înregistrat o îmbunătăţire constantă în ultimul deceniu, efectele recentei crize economice au condus la un profund dezechilibru al sectorului serviciilor de sănătate. Cu o populaţie îmbătrânită, un număr de salariaţi mult inferior pensionarilor şi o retructurare discrepantă, în favoarea asistenţei spitaliceşti, reacţia guvernării actuale, de amputare masivă a cheltuielilor publice, riscă să genereze colapsul sistemului de sănătate. În condiţiile în care ponderea în PIB a cheltuielilor publice este mai mică decât jumătate din media UE, iar cea a cheltuielilor cu sănătatea de 9 ori mai mică decât media UE, România ocupă în ultimele 2 decenii ultimul loc din Europa în privinţa bugetului alocat sănătăţii şi penultimul în ce priveşte cheltuielile publice. În acest context, este de aşteptat o creştere a cheltuielilor publice destinate sectorului sanitar. În acelaşi timp, România trebuie să îşi modifice structura şi să îşi mărească eficienţa cheltuielilor sale pentru serviciile de asistenţă medicală.*

SCIENTIFICAL ARTICLE OF BIBLIOGRAPHIC SYNTHESIS

In a report published on June 29, 2010, The Organization for Economic Cooperation and Development (OECD) showed that Total Health Expenditure in OECD countries increased faster than the economic growth. Average expenditure on health as percentage of GDP increased from 7.8% in 2000 to 9.0% in 2008.

Thus, in Ireland, the proportion of GDP devoted to health increased from 7.5% in 2007 to 8.7% in 2008. In Spain, it increased from 8.4% to 9.0%. France and Switzerland allocated to health over more 50% than OECD average. United States spent $ 7,538 per person in the health sector in 2008, more than double the average of all OECD countries.

The growth rate of expenditure on Health Care Services (16-27%) is much higher than the expenditure on Education Social System (around 3%) (upon Beraldo and Montolio and Speed, quoted 3).

According Eurostat (3), the profile of EU spending in the health sector shows that:

- EU-25 spends on average 7.76% of GDP for health care. EU-15 are allocated on average 8.6% and 5.8% in new member states;
- Cardiovascular diseases, the main cause of mortality in Europe and all industrialized countries, consume about 3% of EU GDP annually (about 135 billion);
- Mental illnesses affect over 27% of adults and costs the European economies up to 4% of GDP;
- Tobacco is the first cause of avoidable deaths in the EU. Diseases and deaths caused by smoking in EU countries require more than 1% of annual GDP (100 billion);
- Obesity conditions costs between 70 and 150 billion per year, representing 2-8% of total healthcare costs in Europe.

Today, the main causes of death are noncommunicable diseases, many avoidable, often caused by lifestyle factors.

This means that the lifestyle determinants, Health, Education and cultural factors are closely related, and Health politics must involve more than the investment in a traditional Health Care System.

The message of these macroeconomic studies is that Health can have a positive impact upon Econoy and not merely a result of economic progress.

This is also the opinion of Barcelona Process (2000) (apud 11) and the Commission (2005) for the EU Health Strategy 2007-2013 (9.10) which concludes that the actions and investments are necessary both to prevent disease health and improve economy.

This argument provides heavy justification for politicians in order to invest more in Health as a means to achieve their economic objectives.

However, the opinion leaders in the medical world have different positions regarding the allocation of health resource.

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Figure no. 1. Annual growh in Health expenditure and GDP, 2000-2008 (%)

Source: OECD (3)

Pfizer and GlaxoSmithKline supports the role of the Pharmaceutical Industry as a key partner for governments, physicians and patients in order to to achieve a "better health status for a greater number of people" and underlines also the potential contribution of medical research, innovation and use of high technologies to improve clinical care. (Apud 11)

European Federation of Pharmaceutical Industries and Associations believes that national governments should give higher priority to improve regional Healthcare. The objective of these reforms is to encourage greater investment and structural reforms in both systems, financing and providing Health Services. Also need incentives, guidance, coordination and expertise to regional Healthcare providers responsible for preparing and administering projects with EU funds. (ibidem)

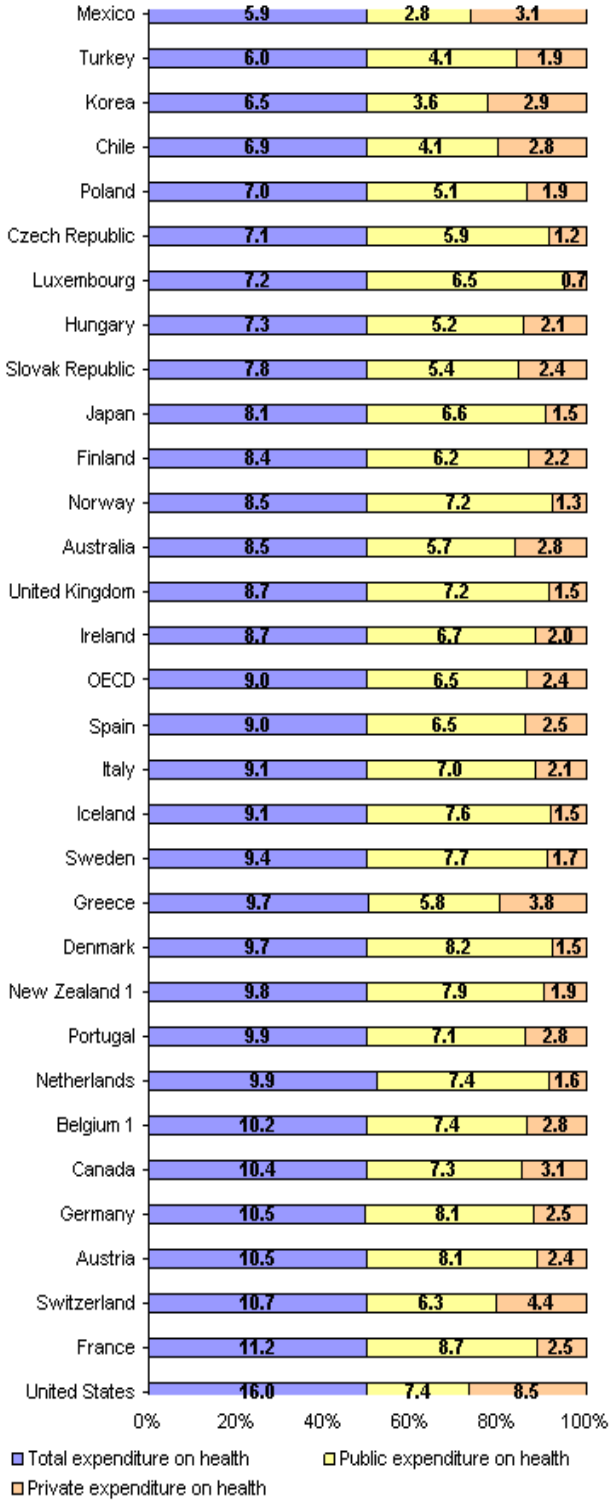
European Public Health Alliance believes that investment in Health should not be devoted to infrastructure improvements in Health or Pharmaceutical industry, but as an allocation of more resources for disease Prevention and Health Promotion. (ibidem)

European Healthcare IT Steering Committee and Industries (ibid) believes that "Health infrastructure is (...) an essential condition for economic growth. The process of building an infrastructure of "modern Healthcare should cover not only hospitals, as traditional symbol of health, but must address also to the other conditions necessary to maintain healthy people (education and prevention).

Standing Committee of European Doctors believes that it is necessary to strengthen the role and activities of The Health and Consumer Protection Commissions and other bodies with similar functions that should have the right and responsibility to influence policies affecting Health. (Ibid)

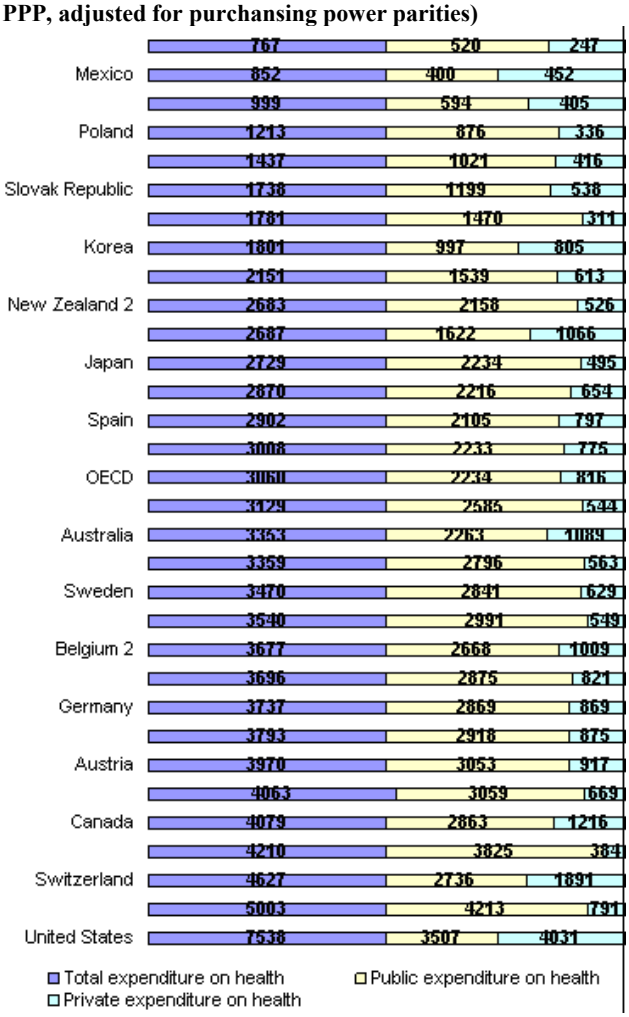
However, the EU budget for 2007-2013 ignores the critical link between a healthy man and healthy economy. (Ibid)

Figure no. 2. Health expenditure as a a share of GDP, 2008



Source: OECD (3)

Figure no. 3. Health expenditure per capita, 2008 (USD PPP, adjusted for purchansing power parities)



Source: OECD (3)

Health expenditure in Romania

Share in GDP of public social expenditure is a synthetic indicator of State's accountability in the production and balancing the welfare. The Social Report of Romanian Academy (1) shows that during the years 1998-2009 Romania has invested less than half of the EU average in the area of social policies: 16.4% of GDP in all European countries that have undergone transition and are now EU member states. This places our country in last postion in Europe in terms of revenue and in the last but one position in terms of expenditure.

According to Eurostat (3), the Health Policy of our country invests less than 8.9 times of the European average, 3.5 times less than Hungary, 5.5 times less than Portugal and 6.5 times less than Spain. The co-payment level in 2009 reached 41% starting from 24% in 2007 and 38% in 2008. Romania annually spends 400 euros for a policyholder, less than to 2500 Euro as it gives the EU and 75 euros for drugs compared with 260 euros which is the average of the European community. Regarding private Health System, the Romanians will spend 420 million euros this year for medical services, 13% more than in 2009.

At this level of Health spending, according to Merck (9), Romania is in the last place in Europe as a percentage of GDP allocated to Health, given that most countries of the world grow THE Health budget allocation of GDP from year to year.

In 2012 will end up out of pocket even more than 600 million for medical services in private Health System, according to Merk Company (9). The cause is obvious: dissatisfaction regarding the inadequate conditions and treatment in most public hospitals. According to the sources (1,3,9), the situation would improve significantly only if Romania will spend more on Health System so that in 2012 to reach 6% of GDP and in 2014 the level of 8%. Average rate of increase of Health budgets would be around 21% and the proportion of GDP allocated to Health in 2014 would allocate close to 85% of EU average in 2009. Estimated Health expenditure per capita in 2014 would reach half the European average today.

As a conclusion

However public services and investment in these services are beyond the phenomena that lead to social blockings the dominant ideology hypothesis seems to wrongly considered the State as being a major consumer of the welfare, ignoring his total amplitude of main welfare producer through Education, Health, Science, Public and Social Security.

Although in terms of crisis / restructuring / social policy similar almost all states lead to increase social protection, in Romania, the present government response is to balance the budget through massive cuts in social areas: Education, Health and Social Assistance, pensions and other social benefits for high social risk groups. This policy is likely to continue into 2011. In addition, there is a trend of disintegration both of public education and Health Systems by underfunding and discreting by the generalization of individual negative examples.It is a strong policy of privatization of these services, with all their negative social consequences. While the poorest segment of the population extends, the likely effect is to increase the social polarization, and to sentence this people to a poor education and poor Health condition. (1,2,3)

Finally, after 20 years, Romania has still a large number of poor and greater inequality than in 1989, and an additional burden on external debt and their accompanying social costs.

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PRIVATE HEALTH INSURANCE IN ROMANIA A RETROSPECTIVE VIEW

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Keywords: *health inssurances, sanitary reform*

Abstract: *In Romania the degree of diffusion of the assurances (for all the categories)is low but it has been observed a tendency of increasing in the last years,even in the context of this economic recession.Once with the apparition of the Law 95/2006 ;regarding the reform in the sanitary field it has been observed a certain effervescence in the favour of the implementing the private health insurances; with a complementary role, as a supplementation of the available funds through the compulsory contribution at the CNAS funds.*

Cuvinte cheie: *asigurări de sănătate, reforma sanitară*

Rezumat: *În România, gradul de penetrare al asigurărilor (toate categoriile) este redus, dar se înregistrează o tendinţă uşor crescătoare în ultimii ani, chiar în contextul acestei recesiuni economice. Odata cu apariţia Legii 95/2006, privind reforma în domeniul sanitar, se constata o anumită efervescenţă, în favoarea implementării unor asigurări private de sănătate, cu rol complementar, ca o suplimentare a fondurilor disponibile prin contribuţia obligatorie la fondurile CNAS.*

SCIENTIFICAL ARTICLE OF BIBLIOGRAPHIC SYNTHESIS

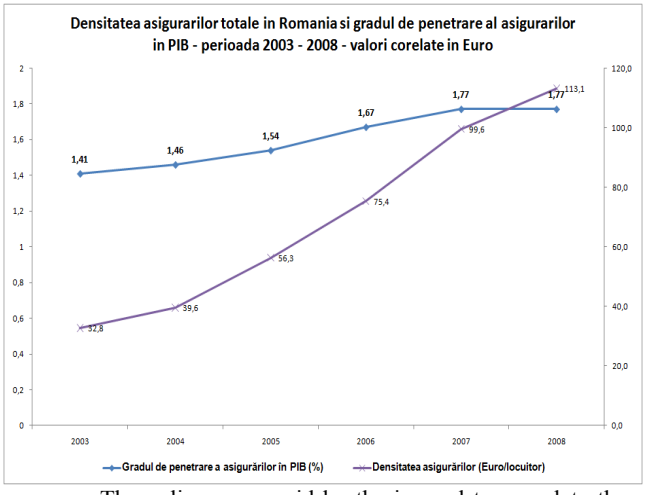
The increase of demand for healthcare services from patients, which tend to be more and more informed about diagnosis and therapeutical procedures, and the ceiling imposed by the National Health Insurance House on medical expenditures, will result clearly in an increase of health care costs, which cannot be entirely covered using the public resources. In a first stage, that ended in 2003-2004, the extra money needed for filling this gap was covered directly by patients themselves, by direct voluntary payment. In recent years, with a new healthcare legislation in place, that is Law 95/2006, the private health insurance developed mainly as a complementary system, regarded as extra contribution, on top of the compulsory social healthcare contribution

Tabel no 1. The evolution of the indicators that define the economic context of the assurances during 2003-2008

Indicator	2003	2004	2005	2006	2007	2008
Insurance to GDP ratio (%)	1,41	1,46	1,54	1,67	1,77	1,77
Insurance density (RON/ inhabitant)	123	160,4	204	265,7	332,4	416,62
Exchange rate Euro/leu	3,7555	4,0532	3,6234	3,5245	3,3373	3,6827
Insurance density (Euro/ inhabitant)	32,8	39,6	56,3	75,4	99,6	113,1

Neither in the past, when it was a slightly economical boom, nor today, when recession strikes, the percentage of people actually covered by this type of insurance did not reached an optimal level, compared with a two-digit yearly development of private healthcare providers.

It is important to be mentioned that, for the moment, in Romania, the overall insurance-to-general population ratio is still low compared to EU, but had a positive trend.



The policy sums paid by the insured to complete the sums paid by CNAS represents a brute sum, from which the emition and distribution expenses supporte by the assurance company asigurator; the policy sums are paid directly by the insured self-employed or in the majority of cases by the employeers for a group of employees.

The city of Bucharest concentrate more than a half of total premium subscription, which is in line with a local GDP much higher than national average, but also with the distribution pathway for private health care insurance – that is – using as corporate employee benefits

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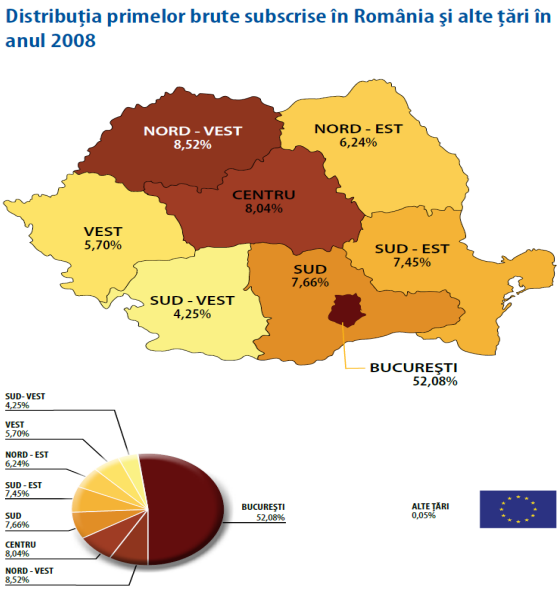

Gross Premium written as on 31.12.2008 (RON)

Non-life insurance type	31.12.2007	31.12.2008	(%)Nominal increase	31.12.2007Share at	31.12.2008Share
I. Accident and sickness insurance	66.163.121	62.500.806	-2,57%	1,20%	0,88%
II. Health insurance	23.728.045	28.209.304	18,73%	0,40%	0,40%

Life-insurance type	31.12.2007	31.12.2008	(%)Nominal increase	31.12.2007Share at	Share at 31.12.2008
B1. Accident and sickness insurance	12.540.058	22.410.702	78,71%	0,90%	1,20%
B2. Health insurance	4.518.787	6.791.043	50,28%	0,30%	0,40%

After a significant increase of private health care insurance during the economic boom, which reached its maximum in 2008, one can see a decrease trend in of subscription starting 2009, which correlates with a decrease of all type insurance subscription.

Gross Premium written as on 31.12.2009 (RON)

Non-life insurance type	31.12.2008	31.12.2009	(%)Nominal increase	31.12.2008Share at	31.12.2009Share at
I. Accident and sickness insurance	62.500.806	62.340.872	-0,26	0,88%	0,86%
II. Health insurance	28.209.304	24.854.679	-11,89	0,40%	0,34%

Life-insurance type	31.12.2008	31.12.2009	(%)Nominal increase	31.12.2008Share at	31.12.2009Share at
B1. Accident and sickness insurance	22.410.702	25.713.927	14,42%	1,20%	1,58%
B2. Health insurance	6.791.043	4.401.750	-35,32%	0,40%	0,27%

The caring for patients with private health assurances allows a constant flux of suplimentary revenues as payments for medical services that will ensure the rapid depreciation of the investments and also a fond of developpment.

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ANALYSING THE MORTALITY ASSOCIATED WITH THE HEART DISEASES IN ORADEA MUNICIPALITY

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Cuvinte cheie: *mortalitate, boli cardiovasculare, decese*

Rezumat: *Studiul răspândirii şi implicaţiile medicale ale bolilor cardiovasculare, a evoluţiei lor în timp, reprezintă modalitatea cea mai adecvată de stabilire a unor măsuri eficiente în prevenirea şi combaterea acestor boli. Analiza mortalităţii cardiovasculare este indispensabilă studiului factorilor de risc, profilaxiei bolilor cardiovasculare, urmăririi corecte a bolnavilor şi repartizării mijloacelor tehnice şi logistice de luptă împotriva acestor boli. Au fost analizate decesele din municipiul Oradea în perioada 2003-2007. Evoluţia mortalităţii prin boli cardiovasculare în perioada 2003-2007 în municipiul Oradea, este sub media pe judeţul Bihor şi ţară, mortalitatea fiind mai mare la sexul masculin şi la grupa de vârstă de peste 65 de ani. Pe grupe mari de boli, mortalitatea prin cardiopatii ischemice deţine primul loc. Vârsta medie la deces prin boli cardiovasculare (ani) prezintă valori cuprinse între 72,0 şi 72,5 ani, de-a lungul perioadei studiate, cea mai mare valoare în anul 2005, iar cea mai mică în 2003.*

Keywords: *mortality, heart diseases, deceases*

Abstract: *The study of the prevalence and the medical implications of heart diseases, and of their evolution in time, represents the best way of taking efficient steps for the prevention and control of these medical disorders. The analysis of the cardiovascular mortality is essential for the study of risk factors, for the prevention of cardiovascular diseases, for the correct observation of disordered patients and for the distribution of technical and logistic means, necessary in the action taken against these diseases. We have considered the deceases that have occurred in Oradea municipality during the period 2003 and 2007. The evolution of mortality due to cardiovascular diseases in Oradea municipality, during the period 2003-2007, has been under the medium level of Bihor county and the situation in our country at large, the death rate being higher in the case of men and persons over 65. By analysing the death rate in terms of large groups of diseases, the mortality caused by myocardial ischemia occupies the first place. The average age at the deaths caused by heart diseases was about 72,0 and 72,5 years for the period we had in view, the highest rates being identified in 2005 and the lowest rates in 2003.*

INTRODUCTION

In Europe, about 4 million deaths occur every year as a result of heart diseases, representing almost half of the total number of deaths (55% of the total number of deaths in case of women and 43% from the total of deaths in case of men). About half of the deaths caused by heart diseases are determined by the myocardial ischemia, which is responsible for 2 million of deaths annually (1).

In the European Union, the situation is almost similar: the heart diseases are also a major cause of death (1,5 million people die annually of heart diseases, which represents 42% of all death cases). Myocardial ischemia causes approximately 600000 deaths annually, respectively 1 in 6 deaths in the case of men and 1 in 7 deaths in the case of women (2, 3).

In Romania the heart diseases represent the main mortality cause, being responsible for 62% of the total number of deaths. The death rate associated with such diseases seems to decrease, but the standardised death rate is much over the average rate in Europe.

PURPOSE OF THE STUDY

The study of mortality caused by heart diseases, with the view of identifying those categories of persons who, by correlation with the heart disease, can represent a priority for the application of preventive and educative measures; the finding of some aspects and correlations between the level of mortality and some socio-economic and cultural factors.

MATERIAL AND METHOD

In the course of the observational, the retrospective and the descriptive study, conducted in Oradea municipality during 2003-2007, we have gathered information concerning the population and the number of deaths caused by heart diseases. The main source of data has been the Medical Certificate that states the deaths. All data have been evaluated by using statistical methods and have been correlated with demographic indicators, using the medical codifications included in the International Classification of Diseases, 10th revision, in accordance with the Basic List – 999 codes. We have used methods such as the ones referring to measuring, description and analysis of the specific mortality.

RESULTS AND DISCUSSIONS

In 2006, in Romania, the deaths associated with the cardiovascular diseases represent the main mortality cause – 742,8 deaths for 100000 persons, being followed, at an

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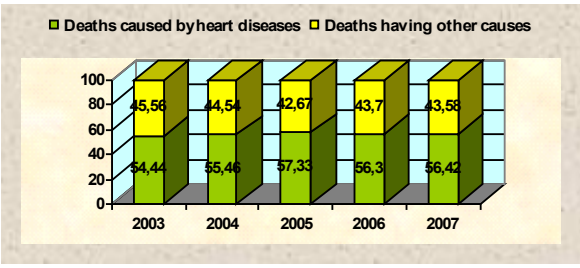
important distance, by neoplasias (210,6 deceases for 100000 persons).

At the inter-county level, the indexes for the standardised cardiovascular mortality varies from 900,2 deaths at 100 000 persons for Satu-Mare county, 575,8 for Brasov county and 530,5 for Bucuresti municipality (4,5). In terms of mortality caused by heart diseases, Bihor county occupies the 8th place at the national level.

During 2003-2007, 5975 persons died of heart diseases in Oradea, which indicates an annual rate of 1195 cases, the lowest annual value of 1168 cases being registered in 2007, and the highest one, of 1234 deceases, in 2004.

Figure no. 1. The death rate due to heart diseases, from the total of deaths having occurred in Oradea municipality, during the period 2002-2007



The evolution of mortality due to heart diseases, during the period 2003-2007, in Oradea municipality is under the medium level in Bihor county and in our country in general (see figure 2), with the highest mortality rate having occurred in 2002; we can also observe a lowering of this rate during the period we had in view.

Figure no. 2. The evolution of mortality caused by heart diseases during the interval 2003-2007 in Oradea municipality, in Bihor county and in Romania

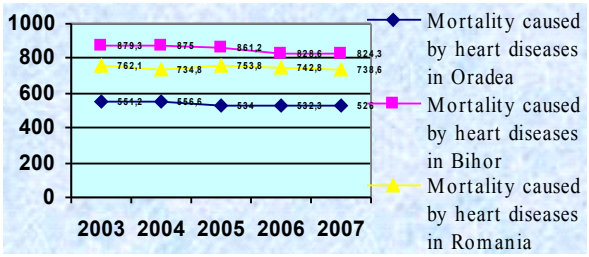
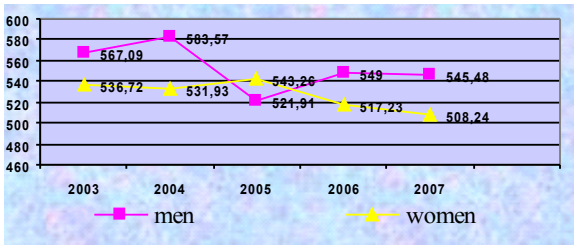


Figure no. 3. The evolution of mortality caused by heart diseases in Oradea municipality, during the period 2003-2007



The percentage of deaths registered in Oradea municipality during the period 2003-2007, caused by heart diseases, related to the sex of the dead persons, indicates the fact that there have been registered more deaths in the case of women (3053), by comparison with the case of men (2922). Although a highest death rate can be associated with women, the feminine mortality is lower than the masculine one, with the exception of 2005.

There haven't been significant changes concerning the rate by heart diseases in terms of age groups, in Oradea municipality, during the period 2003-2007.

Table no. 1. The rate of deaths caused by heart diseases in terms of age groups, in Oradea municipality, during the period 2003-2007

Age groups	2003	2004	2005	2006	2007	Total
0-19	1	6	7	5	6	25
20-34	6	10	3	4	5	28
35-49	74	66	61	58	61	320
50-64	215	231	212	231	219	1108
Over 65	922	923	893	881	877	4396
Total	1218	1234	1176	1179	1168	5975

The evolution of deaths during the period 2003-2007, due to heart diseases in terms of age groups, in Oradea municipality, indicates a decrease in the number of deaths for almost all the age groups.

Table no. 2. The death rate (reported at 100000 inhabitants) due to heart diseases, in terms of age groups, in Oradea municipality, during the period 2003-2007

Age groups (years)	2003	2004	2005	2006	2007	Total
0-19	1,78	12,68	14,05	12,8	15,63	11,39
20-34	11,37	15,23	5,33	6,75	8,1	9,36
35-49	140,57	119,27	109,97	105,27	111,5	117,32
50-54	681,6	721,57	658,53	689,4	463,57	642,93
> 65	1920,68	1914,25	1882,12	1847,28	2031,20	1919,11
Total	701,8	710,6	767,9	762,1	734,8	736,2

The age groups between 60-64 years present relatively low mortality rates, and the evolution of the cardiovascular mortality at these age groups presents little variation from one year to another. With the patients' evolution in age, the number of deaths increases, while the population in terms of age groups decreases, which determines the pronounced increase of mortality values for the group ages over 65 years.

Table no. 3. The cardiovascular mortality in terms of the causes for the deaths, in Oradea municipality, during the period 2003-2007

The cause of the deaths	2003	2004	2005	2006	2007
Hypertension	11,31	11,72	20,88	12,64	12,60
Acute myocardial infarct	128,08	119,07	105,34	106,10	117,54
Other myocardial ischemias	174,25	188,08	190,25	174,72	141,41
Cerebral-vasculr diseases	155,69	147,94	143,94	148,08	145,46

In terms of large groups of diseases, the mortality due to myocardial ischemias occupies the first place, representing about 50 % of the total of cardiovascular mortality for the whole period of time we have in view, while the group of cerebral-vascular diseases represent only 25 %.

In terms of evolution, the mortality caused by chronic myocardial ischemia registers a slow increase until 2006, after which we can observe a decrease with approximately 25% from the value of the mortality, while the mortality caused by acute myocardial infarct and cerebral vascular accident present an approximately stationary evolution till 2006, after which we can observe a slow increase in 2007.

Table no. 4. The masculine and the feminine mortality in terms of deaths causes in Oradea municipality, during the period 2003-2007

sex	The cause of the deaths	2003	2004	2005	2006	2007
masculine	Hypertension	8,50	8,49	14,26	14,27	11,19
	Acute myocardial infarct	181,47	162,41	130,24	119,88	86,14
	Other myocardial ischemias	130,43	167,14	160,66	161,75	163,67
	Cerebral-vascular diseases	159,73	146,36	138,79	147,47	145,58
feminine	Hypertension	13,89	14,67	26,85	11,16	11,19
	Acute myocardial infarct	79,03	79,44	82,31	93,65	86,14
	Other myocardial ischemias	214,51	207,24	243,59	186,44	163,67
	Cerebral-vascular diseases	136,35	149,39	148,16	148,64	145,58

The average age at death is between 72,0 and 72,5 years, during the period that we had in view, the highest rate being registered in 2005 and the lowest one in 2003. The number of persons over 65 years old, from the total of the population, indicates a slow increase during the period we had in view, from values of 9,3% in 2003 to 9,9% in 2007.

Figure no. 4. The evolution of the average age in case of deaths caused by heart diseases, in correlation with the percentage of elderly persons, during the period 2003-2007

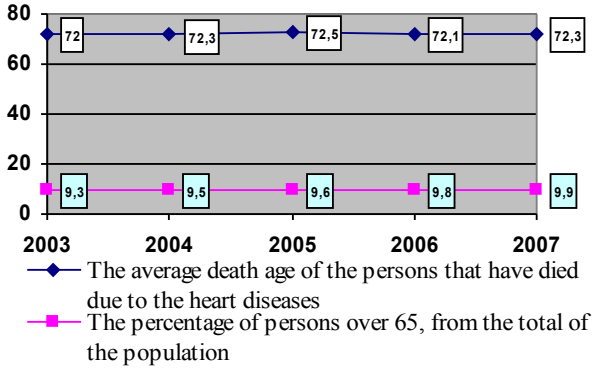


Table no. 5. The evolution of the average age in case of deaths caused by heart diseases, in correlation with the percentage of elderly persons, during the period 2003-2007

(years)age group	The percentage of deaths caused by heart diseases corelated to the age group, from the total number of deaths caused by heart diseases					The percentage of the population of the respective ages, in relation with the total number of the population (%)				
	2003	2004	2005	2006	2007	2003	2004	2005	2006	2007
< 50	6,7	6,4	6,0	5,7	6,2	76,0	75,5	74,9	74,3	74,0
50-64	17,7	18,7	18,0	19,6	18,8	14,7	15,0	15,4	15,9	16,0
65-74	27,9	25,6	25,9	27,3	26,4	6,3	6,4	6,4	6,5	6,6
> 75	47,8	49,0	50,1	47,4	48,7	3,0	3,1	3,2	3,3	3,4

In terms of the percentage of the population divided in large age groups and the percentage of deaths caused by heart diseases, corresponding to the period 2003/2007, we can observe an inverse ratio relation between the two entities. In relation with the percentage of population with large age groups, we can observe a progressive aspect, the lowering of this percentage for persons under 50, from 75,97% in 2003 to 74% in 2007, and for the persons over 50 a slow increase, from 2003 till 2007.

Looking at the deaths caused by heart diseases, in relation with the age groups and taking into consideration the total number of deaths caused by heart diseases, we can speak of an oscillating evolution during the five years we had in view.

CONCLUSIONS

The standardised cardiovascular death rate in Bihor county and Oradea municipality presents the same characteristics as the one registered at the level of the entire country, the tendency towards the decrease of the specific mortality being observed here as well.

During the period 2003-2007, 5975 deaths caused by heart diseases have been registered in Oradea municipality, of which 3053 occurred in case of women and 2922 in case of men.

The main diseases that have caused the death are the following: the chronic myocardial ischemias, the acute myocardial infarct and cerebral vascular accidents that have not been defined as haemorrhage or infarct.

The average death age for the persons who have died due to heart diseases (years) is between 72,0 and 72,5 years, for the entire period that we had in view.

Completing the analysis we have done with the study of other epidemiologic indicators, in relation with the diagnosis and therapeutic means available in Bihor county, we shall manage to obtain a local model, that would allow us to adapt the network of cardiovascular assistance in terms of necessities. The model, if successful, could be adapted and extended later to the situation of other counties, or even to that of the entire country.

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SURVEY ON ASSESSMENT OF THE QUALITY OF LIFE IN PATIENTS DIAGNOSED WITH CHRONIC CONDITIONS WITH A DEGREE OF DISABILITY LIMITING THEIR PERFORMANCE ON DAILY ACTIVITIES

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Keywords: *chronic pathology, invalidity degree;emotional issues*

Abstract: *The present study evaluates the life quality of the persons diagnosed with a chronic pathology that needs to be classified in a invalidity degree through the autoevaluation of the level of the life quality and restrictions imposed by the presence of the chronic pathology*

Cuvinte cheie: *patologie cronică, grad de invaliditate, probleme emoţionale*

Rezumat: *Studiul evaluează calitatea vieţii persoanelor diagnosticate cu patologie cronică care necesită încadrarea într-un grad de invaliditate prin metoda autoevaluării nivelului calităţii vieţii şi restricţiilor impuse de prezenţa patologiei cronice*

INTRODUCTION

The common ground of health care strategies concerning both physical and psychological well-being shapes itself in accordance with the current European social standards and addresses disabled individuals' personal independence from all points of view. Apart from its psychosomatic aspect, disease, that is, loss of health, represents a living condition different from the normal one experienced before the the disease has settled in.

Occupational disease and work-related accidents may lead to partial or complete loss of the ability to work and, thus, to a certain degree of disability, which, in its turn, results in reducing the functional level of an individual affected both physically and psychologically. This will cause the disabled to be assigned into a particular medical and social category.

From this perspective the disabled individuals face various limitations in their daily activities and participation in social life that basically translate into difficulty in solving social or professional problems or in grappling with their disabled condition. All these generate a decrease in the quality of life.

Decision-making and administration forums are responsible with granting protection against decrease in the quality of life while their support should translate into a set of measures intended maintain at high level both qualitative and quantitative indicators of the quality of life. These measures are definitely needed since any disabled individual is entitled to enjoy the same rights as any other healthy person regardless of the origin and nature of their disability.

Social security addresses several areas from which collective effort is needed such as health care, instruction and education, culture, conditions of rest and recreation, the social and political environment, in other words, the living conditions. To the above one should add material aspects (such as housing and the living environment, employment and work conditions, income and expenses), family and social life aspects, as well as respect towards the social and legal order.

PURPOSE OF THE STUDY

With the specific purpose not only of improving the current situation and raising the level of the quality of life for the disabled population groupbut also of becoming involved in offering real support to the members of this category, I have embarked on assessing the quality of life of individuals diagnosed with chronic disease and requiring assignment of a degree of disability. I have resorted to the method of using their own assessment of the quality of life and of the limitations brought along by their chronic condition in what concerns daily routines, the ability to preserve human realtionships with family members, friends, acquaitances and strangers, and the possibility to enjoy an adequate social life.

MATERIAL AND METHOD

I have created an original questionnaire with multiple choice answers centering on the patients' own assessment of the chronic condition and its impact on the quality of life from the point of view of how the physical health and the psycho-emotional state influence daily social activities and the ability to relate to others.

The first part of the questionnaire consists of questions intended to identify and characterize the surveyed respondents. Next come questions intended for respondents to assess not only their own ability to care for themselves and do house chores but also the impact on daily life, human relationships and social activities that their physical health and emotional problems caused by diagnosis and disability may have.

The survey relied on 100 individuals from the county of Sibiu that have been diagnosed with a chronic condition which resulted in thier being assigned a degree of disability. Every eleventh person was selected for the survey out of the total number of disabled individuals in the county of Sibiu. Out of the 100 questionnaires, 7 have proved inconclusive, and thus have not been analyzed, leaving a total of 93 respondents.

RESULTS AND DISCUSSIONS

The survey shows that, out of a total of 93 responding patients, more than half (59.14%) are women and all of them are within 30 and 65 years of age. A third of the respondents (33.34%) have a low level of education, about a quarter of them (24.73%) attended vocational schools while the rest of them, more than two fifths (41.93%) have a medium-to-high level of

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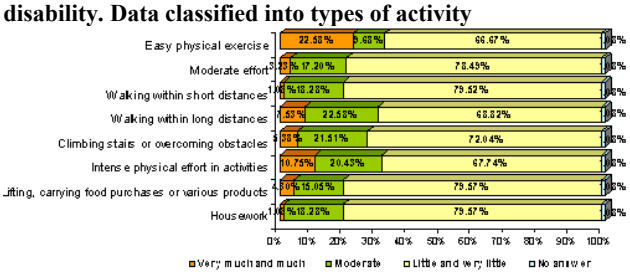
education. The survey also shows that more than half of the respondents (61.29%) live in urban areas of Sibiu county.

Analyzing the data on the patients' own assessment of the ability to perform daily routines prior to being diagnosed and medically assigned a degree of disability, one may notice that the majority of the respondents claim not to have had major difficulty in carrying out these particular activities.

Figure no. 1. The percentage of responding patients and their own assessment of the ability to perform daily routines prior to being diagnosed and medically assigned a degree of disability. Data classified into types of activity

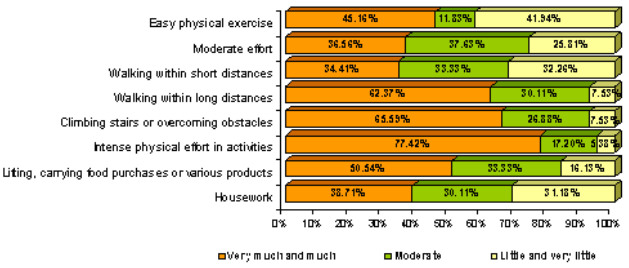


Not to ignore though are the percentages of patients stating that prior to being diagnosed they felt major or moderate discomfort in performing daily activities as well as in maintaining their personal hygiene and getting dressed (19.36%), in lifting and carrying food purchases or other products (19.35%), in performing activities requiring intense physical effort such as practising sports or lifting weights (31.18%), in climbing stairs or overcoming obstacles (26.89%), in walking both long distances (30.11%) and short ones (19.36%), and in doing physical exercise, even easy, fitness exercises such as bends, squats and lunge slides (32.26%). The lack of answers to questions is represented by a percentage of 1.08 for all types of activities (see graph 1).

Analysing the data in graph 2, it is evident that the majority of the responding subjects feel major or moderate difficulty in carrying out daily routines after being diagnosed with a chronic disease and being assigned a degree of disability. This points out that there is a negative impact of the chronic condition on the patients' quality of life.

The analysis also shows that almost two fifths of the respondents (38.71%) feel a major influence of the chronic condition in performing regular daily activities. Also, more than half (50.54%) claim that, after being diagnosed, their ability to lift and carry food products or other items was highly affected and this has resulted in their dependence on other individuals.

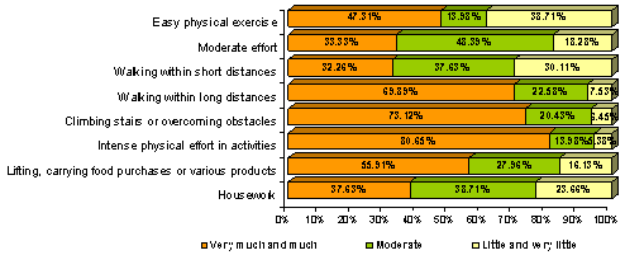
Figure no. 2. The percentage of responding patients and their own assessment of the ability to perform daily routines after being diagnosed and medically assigned a degree of disability. Data classified into types of activity



Just as important is that more than three quarters of the subjects (77.42%) claim that upon diagnosis their ability to perform activities requiring intense physical effort was considerably reduced encountering more than just many difficulties in carrying out these tasks.

We may also notice high and impressive percentages of respondents (65.59% and 62.37%) who claim that after being diagnosed feel great difficulty in climbing stairs and overcoming obstacles as well as in walking long distances. We find relatively equal percentages (34.41% and 36.56%) of patients who claim to encounter great difficulty in walking even short distances and in carrying out daily routines that require moderate effort. In addition, more than two fifths of respondents (45.16%) state that their chronic condition has considerably affected their ability to do physical exercises such as bends, squats and slide lunges.(see graph 2)

Figure nr. 3. The percentage of responding patients and their own assessment of the ability to perform daily routines a year after being diagnosed and medically assigned a degree of disability. Data classified into types of activity

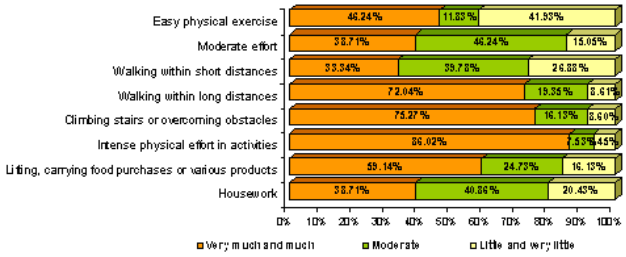


Analysing the same aspects as before, one may notice that the respondents' situation has not improved even a year after being diagnosed. The percentage of the patients claiming that they encounter major difficulty in performing daily rutines has actually increased compared to the period represented in the previous graph.

The analysis of graph 3 shows that the greater majority of responding patients display their dissatisfaction with the impact of their chronic condition on the ability to care for themselves and do housework and this clearly points to a drop in their quality of life.

Compared to the previous studied period, a considerable percentage of patients confirm the presence of discomfort generated by their chronic disease and causing their dependence on other individuals since most of them are unable to carry out daily household routines. They also claim that, even if still able to perform these routines with great difficulty, it still may mean that in a couple of years they will end up completely dependent on their family members or other individuals.

Figura nr. 4. The percentage of responding patients on their own assessment of diagnosed chronic condition and its impact on the quality of life, their condition being perceived as limitation on daily routines and various types of activities

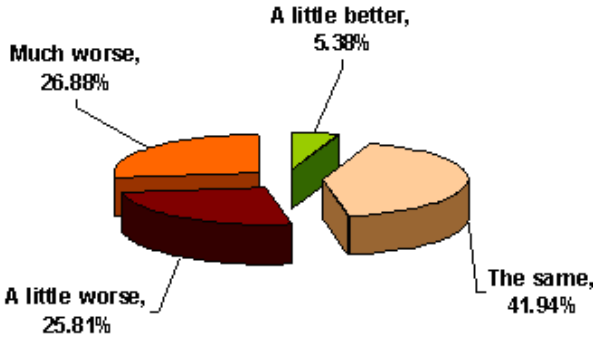


According to this data, three quarters of the patients (79.57%) claim to meet major and moderate difficulty in performing household activities such as maintaining their personal hygiene and getting dressed. More than 80% of respondents also claim that their chronic condition brings along limitations in lifting and carrying food produts or other personal use items while the greatest percentage of patients feel the major impact of their chronic disease on performing activities that

involve intense physical effort, on climbing stairs or overcoming obstacles, and on walking long distances. One may also notice that a considerable percentage also meet major and moderate difficulty in walking even short distances, in carrying out routines that require moderate effort and in doing physical exercise.

The analysis further points out that most responding patients voice their dissatisfaction with the influence that their chronic condition has on the quality of life and perceive it as a limitation brought on their daily routine.

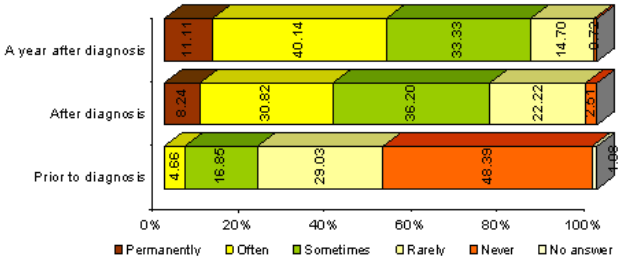
Figure no. 5. The percentage of responding patients on their own assessment of health as compared to their health state a year before



Graph 5 brings forward the fact that only 5.38% of the patients feel a slight improvement of their condition compared to their same condition a year before. More than two fifths of the respondents (41.94%) feel that their health is the same it was a year before. Significant, though, is the high percentage of respondents (52.69%) who claim a slight worsening (25.81%) and even a major worsening (26.88%) of their health when comparing it to what it was like a year before.

These results lead to the conclusion that all the responding patients express their disappointment in their health state when comparing it to the one a year before, since this definitely reduces their quality of life.

Figure no. 6. The percentage of responding patients on their own assessment of the influence of physical and emotional health on daily routines prior to, in the period after and and a year after being diagnosed and medically assigned a degree of disability



Graph 6 shows that not only physical health but also emotional problems can more or less influence the patients' ability to perform daily routines not only from the point of view of the time allotted to such routines but also from that of the quality of work, power of concentration and focus needed to carry out those activities.

It can be easily noticed that prior to diagnosis and medical assignment of a degree of disability, the responding patients claim that their physical health and emotional state did not significantly influence their ability to carry out daily activities. Only a little more than a fifth of them (21.51%) state that they often (4.66%)encountered or sometimes (16.85%) met difficulty in carrying them out.

The analysis also shows that a percentage of 8.24 of the patients feel the impact of physical health and emotional problems generated by the chronic condition claiming that it brings permanent limitations in their ability to carry out daily activities while a 30.82 percent often feel the influence of their physical health and emotional issues on this ability.

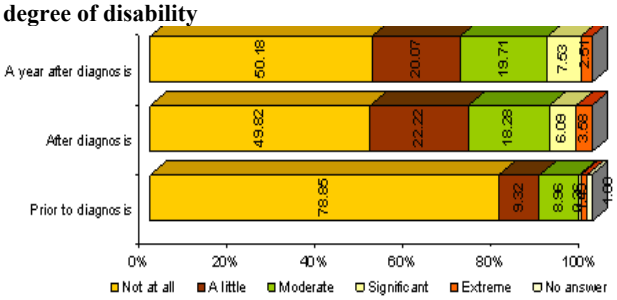
Moreover, the percentage of those who only sometimes feel the impact of these factors on their abilities has doubled from the moment prior to diagnosis to the one immediately after diagnosis (from 16.85% to 36.20%) while the percentage of those claiming they never encountered such limitations prior to diagnosis dropped significantly (from 48.39% to 2.51%)

Analysing the data on the assessment of physical and emotional health and its impact on daily life a year after diagnosis, the constant decrease in the respondents' abilities becomes evident. This reflects both a decrease in this population group's quality of life and an increase in their dependence on others generated by their inability to care for themselves and do household activities

The analysis of graph 7 shows that prior to diagnosis and assignment of a degree of disability, more than three quarters of respondents (78.85%) did not feel any impact of physical health or emotional problems on their ability to preserve human relationships while the rest of them claim that it has an insignificant impact on their realtionships with family, friends, neighbors or other acquaintances.

One may also observe that, in the period after diagnosis, the percentage of patients who were previously not afected by their physical and emotional problems in their relationships drops almost to half (49.82%). This aspect generates an increase in the percentage of those who feel a slight, moderate or even significant and extreme influence of their physical health and emotional problems on healthily preserving human relationships around them.

Figure no. 7. The percentage of responding patients on their own assessment of the impact of physical and emotional health on human relationships, prior to,in the period after and a year after diagnosis and medical assignment of a degree of disability

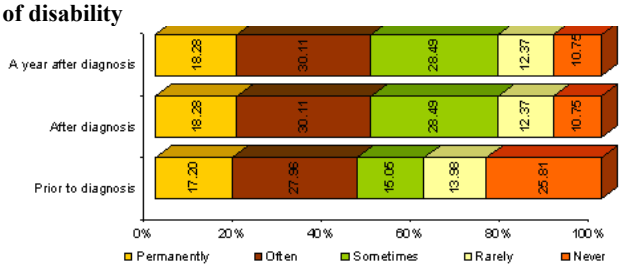


Looking at the data for a year after diagnosis, one may notice the resemblance with the results obtained in the period immediately after diagnosis since the patients' situation has not significantly changed.

As graph 8 shows, prior to being diagnosed a 17.20 percentage of the respondents claim that physical and emotional health permanently limited their abilities to lead an adequate social life reducing their option to visit friends and relatives prior to diagnosis. At the same time, more than two fifths of the respondents (43.01%) declare that they often (27.96%) or sometimes (15.05%) dealt with this issue. The rest of about a third (39.79%) claim that their physical and emotional health rarely (13.98%) or never (25.81%) prevented them from becoming involved in social activities.

Figure no. 8. The percentage of responding patients on their

own assessment of physical and emotional health and its impact on social activities prior to, immediately after and a year after being diagnosed and medically assigned a degree of disability



On futher analysis, it is evident that both in the period after and a year after diagnosis, the percentage of responding patients is much the same; 18.28% claim they have permanently encountered limitations in such activities as visiting friends and relatives, which were generated by their physical and emotional health both immediately after and a year after being assigned a degree of disability. 30.11% of the subjects have stated that they often meet difficulty in performing social activities while 28.49% only sometimes feel the influence of their physical and emotional health on this aspect of their life.

In addition, equal shares of subjects (12.37%) state that their emotional and physical states experienced immediately after and a year after diagnosis rarely reduce their opportunities to visit friends and relatives.

Still equal percentages of respondents (10.75%) claim that immediately after and a year after diagnosis they have not encountered such difficulty.

Hence, this survey clearly points out that physical and emotional health have a great impact on the patients' ability to participate in social activities which reduces the quality of life and the patients' fair chance at having an adequate social life.

CONCLUSIONS

1. Prior to being diagnosed and assigned a degree of disability, the majority of respondents claim not to have had any significant difficulty in performing daily routines.
2. Soon after being diagnosed and medically assigned a degree of disability, most subjects have felt major and moderate difficulty in carrying out daily routines.
3. A year after being diagnosed and medically assigned a degree of disability, a considerable percentage of subjects claim to experience the discomfort of their chronic condition which determines their dependence on other individuals as most of the patients are unable to perform housework or, if able to do so, encounter major difficulty.
4. Most patients express their disappointment in the influence that their chronic condition has on the quality of life and they perceive it as a limitation brought on carrying out daily activities.
5. Almost all responding patients express their dissatisfaction with their physical health when comparing it to the one a year before claiming that it reduces the quality of life.
6. Both physical and emotional health more or less influence the patients' ability to carry out daily routines, both from the point of view of time allotted to these activities and from the point of view of quality of work, concentration and focus required by these specific activities.
7. A year after diagnosis and assignment of a degree a disability, the constant decrease in patients' ability to perform daily routines is evident. This clearly reflects a drop in the quality of life as well as an increase in their dependence on others as they are unable to care for themselves and do house chores.
8. Physical health and emotional problems may be considered risk factors in maintaining human relationships with family members, friends, neighbors or other aquaintances. Prior to diagnosis only a small percentage of the responding patients claim to have dealt with difficulties of this kind. In the period after and a year after diagnosis one can see an increase in the percentage of those who state that physical and emotional health impact significantly on their ability to maintain appropriate relationships with family, friends, neighbors and other people around them.
9. Physical and emotional problems have a significantly negative impact on the patients' ability to participate in social activities and this reduces their quality of life as well as their fair chance at leading an adequate social life.

All these studied aspects reflect the major negative impact of the chronic disease or condition and the physical and emotional health on the patients' ability to perform daily routines, to maintain human relationships and lead a social life.

This survey also shows that respondents claim a drop in the quality of life especially during the period after and a year after being diagnosed and medically assigned a degree of disability by being unable to care for themselves and do their own housework.

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DESCRIPTIVE STUDY OF ANTHROPOMETRICAL INDICATORS FOR A 942 LOT OF PERSONS FROM RURAL AND URBAN ENVIRONMENT IN BACAU COUNTY

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Keywords: *anthropometrics indicators, body mass index, harmonic deviation*

Abstract: *The purpose of the study was to compare anthropometrical indicators measured in a populational group of 942 persons from Bacau county with standards on Moldova. The study analyze high and weigh parameters for children under 18 years old and Body Mass Index for adults. The average BMI in groups on ages shows a normal weigh for the group of age 18-30 and a tendecy of overweigh for all other groups of ages. In an analysis on sex groups we can notice the same normal average of BMI at the age group of 18-30 and a overweigh in the rest of the groups on ages, especially in women groups. The diferences for the parameters high and weigh in the groups under 18 compared with the standards fits into -1σ for weigh and -1σ for high (group of girls 11 years old from rural and group of boys 17 years old from urban) and +1σ for the group of boys 17 years old from rural. Either for group of girls 11 years old from rural or for the group of boys 17 years old from urban, both the weigh and the high are in the same class of standard deviation, meaning an harmonic decrease of these too parameters.*

Cuvinte cheie: *indicatori antropometrici, indice de masa corporală, deviatie armonica*

Rezumat: *Scopul studiului a fost de acela de a compara indicatorii antropometrici măsurați într-un lot populațional de 942 persoane din județul Bacău cu standardele pe zona Moldovei. Pentru copii sub 18 ani s-au analizat parametrii înălțime si greutate față de valorile tabelare standard , iar pentru adulții peste 18 ani s-a analizat Indicele de Masă Corporală. Media IMC pe grupe de varstă indică o greutate normală a grupei de varstă 18-30 ani si o tendință de supragreutate la toate celelalte grupe de varstă din lotul studiat. La analiza pe sexe, se observă aceeaşi medie normală a IMC la grupa 18-30 ani si o supragreutate în celelalte grupe de varstă cu tendința mai accentuată la loturile de sex feminin. Diferențele pentru parametrii înălțime şi greutate la loturile sub 18 ani față de standarde se incadreaza in -1σ pentru greutate şi -1σ pentru înălțime (lotul fetelor de 11 ani din rural, lotul băietilor din urban 17 ani); +1σ pentru înălțime (lotul băieților din rural 17 ani). Atât in lotul fetelor de 11 ani din rural cât şi în lotul băieților din urban 17 ani, şi înălțimea si greutatea sunt în aceeaşi clasă de deviație standard, deci este o scădere armonică a celor doi parametri.*

INTRODUCTION

The complexity of the epidemiological process and of clinical manifestation of different type of nutrition disorders, are obstacles in an efficient implementation of national heath programmes aimed to combat nutrition disorders and associated pathology. Thus, clinical-epidemiological researches in order to determine heath status correlated with nutritional status, life style and associated morbidity, bring valuable information in designing and implementing national prevention programs. Epidemiological researches allow also to assess the present heath status and guide in developing health politics in order to decrease the weaknesses points and reduce the threatenings prioritised in a Swot analyze.

PURPOSE OF THE STUDY

The present study has been carried out in bacau county and it has no ambition to extrapolate the results at the county level, but the results obtained compared with the standards on moldova, will add information for the epidemiological picture of the nutritional status, allowing the prevention actions in order to decrease the consequences on heath status.

MATERIAL AND METHOD

In order to achieve the objectives it was conducted a descriptive study on a population lot of 942 persons selected from one urban locality and one rural. The selection of these localities it was done in an aleatory mode, by choosing them from a list of urban and rural localities from Bacau county. People participating in the study were selected from the family practitioners lists, who were chose using some criteria:

1. The heterogenity of persons (different socio-economics levels, different levels of training)
2. To assure an equilibrated repartition on age groups and sex
3. The compliance of persons involved in the study
4. Disponibility of the medical practitioners to help in the study process.

From the ethnical point of view, the most great of the participants in the study were Romanians but there were also other ethnics, without taking into consideration this criteria in interpretation of the results. It was also a great concern in eliminating as much as possible the interpersonal differences in measuring weight and height. The data collected were prelucrated using the statistical soft EPI INFO/SPSS.

In interpreting the results, were analyzed different parameters for different groups of ages: for children under 18 years old was compared the weight and height with standards and for adults The Body Mass Index, being a more valid indicator of nutritional status and of the health status.

RESULTS AND DISCUSSIONS

BMI ANALYSYS

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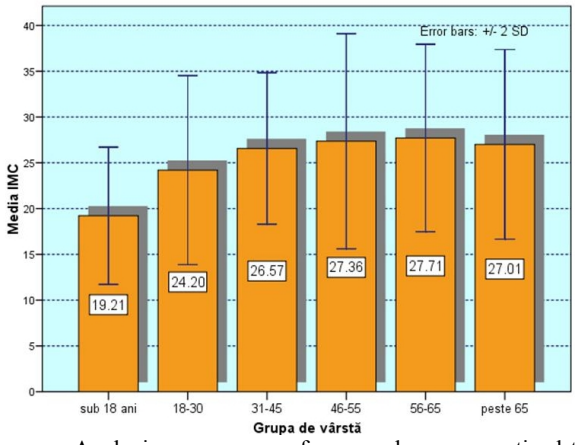
The average bmi on groups of ages shows a normal weight for the 18-30 years old age group and a tendency of overweight for all other ages groups.

Figure nr. 1.The ICM analysis: The Media+/- standard deviation on age groups

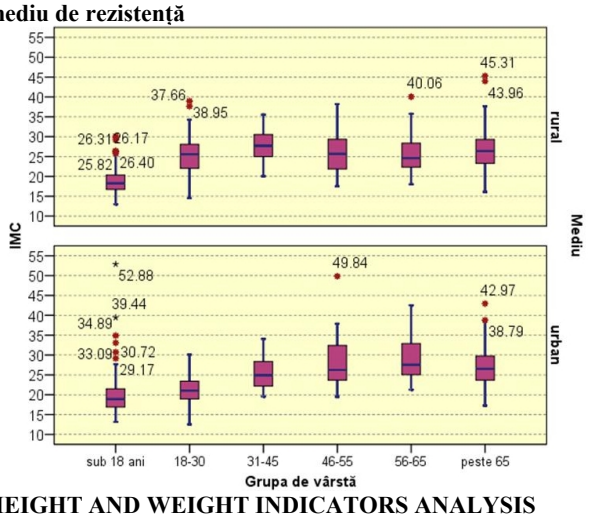


Analyzing on groups of ages and sex, we noticed the same normal value of BMI indicator for the 18-30 years old either for women and for men groups, with bigger values for the feminine lot.

In a box plot graphic showing the linear distribution of the values, we notice big values beyond the upper limit, especially for the extreme groups of ages, indicating that at these groups of ages the parameter BMI is not such a valid parameter of study, being biased by other factors such as the growing process for the ages under 18 or by the ageing process for the age group after 65 years old.

Analyzing the distribution of BMI values on residences environments groups, we can see bigger values in the urban lot compared with the rural.

Figura nr. 2. Graficul "box plot" pentru analiza IMC pe mediu de rezistenţă



HEIGHT AND WEIGHT INDICATORS ANALYSIS

Weight analyze for youth under 18 years old, shows lower values then standards for the following groups: feminine 11 years old , rural group and 17 years old , masculine urban group. The differences are statistic significant but still small and fit in a -1σ standard deviation. A possible explanation of low weight compared with standards may be aleatory election of participants or it can reflect imparities in the socio economical conditions.

Height analyze indicates lower values compared with the standards for the group of girls 11 years old rural, girls 17 years old from rural, boys 11 years old from rural and boys 17 years old from urban ($p<0.05$, difference statistical significant that fits in a -1σ standard deviation).

The average value for high in the masculine, rural 17 years old group is bigger then standards.

CONCLUSIONS

1. BMI analyze on age groups, sex and residential environment in adult lot indicates a normal weight for the 18-30 years old group and a tendency of overweight for all other age groups, with bigger values for feminine groups in the urban area.
2. For youth under 18 years old there are not great differences compared with standards for the parameters height and weight. The differences fit into -1σ standard deviation either for weight or for height, being in the same class of standard deviation and indicating an harmonic decrease of these two parameters.

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PROFESSIONAL STRESS MANAGEMENT

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Keywords: *workplace stress, management*

Abstract: *Regarding actual life conditions one of the most important facet of stress is the stress at the workplace. The professional stress is situated on the second place in the hierarchy of the health problems at the workplace, after the lumbar ache and affects a third from the employees of the European Union. The stress effects at the work place may manifest in the behavioural, psychological and physiological plan.*

Cuvinte cheie: *stres profesional, management*

Rezumat: *În condițiile vieții actuale, una dintre cele mai importante fațete ale stresului este stresul la locul de muncă. Stresul profesional ocupă locul doi în ierarhia problemelor de sănătate la locul de muncă, după durerile lombare şi afectează o treime dintre angajații Uniunii Europene. Efectele stresului la locul de muncă se pot manifesta în plan comportamental, fiziologic şi psihologic.*

SCIENTIFICAL ARTICLE OF BIBLIOGRAPHIC SYNTHESIS

Modern society offers us many advantages, things that we can't be deprived, but also many sources of stress that earlier or later will reveal their negative effects and we will be transformed in ''stressed persons''.

Professional stress is situated on the second place in the hierarchy of the professional health issues in the European Union, after the lumbar ache. Affects one in three employees, meaning more than 40 million employees from the European Union countries. Also, it is responsible for the apparition of the cardiovascular diseases in 16% from the entire men and in 22% from the entire women that suffer at present from these affections.

Stress is a state of intense tension of the organism forced to mobilize all the defending means to face a threatening situation. (Dictionary of psychology Larousse). Hans Selye (1976) considers the stress, as a nonspecific response of the organism at any solicitation directed on it, being considered a physiological condition identifiable and triggered by psychological factors having as a consequence the affection of the psychic and somatic echilibrum of the individual.

The stress represents a complex of emotional reactions, cognitive, behavioural and psychological ones regarding varied aspects of the content of work, organising of the work and work environment. The positive stress (eustress) acts as an energising factor on the human organism having as effects the intensifing realisation of the proposed objectives at high quotes, the negative stress (distress) can't be controled and may affect in a negative way the functional physiological systems. May affect the health by determining the apparition of different diseases such as: myocardial infarction, asthma, migrena, psychic affections (anxiety, depression, suicide), muskulo skeletal disorders, gastro intestinal disorders. During life and profession we are exposed to minor or major events that may determine the apparition of stress.

To have a clearly and fully understanding of this issue we need a short classification of the different types of stress that we may be confronted to. The stadiums of stress (after Selye) are the following: alarm reaction, resistance stadium and exhaustion stadium. The alarm reaction is the first answer of the organism, this proces meaning the "general mobilisation" of the defence forces of the organism. In the acute phase of the alarm reaction, the general resistance of the organism declines under the medium level.

The complete answer is not reduced to the alarm reaction because if the nocive agent continues to action it is produced the stadium of resistance or adaptation.

In other words not even one organism founds itself in the permanent stadium of alarm, the initial reaction being followed by the stadium of resistance.

The second stadium, the resistance one is distinguished from the first one through the chemical and physiological reactions that are produced. After the organism has adapted, in the stadium of resistance the capacity of the organism grows over the level medium resistance. If the person is exposed for long time to the action of a nocive agent, the adaptation obtained disappears. This way the third stadium is reached, which symptoms are similar to the ones present in the alarm stadium. In the exhaustion stadium the resistance is smaller than level of medium resistance.

The stress factors are very different. They may be of psychic order (conflicts, professional or familial discontent, exhaustion) of socio-cultural order or of physical order (pain, infectious diseases). The potential stress factors in our life may affect almost everybody in any organization; meanwhile others affect only those that play certain roles. Interpersonal conflicts are a strong factor, especially for those with accentuated tendencies of avoiding it.

The whole range of conflicts, from the personalities clashing to intergroups argues has great chances to determine stress, when drives to real or only perceived attacks to the integrity or to the good opinion of one self. In the case of conflict between employment- family the stress results from the conflict of roles being the member of a family or the member of an organization. The uncertainty of the job is also an important factor of stress. A certain job represents an objective for almost anyone and when this one is menaced the stress may come out.

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The ambiguity of the role exists where the objectives of the job or the way to accede to them are unclear. The lack of a directive may prove stressfull, especially for those that can hardly tolerate such an ambiguity. Near those general factors one may encounter other stress factors: the lack of a workplace, a good workplace may be stressfull when the employee is permanently unsatisfied, has no advancing perspective or of a significant change, hasn't the certainty of the presence at the right job and in the same time he doesn't know what else he could do.

The organization or even the community may be stressfull when the demandings are conflictual, the objectives unclear or the resources inadequate, if there are changes that are not planned adequately or are unconsulted or if there is a conflict between the satisfaction of the needs and the expectations.

Other causes of stress may be: unproper work conditions (noise, illumination, misery, humidity, excessive heat/cold), a weak time management, uncertain financial future, lack of support procedures and supervision.

The workplace may be stresfull if the employee has too little or to many things to do, if the job is too easy or too heavy, if the employee has to take decisions without being properly informed or without proper authority, if he has terms that he can't control or if he has the responsibility of others life.

The stress may be generated by the relationship with colleagues, subordinates, superiors, the administration board, the beneficiaries, members or persons from other organisations.

A special importance should be given to the autoinduced factors; they are specific to the persons that don't treat themselves correspondingly.

They may be due to the physical neglecting that next to the own stress potential may determine the capacity of resisting to other stress factors or to abandoning the relaxing periods. Among the external stress factors that evade the control we may mention: legislative changes, the decisions of the financer, the traffic, the common transport.

The stress effects at the work place may manifest in a behavioral, psychological and physiological plan. The behavioral reactions are activities practiced openly, that the stressed individual uses in his trial to cope to stress.

They include: attitude of solving the problem, of retiring and of use of substances that gives dependency. Psychological reactions imply first the emotional and cerebral processes.

The psychological reaction that is more often met is the usage of the defending mechanisms (psychological efforts to reduce the anxiety associated with stress). Regarding the physiological reactions at stress there are proves that stress at the work place is associated with the irregular function of the heart, with hypertension, accelerated pulse, a growing colesterol.

Stress has been associated with the beggining of some diseases such as: respiratory ones and bacterian infections.Some of the employees consider the stressfull conditions of work as a needed amiss-the company has to cope with the employees pressure and to assure their health in order to remain productive and profitable in the actual economic conditions.

The stressing conditions are associated with the growing of the absenteeism, the delaying and with the intentions of the employees to leave their workplace, all those showing a negative effect on the company. A healthy organisation is defined as an organisation with a small rate of falling ill, of the infirmity of the work force, and the politics in favor to the employees determine benefits for the organisation.

The researchings have identified organisational characteristics associated with health, with a minimum level of stress at the work place and a high level of the productivity (recognising the performance to the employees, opportunities of developping the carreer, organisational culture that valorises the employee).

American companies promote classes for the stress management for their employees. The programs of stress management teach the employees about the nature and causes of the stress, for exemple: the time management and relaxing exercises. Part of the organisations promote individual consultations for the emplyees to discuss their familial problems or problems related to the workplace.

Those programes may rapidly reduce the symptoms of stress: anxiety, sleep disorders and have as advantage that they are easy to apply and cheap.

The stress due to the work place represents a menance to the employees health and the searchings regarding the stress at the work place has extended a lot in the last years.

But, in spite this attention, the confusion connected to the causes, effects and the prevention of the stress at the workplace persists.

Not but that, the prevention of the stress should be realised at the level of organisation, it is important that any individual realises how to administrate stress, to assure its professional succes on a long term and to maintain its physical and mental health.

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THE ELDER'S DEPRESSION –A MAJOR RISK FACTOR IN AUTOANALYTICAL CONDUCT

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Keywords: *suicide, depression, mental disorder*

Abstract: *Suicide is a worldwide important public health problem, due to the loss of human lives and the devastating effects on those left behind and society. The literature review shows a lot of risk factors related to suicide. Among them, the psychiatric pathology seems to play a major role. For this reason, the prevention of depression and suicide is one of the main targets of The European Health Program. The paper presents two suicide case reports autopsied at the Forensic Service of Covasna County, during the present year, which have as common characteristics victim's elder age, ruthless of suicide method, atypical for women and the presence of mental disorders in the medical history.*

Cuvinte cheie: *suicid, depresie, tulburare psihică*

Rezumat: *Suicidul este o importantă problemă de sănătate publică în întrega lume, datorită pierderii de vieţi omeneşti şi a efectelor devastatoare asupra celor lăsaţi în urmă şi societăţii. Revizia literaturii arată că există o mulţime de factori de risc asociaţi cu suicidul. Între aceştia, patologia psihiatrică pare a juca un rol major. Din acest motiv, prevenirea depresiei şi a suicidului este unul din obiectivele principale ale programelor europene în domeniul sănătăţii. Lucrarea prezintă două cazuri de suicid, autopsiate la SML Covasna, în anul în curs, care au ca şi caracteristici comune vârsta înaintată a persoanelor, maniera dură de comitere a suicidului, atipică sexului feminin şi prezenţa tulburărilor psihice în antecedente.*

INTRODUCTION

Suicidal act, the eternal human dilemma, often appears as a compact wall, impenetrable, whose appearance may be different on each side, it depends on where you look: suicide as an irrational, pathological act, suicide as the ultimate freedom of the individual to choose, suicide as expression of the idea of dignity.

Albert Camus in "The Myth of Sisyphus", said: "There's only one truly important philosophical problem: the suicide. To determine whether or not life is worth living is to answer the fundamental question of philosophy. (... ....). For the beginning think about this being eroded by inside. The society has no great contribution in this beginning. The worm is inside of the human heart. There should be sought. This deadly game that leads from lucidity of existence to the evasion in the outside world, should be followed and understood. " (1).

In a concise definition, suicide is "intentional self-generated death", the word "suicide" has its origin from the Latin words "sui ed caedere" which means "him" and "to kill". (2,20)

As a form of behavior, suicide is an act of aggression, many factors were considered to be involved in its genesis (2, 20). As Friedrich Hacker mentioned: "At the origin of aggressively it is found the game of mixed hereditary factors, psychological and cultural influences, central nervous system structure and, also, hormonal mechanisms and social patterns. (7)

Risk factors for suicide are divided in several categories: biological, psychological, economic, social - networking, but usually they are intricate, being involved with different weights in the genesis, precipitation and the onset of suicidal act.

Among the biological factors, the depressive moods are considered to have the most important role in the genesis of suicidal thoughts, according to some authors reaching 35-80%percent.

Depression is one of the most undesirable psychiatric conditions, not only due to significant impairment of functional capacity of individuals, but also because its most feared complication: the suicide. Unipolar depression, one of the leading causes of disability worldwide, is characterized by a depressive mood, hopelessness, helplessness, a strong feeling of guilt, sadness, low self-respect, self-injury and suicidal thoughts. Up to 15% of patients with unipolar depression eventually commit suicide. Latest statistics of the U.S. show that approximately 17% of the adult population of America (regardless of race, ethnicity or socioeconomic) has at least one major depressive episode over the life and another 5% of the population has different forms of small or medium depression. (10,11,12). In Europe it is considered that one of four person shows a form of mental disorder at least once in their life, and depression is one of the most common disease, affecting one of six women, and it is estimated that until 2020, will become the most common disease in developed countries and the second leading cause of disability. In the European Union there are approx. 59000 suicides annually, 90% are attributable to mental illness. (27).

The most harmful complication of depression is the suicide. The risk of suicide, low in childhood, increases during the adolescence due to profound changes of the individual characteristic of that period, then follows a plateau period between 25-45 years, and later, it grows once aged again, reaching a high rate over 65 years. A rate of almost 10% of major depression begins after the age of 60 years. Should be

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also noted that about one third of patients who experienced a major depressive episode will present another major depressive episode in the next five years. The recurrence rate increases in direct proportion to the number of depressive episodes, which extends directly proportional suicidal risk . It is considered that the expression of three or more major depressive episodes in history makes the likelihood of recurrence of depression over the next three years to be 85% (6,8,9,19,21,22).

In elder people, realized suicide is more common than attempted suicide and is characterized by a long premeditation, by association with health problems, by psychiatric and somatic frequency major accidents, by the presence of solitude and the idea to give grandeur to death. (24)

"European Pact for Mental Health and Well-Being" adopted at the EU High Level Conference "Together for mental health and welfare ", held in Brussels from 12-13 June 2008, supports the adoption of measures to improve quality of elderly' life. Particular attention should be paid to both research on the mechanisms and causes of neurodegenerative disorders and other mental illnesses and their prevention and treatment. It is, also, necessary to assess co-morbidities and to train health professionals in this field, as an interdisciplinary approach to complex situations associated with mental health problems will bring added value. Care for the elderly means both to protect their right to a dignified and active old age, and to ensure the social cohesion.

CASE PRESENTATION

The cases presented are of some elderly, in which the common features are the presence of a depressive disorder in their medical history and the violent means of committing suicide, by cutting the cervical region with a cutting object (knife).

CASE I

IA, 77 years old, female, retired, romanian nationality, moved several years ago from Bucharest to St. George. This thing led, by default, to the stop of her social networking. She was living alone in a studio, didn't have children, the closest relatives were some nephews. From the medical documentation found in the victim house results that she was suffering from affective disorders since 2004 (at age 74 years), which required hospitalization in the psychiatric ward, then followed by chronic antidepressant drug treatment; the last prescription was dated 3 days before her death.

During the research we found a chic flat, reflecting the membership to a medium socio-economic level and a certain concern for appearance. The door was locked inside. The woman's body was found in the bathroom, fell on her right side, in front of the toilet bowl. Between the victim's body and toilet bowl was a pool of blood; her hands were bloody. Cervical region, at the left side, reveals three cut wounds, two of which are located higher, one almost a continuation of the other, and a lower one, with a thin region between them. The wounds measured approx. 3.5 cm each, with very fine cut injuries adjacent on the skin surface, next to the extremity of wounds (test lesions). The wound is interesting the skin plane, until the subjacent muscle plane, which can be seen trough the wound edges.

A special feature of the case is the adjacent pedantry relating with the death act, as much as the word "elegance" may be associated with the gesture of the suppression of life, revealed by the attention given to details. A towel is placed next to the neck, below the wound, under shirt, in order that the blood drained wouldn't dirty clothes (when the dead body was found, the towel was full of blood).Over trousers, a white cloth is wrapped, all-purpose protective clothing. Around the toilet bowl leg rests another rolled towel. Knife rests on the back of the toilet bowl. Another knife, shorter and less sharply, was found sideways, near the toilet bowl. Putting together the aspects found at the crime scene and making the links with the direction of blood traces inside of toilet bowl we can conclude that she had cut his neck over the toilet bowl, allowing blood to flow in, in the attempt to not dirty with the blood of her tragic death blood the life left behind.

The autopsy revealed that the anterior jugular vein was sectioned, it being caught in the path of cut cervical wound; we, also, found anemia of visceral organs and degenerative changes characteristic of aging. Death was interpreted as due to massive external bleeding, consecutive to the section of jugular vein; the presence of hesitation injuries, multiple number of wounds and damaged region accessibility suggest a self-inflicted nature of the lesions, in the same direction converging the criminalist aspects found at the crime scene.

CASE II

M.R, 74 years old, female, retired, hungarian nationality, domiciled in the St. George city. She was living alone in a studio, the only relative who was visiting her was a nephew. She had a daughter, but they interrupted connections for years. She can change her place only with the carriage, in a difficult way, due to a failed operation bilateral hip prosthesis, in the context of obesity.

The crime scene research showed the body of a old obese female person, lying in her bed in the bedroom, on the back side, the carriage placed next to the bed. The woman is dressed in a white nightgown, soiled with blood at the top, hands are defiled with blood. On the vertical side of the bed, in his frame, there are fitted 2 help - straps to support the mobilization and, can be also seen a knife full of blood; over the bed, from the ceiling hangs another strap to support the mobilization. On the left side of the cervical region there is a cut wound and, on her clothes, dry blood spots. Pillows and bedding around the person are soaked with blood. Near the bed is a towel full of blood and clots. Signs of struggle were not found inside of the room. Blood is limited around the dead body, having the issue of leakage. Neighbors told that she was suffering with depression and had 3 previous suicide attempts , including one in the same year, two of them by ingestion of drugs, and one by hanging. A note expressing regrets was found in the same room, in which she motivates her gesture by the impossibility to endure the pain and inability to mobilize.

The autopsy revealed two cut wounds in the cervical region, on the left side, overlaid with horizontal direction from left to right, ending with an aspect of "mouse tail", with a small flap on the right between them and multiple skin hesitation injuries on the left side. After opening the wound it was noticeable that it was not particularly deep, the facial vein appears cut inside of wound.

It was concluded that death was due to external bleeding by cutting facial vein. The superficial appearance of cervical wound, the presence of hesitation injuries and damaged region accessibility suggest a self-inflicted nature of the lesions.

What is significant in this case is the perseverance in repetition of self-destroying act and the intensity of desire to die, giving the resources to overcome physical disability and to commit the act. The person is obese, hard to be mobilized, virtually immobilized in bed without aid of another person. In order to stand up is necessary to catch with the hands the system of straps installed around bed (over this and on the right side); we can deduce from this that moving up to the kitchen to procure the knife used by the deceased needs an enormous effort comparing with the possibilities of her current mobilization. It is remarkable in this case as well the focus on details: the knife that she used to make the wound is placed up on bed and the wound area had also a towel put around to absorb

blood, it fell later near the bed.

CONCLUSIONS

The analysis of presented cases shows the common characteristics of the two victims:

- Both victims are old persons, who live and maintain themselves without immediate family support. The deficit of social networking is amplified by the loss of social support circle (known people, friends, neighbors) as a consequence of changing domicile in the first case, and due to the invalidating organic pathology, which limits travel opportunities in the second case;
- both people have insufficient income to purchase daily living expenses and necessary drugs;
- both persons have a history of depressive disorder and even suicide attempts failed in one of the cases;
- In both cases, suicidal method chosen is tough, violent, with definite purpose, uncharacteristic for females, although both had access to / could use medication with potential lethal effect, prescribed for depressive illness. This medication could induce a less-painful death, drug poisoning being preferred by women in attempted suicide cases.

Situations like the ones presented below should be an alarm signal regarding the pathology of alone elder. The depression often occurs in the context of lack of socialization, superimposed on the organic degenerative background of changing of brain function, according to chronological age.

The international suicide management programs put together the predictive value of attempted suicide and hermeneutical significance of "cry for help", with the supervision of the risk populations and the evaluation of the risk factors, the fallow-up and monitoring of depressive moods and the decreasing of factors involved in passing to the act, with the availability of entourage in understanding the moral suffering and desperation in people at high risk. Risk of mental disorders increases with age; it is not only Alzheimer which is important, there are a lot of other problems such as depression, stress and psychotic disorders. Therefore, elderly people must be regarded as a key target group in promoting mental health and well-being.

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THE ROLE OF DENTAL MEDICINE IN SCHOOLS TODAY. THE CASE OF THE DENTIST'S OFFICE IN "AUREL LAZAR" THEORETICAL HIGH-SCHOOL, ORADEA

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Keywords: school medicine, communication, prevention, curative activities

Abstract: *The activity of dentists activating in schools should be centered on the adequate and constant information of pupils about the importance of preventing dental caries and dental-maxillary affections. The prevention of dental affections, alongside the early detection and curative treatments in early stages not only reduce the risk of complications, but also diminish the physician's effort and the work of other factors involved in the health care system. Medical (and dental) assistance of students is free, as it is insured from the national health insurance fund.*

Cuvinte cheie: medicină şcolară, comunicare, prevenţie, activităţi curative

Rezumat: *În activitatea sa, medicul de medicină dentară şcolară trebuie să se bazeze pe o informare corespunzătoare şi constantă despre importanţa profilaxiei cariei dentare şi a afecţiunilor dento-maxilare. Prevenirea îmbolnăvirilor, sau depistarea precoce şi tratamentul curativ în faze incipiente, scade riscul complicaţiilor, dar uşurează şi efortul depus de medic şi de factorii angrenaţi în sistem. Asistenţa medicală şi stomatologică a elevilor este gratuită, fiind asigurată prin finanţare de la bugetul de stat, din fondul de asigurări de asigurări sociale de sănătate.*

INTRODUCTION

Until recently, school medicine was perceived as a domain placed at the periphery of other medical specializations, especially as regards dental medicine. Even today there are voices that advocate for ceasing the activity of medical cabinets in schools. The inefficiency of the system, as well as the insufficient involvement of doctors working in schools, are often used as arguments in supporting the idea referred to before.

The first part of this study emphasizes, starting from the competences and attributions of medical school dentists, their role in the prevention of specific oral cavity diseases and in curative care. The second part presents a study that aims to point out at: (1) the importance of school dentists in supervising the oral health of school pupils and in applying methods of prevention and cure, (2) the central function of communication, not only between doctors and patients, but also between physicians and teachers, or physicians and the local authorities (3) the importance of doctors' commitment to provide quality health care. Given the context in which school medicine faces the challenge of decentralization, we believe that those working within the system must bring into question both the need for a better management of both human resources and investments in this area, and to highlight the role of their activity in society.

PURPOSE OF THE STUDY

The purpose of this article is not simply to contradict those who criticize school medicine. We all know that the changing of a system for the better can not occur overnight, while professional integrity is a matter that concerns each individual in particular. Rather, we intend to bring into focus the need to support primary medicine in schools, which is an important factor in maintaining people's health, both on average and long-term.

MATERIAL AND METHOD

The present study is based on the evaluation of 400 subjects, from the 530 students of "Aurel Lazar" High School in Oradea. Their observation sheets were completed at the request of the school dentist, with patients' consent to be consulted, between January 2008 and July 2010.

RESULTS

In accordance with the current legislation (1), both prevention and dental treatments are provided free to the pupils from the primary, secondary and the high-school system of education in Romania.

Of course, prevention of diseases represents a central element of the school physicians' activity, who should give priority to pupil's relevant and consistent information about the dangers of overlooking dental hygiene measures. At the same time, the prophylaxis of dental caries and oral-dental diseases represents another important aspect of their work in schools. In this way, the periodic examinations of pupil's oral-dental apparatus becomes compulsory at every six months, as well as their registration, with the aim of maintaining their oral health, and educating students to achieve the prevention of dental caries, and to detect the onset of clinical signs of dental problems. Early diagnosis and curative treatments diminish the risk of complications and, not ultimately, facilitates efforts of both doctors and the factors involved in the health care system.

The cases beyond the competence of medical school dentists are sent to specialists, such collaboration being absolutely necessary and normal.

The medical and stomathologic assistance of pupils is provided through funding from the state budget, namely the health insurance fund (2).

In Romania, school dentists' offices are struggling to regain credibility as, for many years, they encountered problems related to the lack of materials, old equipment, requiring frequent repairs, mostly paid for by the physician. Cost standards for the activity of the cabinet would be reasonable, and materials can be purchased at fair prices, as the offer is very rich and diverse.

A real help in the successful carrying out of doctor's duties is the effective doctor-patient communication, which might draw pupil's attention upon the importance of medical acts, of

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prevention and prophylaxis in maintaining personal health. The confidence of young patients, once gained both by doctor's patience (the result of the medical staff's experience in dealing with pupils) and given the certain facility in achieving prevention (this medical act is not painful for the patient), will probably increase the number of pupils seeking medical advice in school medical cabinets. Equally important in this respect is, as indicated above, the information of patients, the collaboration with principals and head-teachers.

In general, students are informed with regards to the appropriate use of toothbrush and toothpaste (the correct way and the time needed for a proper brushing of teeth) but also of other elements necessary to maintain dental hygiene, such as flossing or mouthwash. They are also informed about the crucial role of nutrition, as certain types of food have cario-protective role, due to chemical constituents which models the effect of the cariogen hidrocarbonates (e.g. phosphates from unrefined cereals, or chewing gum, cheese, milk, certain fats, oligoelements such as fluorine or cocoa from chocolate or glicirizine from licorice). (3)

The supervision of children at a school medical office is easy, given students' easy access to the dentist.

We should point out here that the examination of each student takes place twice a year, the school we refer to here having 530 students. In agreement with principals and head-teachers, pupils are sent, by rotation, during classes, until all those that give their consent are registered (on average 75% -80%, as reflected by the consultation register). At the first consultation, the observation sheet of the student is opened, on which all medical consultations the child will attend during school are subsequently recorded. The pupil is informed of any dental problems he/she might have.

Emergencies are also solved at the school's dentist's office, if these occur during school hours.

It is worth mentioning here that approximately 25% of students with dental problems, learning in the school this study has focused on, choose to solve these problems in the school's medical office (caries lesions and sometimes even extractions). This confirms Rodica Luca's observation, that, between 5 and 17 years, 83% of the caries are placed on the vestibular and oral surfaces (4), therefore these can be solved by simple fillings or sealing. As a particularity, with children, dentists should use the conservation techniques of the dental pulp, as formative body, especially as its potential for healing remarkable at such ages. Because of this, and due to the increased reactivity of the young organism, favorable results are widely expected. (5) There are also emergencies that have been solved (about one case per week).

The vast majority of students that are treated in school come from rural areas (they commute or live in boarding school), as they rarely have access to dental surgeries in the village where they live, or have limited financial possibilities. There are also pupils that live in urban areas, who may be included in this last category (social cases). Due to the current economic context of our country, there is a tendency towards the equalization of the two categories referred to above. As mentioned, an important advantage for students is the fact that the treatment is free of charge, which benefits both the family budget, and the National Health Insurance system, which should otherwise spend more money if students were treated at various private dentist offices, who signed contracts with the Health Insurance system.

In what follows we shall present some relevant cases that may help doctors better understand the psychology student and the way they perceive the role of oral hygiene, as related to personal health.

Case 1. DT, pupil, 11 year old, living in urban areas, comes at the dentist's office of "Aurel Lazar" high-school, for a first examination, in March. 2009. Multiple lateral carious lesions are observed and recorded; the four "six years" molars appear as root debris. The pupil does not accept treatment. Examination 2, 09. 2009: the same situation is observed, but dental pain is present, as a result of carious processes development. Emergency treatment is provided, calming dressing on 2.4. However, the patient does not accept further treatment.Examination 3, 04. 2010: on the occasion of the periodic consultation, the doctor observes that the student began dental treatment, molar debris was extracted and carious lesions were treated. The pupil expresses the wish to continue treatment until the eradication of all dental problems, but in a private dentist office, where s/he was taken by parents. The treatment was free, as the private cabinet had contract with Health Insurance system.

Case 2. T.I., student, lives in rural areas, 11 year old. Examination 1 - 03. 2009. Carious lesions are observed on 1.6., 3.6., 4.6. The pupil does not want treatment in the school dentist's office. Examination 2, 09. 2009. The doctor observes that carious lesions were treated properly, with fillings.

Case 3. D.S., lives in rural areas, 15 years old. Examination 1, 01. 2008. Multiple carious lesions on the first examination. The pupil presents regularly for treatment and within three months all the problems of oral health are solved in the school dentist's office.

Case 4. P.C. lives in rural areas, 16 year old. Examination 1, 10. 2008. Multiple small lateral cavities. Examination 2, 04.2009. Similar situation to the one observed on the occasion of the first consultation. Examination 3, 01. 2010. Following consultation in the school dentist's office, the subject decides to begin treatment, which lasts until 3/25/2010, according to records. Treatment on 4.6., 4.6, 4.7., 3.6., 3.7., 2.7., with complete filling and intermediate treatments.

Case 5. P.C., living in urban areas, students, grade 12. Examination 1, 03. 2010, lateral carious lesions. Decides to begin treatment at the school dentist's office, which lasts until 28.05.2010, according to the observation form. Receives treatment for gangrene on 3.5, 3.6., 2.6., 1.5., with the corresponding final restorations, but also intermediate treatments, cementing Coronet 1.4., scaling.

CONCLUSIONS

These are just some examples to illustrate the fact that students decided to treat their teeth (most of them in the school dentist's office, but also in private dentist's offices), after having been consulted and kept informed about their oral health problems by the school dentist, which eventually lead to the improvement of their oral health. Such actions may contribute to improving the oral health of the population at large, on both medium and long term. It is true that receptivity increases with age, but problems detected earlier are easier to be solved, which again draws attention upon the crucial role of prophylaxis, which raises primary medicine at the level of necessity.

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HYPOXIC-ISCHEMIC ENCEPHALOPATHY IN ADULT

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Keywords: *cerebral hypoxia, diffuse cerebral ischemia, brain tissue damage, posthypoxic neurological syndromes*

Abstract: *Hypoxic-ischemic encephalopathy (HIE), is one of the most frequent and dramatic urgency found in neurological brain diseases of adults. This is a neuro-vascular and neuro-metabolic syndrome, caused by a shortage of supply of oxygen and glucose or their metabolism in the brain. HIE results from a global hypoperfusion or oxygenation deficiency rather than from infarction in a specific vascular cerebral territory. In adults, common etiologies include hypotension, cardiac arrest followed by succesful resuscitation, and carbon monoxide poisoning. The prognosis is favorable with recovery in case of mild or moderate hypoxia of short duration. Prognosis is unfavorable in hypoxic-ischaemic encephalopathy after severe damage.*

Cuvinte cheie: *hipoxie cerebrală, ischemie cerebrală difuză, leziuni tisulare cerebrale, sindroame neurologice posthipoxice*

Rezumat: *Encefalopatia hipoxic-ischemica este unul din cele mai frecvente şi dramatice afecţiuni cerebrale întâlnite în urgenţa neurologică a adultului. Este un sindrom neuro-vascular şi neuro-metabolic, determinat de un deficit al aportului de oxigen si glucoză sau de metabolizare a acestora la nivelul creierului. HIE rezultă mai degrabă dintr-un deficit global de hipoperfuzie sau oxigenare decât dintr-un infarct într-un teritoriu vascular cerebral specific. La adulţi cauzele comune sunt hipotensiunea, stopul cardio-respirator urmat de resuscitare eficientă, intoxicarea cu monoxid de carbon. În cazul unei hipoxii uşoare sau moderate, de scurtă durată, prognosticul este favorabil. Prognosticul este nefavorabil în encefalopatia hipoxic-ishemică după leziuni cerebrale severe*

Cerebral hypoxia can be classified according to severity and location, in:

- **diffuse cerebral hypoxia**: mild to moderate impairment of global brain function caused by low levels of oxygen in the blood.
- **focal cerebral ischemia**: a localized and temporary reduction of brain tissue oxygenation. Neuronal damage is usually reversible. Ex: TIA.
- **cerebral infarction:** a long-term blockage of blood flow to a region of the brain. Significant irreversible damage occurring in the area after obstruction.
- **global cerebral ischemia**: a complete and diffuse stop of blood flow to the brain (eg. severe systemic hypotension in shock, cardio-respiratory arrest). (1)

Depending on the cause of the reduction of oxygen to the brain, cerebral hypoxia may be: hypoxic, hypemic / anaemic, ischemic and hystotoxic. (see Table no. 1) (2)

Neurophysiology

The brain needs 3.3 ml O2/100g/min and 8 mg glucose/100g/min under basal cerebral condition at a blood flow to an average of 55 ml/100g/min (ie 750 ml / min) representing 15 -20% of total cardiac output at rest. Blood flow of gray substance (cortex) is 4-5 times higher (70-80 ml/100g/min) than that of white matter (15-20 ml/100g/min). In people over 60 years, cerebral blood flow is 30-40 ml/100g/min.(2)

Neurophysiopathology

In case of reduction of O2 concentration in the blood, the body respond to compensate by redirecting systemic blood flow and increasing cerebral blood flow, up to 2 times normal. If this increasing is sufficient to meet the brain needs of O2, then symptoms characteristic of hypo / anoxia of brain does not appear. If the adaptive response of O2 deficit is not corrected, the symptoms begin to appear. (3), (4)

When brain hypoxia appear, brain tissue suffering is not equal in all territories, newer developed phylogenetically formations are the most sensitive. By microelectrodes studies has been showed that signs of distress tissue in different areas (demonstrated by lack of neuronal electrical activity) is installing in variable periods of time after the onset of hypoxia, namely:(5)

- at 10-12 seconds for the cortex, Ammon's horn, Purkinje cells
- at 25-27 seconds for caudate nucleus
- At 35-37 seconds ventral nucleus of the thalamus
- At 30-40 seconds for bulbar gray substance

The most common causes of acute cerebral hypoxia is the dropping of cerebral perfusion (global cerebral ischemia) caused by cardio-respiratory arrest and severe hypotension (haemodynamic shock). Sustained severe hypoglycaemia, sustained seizures (status epilepticus) over 1-2 hours may also cause permanent brain damage. Global cerebral ischemia is more aggressive, because in addition to the energy shortage is leading to accumulation of lactic acid and free radicals, which are removed during normal blood flow conditions as they accumulate.

Shortage of energy substrate (O2, glucose) in the brain has these negative effects: impaired Na-K pump results in prolonged neuronal depolarisation and release of excess glutamate from the synapses. It then activates NMDA and AMPA receptors, leading to a massive influx of Ca in neurons with consequent activation of catabolic enzymes and NO production and formation of free radicals. They cause irreversible neuronal damage and neuronal death. Therefore

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modalities of seeking to neutralize the action of glutamate are therapeutic measures underlying the neuroprotective strategies. (6)

Table no. 1. Classification of cerebral hypoxia according to the causes of reduction of oxygen concentration in the brain

Type	Circumstances	Causes
Hypoxic hypoxia	reduction of oxygen concentration in the atmosphere, acute respiratory disease	• high altitude • Breathing ineffective (ALS, Guillain-Barre sdr) • obstruction of air routes • asthma
Hypemic/ anaemic Hypoxia	reduced capacity of anaemic blood (Hb) in oxygen fixation	• Reducing the number of red blood cells, the Hb (anaemia) • abnormal Hb (sickle cell) • CO intoxication
Ischemic hypoxia	Stenosys / obstruction of cerebral circulation and decreased bloodflow to the brain	• Stroke • myocardial infarction • shock
Hystotoxic hypoxia	O2 is in normal concentration in blood, but can not be metabolized in tissues	• metabolic intoxication (cyanide)

Incomplete combustion of glucose in hypoxia leads to the formation of lactate and H which contributes to the development of cerebral edema (initially cytotoxic and then interstitial) and to intracranial hypertension syndrome (ICH). Damage to small vessels (vascular endothelium) leads to accumulation in the interstitial space of fatty acids, lactic acid, electrolytes, arachidonic acid (proinflamatory and chemotactic function). These metabolites of plasma origin and local perivascular inflammation do not appear in conditions of complete ischemia (vascular obstruction), but occur at the stage of reperfusion (the so-called *injury of reperfusion)*.(7)

Symptoms and signs of cerebral hypoxia:

Depending on the duration of cerebral hypoxia the following clinical events are observed (see Table no. 2): (8), (9)

Tabel no. 2. Clinical signs which occur depending on the duration of cerebral hypoxia

Duration of hypoxia	Clinical signs
Up to 1 minute	Unconsciousness, convulsions, miosis, abolished pupillary reflex
After 2 minutes	Mydriasis, the abolition of corneal reflex
After 5 minutes	Cerebral cortex suffering irreversible damage
After 15 minutes	Irreversible damage at brain stem and the spinal cord

Clinical applications

In one patient with a short episode of global cerebral ischemia (syncope), within seconds, electric energy deficit causes the decrease of the neural electrical activity and the patient loses consciousness.

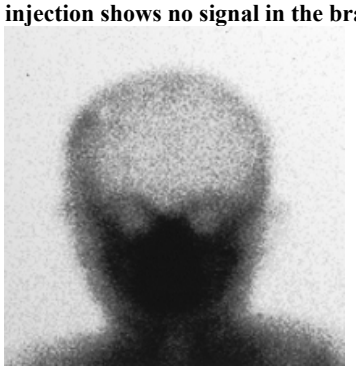
Neurons and glial cells are viable, and if circulation is restored promptly, the patient regains consciousness. If ischaemia lasts longer, at first is compromised the integrity of neuronal membranes and then the neuronal metabolism resulting in neuronal cell death by apoptosis. 4-5 minutes of ischaemia may irreversibly damage cortical pyramidal cells (layers 3,5,6) and hippocampus (CA1), neurons in the corpus striated and Purkinje cells. Ischaemia lasting longer leads to irreversible damage in thalamus and brain stem. Spinal cord remain unaffected for longer periods, even after the rest of the CNS was severely injured. An explanation of this selective vulnerability is that neurons more susceptible are the ones that most likely produce more glutamate.

Severe hypoxia which harms the cortex, basal nuclei and brain stem is resulting in brain death.

This is a clinical and paraclinical terminal condition characterized by a lack of response to external stimuli, absence of brain stem reflexes, isoelectric EEG and absence of brain perfusion. Lack of cerebral perfusion is due to blocked arterioles (by endothelial edema = no-reflow phenomenon) and because of cerebral edema. In this case the differential diagnosis is made with deep general anesthesia, various poisoning, hypothermia, conditions that can lead to coma and isoelectric EEG.

If a patient who is in brain death is artificially ventilated for a longer period, the brain goes through a process of enzymatic autolysis (liquefaction by autolysis), which was called by the term of *respiratory brain*. It has been replaced with the term of *nonperfused brain.*

Figure no. 1. Appearance of nonperfused brain. Radionuclide injection shows no signal in the brain



Diffuse cortical neuronal loss, thalamic or combined (but with unaffected brainstem) leads to severe dementia or persistent vegetative state (characterized by loss of cognitive functions and emotions but with preservation of sleep-wake cycle, autonomic functions and spontaneous breathing).

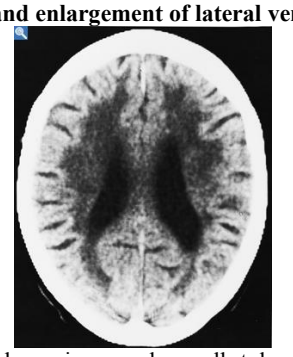
In some patients with epilepsy (after repeated episodes of generalized seizures) or in patients with short episodes of cardio-respiratory arrest, lesions with neuronal loss in hippocampus and bilateral gliosis (hippocampus sclerosis) occur, which can lead to Korsakoff amnesia, characterized by a deficit in establishing new information (anterograde/ posttraumatic amnesia), and a less severe deficit in evoking old memories (retrograde amnesia).

White matter is rarely affected in cases of acute cerebral hypoperfusion. An exception is the case of acute CO intoxication in which after a few weeks after injury appears an autoimmune response in subcortical myelin layers. In situations of chronic cerebral hypoperfusion occurs a subcortical axonal demyelination.

On CT or MRI examination that demyelination is called leucoarayosis (from Gr: *leucos* = white ,*araios*= least dense, thin). It is associated with small vessel disease (in chronic hypertension, cerebral amyloid angiopathy, CADASIL desease, Binswanger's desease) and lead to dementia. White matter pathology is usually associated with subcortical incomplete infarctions and hemorrhages.

Fig no. 2. CT in a patient with Binswanger's disease:

hypodense diffuse white matter around the ventricles (leucoarayosis) and enlargement of lateral ventricles.



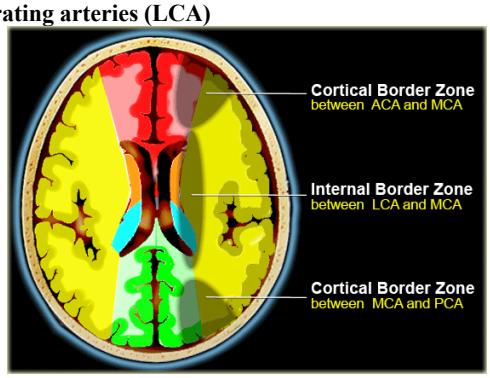
Severe hypoxia may be well tolerated if it occurs progressively. Some patients with severe chronic lung disease does not show signs of impairment of consciousness even when arterial oxygen partial pressure is 30 mmHg. This value, when suddenly occurs to a healthy individual, causes coma. (8), (9), (10)

Posthypoxic neurological syndromes

They are: coma or persistent vegetative state, dementia, extrapyramidal syndrome (parkinsonian) with cognitive deficit (in CO poisoning), coreoathetosis, cerebellar ataxia, myoclonus, Korsakoff's disease.

If injuries are caused by global ischaemic hypoperfusion, the patient may present specific manifestations of watershed strokes (border zone): visual agnosia (Balint's syndrome or cortical blindness) when the lesion is between the territories of MCA and PCA, proximal upper limb motor deficit, sometimes to the leg when damage is located between MCA and ACA territories.

Fig no. 3. Different border zone strokes, cortical or deep, between the territories of arteries MCA, PCA, ACA and penetrating arteries (LCA)



Balint's syndrome is characterized by a parieto-occipital bilateral ischaemia, manifested by optic ataxia, oculo-motor apraxia and psychic paralysis of gaze.

Seizures can occur, often resistant to therapy, and of which myoclonus is common and shows a sign of seriousness. (8), (9)

Late anoxic encephalopathy

It is a relatively rare phenomenon in which the initial improvement, apparently complete, is followed by a variable period (between 1-4 weeks) of a relapse: apathy, confusion, irritability, occasional agitation or mania. Most subjects survive the phenomenon, but some remain with severe mental and motor disorders and in some cases death occurs. (8),(9)

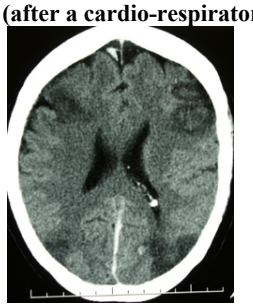
Prognostic

Improving in case of mild or moderate short lasting global hypoxia (seconds), with some minor temporary effects. Focal signs apear in case of localized persistent ischaemia. Could follow a state of permanent dementia or a state of superficial coma (or permanent vegetative state).

Prolonged severe hypoxia leads to irreversible brain damage, as evidenced by: the presence of fixed mydriasis and paralysis of eye movements for 24-48 hours, GCS less than 7. This is diagnosed after the exclusion of other causes (intoxication, deep anesthesia, hypothermia).

Family impact is significant. They have frequently idealized perspectives (often inspired by the media) making it difficult to accept unfavorable prognosis. Therapeutic decision is often influenced by complex ethical situations (brain death, organ transplants).(8),(9)

Fig no. 4. border zone infarction (watershed) between cortical territories ACA, MCA and PCA in a patient with Balint's syndrome (after a cardio-respiratory arrest).



Therapy

It is made by urgent initiation of the following measures: removing the cause of hypoxia, recovery of cardiac and pulmonary function (by resuscitation, respiratory support, defibrillation, pacemakers), oxygen (hyperbaric O2 in CO intoxication), blood glucose and blood pressure control, therapy and prevention of aggravation of focal cerebral ischemic injury, induction of controlled hypothermia - the cooling blankets (core T at 33 ° C) for 2 hours, immediately after resuscitation (is reducing cerebral metabolic needs and may improve prognosis).

To be given corticosteroids, prevention of cerebral edema, anticonvulsants (midazolam or neuromuscular blockers in cases of resistance to therapy, anesthesia). Myoclonus can be treated with clonazepam 8.12 mg / day. Fever and chills are treated with antipyretic, low body temperature from outside (cold applications) or neuromuscular blockade. (8),(9),(11),(12)

CONCLUSIONS

After those presented can be said of hypoxic-ischemic encephalopathy in adults that is caused by a shortage of supply of oxygen and glucose or their metabolism in the brain. The most common causes are cardio-respiratory arrest and haemodynamic shock. Brain tissue lesions are variable and depend on the duration and severity of the hypoxic / ischaemic phenomenon (from reversible to irreversible) and different degrees of sensitivity to hypoxia of different brain areas. Clinical manifestations vary depending on the duration, severity and localisation of the phenomenon and the causes of reduction of O2 concentration in the blood.

It is made a clinical diagnosis (based on history, signs and symptoms) and laboratory diagnosis (based on laboratory investigations, imaging and neurophysiological data).

Posthypoxic neurological syndromes can include: coma or persistent vegetative state, dementia, extrapyramidal syndrome with cognitive deficit (in CO poisoning), coreoathetosis, cerebellar ataxia, myoclonus, Korsakoff amnesia. Late postanoxic encephalopathy phenomenon may also be present.

The prognosis is favorable with recovery in case of mild or moderate hypoxia of short duration. Prognosis is unfavorable in hypoxic-ischaemic encephalopathy after severe damage.

Hipoxic-ischemic encephalopathy requires the

establishment of therapeutic measures as early as possible (in the ambulance, in pre-hospital, in the emergency room, the ICU unit) which aims: removing the cause of hypoxia; resuscitation, hemodynamic, metabolic and electrolyte balance, oxygen (with respiratory support), focal brain lesion therapy, prevention of cerebral edema, anticonvulsants, antipyretics.

It is very important the effective collaboration between physicians of different specialties which are coming in contact with the patient with hypoxic-ischemic encephalopathy and efficent resolution of ethical issues (brain death diagnosis, the possibility of organ transplantation).

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IMAGING OF CENTRAL NERVOUS SYSTEM IN MULTIPLE SCLEROSIS

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Keywords: *multiple sclerosis, imaging criteria, magnetic resonance imaging, white matter, grey matter*

Abstract: *The diagnosis and monitoring of patients with Multiple Sclerosis (MS) requires magnetic resonance imaging (MRI), that should be acquaired according to a standardized and reproductible protocol, consistent with international guidelines. Hyperintensities on T2 or FLAIR sequences are a very sensitive finding in patients with MS but is not specific of the underlying pathology. Among patients with clinically isolated syndrome, the presence of spatially disseminated lesions on the initial MRI is highly predictive of the conversion to clinically define MS. New sequences such as MR spectroscopy, diffusin tensor imaging, magnetization transfer imaging allow more sensitive quantification of such alterations. Molecular imaging by Positrons Emission Tomography is a very promising technique with high tissue specificity. It should improve our understanding of the pathophysiologic mechanisms involved in MS.*

Cuvinte cheie: *scleroza multiplă, criterii imagistice, imagistica prin rezonanţă magnetică, substanţa albă, substanţa gri*

Rezumat: *Diagnosticul şi monitorizarea radiologică a pacienţilor cu Scleroză Multiplă (SM) necesită un protocol de achiziţie în imagistica prin rezonanţă magnetică (IRM) standardizat şi reproductibil, în concordanţă cu recomandările internaţionale. Existenţa hipersemnalelor pe secvenţele T2 sau Flair reprezintă o anomalie foarte sensibilă la pacienţii cu SM, dar acest semn nu este specific unui mecanism fiziopatologic demielinizant. La pacienţii cu sindrom clinic izolat, prezenţa leziunilor diseminate în spaţiu pe IRM iniţial este extrem de predictivă pentru conversia la SM clinic definită. Noi secvenţe, cum ar fi spectro-RM, imagistica de difuzie, imagistica prin transfer de magnetizare, permit cuantificarea mai sensibilă a acestor alterări. Imagistica moleculară prin tomografie cu emisie de pozitroni este o tehnică foarte promiţătoare cu înaltă specificitate tisulară. Ea ar trebui să amelioreze înţelegerea noastră asupra mecanismelor fiziopatologice implicate în SM.*

SCIENTIFICAL ARTICLE OF BIBLIOGRAPHIC SYNTHESIS

Central nervous system imaging has become a mandatory procedure in diagnosing and monitoring inflammatory demyelinating disorders, particularly for the most common of them, the Multiple Sclerosis (MS). The most dominant of the techniques is the so-called conventional magnetic resonance imaging (MRI), generally used in hospital practice, but non-conventional imaging sequences are nowadays in full progress and may become interesting means of improving our knowledge on disease physiopathology.

Magnetic resonance imaging and Multiple Sclerosis diagnosis

The central role of MRI in diagnosing and monitoring the activity of the disease and among the therapeutic tests explains the need for a standardized and reproducible acquisition protocol. For this purpose suggestions have been made in order to standardize the methods and to adapt the acquisition techniques to the pathophysiology of the disorder. A magnetic field of at least 1.5 Tesla is recommended and the following sequences also:

- T2 fast spin echo (FSE) in axial sections of 3 mm thick maximum along the bi-callous plan.
- Fast fluid attenuated inversion recovery (FLAIR) in axial and sagittal sections.
- T1 echo spin preceded by at least 5 minutes by injecting a 0.1 mmol/kg standard dose of Gadolinium (severe kidney failure does not allow a gadolinium injection the risk of systemic fibrosis being present) (1).

Medullary MRI is advisable in case of primary medullary symptoms or if the cerebral MRI result is not ambiguous for the MS diagnosis. The Gadolinium injection should not be given systematically therefore it is being recommended only if the medullary MRI has been performed at a distance from the contrast cerebral MRI. Two planes, sagittal and axial should be study. The sections should be close to each other and should not exceed a 3 mm thickness.

The MRI monitoring is not usually systematical but it may become appropriate in cases of inexplicable aggravations, in cases of re-assessing the number of lesions prior to initiating any new treatment, or in case one should suspect a secondary/intercurrent pathology. If a MRI should be indicated in such cases, it should be performed following an identical protocol, in order to obtain an interpretation compared to the previous tests.

T2-weighted or FLAIR are highly sensitive to the plaques appearing as hyperintensity areas. These hyperintensities are not typical to a pathological mechanism and reflect a combination of inflammation, oedema, demyelination, axonal loss, and gliosis. In the supratentorial level these lesions are placed periventricular, subcortical and juxtacortical. At the periventricular level the lesions are usually ovoid, placed perpendicularly to the big axle of the lateral ventricles, and frequently touch the lower side of the callous body. On the T2-weighted it is sometimes difficult to distinguish certain periventricular or juxtacortical lesions, due to the hyperintense adjoining cerebrospinal fluid (CSF). Thus, FLAIR sequences are preferred because the liquid intensity is blocked (2).

Being more visible on T2-weighted images than on FLAIR, the subtentorial lesions usually touch the cerebellum peduncles, the 4th ventricle floor and the pons.

More recently the cortical lesions are being identified in

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MS: are find focal leucocortical lesions, intracortical lesions, and subpial lesions. These lesions can be identified in an almost identical proportion as those hystologically documented using high resolution MRI (7T or 9.4T) (3.4).

A variable number (10-20%) of hyperintense lesions in T2-weighted is also visible as a hypointensity in T1-weighted sequences. Moderate hypointensity areas do not persist during the evolution of the disease. These areas would reflect a reversible oedema or a partial demyelination, while persistent hypointensities (with an intensity similar to the CSF) called 'black holes' reflect a tissue destruction combined with a permanent axonal loss.

The intravenous injecting of the paramagnetic contrast substance (gadolinium) and the acquisition of the conventional T1-weighted sequence allow the discovery of areas of blood- brain barrier breakdown, secondary to the inflamation and thus the visualization of the active lesions. The most recent lesions (not more than 3 months old) are contrast-enhanced while older lesions are not.

Where the medullary MRI is concerned, the most accurate sequences are the T2-weighted ones which allow to distinguish the hyperintensity areas in more than 70% of the patients. Such lesions are more often seen at the cervical level, they are found at the height of less than 2 rachidian segments, and they are asymmetrical on the axial sections. At an acute phase one may notice a segmental medullary expansion as well as contrast-enhanced.

Nowadays there are several methods available to measure the cerebral volume. These methods have shown that cerebral atrophy occurs early in MS. The atrophy affects the cortical and subcortical white matter as well as the grey matter: while the atrophy of the white matter seams to evolve on the entire duration of the disease, the atrophy of the grey matter seems to evolve when the disease is more advanced (5).

Due to the appearance of new techniques of processing the images the measuring of the medullary atrophy becomes possible. One should note that in progressive forms of the disease, the medullar atrophy can be detected during the first years, especially on patients presenting a great number of medullary lesions. In this case the atrophy is segmentary conferring to the medulla an irregular caliber (6).

In 1997 Barkhof et al. have advanced the first MRI criteria focused on the number of lesions, their location (periventricular, juxtacortical or subtentorial), and on the presence of active lesions that are contrast-enhanced. Due to their being specific to MS this pattern has been included by MacDonald et al. among the diagnosis criteria in 2001 and stand at the basis of the radiological demonstration of spatial and temporal dissemination (7). According to Barkhof et al. 3 out of the following 4 criteria should be present in order to set a spatial dissemination diagnosis in MRI:

- at least 9 hyperintensity lesions in T2-weighted or a lesion contrast-enhanced;
- a infratentorial lesion;
- a juxtacortical lesion;
- 3 periventricular lesions..

All the lesions should exceed 3 mm in diameter. As for dissemination in time its existence can be proven radiologically through the presence of a new MRI lesion obtained 3 months after the first clinical episode. It may be the case of a contrast appearance or a new lesion in T2. Although they may appear complex at first, these criteria have allowed a more facile determination of the diagnosis in MS having the purpose of offering the patients the most rapid treatment. The 2001 MacDonald et al. criteria have given room to disapproving opinions and consequently they have been revised in 2005 (8).

The limits of the initial criteria are first and foremost interesting as they give a far minor but still very specific to MS importance to medullary lesions. As a result of the 2005 alterations a medullary lesion can be validated as an infratentorial lesion and any Gd-enhancing medullary lesion is equivalent to a cerebral one. A major second change concerns the definition of dissemination in time. A 3 months interval seemed too restrictive. Thus the appearance of a new T2 lesion on a checking MRI taken at any time after a reference MRI taken in its turn 1 month after the clinical episode is relevant enough to define this dissemination in time. Despite all the alterations, these criteria remain moderately sensitive (60 %) and specific (88%).

In 2006 Swanton et al. suggested some simplified criteria according to which dissemination in space is proven by detecting a T2 hyperintensity lesion, suggestive in 2 out of the following 4 locations: juxtacortical, periventricular, subtentorial and medullary. Dissemination in time requires the presence of a new T2 lesion on a distanced MRI, regardless of the time frame between the first imaging and the clinical episode. Compared to the MacDonald et al. criteria in a retrospective multi-central study, these new criteria bear an identical specificity (87%) for the MS diagnosis, but a higher sensitivity (71%) and do not require pathological contrast-enhanced (9,10).

Clinical isolated syndromes (CIS) manifesting themselves as optic neuritis, myelitis, brain stem damaged, are very frequently the first symptoms of MS. Still not every CIS evolves to a definite MS. In a 2008 study D.H.Miller`s team of researchers present their results after 20 years of studying a group of 107 patients with MS. They concluded that 63% of these patients have undoubtedly developed MS. Patients with an abnormal initial MRI (one or more T2 hyperintensity lesions) present a higher risk than the ones without cerebral abnormalities (82% vs. 21%). Within the group presenting an abnormal MRI the average time frame of evolving to definite MS is of 2 years compared to a 6 year frame in the case of a normal initial MRI (11).

The contribution of the new sequences and techniques:

1. Spectro-MRI:

Magnetic resonance spectroscopy is different from the other MRI techniques as the measured signal does not come from protons found in water molecules but from protons found in organic molecules located in certain tissues like N-acetylaspartate (NAA), coline, lactate, glutamate, or myoinositol. Spectro-MRI provides information on 2 pathological processes within MS: inflammatory demyelination and neural loss in injured or apparently normal tissues.

The increasing of coline, lactate, and macromolecules is associated with active inflammation and demyelination. This local increase may occur a few weeks earlier than T2 hyperintensities do and in some patients can be seen even in white matter areas that appear normal, indicating an inflammatory strike that exceeds by far the plaques visible in conventional imaging. A special role is held by NAA, a specific metabolite of the neural segment. Thus, a decrease in the NAA signal may be interpreted as a neural disorder. NAA signal abnormalities are distinguished at the level of visible lesion, but also in the apparently normal white matter, suggesting a diffuse neural dysfunction.

The role of the grey matter in the pathophysiology of the disorder can be emphasized with the help of spectro- MRI. A decrease in the NAA level has been observed in the cortical and deep grey matter. This sequence along with the measurement of the thalamic atrophy in T1-weighted allowed the assessment of the neural loss (approx. 30%) within the medio-dorsal nucleus of thalamus in patients with MS: values consistent with the neural loss measured on post-mortem brains. Still, variations of the NAA level may reflect a diminution in the number of neurons as well as neural atrophy or a metabolic dysfunction (12).

Table no. 1. MRI criteria for dissemination in space (DIS) and time (DIT) for MS. Rovira and Leo

	McDonald 2001	McDonald 2005	Swanton 2007
DIS	3 or more of: - 9 T2 lesions or 1 Gd-enhancing lesion - 3 or more PV lesions - 1 or more JC lesions - 1 or more PF lesions 1cord lesion can replace 1 brain lesion	3 or more of: - 9 T2 lesions or 1 Gd-enhancing lesion - 3 or more PV lesions - 1 or more JC lesions - 1 or more PF lesions A SC lesion can replace an infratentorial lesion An enhancing SC lesion is equivalent to an enhancing brain lesion Any number of SC lesions can be included in total lesion count	≥1 lesion in each of ≥2 characteristic locations: - PV - JC - PF - cord All lesions in symptomatic regions excluded in BS and SC syndromes
DIT	A Gd-enhancing lesion at least three months after CIS onset With reference to a prior scan, a new T2 lesion at least three months after CIS onset	A Gd-enhancing lesion at least three months after CIS onset With reference to a baseline scan, a new T2 lesion obtained at least 30 days after CIS onset	A new T2 lesion on follow up MRI irrespective of timing of baseline scan

2. Magnetization transfer imaging:

This particular technique measures the interaction between free protons (water and fat) and protons attached at macromolecules. The calculation of these exchanges takes the shape of a ratio called ”magnetization transfer ratio” (MTR). Post-mortem studies have shown that MTR, as a parameter suggested by many groups as appropriate to specifically assess demyelination and remyelination, is correlated with the degree of demyelination, but also with the number of residual axons. So this method does not seem specific enough to emphasize the myelin. The decreasing of MTR precedes the appearance of T2 hyperintensities and it is more relevant when the lesion is being visible under the shape of a T1 hypointensity. A decrease of the MTR is also made obvious within the apparently normal white and grey matter in MS patients, consolidating the concept of diffuse pathology (13).

3. Diffusion imaging:

This method measures the microscopic movements of the water molecules at tissue level. Inside the well-organized tissues like white substance or grey substance the water molecules have a reduced mobility. The diffusion process is consequently lower in such tissues. The interruption of the white substance fasciculi as well as the alteration of the axonal membranes permeability cause an increase in the apparent diffusion coefficient (ADC), in the medium diffusivity (MD), and in the fractional anisotropy which measures the leading direction of the diffusion process. These alterations are classically observed inside the demyelination plaques presenting a major increase especially in the ADC at the level of contrast-enhanced lesions. It has also been demonstrated that these parameters are disturbed at the level of the apparently normal cerebral tissue, suggesting that the presence of micro-structural alterations is still undetectable by means of conventional sequences (14).

Using a diffusion sequence for more than one direction allows one to determine the orientation of the axons and to assess the quality of the white matter fasciculi. This technique called tractography is used to determine the cortico-spinal fasciculi trajectory and to quantify the number of T1 and T2 lesions and the alteration of diffusivity at their level.

4. Functional MRI:

This is an indirect imaging method of the cerebral activity at a higher temporal resolution. Its purpose is to detect the transitory hemodynamic response triggered by the neural activity. It gives additional valuable information on the cortical strike in MS. Using the functional MRI while performing a motor, visual, or cognitive task on patients, points out a problem in recruiting the areas normally implicated in achieving such tasks and in activating new cortical areas compared to the healthy-control group. These functional changes, a proof of the existence of compensatory mechanisms, occur early, from the first clinical episode and continue with the evolution of the disease and the extension of the tissue damage. From the pathophysiological point of view, it is not known if this cortical reorganizing is a consequence of the axonal recovery, of the synaptic plasticity, or the preexisting parallel neural circuits (15).

5. Positron emission tomography (PET):

The advantages of this technique consist in the specificity, sensitivity, and the possibility to perform a reliable quantitative imaging. From another point of view, we are dealing with a complex and expensive method.

Neuro-inflammation imaging is possible through the ligands of the peripherical receptors of benzodiazepins, having as reference tracer (11C) - PK 11195. This tracer has already allowed the visualization of the microglial inflammation in MS, and in other degenerative neurological disorders (16).

6. Other sequences:

The sequences able to identify the cortical plaques (“double inversion recovery”, 3T and 7T high resolution MRI) which sensitivity/specificity is being studied or the T2 relaxometry whose early component would then be the reflection of the water contained by the myelin (17).

A special interest is carried by the usage of new contrast agents containing nano-particles (US - PIOs) which are actively phagocyted by monocytes and circulating macrophages, allowing the identification of the macrophage component of the cerebral inflammation at lesion level but also inside the apparently normal white matter (18).

In conclusion, the central nervous system imaging in MS has known a great development in the last 10 years. Nowadays, MRI represents a mandatory examination procedure indispensible in determining an early diagnosis, initiating the appropriate treatment, and monitoring patients. The multiple pathophysiological components of this disorder (lymphocyte and microglial inflammation, demyelination, neural-axonal damage) justify the development of higher tissue specificity techniques, thus revealing a wider research field regarding so-called non-conventional MRI sequences, new contrast agents, and molecular imaging. The following years shall undoubtedly be marked by major developments in this field.

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NEURO-OPHTHALMOLOGIC MANIFESTATIONS OF DEMYELINATING DISEASES

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Keywords: *demyelinization, autoimmune, optical neuritis*

Abstract: *Among all demyelinating diseases, the most frequent one in practice as well as in life is, beyond any doubt, multiple sclerosis (MS). Although the etiology of this condition is not known exactly (a lot of predisposing factors being involved), the disease has an obvious genetic predisposition and its pathogenetic mechanism is autoimmune. The clinical manifestations of MS are multiple and various, depending on the level the demyelinating injuries are produced at. The most frequent inception is through visual signs and symptoms, the neurological signs generally breaking out a bit later. The diagnostic of MS supposes firstly being familiar with the ways of manifestation of the disease, specific neurological and eye investigations and, of course, a closer cooperation between the neurologist and the ophthalmologist. It is equally important to establish the etiology of retro bulbar visual neuritis (a common manifestation of MS), through a strict history and specific paraclinical, biochemical and serological tests, so that the MS diagnostic should involve great responsibility on the part of the neurologist to inform the patient on the clinical manifestations and the progressive evolution of the disease. Since there still isn't any etiological treatment of MS, its treatment is immunomodulator / immunosuppressive, symptomatic and rehabilitating.*

Cuvinte cheie: *demielinizare, autoimun, nevrită optică*

Rezumat: *Dintre toate bolile demielinizante, cea mai frecvent întâlnită în practică şi în viaţă este fără îndoială scleroza multiplă (SM). Deşi etiologia afecţiunii nu se cunoaşte cu exactitate (fiind implicaţi mai mulţi factori predispozanţi), boala are totuşi o clară predispoziţie genetică, iar mecanismul patogenetic este unul autoimun. Manifestările clinice ale SM sunt multiple şi variate, în funcţie de nivelul la care apar leziunile demilienizante. Debutul cel mai des întâlnit este prin semne şi simptome vizuale, semnele neurologice apărând de regulă ceva mai târziu. Diagnosticarea SM presupune în primul rând cunoşterea formelor de manifestare ale bolii, investigaţii specifice neurologice şi oftalmologice şi bineînţeles o colaborare strânsă între neurolog şi oftalmolog. Este de asemenea important de stabilit etiologia nevritei optice retrobulbare (o manifestare comună a SM), printr-o anamneză riguroasă şi prin teste paraclinice, biochimice şi serologice specifice, întrucât diagnosticul de SM, implică o mare reponsabilitate a medicului neurolog de a informa pacientul cu privire la manifestările clinice şi la evoluţia progresivă a bolii. Întrucât nu există încă un tratament etiologic al SM, tratamentul este în principal imunomodulator/imunosupresor, simptomatic şi recuperator*

SCIENTIFICAL ARTICLE OF BIBLIOGRAPHIC SYNTHESIS

Demyelinating disease refers to any kind of affection that produces damage/destruction of the myelin sheath of the nerves in the Central Nervous System (CNS).

The most frequently met demyelinating disease is multiple sclerosis. (MS).

MS is a chronic disease which is characterized by axonal demyelination at the level of CNS, but through an inflammatory and degenerative device that are the base of neurological damage.

Described for the first time by Charcot in 1868, MS is an incompletely understood disease with unknown aspects regarding its etiology and pathogenesis. Conducting studies on monozygotic twins in comparison to bizygotic twins, it has been proved the certain existence of a genetic predisposition for MS. Apart from genetic factors, there are predisposing ones, such as environmental factors, infectious, smoking (although the device is still unknown).

No matter the etiology of the disorder, the pathogenetic device is considered of having autoimmune nature, a fact which has been scientifically proved through auto reactive HT1 lymphocytes. They activate themselves and migrate in the CNS where they are exposed to various auto antigens and, by reactivating themselves, they lead to inflammatory falls which has, as a final result, axonal demyelination as well as the loss of oligodendrocytes and axons. The necessary and compulsory condition for producing the inflammatory/immune assault upon the CNS structures is a complex, focal modification at the level of the blood-encephalic barrier which leads to modification of its permeability.

From the point of view of the correlation between these pathogenic and clinical processes, the inflammation or demyelination episodes manifest through clinical flares (falls followed by remissions), while the axonal degeneration is the major cause of the progressive and irreversible disability, which is more often met with progressive forms.

The damage may occur in every region on the CNS –

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visual nerve, spinal cord or in the cerebral parenchyma but most of the focuses are located in the white matter and specific-periventricular. Demyelination finds itself in different stages of evolution and may coexist with focuses of dysfunctional incomplete demyelination whose final stage is represented by the astroglial scar, from which the old name of *multiple sclerosis*.

The signs and neuro-ophthalmologic symptoms from MS are multiple and various, depending on the affected nerves. The disease may begin with motive symptoms (fatigue, ataxia, spasticity) or sensory (paraesthesia, feelings of burn or pain, Lhermitte sign etc.), but it most frequently starts with visual symptoms. On average, the period between the beginning of the visual symptoms and the neurological ones is 9 years.

Visual neuritis is the most often clinical symptom of presentation of Ms (25% of the cases), especially with young patients. It consists in the inflammation of the visual nerve with its demyelination, having as a result the reduction of visual ability of the respective eye (rarely bilateral). It is usually about a retro bulbar visual neuritis, only in third of the cases manifesting itself as papillitis.

It seems that about 78% of the visual neuritis cases are due to MS!

Visual neuritis manifests through different degrees of visual dysfunctions – from light to severe and even blindness. It is often accompanied by pain (or discomfort) at the movements of the affected eyeball – which precedes fogginess of the sight or occurs at the same time. The sight usually diminishes suddenly, stagnates for a few days and then it recovers spontaneously in a few weeks or months. The sight retrieves totally after the first attack, the visual prognosis diminishing with each subsequent attack. Even after the complete recovery of the visual acuteness, the examination of the fund eyes generally indicates a temporary visual atrophy (rarely generalized) – frequently met with optical neuritis in MS.

The most common brack of eyeshot which accompanies visual neuritis is the diffuse reduction of sensitiveness in central area (at 30 degrees), followed by arched scotoms, central or centrocecal scotom, bracks within the dial, etc.

Visual neuritis is also accompanied by discromatopsy, especially in red-green spindle and by an afferent pupillary brack.

Although the patient's sight is very weak or blurry, the fund eyes examination in the acute phase of retro bulbar neuritis (visual atrophy occurs later) – "the patient cannot see anything, the physician cannot see anything". Therefore, in this stage of the disease, the diagnosis is suggested by pupillary signals, by the bracks of the eyeshot, by the affectation of the chromatic sense and by the quick reduction of the sight. Visual evoked potentials (VEP) which reveal the delay of the conduct of the impulses through the visual nerve, represents an additional element for diagnosing, though it is nonspecific – alteration of VEP possibly reoccurring in the case of glaucoma or of ischemic visual neuropathy.

Very suggestive for MS is the fluctuation of the sight together with the growth of body temperature – either during a hot bath or after persistent physical activity (Uhthoff sign). The explanation consists in the alteration of neural conductivity through demyelinating nerves due to the high temperature.

In evaluating visual neuritis, for guiding the differential diagnosis, history is extremely important. The patient has to be asked whether he has been exposed to various toxins (mercury, lead, etc.), whether he is aware of certain diseases (sarcoidosis, lupus or other vasculitis, syphilis, etc.) or some viral or bacterial infection, whether he has taken medicines (etambutol, isoniazid, contraceptive, drugs) or whether he uses alcohol or tobacco excessively.

Another frequent visual signal which occurs in MS is *diplopia,* due to affecting the afferent visual system, with abnormalities of ocular movements. There are likely to occur *nystagmus* and *internuclear ophthalmoplegia*. Nystagmus in internuclear ophthalmoplegia is specific. Nystagmus occurs at the eye which is in abduction, at the horizontal look. When internuclear ophthalmoplegia is bilateral, nystagmus occurs at the eye in abduction in both directions, and the diagnosis of MS is almost certain. Less frequent visual signs in MS are paralyses of oculomotor muscles, hemianopsis intermediary uveitis (10% of the cases occur in the context of MS) and retinal periflebita.

Internuclear ophthalmoplegia, intentional tremors, cerebellar ataxia, motive and sensorial symptoms, emotional disturbances – all of these suggest MS.

Positive diagnosis of MS is set on the basis of the history, of the clinical signs and paraclinical investigations. Very useful and absolutely necessary for the diagnosis are complete ophthalmologic consultation, testing the eyeshot = VEP – which can trace alterations even in the absence of visual symptoms. Ophthalmologic examination should contain, beside fund eyes examination, testing the chromatic sense, the red glass exam (in the event of diplopia) and biomicroscopy and visual tonometer – for settling the differential diagnosis.

Blood tests and serological tests (for VIH, syphilis, Lyme disease) help establishing the etiology of visual neuritis.

The establishment of the diagnosis for sure of MS is done on the basis of cerebral NMR and cervical column (native and with contrast substance), possibly lumbar puncture with RCL examination and NMR spectroscopy.

Because of the fact that it is not known for sure the cause of the disease, despite the great number of researches for the past few years, there isn't an etiological treatment to lead to its cure. Numerous efforts for elucidation the pathogenic devices of the disease, are at the base of some therapeutical schemes that eventually lead to the alteration of the natural evolution of the disease.

The treatment of MS contains, beside the treatment which alters the natural evolution (immunomodulator, immunosuppressive), the treatment of the flare, the symptomatic and recovery ones.

In the case of acute flares of the disease, the treatment consists in administrating intravenous SoluMedrol, followed by Prednisolon orally. The scheme is established by the neurologist and it adapted to each case. It is not recommended the treatment only with corticosteroids orally administrated, as it doubles the rate of relapse of visual neuritis. After the acute phase treatment, immunomodulators are administrated (beta 1a/1b interferon, acetate glatiramer) or immunosuppressive (mitoxantrone, cyclophosphamide, methotrexate, etc.), depending on the form and progress of the disease.

Devie visual neuromyelitis is a pathological entity related to MS. It is a rare disease which can occur at all ages and which consists of bilateral visual neuritis quickly followed (within days or weeks) by transverse myelitis (demyelination of spinal cord) with paraplegia.

Schilder disease (diffuse mielinoclastic sclerosis) is also a very rare disease, progressive, generalized, which starts before the age of 10. It represents one of the causes of cortical blindness acquired by children of this age. It may cause bilateral retro bulbar visual neuritis or papillary edema (in 20% of the cases), because of the light growth of intracranial pressure. As the disease progresses, spastic paralysis occurs. The cause of this disease and its treatment are unknown, the decease intervening within 1-2 years form the inception of the disease.

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AMAUROSIS FUGAX

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Keywords: *Amaurosis fugax, arterial emboli, ocular hypoperfusion, arterial vasospasm*

Abstract: *Amaurosis fugax (Latin fugax meaning fleeting, Greek amaurosis meaning darkening, dark, or obscure) is a transient monocular visual loss.In 1990, the causes of amaurosis fugax were better refined by the Amaurosis Fugax Study Group, which has defined five distinct classes of transient monocular blindness based on their supposed cause: embolic, hemodynamic, ocular, neurologic, and idiopathic. Concerning the pathology underlying these causes (except. idiopathic), "some of the more frequent causes include atheromatous disease of the internal carotid or ophthalmic artery, vasospasm, optic neuropathies, giant cell arteritis, angle-closure glaucoma, increased intracranial pressure, orbital compressive diseaseand blood hyperviscosity or hypercoagulability. Amaurosis fugax este o scădere vizuală monoculară tranzitorie.*

Cuvinte cheie: *amauroza fugace, embol arterial, hipoperfuzarea oculară, vasospasm arterial*

Rezumat: *Amauroza fugace (fugax latin are sensul de efemer, amaurosis în greacă înseamnă întunecare, închisă la culoare sau obscur) este o scădere vizuală monoculară tranzitorie. În 1990, cauzele amaurozei fugace au fost stabilite de Grup Studiu Amaurosis Fugax, care defineşte cinci cauze ale orbirii monoculare tranzitorii: embolic, hemodinamic, ocular, neurologic şi idiopatic. În ceea ce priveşte patologia care stă la baza acestor cauze(cu excepţia idiopatică) unele dintre cele mai frecvente cauze includ boala ateromatoasă a arterei carotide interne sau oftalmice, vasospasm, neuropatii optice, arterita cu celule gigant, glaucomul cu unghi închis, creşterea presiunii intracraniene, boala compresivă orbitală şi hipervâscozitate sau hipercoagulabilitate.*

SCIENTIFICAL ARTICLE OF BIBLIOGRAPHIC SYNTHESIS

Amaurosis fugaux – General characters

The transient monocular visual loss occurs due to a reduction in retinal artery, ophthalmic artery or ciliary artery blood flow, leading to a decrease in retinal circulation which, in turn, causes retinal hypoxia.Emboli are described as coming from an atherosclerotic carotid artery, any emboli arising from vasculature preceding the retinal artery, ophthalmic artery, or ciliary arteries.

- Atherosclerotic carotid artery: Amaurosis fugax may present as a type of transient ischemic attack (TIA), during which an embolus unilaterally obstructs the lumen of the retinal artery or ophthalmic artery, causing a decrease in blood flow to the ipsilateral retina. However, a severely atherosclerotic carotid artery may also cause amaurosis fugax due to its stenosis of blood flow, leading to ischemia when the retina is exposed to bright light.Unilateral visual loss in bright light may indicate ipsilateral carotid artery occlusive disease and may reflect the inability of circulation to sustain the increased retinal metabolic activity Atherosclerotic ophthalmic artery: Will present similarly to an atherosclerotic internal carotid artery.
- Cardiac emboli: Thrombotic emboli arising from the heart may also cause luminal obstruction of the retinal, ophthalmic, and/or ciliary arteries, causing decreased blood flow to the ipsilateral retina; examples being those arising due to atrial fibrillation, valvular abnormalities including post-rheumatic valvular disease, mitral valve prolapse, and a bicuspid aortic valve, and atrial myxomas.
- Temporary vasospasm leading to decreased blood flow can be a cause of amaurosis fugax. Generally, these episodes are brief, lasting no longer that five minutes. These vasospastic episodes are not restricted to young and healthy individuals. Observations suggest that a systemic hemodynamic challenge provokes the release of vasospastic substance in the rentinal vasculature of one eye.

- Giant cell arteritis: Giant cell arteritis can result in granulomatous inflammation within the central rentinal artery and posterior ciliary arteries of eye, resulting in partial or complete occlusion, leading to decreased blood flow manifesting as amaurosis fugax. Amaurosis fugax caused by giant cell arteritis may be associated with jaw claudication and headache but it is possible for these patients to have no other symptoms.

- Malignant hypertension can cause ischemia of the optic nerve head leading to transient monocular visual loss.
- Drug abuse-related intravascular emboli
- Iatrogenic: Amaurosis fugax can present as a complication following carotid endarterectomy, carotid angiography, cardiac catheterization, and cardiac bypass.

Ocular origin of the Amaurosis fugax:

- Optic disc drusen
- Posterior vitreous detachment
- Closed-angle glaucoma
- Transient elevation of intraocular pressure
- Orbital hemangioma
- Orbital osteoma

Neurologic origin of the Amaurosis fugax:

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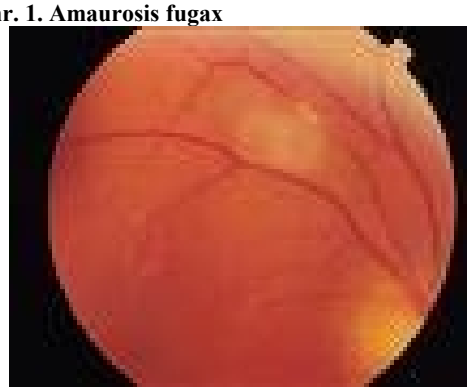
- Optic neuritis
- Compressive optic neuropathies

Figure nr. 1. Amaurosis fugax



- Papilledema: "The underlying mechanism for visual obscurations in all of these patients appear to be transient ischemia of the optic nerve head consequent to increased tissue pressure. Axonal swelling, intraneural masses, and increased influx of interstitial fluid may all contribute to increases in tissue pressure in the optic nerve head. The consequent reduction in perfusion pressure renders the small, low-pressure vessels that supply the optic nerve head vulnerable to compromise. Brief fluctuations in intracranial or systemic blood pressure may then result in transient loss of function in the eyes." Generally, this transient visual loss is also associated with a headache and optic disk swelling.
- **Multiple Sclerosis can cause amaurosis fugax due to a unilateral conduction block, which is a result of demyelination and inflammation of the optic nerve, and "...possibly by defects in synaptic transmission and putative circulating blocking factors."**
- Migraine
- Pseudotumor cerebri
- Intracranial tumor
- Psychogenic

TMVL caused by vascular arterial ischemia

TMVL most often results from impaired perfusion in the ophthalmic, retinal (central or branch retinal arteries), choroidal (posterior ciliary arteries), or optic nerve (posterior ciliary arteries) circulation (Figs. 4-6 and 4-7)

There are three main mechanisms responsible for episodes of vascular arterial TMVL. They comprise

1. arterial emboli that originate in proximal arteries or the heart (usually to the ophthalmic artery, central retinal artery or its branches),
2. ocular hypoperfusion secondary to hemodynamic impairment (stenosis or occlusion of the aortic arch, carotid or ophthalmic arteries, reduced cardiac output or systemic hypotension),
3. arterial vasospasm (usually involving the central retinal artery). Each of these mechanisms may occur separately or in association with each other. The characteristics of the episode of TMVL and the fundus appearance help characterize the mechanism (Figs. 4-8, 4-9, 4-10, 4-11, 4-12, and 4-13).

1 Retinal Emboli

TMVL was first linked to retinal arterial emboli 50 years ago when white fragments were observed by ophthalmoscopy to travel through the retinal arterial vessels during episodes of TMVL. These emboli originate most often from an atherosclerotic plaque at carotid bifurcation (Fig. 4 – 14) and less commonly from the aortic arch or ophthalmic artery (fig. 4 – 15). Patients with this symptom typically complain of TMVL that lasts a few minutes at most.

2 Anterior Circulation Stenosis

Severe stenosis of the carotid or ophthalmic arteries or stenosis of the aortic arch (in severe aortic arch atherosclerosis or Takayasu arteritis) may cause TMVL by hypoperfusion rather than embolism.

3 Hypotension

Reduced cardiac output or systemic hypotension may also produce TMVL. Although TMVL is not typically an isolated symptom of systemic hypotension, which generally also causes lightheadedness, confusion, and binocular visual loss, the combination of drop in systemic blood pressure and asymmetric anterior circulation stenosis may cause TMVL alone, particularly orthostatically induced TMVL.

4 Chronic Ocular Hypoperfusion

Chronic ocular hypoperfusion of any mechanism may be associated with transient but prolonged visual loss (several minutes to hours) and positive visual phenomena. It may be induced by situations that further decrease perfusion pressure (postural change) or increase retinal oxygen demand (exposure to bright light). Borderline ocular perfusion may not be able to maintain retinal metabolic activity when blood flow is diverted to other tissues as after eating a meal or during exercise. Chronic hypoperfusion of the eye may also induce delay in the regeneration of visual pigments in the photoreceptor layer of the retina, resulting in blurred or absent vision that persists until regeneration of visual pigment occurs. Impaired dark adaptation may be a consequence of this phenomenon. In these cases, examination often shows venous stasis retinopathy or the ischemic ocular syndrome (dilated retinal veins, retinal hemorrhages, retinal or iris neovascularization, ocular hypotony or hypertony, anterior chamber cells and flare, cataract, and corneal edema) (Figs 4-11 and 4-12)

5 Other Causes

Less common causes of TMVL are vasculitis and radiation toxicity. Giant cell arteritis commonly causes TMVL by compromising the optic nerve circulation, more commonly than the retinal arterial low. TMVL from isolated choroidal ischemia is rare and should point to a vasculitic process such as giant cell arteritis (Fig. 4-13). TMVL is rarely a premonitory sympthom of ischemic optic neuropathies. In those cases, arteritic (rather than nonarteritic) ischemic optic neuropathy should be suspected.

Idiopathic TMVL in Young Individuals (Vasospasm)

Young people who have no evidence of vasculopathy may have episodes of TMVL secondary to reversible vasospasm of retinal arteries. Rare case reports have documented this phenomenon. Such vasospasm may be the basis for the TMVL of so – called retinal migraine, which remains a debated entity. In listening to the patient`s history, it is impossible to distinguish TMVL as an isolated symptom of vasospasm from TMVL of other causes. There-fore, vasospasm should remain a diagnosis of exclusion.

6 Natural History of TMVL

The natural history of patiens with TMVL depends on the age of the patient and the etiology of the TMVL (Table 4-2)

7 Retinal Stroke

A major adverse outcome is persistent visual loss, mostly resulting from branch or central retinal artery occlusion (Figs. 4-15 and 4-16). Besed on several natural history studies, the aggregate risk of permanent ipsilateral visual loss is about 1 % to 2 % per year.

8 Cerebral hemispheric stroke

TMVL may also herald a cerebral infraction (Fig. 4-17). When carotid occlusive disease is related to atherosclerosis, TMVL is a marke of systemic atheromatous disease and is associated a higher risk of vascular death.

The NASCET study showed a 25% 3 year risk of

stoke in patients with hemodynamically significant carotid stenosis causing ipsilateral TMVL, cerebral hemispheric transient ischemic attack (TIA), or mild stroke. However, the risk of stroke doubles in patients presenting with a hemispheric TIA compared with an episode of TMVL (see later).

Death

The risk of death in patients with TMVL and atheromatous carotid stenosis is approximately 4% per year, mainly related to myocardial infarction. Patients with retinal and hemispheric TIAs are equally vulnerable.

These data suggest that TMVL is a marker for systemic arteriosclerosis and should prompt immediate comprehensive patient evaluation

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ORAL CANDIDOSIS PREVALENCE ON PATIENTS WITH PREMATURE OVARIAN INSUFFICIENCY

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Keywords: *oral infection with Candida, precocious menopause*

Abstract: *The oral infection with Candida is opportunistic, the pathogen agent using the diminishing of the resistance of the organism, in order to become consensual, pathogen. Starting from the premises that the secretion rhythm of the saliva and the salivary pH depend on the concentration of the circulating estrogen, we intended to research on the risk factors favoring the development of the oral candidosis on women with hyper-estrogenism. So we analyzed the quantity of saliva after the stimulation, as well as the salivary pH on a 53 patients group with precocious ovary insufficiency, compared with a testimony group of 50 healthy women. The patients with precocious ovarian insufficiency had an un-stimulated salivary flux inferior to the one of the testimony group and a lower salivary pH. The oral candidosis confirmed on the Sabouraud culture was present on 13,2 % from the patients with precocious ovarian insufficiency and on 2% of the women from the testimony group, with a positive correlation (p=0,024) between the presence of the oral candidosis and the premature ovarian insufficiency. It can be mentioned, with a 99% certainty (p=0,000), the presence of the positive correlation between the premature ovarian insufficiency and the oral candidosis prevalence. The conclusion of the research: the oral health of the patients with precocious menopause is altered by hypo-estrogenism that attracts the hypotrophy of the oral mucosa, diminishing the salivary pH and the salivary flux and structurally and functionally modifying the pathologic reproduction of the species of Candida in the oral cavity.*

Cuvinte cheie: *candidoză orală, insuficiență ovariană prematură*

Rezumat: *Infecția orală cu Candida este una oportunistă, agentul patogen folosindu-se de diminuarea rezistenței organismului pentru a deveni din comensual, patogen. Plecând de la premiza că ritmul de secreție al salivei şi pH-ul salivar depind şi de concentrația estrogenilor circulanți, ne-am propus să cercetăm factorii de risc care favorizează dezvoltarea candidozei orale la femeile suferinde de hipoestrogenism. În acest sens am analizat cantitatea de salivă bazal şi după stimulare, precum şi pH-ul salivar la un lot 53 de paciente cu insuficiență ovariană precoce, comparativ cu un lot martor de 50 femei sănătoase. Pacientele cu insuficiență ovariană precoce au avut un flux salivar nestimulat inferior femeilor din lotul martor şi un pH salivar în salivă mai scăzut. Candidoza orală confirmată pe mediul de cultură Sabouraud a fost prezentă la 13,2% din pacientele cu insuficiență ovariană precoce şi la 2% la femeile din lotul martor, existând o corelație pozitivă (p=0,024) între prezența candidozei orale şi insuficiența ovariană prematură. Se poate afirma cu o confidență de 99% (p=0,000) prezența corelației pozitive între insuficiența ovariană prematură şi prevalența candidozei orale. Concluzia cercetării: sănătatea orală a pacientelor cu menopauză precoce este alterată de hipoestrogenism, condiție care antrenează hipotrofia mucosei orale, diminuează pH-ul salivar şi fluxul salivar, modificări structurale şi funcționale favorabile înmulțirii patologice a speciilor de Candida în cavitatea orală.*

INTRODUCTION

The premature ovarian insufficiency is defined as amenorrhea with more than 4 month duration, before 40, with high levels of gonadotrofine, mainly FSH (over 40UI/I). The affection is also called precocious menopause and recognizes many ethyologies: iatrogenic, self-immune, genetic, toxic (1). The monitoring of the patients with premature ovarian insufficiency aims at the avoidance of the complications due to hypoestrogenism, as the cardio-vascular diseases, the osteoporosis, the atrophy of the genital tract (2).

Through techniques of immune-hystochemistry receptors for estrogen hormones have been emphasized (3). The estrogens maintain the trophicity of the normal functions of the mucosa of the oral cavity and so the balance of the micro-organisms from the oral cavity. The salivary secretion as well as the salivary pH is correlated with the level of the circulating estrogens (4). It was found out that hypo – estrogenism produces glosodinie, xerostomie and diminishes the sensitivity over the bitter taste at 40% from the women at menopause. Another cause, besides the lowering of the circulating estrogens that produces the sensation of burning at the level of the tongue is candisosis (5). At 40 – 60% from the healthy women, different species of Candida can be emphasized inside the buccal cavity, the levura being a part of the normal flora of the mouth (6,7)

PURPOSE OF THE STUDY

Starting from the fact that the rhythm of secretion of the saliva and the salivary pH depend also on the concentration of the circulating estrogens, we intend to research on the factors of risk that favor the development of the oral candidosis on women with hypo – estrogenism. So, we analyzed the quantity of basal saliva after stimulation, too, as well as the salivary pH on a

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group of women affected by the precocious ovarian insufficiency.

Another objective of the study is the research of the prevalence of oral candidosis on women with precocious menopause, compared to women with normal ovarian activity.

The third objective was to elaborate a practical guide for the patients with precocious menopause, as well as for the doctor, in order to prevent and heal the oral manifestations caused by hypo-estrogenism.

MATERIAL AND METHOD

The study was done during the period 2006-2008. it was a transversal research in two sanitary units (the Clinic of Endocrinology and the Ambulatory of Stomatology from Sibiu).

The group was of 53 patients with premature ovarian insufficiency.

The patients were asked to fill in a form concerning the moment of amenorrhea and the oral subjective and objective symptoms (sensation of dry mouth, burnings on the tongue, taste modifications, loaded tongue, creamy deposits on the intern face of the cheeks).

The diagnosis of precocious ovary insufficiency was put after the anamnesis, the clinic exam and the hormone dosage. The oral candidosis diagnosis was represented by the finding of the pseudohife on the wet frotiu, with confirmation in the Sabouraud culture. The prelevations for the frotiu were done at the level of the oral mucosa. More profound and suspect lesions maybe produced by Candida have been examined hystologically on the tests obtained through biopsy.

There have been collected basal saliva tests (without stimulation) and after stimulation in GC Salivar Check Buffer testers. The salivary flux (degree of hydration of the saliva) and the pH of salivary break. The stimulated salivary flux was determined after stimulation through 30 minutes mastication of a cube of sterile paraphine from the kit. The pH was determined by pouring one drop of saliva on the paper band of the pH kit and the comparing after 2 minutes of the color with the one of the reference set.

RESULTS

The research analyzed the testimony group of 50 healthy women, with present menstrual cycles, aged between 37+-8,32 and 53 patients suffering from premature ovarian insufficiency, with the following characteristics (Tab.nr.1).

Tabele no. 1. Representing the characteristics of patients with early ovarian failure

	Precocious ovarian insufficiency	Testimony group	P Likelihood ratio
Average age	36 ± 6,40 ani	37±8,32 ani	
Buccal accuses	17(32,07%)	3(6,0%)	
Un-stimulated salivary flux Salivary flux after stimulation	0,32±o, 0,06 ml/min. 1,3±0,09 ml/min	0,39±o, 0,04 ml/min 1,7±0,05 ml/min	p=0,000
Salivary pH	6,7±0,8	7,1±0,9	p=0,000
Suspected, at clinical exam, of oral candidosis	9(16,98%).	2(4%)	
Candida present inside the oral cavity	31(58,49%).	17(34,0%)	p=0,012
Oral candidosis confirmed on Sabouraud culture environment	7(13,20%)	1(2,0%)	p=0,04

DISCUSSIONS

The total number of patients with premature ovarian insufficiency in study was of 53 with an average age of 36±6,40. The ethyology of the premature ovarian insufficiency was the ovarectomy: 31 (58,49%), self-immune: 13 (21,52%) and Turner syndrome: 9 (16,98%).

The patients with precocious ovarian insufficiency presented buccal accuses: in 32% of the cases compared with 6% of healthy women.

After the statistic analysis a conclusion could be drawn with a 99% precision (p=0,000), that there is a significant statistic difference between the salivary flux of the patients with premature ovarian insufficiency, compared with the women from the testimony group. Thus, the level of the salivary flux was lower at the patients with ovarian insufficiency (0,32 – un-stimulated; 1,30 – stimulated), compared to the testimony group (0,39 – un-stimulated; 1,70 – stimulated).

As for the salivary pH a conclusion can be drawn with a 99% precision (p=0,000), that there was a significant statistic difference between the level of the salivary pH in the stimulated saliva of the patients with premature ovarian insufficiency from the testimony group. Thus, the level of the salivary pH in the stimulated saliva is lower at those with ovarian insufficiency (6,7), compared to the women of the testimony group (7,1).

At the patients with clinic precocious ovarian insufficiency, the diagnosis of buccal candidosis was suspected on 9 (16,98%) while only 2(4%). women of the clinic testimony group were suspected of buccal candidosis .

The patients with precocious ovarian insufficiency had Candida in the buccal cavity in 31 (58,49%) of the cases, while Candida was found in the buccal cavity only at 17(34%) of the women from the testimony group. It comes out that the premature ovarian insufficiency represents a factor of risk for the oral candidosis (the relative risk was of 1,72%).

At the patients with precocious ovarian insufficiency the oral candidosis was confirmed on the Sabouraud culture for 7 (13,20%), while the testimony group confirmed it on only one person.

The estrogens are confirmed in the modulation of the cells growth, the differentiation and the regulation of the reproduction function. The steroid sexual hormones seem to play a significant role in the physiology of the oral cavity. They modulate the maturation of the epithelial cells, including those from the buccal mucosa (8).

The lowering of the estrogens during menopause affects the process of maturation of the buccal epithelia, leading to its weakening. The atrophied epithelia lead to different infections, including the fungi ones (9,10).

A series of studies showed that the therapy of hormone substitution prevents these things at post- menopause women, suggesting the role of the feminine sexual hormones for the maintenance of the troficitate of the buccal mucosa. (11,12). The salivary secretion is regulated by many hormones among which the estrogens play a very special role. During the menstrual cycle, the pregnancy and the menopause, the composition of the saliva pH is modified.

The estrogens contribute at the maintenance of the acid-basic balance in the buccal cavity through many mechanisms. Normally the mouth is easily acid.

Candida, on some researchers, blocks the estrogen receptors from the buccal mucosa; as a result, it can be said that the presence of candida in high quantity in the oral cavity can produce local estrogenism, inducing a sensitivity of the receptors to estrogens. The blocking of the estrogen receptors can lead to the relative domination of the progesterone and the testosterone that raise the risk of hypoestrogenism (13).

The substitution treatment with estrogen raises the neutralizing effect of the saliva (raises the pH) and also raises the salivary secretive debit (14).

The cited studies suggest that the estrogens play an

important role in maintaining the troficitate of the buccal mucosa and of the salivary glands. After menopause, the salivary flux diminishes (15, 16, 17, 18).

Turner syndrome associates with intense signs and symptoms of hypoestrogenism (19, 20). Oral candidosis often associates with the angular cheilitis (Fig.nr.2).

Figure. no. 1. A. The patient AV, 32 years old, Turner syndrome

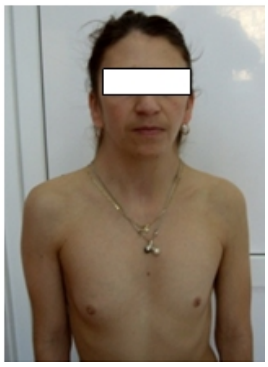
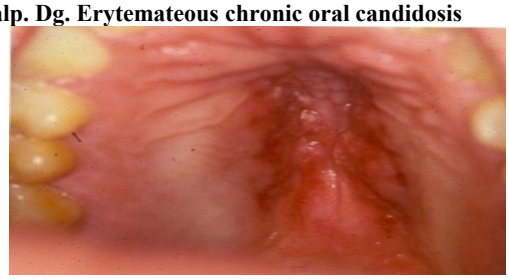


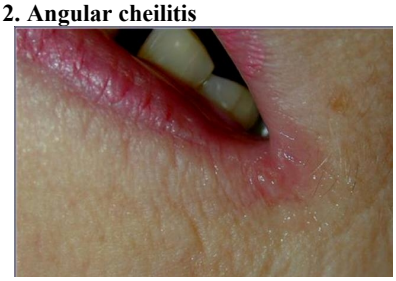
Figure no. 1. B. Ogival palate, pterygium colli, low insertion of scalp. Dg. Erytemateous chronic oral candidosis



The intimate mechanisms through which the estrogen lack influences the oral manifestations favoring the development of Candidosis in the oral cavity are not known, but the reduction of the number of estrogen receptors in the buccal mucosa and in the salivary glands could be a first cause. The histological aspect of the oral mucosa is similar to the vaginal mucosa. The vitality dependency of the vaginal mucosa on estrogen is already proved, the atrophic modifications due to am estrogen lack could be extrapolated on the oral mucosa. In a precocious menopause the raised prevalence of the oral candidosis could be due to hypo estrogen, pH lowering of the salivary flux (Fig.3).

The estrogen substitution treatment in precocious ovarian insufficiency could prevent and heal the oral manifestations of this patient. For that we need random clinical studies, controlled on long term, in order to prove the benefits of the estrogen substitution treatment on the oral discomfort at precocious menopause (21,22).

Figure no. 2. Angular cheilitis



Angular cheilitis (fig.2) was the most frequent form of oral candidosis at the patients with precocious menopause and those with Turner syndrome.

The hyperplasic chronical candidosis was present at a patient with precocious menopause. It can be taken for leucoplakia (white persistent spots on the cheeks and tongue). Leucoplakia is a pre-cancer state. (23).

For a differential diagnosis in such a situation a biopsy for differential diagnosis was needed. (fig.4)

Figure no. 3. Mechanisms involved in the pathogenesis of the oral candidosis in precocious menopause

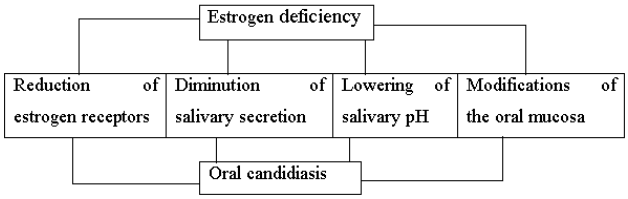
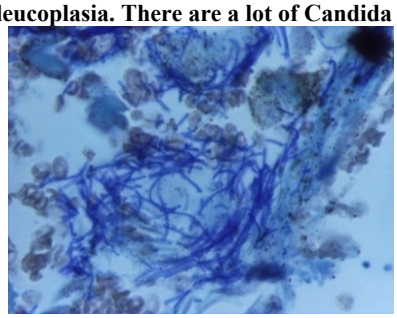


Figure no. 4. Biopsy on the buccal mucosa in a patient suspect of leucoplasia. There are a lot of Candida pseudihife



CONCLUSIONS

1. În ce priveşte acuzele orale se poate confirma cu o confidenţă de 99%, că există o corelaţie între insuficienţa ovariană prematură şi acuzele orale. 32,1% dintre pacientele cu menopauză precoce au prezentat acuze orale faţă de 6% din lotul martor.
2. Pacientele cu insuficienţă ovariană precoce au avut un flux salivar nestimulat (bazal) inferior femeilor din lotul martor şi un pH salivar mai scăzut.
3. Se poate afirma cu o confidenţă de 99% (p=0,000) că există o corelaţie între insuficienţa ovariană prematură şi suspiciunea de candidoză orală.
4. Confirmarea candidozei orale pe mediul de cultură Sabouraud a fost la 13,2% din pacientele cu insuficienţă ovariană precoce şi de 2% din lotul martor. Rezultă o corelaţie pozitivă între prezenţa candidozei orale şi insuficienţa ovariană prematură (p=0,024).
5. În menopauza precoce prevalenţa crescută a candidozei orale s-ar putea datora hipoestrogenismului, scăderii pH-ului şi fluxului salivar.
6. Tratamentul de substituţie estrogenic în insuficienţa ovariană precoce ar putea preveni şi trata manifestările orale la aceste paciente. Pentru acest deziderat sunt necesare studii clinice randomizate, controlate pe termen lung care să dovedească beneficiile tratamentului de substituţie estrogenic asupra disconfortului oral în menopauza precoce.

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THE OPTIMIZATION OF BACTERIOLOGICAL INVESTIGATION IN THE CASES OF PULMONARY TUBERCULOSIS WITH NEGATIVE MICROSCOPIC EXAMINATION, FOR ACID- FAST BACILLI (AFB), OF SPONTANEOUS SPUTUM CULTURE

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Keywords: *tuberculosis, bacteriological confirmation, induced sputum, bronchial lavage*

Abstract: *Introduction. Tuberculosis continues to remain a major public health issue in Romania, the level of TB incidence at present placing our country among the first places in the European Union. Pulmonary tuberculosis (TB) is the most common way of localization of the disease in the adult patient (over 90%), the level of bacteriological confirmations of newly proven cases being, over the last few years (2006-2008), around 50%-70%. Aims. The evaluation of the input of special techniques for cough and expectoration induction (sputum induced by aerosol exposure with 5% of saline solution), along with methods of sputum culture (normal saline solution lavage and bronchial aspirate by fibrobronchoscopical examination.) Materials and methods. The object of study was a group of patients hospitalized with the diagnosis of pulmonary tuberculosis who, apart from the standard process of sputum culture and processing, received treatment by means of ultrasonic aero Venturi type face-mask, together with lavage and bronchial aspirate by endoscopic examination. The recorded issues were: the aspect of products taken, the results of bacteriological examinations carried out for negative sputum-smear for acid-fast bacilli (AFB), by means of microscopy and culture (C) of the products taken, adverse effects and necessary costs. Results. Bacteriological examinations of induced sputum proved to be valid through microscopic examination (M+) for seven patients and through culture (M-,C+) for nine patients, having a diagnostic sensitivity of 18,1%. Then, the examinations of bronchial lavage liquid confirmed 4 patients (4%) through microscopy and 8 patients (8%) through culture, with a diagnostic sensitivity of 14%. The methods used were considered to be accurate and valid, with minor adverse events, applicable to routine practice and also low cost. Conclusions. The results of this study prove the importance in implementing all the recommendations made by the Tuberculosis National Control Programme concerning sputum culture, in order to obtain the best results (bacteriological confirmations) in pulmonary tuberculosis.*

Cuvinte cheie: *tuberculoza, confirmare bacteriologică, sputa indusă, lavajul bronşic*

Rezumat: *Introducere. Tuberculoza continuă să rămână o problemă majoră de sănătate publică în România, nivelul incidenţei actuale (99,9‰) situând ţara noastră pe primul loc în Uniunea Europeană (UE). Tuberculoza pulmonară (TB) este cea mai frecventă localizare a bolii la pacientul adult (peste 90%), iar nivelul confirmărilor bacteriologice a cazurilor noi declarate a fost în ultimii ani (2006-2008) între 50-70%. Obiectiv. Evaluarea aportului tehnicilor speciale de provocare a tusei şi expectoraţiei (sputa indusă prin aerosolizare cu soluţie salină 5%), completate cu tehnici de recoltare a sputei (lavaj cu ser fiziologic şi aspiraţie bronşică prin examen fibrobronhoscopic), la creşterea procentului de confirmare bacteriologică la pacienţii cu TB pulmonară, la care examenul microscopic (M) pentru BK din sputa recoltată spontan, a fost negativ. Material şi metodă. S-a luat în studiu un lot de pacienţi internaţi cu diagnosticul de tuberculoză pulmonară, la care pe lângă aplicarea metodelor standard de recoltare şi prelucrare a produsului patologic (sputa), s-a efectuat tehnica de recoltare şi îmbunătăţire a produsului patologic prin aerosolizare ultrasonică pe masca Venturi, completată cu lavajul şi aspiraţia bronşică prin examen endoscopic. S-au consemnat: aspectul sputei recoltate spontan, rezultatele examenelor bacteriologice pentru BK efectuate prin microscopie şi cultură (C), reacţiile adverse apărute şi costurile necesare. Rezultate. Examenele bacteriologice ale sputei induse au arătat o confirmare prin examen microscopic (M+) la şapte pacienţi (7%) şi prin cultură (M-; C+) la nouă pacienţi (9%), având o sensibilitate diagnostică de 18,1%, iar examenele lichidului de lavaj bronşic au confirmat patru bolnavi (4%) prin microscopie (M+) şi opt pacienţi (8%) prin cultură, cu sensibilitate diagnostică de 14%. Metodele aplicate au fost considerate sigure, cu reacţii adverse minore, posibil de aplicat în practica de rutină, fără costuri mari. Concluzii. Rezultatele studiului demonstrează importanţa aplicării tuturor recomandărilor Programului Naţional de Control al Tuberculozei (PNCT) privind recoltarea sputei, în vederea obţinerii celor mai bune rezultate (confirmări bacteriologice) în tuberculoza pulmonară.*

INTRODUCTION

The current level of incidence for TB in Romania, (99,9‰)(8) places our country on the seventh place among the countries in the European Region of the World Health Organization (WHO) and on the first place in the EU. What can be noticed from the data analysis concerning the bacteriological confirmation of cases with pulmonary localization is the preservation of a low value for new cases and relapses both country level and local level, around 50%-70% confirmations[(8)]. There is still a significant percentage of new cases of TB bacteriologically unconfirmed, the ones for which the alternative

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of whether implementing an anti TB treatment or not raises enough dilemmas.

PURPOSE OF THE STUDY

The purpose of this study is to evaluate the contribution of special techniques for: the generation and culture of valid samples of sputum (induced sputum and fibronchoscopic examination with aspirate after bronchial washing), the optimization of bacteriological investigation (rise of etiological confirmations), techniques used on patients suspect of pulmonary tuberculosis but still with negative microscopic examination for acid-fast bacilli (AFB), of spontaneous sputum culture.

MATHERIAL AND METHOD

The study was conducted between 01.01.2007-31.12.2009 on a group of 98 patients hospitalized at Spitalul de Pneumoftiziologie in Mihaiesti, Valcea, diagnosed with pulmonary TB.

What was insisted upon was the application of standard methods of sputum culture and processing, according to PNCT[6]. as an accepted alternative of sputum culture, there were three samples of sputum used, (necessary for a bacteriological examination), daily, every 6-8 hours.

The procedure was repeated uninterruptedly for three days, after knowing the result of the previous examination, reaching to up to three check-ups (bacteriological examinations). What was used for the patients who could not expectorate and for the ones with three bacteriological examinations with negative sputum result, was the method of cough and expectoration induction, with 10 ml of hypertonic saline solution 5%, making use of an ultrasonic nebulizer and a Venturi type face-mask. This procedure was implemented after the technique had been explained, the patient had given the written agreement and the spirographic examination had been done.

The test was considered finished with a positive result when the patient managed to collect, al least 3ml of sputum.The fibronchoscopic examination completed with broncho alveolar lavage and ended with bronchial aspirate was applied to patients with negative microscopical examination for acid-fast bacilli (AFB) from the spontaneous sputum culture or after aerosol intake. The investigation was preceded by the patient's anamnesis, clinical examination, EKG examination and spirogram, accomplished only after the patient's written agreement, using local anesthesia with lidocaine, 1% and 2% and 20 ml of sterile saline solution for bronchial lavage. The sputum collected after the aerosol exposure and the bronchial lavage liquid were processed and bacteriologically investigated through microscopic examination and culture in view of identifying the etiologic agent, M. Tuberculosis.

RESULTS

The study group included 98 patients: 36 women (37%) and 62 men (63%), ages 18-69, the average age being 46,4 years, (Table 1), 84% new cases recorded and 16% relapses, according to therapeutic history.

In what concerns the aspect of sputum collected at hospitalization, there were concluded the following: on one hand, in female patients mucous aspect was found in a 53% percentage, compared to 39% in male patients; on the other hand, muco-purulent aspect was more frequently met in male patients, 45%, compared to 31% in female patients.

For 70% of the patients, 44 male and 26 female, the results of the sputum bacteriological examination at hospitalization, were negative. The induced sputum was collected for 88% of the patients, three patients refused the test and seven patients interrupted the procedure because of an adverse reaction.

The results of the bacteriological examination of the sputum obtained after exposure to aerosols illustrated 16 cases of bacteriological confirmation, seven patients were recorded with positive examinations in microscopy and culture, while for nine patients the microscopic examination was negative and the culture one, positive (Figure1). There were 85 patients fibronchoscopically examined, out of which 55 men and 30 women, four patients refused the investigation, in two cases the patient was uncooperative and seven patients were confirmed positive through the previous method (induced sputum).

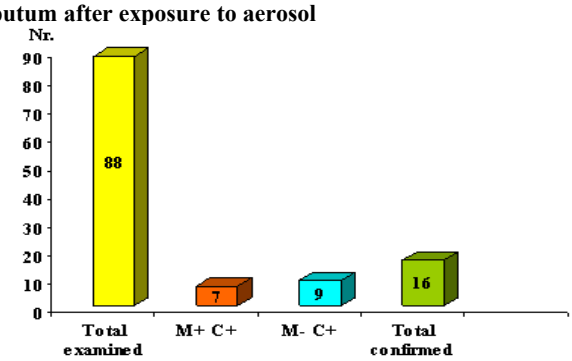
Table no. 1. Age and sex distribution of patients

STUDY GROUP						
Age (years)	Female		Male		TOTAL	
	frequency(no.)Absolute	Relative frequency(%)	frequency(no.)Absolute	Relative frequency(%)	frequency(no.)Absolute	Relative frequency(%)
< 30	5	14	6	10	11	11
31 – 40	12	34	12	19	24	25
41 – 50	9	25	17	27	26	26
51 – 60	7	19	16	26	23	24
61-70	3	8	11	18	14	14
TOTAL	36	100	62	100	98	100

Table no. 2. Aspects of spontaneous sputum culture at hospitalization

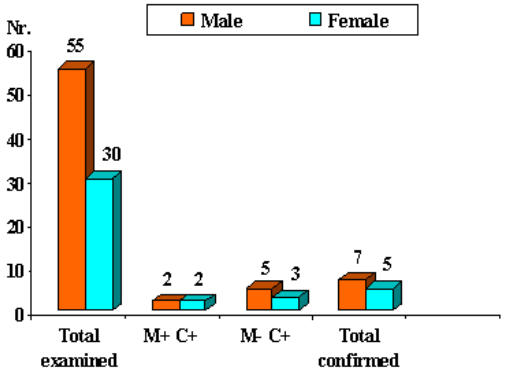
STUDY GROUP				
Sputum aspect	Female		Male	
	Absolute frequency (no.)	Relative frequency (%)	Absolute frequency (no.)	Relative frequency (%)
Sero-mucous	19	53	24	39
Muco-purulent	11	31	28	45
Hemoptoic	2	5	5	8
Salivary	4	11	5	8
TOTAL	36	100	62	100

Figure no. 1. Result of bacteriological examination of sputum after exposure to aerosol



The bacteriological examination carried out of the bronchial lavage liquid was registered positive for four patients both through microscopy and culture, as for eight patients it was negative at the microscopic examination and positive at the culture examination.(Figure 2).

Figure no. 2. Results of bacteriological examination achieved out of bronchial aspirate



By means of the two methods applied (induced sputum and bronchial lavage), there were 28 patients diagnosed with pulmonary TB, representing 28% of the patients, 18 patients were new cases (22% of the group) and 10 patients were part of the second category (66% of the relapses).

The adverse events encountered during aerosol exposure and fibronchoscopy were minor in the majority of cases (salty taste, throat irritation, cough, dysphagia or irreversible hoarseness) and the average cost for an endoscopic examination was estimated to 40,55 RON.

DISCUSIONS

What is essential in pulmonary TB management for initiating, monitoring and evaluation of the treatment is the earliest bacteriological confirmation possible, the "golden standard" of laboratory investigation. In negative microscopic TB, where the diagnosis is based firstly on the clinic and radiologic(5) criteria a diminished interest can be noticed concerning the indication of techniques for valid sputum samples' generation and culture. In specialized literature Anderson et al(1), proved that the usage of induced sputum and bronchoscopy in the diagnosis of patients suspect of TB, but with negative microscopic examination, contributed to the improvement of the bacteriological confirmation percentage by 12% up to 19%.

In our country, modern methods of etiological confirmation of the disease (gene tests), could not be introduced in routine practice because of the expensive costs, the complexity of the procedure and last but not least, because of the insufficient funding for health system.

The quality of the collected product (sputum) is influenced by saline aerosols generated by the nebulizer through an effect of irritation and osmosis; in the study group sputum was obtained in 89% of the patients.

Conde et al(2) obtained sputum in 97 % of their patients and Peri et al(9) obtained sputum in 73 (89%) of the patients, 26 of whom had negative AFB smear and 47 were unable to expectorate before sputum induction.

The sensitivity gained by this method for supporting the diagnosis for pulmonary TB was of 18,1%, literature data showing values ranging from 20,5%(10) to 33%(7). Lacking major adverse effects, the procedure is simple, cost effective and cand be performed in the sputum collection chamber of any stationary.

Although bronchial endoscopy is considered to be an invasive technique and many doctors refuse to use it, in the study conducted there were examined 87% of the patients, only 4 of them refusing the procedure. Diagnostic sensitivity of 14% in the group under study is similar to results published in literature(1). The adverse reactions after the bronchoscopic investigation performed with local anesthesia were minor, that is why the method was considered to be safe, low cost and applicable to routine practice on condition that all indications and contraindications are strictly followed.

CONCLUSIONS

Bacteriological examination of sputum is essential for a reliable diagnosis of pulmonary TB; therefore all PNCT recommendations concerning sputum culture in view of obtaining the best results at the laboratory examination are mandatory and need to be taken into consideration.

Sputum induced through saline aerosols and fibronchoscopic examination along with lavage and bronchial aspirate are two efficient culture methods for increasing the percentage of bacteriological confirmations, in the diagnosis of pulmonary TB.

The procedures are considered to be safe, they can be applied in routine practice, the adverse events are usually minor and the costs are reduced.

Assistance in cases of microscopy pulmonary TB, needs a higher degree of professional perseverance in the bacteriological investigation of casuistry which often generates a dilemma whether the process of active tuberculosis exists or not.

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BRONHO-PULMONARY CANCER: MORFO-PATHOLOGICAL FORMES

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Keywords: *histopathological classification, benign tumors, malignant tumors*

Abstract: *The primitive bronchopulmonary cancer includes the cases of cancer that develops primitively from the bronchic glandular epithelium, next invading the pulmonary parenchyma. It is the most important and frequent form of pulmonary tumor representing more than 90% of the primitive malignant and benign tumors. The histological classification of the bronchopulmonary cancer is complex and extremely important from the point of view of the neoplasia evolution, the choice of the possibilities of treatment and of the prognosis.*

Cuvinte cheie: *clasificarea histopatologică, tumori benigne, tumori maligne*

Rezumat: *Cancerul bronhopulmonar primitiv include cazurile de cancer care se dezvoltă, în mod primitiv, de regulă din epiteliul glandular bronşic, invadând ulterior şi parenchimul pulmonar. Este cea mai importantă şi frecventă formă de tumoră pulmonară, reprezentând peste 90% din tumorile primitive maligne şi benigne. Clasificarea histologică a cancerului bronho-pulmonar este complexă şi este extrem de importantă din punctul de vedere al evoluției neoplaziei, a alegerii modalităților terapeutice şi a prognosticului.*

SCIENTIFICAL ARTICLE OF BIBLIOGRAPHIC SYNTHESIS

The primitive bronchopulmonary cancer includes the cases of cancer that develops primitively from the bronchic glandular epithelium next invading the pulmonary parenchyma. It is the most important and frequent form of pulmonary tumor representing more than 90% from the malignant and benign tumors. (1)

Some authors (especially the broncholog) consider that the correct name would be bronchogenoic or bronchogenetic cancer (Lemoine). Most use the name of pulmonary cancer or bronchopulmonary cancer that doesn't exclude the ideea of the predominant bronchogenetic origin reflecting even better the coaffection bronchic and parenchymal and is not incorrectly from the anatomical point of view because the bronchi are constitutive part of the lung. Like wise correct is the name of carcinoma. (1)

Rarely met and mistaken for the consumption in the antiquity and with other consumptive lung diseases, was the lung cancer observed for the first time without being individualized in the antiquity, in the XVI-th century, by Paracelsus and by Agricola as *male metallorum*, at the miners from Schneeberg (1531) and from St. Joachimstal (1556). The diagnosis was established retrospectively later by Hesse and Härting (1879). Meantime Bayle (1810) described it under the name of cancerous consumption, considering it the sixth form of consumption. The worth of being individualized as a nosologic entity under the name of "the lung's encephaloid" is attributed few years later to Laennec. Stokes (1837) establishes the diagnosis procedure. Walsche (1843) gives it the first the name of lung cancer.Wolf (1895) points out the association with the tuberculosis. Waldayer mentions, the first, the epithelial origin of the cancerous tumor. (1)

Until the end of the XIX century are studied minutely, its clinical aspects (Jaccoud, Darolles, Marchiafanas) and morph- pathological ones (Virchow, Ménetrier). In the first decades of the XX century are specified the radiologic aspects of the disease in its manifest stadium, correlated with the morphologic ones (Letulle, Huguenin, Delarue). Later, by introducing new methods of bronchoscopic investigation, citodiagnosis, biopsic, funcţional respiratory ones becomes possible the diagnosis of the disease in a precocious phase, still operable (Adler, Lemoine).

Exeresis surgery developed and perfected on a large scale after 1946 (Overholt, Bjôrk, Derra, Cărpinişan) and offers, for the first time, the posibility of a terapeutical solution of the cases, with the condition of realising an early sistematic diagnosis.

Morphopathological aspects of the bronchopulmonary cancer:

The morphopathological aspects of the bronchiopulmonary cancer are extremly varied raported to: the size of the tumor;.the localization on a central or peripherical bronchia; degree of intratoracic and extratoracic extension and especially with; the histological type.

The statement of those elements is of a maximal importance for choosing the exploratory methods, establishing the optimal modalities of treatment and of the prognosis (3). From a morphopathological point of view two elements are essential: the localization of the tumor central or peripherical from the beginning; histological type.

The histological classification of the bronchopulmonary cancer is complex and extremely important from the point of view of the evolution of the neoplasia, of choosing the therapeutic possibilities and of the prognosis. Lung tumors have been classified by OMS, classification that was redacted in 1981 and 1999 (13, 15). Pulmonary tumors are composed from more different histological types with a varied degree of malignity, from complete benign to an extremely aggressively.

The next classification is redacted by OMS (From Travis

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WD, Colby TV, Corrin B, et al. *WHO histological typing of lung and pleural tumors*, 3rd ed. Geneva: World Health Organization, 1999):

Epithelial tumors:

I. Benign

1. Papilloma: a. with squamous cells (exofitic, inverted); b. glandular, c. glandular and mixt squamous;
2. Adenoma: alveolar; papillar; of the salivary gland type (mucouse, pleomorph); Mucinous Cyst adenoma.

II. *Pre -invasive lesions*: squamous dysplasia, carcinoma in situ, atypical hyperplasia adenomatous, diffuse idiopathic hyperplasia with neuro endocrine cells;

III. Malign:

1. Carcinoma with squamous: a. papillar; b. with clear cells; c. with small cells; d. Basaloid;
2. Carcinoma with small cells: a. carcinoma with mixt cells ;
3. Adenocarcinoma; a. Acinar; b. papillar; c. bronchioloalveolar: nonmucinous, mucinous, mixt: nonmucinous and mucinous or type of intermediate cells; d. solid with mucine; e.with mixt subtypes, variants: adenocarcinoma with well differentiated fetal cells, adenocarcinoma with mucinous cells(colloidal), cystadenocarcinom mucinous;
4. Carcinoma with large cells: a. carcinomawith neuro endocrine large cells; b. carcinoma combined with large neuro endocrine cells; c. basaloid carcinoma ; d. carcinoma limfo epithelial-like; e. carcinoma with clear cells; f. carcinoma with large cells with rhabdoid phenotype;
5. Adenosquamous Carcinoma;
6. Carcinoma with pleomorph elements, sarcomatoid or sarcomatous;
7. Carcinoma with giant cells or fusiform: a. pleomorph: with fusiform cells or large cells; b.carcinosarcoma; c.pulmonary blastoma ;
8. . Carcinoid tumors: typical and atypical; I
9. Carcinomas of the salivary glands type: mucoepidermoid, adenoid cystic;
10. Unclassified

Tumors of soft tissue: Tumors localized fibrous, epitheloid hemangioendothelioma, pleuropulmonary blastoma, chondroma, pleural fibrous calcified pseudotumor, congenital peribronchial myofibroblastic tumor, diffuse pulmonary lymphangiomatosis, desmoplastic round cells tumor;

Mesothelial tumors: *Benign* – adenomatoid tumor, *Malignant* mesotheliom, Sarcomatoid mesotheliom (desmoplastic, biphasic);

Divers tumors:

1. Hamartoma,
2. Sclerosing hemangioma,
3. Tumor with clear cells,
4. Tumor with germinative cells (mature teratoma, immature teratoma, tumor with other cells),
5. Thymoma,
6. Melanoma malignant

Limphoproliferations: 1.Interstitial lymphoid pneumonia, 2.Nodular lymphoid hyperplasia, 3. Lymphoma with B cells type marginal area with a low degree of associated lymphoid tissue (MALT), 4.Lymphoid granulomatosis

Secondary tumors

Unclassified tumors

Tumoral type lesions: 1. Tumor, 2. meningothelioma multiple nodules, 3. Histiocytosis with Langerhans cells, 4.Inflammatory pseudotumors (mioinflamator), 5.Organized localized pneumonia, 6.Amyloid tumor (nodular amyloid), 7.Hyalinizing granuloma, 8.Lymphangioleiomyomatosis, 9.Micronodular pneumocystic hyperplasia, 10.Endometriosis, 11. Inflammatory bronchial polyp

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GENERALITIES ON PARANEOPLASIC SYNDROMES IN BRONCHOPULMONARY CANCER

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Keywords: *paraneoplastic syndrome, bronchopulmonary cancer, clinical and biological manifestations*

Abstract:*Paraneoplastic syndromes are nonspecific clinical and biological manifestations that appear in patients with maligne neoplasia. Those manifestations may precede the tumour sympthomatology, may appear concomitantly with this one or may pursuit it.In general, paraneoplastic syndromes have a great importance, because are present in 15% of the patients with cancer and 70% of the patients with bronchopulmonary cancer may present one of the syndromes during the evolution of the disease. The paraneoplastic syndromes appear only if there is a maligne tumour. The sympthomatology of the paraneoplastic syndromes is varied and polymorph, each syndrome presenting a specific clinical and biological picture.*

Cuvinte cheie: *sindrom paraneoplazic, cancer bronhopulmonar, manifestari clinice şi biologice*

Rezumat: *Sindroamele paraneoplazice sunt manifestări clinice şi biologice nespecifice care apar la bolnavii cu neoplazii maligne. Aceste manifestări pot preceda simptomatologia tumorii, pot să apară concomitent cu aceasta sau pot să o urmeze. În general, sindroamele paraneoplazice au mare importanţă, deoarece sunt prezente în până la 15% dintre pacienţii cu diagnosticul de cancer, şi până la 70% dintre pacienţii cu cancer bronhopulmonar pot prezenta unul dintre aceste sindroame pe parcursul evoluţiei bolii. Pentru ca sindroamele paraneoplazice să apară, este neapărat necesar ca în organismul bolnavului să se dezvolte o tumoră malignă. Simptomatologia sindroamelor paraneoplazice este variată şi polimorfă, fiecare sindrom exteriorizându-se printr-un tablou clinic şi biologic aparte.*

SCIENTIFICAL ARTICLE OF BIBLIOGRAPHIC SYNTHESIS

Short History

The first report of a paraneoplastic syndrome was made in 1825 by Trousseau and described the growing incidence of the venous trombosis in patients with cancer, since then it has been proved with a large frecquency the existent retionship between tumors and particular paraneoplastic syndromes.(43,59)

In 1928 it has been described by Brown for the first time, the Cushing Syndrome in a patient with hirsutism, diabetes mellitus, arterial hypertension, adrenal hypoplasia, and small cell pulmonary cancer. (8, 22, 28)

In 1942 Guichard described leukemias that appeared in some types of cancers and called them paraneoplasia. In 1957 Schwartz and Bartter described a syndrome that consists of hyponatremy of dilution and renal loss of sodium in 2 patients with bronchopulmonary cancers. Bouden in 1962 gave the name to the paraneoplastic syndromes. (26)

The area of the paraneoplastic syndromes has constantly evolved and nowadays contains more fields from the chapters of medical pathology.

Definitions. Generalities.

Neoplastic syndromes are biological and clinical nonspecific manifestations that appear in patients with maligne neoplasia.Those disturbances are not caused by the direct, mechanical, local action of the tumor on the organ and tissue in which it develops, it is not in a direct rapport with the local action of the metasthasis of the primitive tumor. Those manifestatios may precede the sympthomatology of the tumor, may dissappear simultaneoustly with this one or may follow her. Usually, these syndromes disappear with the removal of the tumor and reappear in case of tumor recidive and methasthasis. (3,5)Paraneoplastic syndromes associated to the bronchopulmonary cancer are numerous and extremely varied. They are produced through the secretion of ectopic hormones by the tumoral tissue.The producing of ectopic hormones or its precursors that are peptides is characteristic to all types of cancer but, in the bronchopulmonary cancer the incidence of the clinical manifestations correlated with the secretion of ectopic hormones is relatively high. It appears that the clinical syndromes may appear only if the neoplastic tissue is capable of metabolising the polipeptides precursors in bioactive hormones. (5)

Paraneoplastic manifestations appear more frequently in the small cells pulmonary carcinoma and rarely in the epidermoid carcinom and adenocarcinom, but there is no ectopic hormones secretion specific for a certain histologic type. (5)

Clinical formes

Are very numerous and may be classified as follows:

1. Paraneoplasic syndromes with clinical manifestations: endocrine, metabolics, neurologics, muscular, ostheo-articular, cutaneous, cardiovascular, hematologic, renale, hepatic, digestive, sarcoid reactions.
2. Biological manifestations without clinical expression: the apparition of isoenzymes, substances with an embrionar character, biochemical manifestations, immune manifestations.
3. Syndromes and symptomes that appear during the acute phase of evolution of maligne tumors (weight loss, muscular atrophy, dehidratation, prolonged fever, itchiness).

The most frequent paraneoplastic syndromes present in the bronchopulmonary cancer are:

Systemic manifestations: anorexia, cachexy, fever,

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deprimation of the immunity, ortostatic hypotension.

Endocrino metabolic syndromes: (12% from the patients): Ectopic secretion of ACTH (Cushing syndrome); inappropiate secretion of ADH with hyponatremia (Schwartz-Bartter syndrome); hipercalcemy and hypophosphatemie; hyperthyroidism; ginecomasty; acromegaly.

Neuro miopatic syndromes (1% of the patients): Polimiositis-dermatomiositis; miastenic syndrome (Eaton-Lambert); peripheral neurophaties; subacute cerebellar degenerescensis, encefalopathy (cerebral encephalitis, limbic encephalitis, cerebral encefalitis, mioclonia-opsoclonia).

Conjunctive and bone tissue manifestations: digital hipocratism; pulmonary hypertrofic osteoarthropathy; Sclerodermy;

Vascular manifestations: migratory tromobophlebitis; non-bacterial thrombotic endocarditis, hemathologic manifestations (1-8% of the cases): anemy (simple, hemolytic); medullary aplasia; leukemoid reaction or leukoeritroblastic; IDC; hypofibrinogenemia;

Other manifestations: membranous glomerulopathy; Acanthosis nigricans

PROGNOSIS: The prognosis of the paraneoplastic syndromes is in general the same with the prognosis of the causing tumour. The syndromes disappear with the removal of the tumor and reappear with the recidive of the tumor. The presence of the paraneoplastic syndrome darkens more the prognosis, the sum of its sympthomathology worsening the clinical aspect and the evolution of the cancer and sometimes complicating and making difficult the possibilities of treatment. Usually, the paraneoplastic syndromes have a severe evolution, nonfavorable, than similar syndromes that appear in patients without maligne tumours.

TREATMENT: The treatment addresseses, directly to the paraneoplastic syndrome and heads against the maligne neoplasia that conditioned its apparition, in general, the treatment is of the maligne tumor having as effect the atenuation or the dissparition of the paraneoplastic manifestations.

But, there are cases that need a pathogenic or symptomatic treatment for the paraneoplasia besides the treatment for tumour or its metastasis.

It has been showed that the maligne neoplasia may be modified fundamentaly without its disappareance, but with the disappareance of the paraneoplastic syndrome.

There are cases in which the treatment of the paraneoplasia may influence indirectly the neoplasia or with a citostatic treatment, the palliation of the paraneoplastic syndromes may be obtained, without the significant tumor influence (29).

Sometimes, citostatic treatment has no evident action on the tumor, but produces a significantly diminishing subjective sympthomatlogy and improves general condition.

On the whole, every case of paraneoplastic syndrome has a treatment against the tumor and a treatment against the paraneoplastic syndrome.This treatment is different with the clinical picture of the paraneoplasia.

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FAMILY GASTRIC CANCER SYNDROMES

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Keywords: *gastric cancer, familial syndromes*

Abstract: *The syndromes of familial gastric cancer were recently described. Ten years ago, Guilford was the first scientist who identified a germline mutation of CDH1 (E-cadherine) gene in a Maori family from New Zeeland. Other similar discoveries in families with agregability of gastric cancer led to an international symposium in Vancouver were the syndromes of familial gastric cancer were defined.*

Cuvinte cheie: *cancer gastric, sindroame familiale*

Rezumat: *Sindroamele de cancer gastric familial reprezintă o patologie documentată recent în literatura medicală. Guilford a fost primul cercetător care, în urmă cu 10 ani, a identificat o mutaţie germinală a genei CDH-1 (E-cadherina) la o familie Maori din Noua Zeelandă. Această descoperire a fost urmată de semnalări similare în cadrul familiilor cu agregabilitate de cancer gastric, ceea ce a determinat organizarea unui simpozion la Vancouver în care s-au definit sindroamele de cancer gastric familial.*

SCIENTIFICAL ARTICLE OF BIBLIOGRAPHIC SYNTHESIS

Until recently, evidence supporting the existence of a distinct syndrome of hereditary gastric cancer have been indirectly based on clinical evidence. Bonaparte family is one of the most famous in the world, primarily on historical considerations, but also from a health perspective, given the high incidence of gastric cancer reported: Napoleon's father and grandfather, a brother and three sisters, all have died of gastric cancer, some of them at a young age (2). More recently, it was reported in the literature of New Zealand Maori family (originally described by Jones in 1964), the period of 30 years died 25 members due to gastric cancer with no evidence of associated malignancies. Guilford was the first scientist who in 1998 documented the existence of germinal mutations in the gene CDH1 (E-cadherin) from a study of this family (12). A number of other researchers recently reported gene mutations in CDH1 germ (Richards et al. In 1999, Dussaulx-Garin et al. In 2001, Humar et al. In 2002, Oliveira et al. In 2002), which is associated with literature known as hereditary diffuse gastric cancer (25).

Emergence of new hereditary cancer syndrome caused organizing a symposium in Vancouver (International Gastric Cancer Linkage Consortium) in 1999 in which a group of geneticists, gastroenterology, surgeons, oncologists and molecular biologists have issued consensus statements and guidelines for familial gastric cancer.
According IGCCL gastric cancer there are four categories of family:

- Hereditary diffuse gastric cancer (HDGC)
- Familial diffuse gastric cancer (FDGC)
- Familial intestinal gastric cancer (FIGC)
- Gastric cancer in other familial cancer syndromes.

That gastric cancer syndromes can be characterized morphologically or entities not covered in the above are called familial gastric cancer syndromes (FGC) (21).

5.1. Hereditary diffuse gastric cancer (HDGC) defined (5) family as cancer, germinal Mutation substrate that meets the following criteria:

1. two or more documented cases of diffuse gastric cancer relatives Grade 1 or 2, with at least one diagnosis made before 50 years
2. three or more cases of documented diffuse gastric cancer in relatives of grade 1 or 2, regardless of age onset.

These criteria were based on a recently completed study by Brooks-Wilson et al., Which proposed that the diagnosis of hereditary diffuse gastric cancer should be suspected if a person or family meets one of the following circumstances (4, 15)

1. two or more cases of diffuse gastric cancer family, with at least one diagnosis made before 50 years;
2. three or more cases of gastric cancer in the family, regardless of age, with at least one documented case of diffuse gastric cancer;
3. an individual diagnosed with diffuse gastric cancer before 45 years;
4. an individual diagnosed with diffuse gastric cancer and lobular breast cancer (no other inclusion criteria);
5. a family member diagnosed with diffuse gastric cancer and another with lobular breast cancer (no other inclusion criteria);
6. a family member diagnosed with diffuse gastric cancer and another with colon cancer with signet ring cells (no other inclusion criteria).

Hereditary diffuse gastric cancer is between 1-3% of all gastric cancers (9). It is a poorly differentiated adenocarcinoma that infiltrates the stomach wall causing thickening it (linita plastic) without forming a distinct tumor mass. The average age of onset is 38 years, as far described cases with onset between 14 and 69 years. Cumulative risk of gastric cancer by the age of 50 years is estimated at 21% to 49% for males and females (11), increasing to 80 years from 67% to 83% for males and females (10) . Women behave and a 39% risk for breast cancer (27).

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HDGC is transmitted by autosomal dominant pattern, altered gene is passed from one parent. So far, only discovered gene whose mutations are associated with HDGC is E-cadherina (CDH1). Risk of transmission of the mutation of the sample to each descendant is 50%. Once inherited this mutation, it is considered that the risk of developing gastric cancer is 2,000 times higher than the control population (31). It was considered and the possibility of a de novo mutation in the E-cadherinei, but the situation has not hitherto been documented. Thus, if none of the parents of a sample with an apparent autosomal dominant mutation is not affected by possible non-medical explanations as alternative paternity or adoption Unravelled (10).

To date 56 have been documented germ of CDH1 mutations, 43 were found in HDGC group and 13 in families with FDGC (21). In contrast to somatic mutations in sporadic diffuse gastric cancer, which are concentrated in the exons 7-9, where HDGC lesions were documented throughout the CDH1 gene, not reported any "hot spot" to represent a fragile locus high, exposed to mutations (3, 8, 11). These mutations have been described in families from different geographical areas and different ethnicities. Guilford et al. (12) were first identified germinal mutations of CDH1 gene in three families of Maori ethnicity in New Zealand in 1998 cecetători other families showed similar abnormalities in Europe, Africa and America (16, 22, 33).

As with other genes that predispose to hereditary cancer syndromes, one allele undergoes mutation germ, most of which are deletions (83%) resulting in the emergence of active protein, a rate of 17% is represented by nonsense mutations unknown functional significance (23). Frequently encountered and somatic mutations of the other allele (loss heterozigozității) bialelică inactivation leading to reduction or absence imunoreactivității E-cadherinei in gastric cancer cells. Similar cases of sporadic gastric cancer, the main mechanism of inactivation of wild allele is hipermetilarea CDH1 gene promoter. (9).

Other candidate genes are the suppressor genes HDGC FEZ1/LZTS1 and SMAD (13, 14.30), RUNX3 (19) or caspase (26).

5.2. Diffuse gastric cancer families (FDGC) is cancer that has agregabilitate family to meet all criteria HDGC. These cases have been identified so far 13 germ of CDH1 mutations. Among patients with diffuse gastric cancer and family agregabilitate, 70-80% fall in group FDGC. A study in the western region of Poland in 2001 aimed at determining the prevalence of families with genetic cancer syndromes revealed 113 families with FDGC. As a feature, it appears that both hereditary diffuse gastric cancer, and especially the diffuse family tends to locate in the region cardiei, showing a more aggressive than sporadic gastric cancer (20).

5.3. Familial intestinal gastric cancer (FIGC) was defined according to gastric cancer incidence in the population. Thus, in countries with high incidence (Japan, Portugal) have used similar diagnostic criteria for HNPCC Amsterdam criteria: (a) at least three relatives with intestinal gastric cancer and one of them is relative degree one with the other two; (2) at least two successive generations affected; (3) to one of the relatives, the diagnosis is made before 50 years. In countries with low incidence (USA, England), FIGC was defined as: (a) at least two grade 1 or 2 relatives affected by intestinal gastric cancer, one diagnosed before 50 years (2) three or more relatives with intestinal gastric cancer, regardless of age of onset. At present there is no mutation was identified in families with germ FIGC (23).

5.4. Gastric cancer in other familial cancer syndromes is reported that a significant proportion: nonpolipos hereditary colon cancer, familial adenomatous polyposis, SDR. Peutz-Jeghers, SDR. Cowden and SDR. Li-Fraumeni (5).

5.4.1. Nonpolipos hereditary colon cancer (HNPCC) is a well characterized familial cancer syndrome that comprises about 5-10% of all cancers rectocolonice (CRC). In this entity describes two distinct syndromes: SDR. Lynch I, which includes patients with increased risk of developing CRC and SDR. Lynch II, which covers those who associate an increased risk of extracolonice cancers (stomach, ovary, endometrium) (24). Gastric cancer is the most common malignancies associated with HNPCC, as seen in 13-20% of these patients (6,7), intestinal type is more common (9). Occurs due to defects in mating system errors repair genes, hMLH1 and hMSH2 gene mutations are seen in more than half of cases. Abnormalities of these two genes are associated with complete inactivation of the MMR system (missmatch repair), while other mutations, such as those present in the hPMS1 and PMS2 genes are associated with incomplete inactivation (1). A study (26) conducted in Korea showed a risk of 2.1 for gastric cancer patients with HNPCC and their first degree relatives, the relative risk was 11.3 times higher at young age.

5.4.2. Familial adenomatous polyposis (PAF) is an autosomal dominant disease that occurs through mutation of APC gene and colorectal cancer typically presents with early onset secondary malignizării multiples present in the colon polyps. They are also developing in the upper gastrointestinal tract. Ribbons gland polyps are the most common gastric polyps in the PAF, some of whom may develop into malignant (9, 32).

5.4.3. Peutz-Jeghers Syndrome (PJS) associated with the presence of multiple polyps that can interest any segment of the gastrointestinal tract, especially jejunum. Malignant degeneration of these polyps is rare. Several cases of gastric cancer associated with PJS have been described in the literature associated with gene inactivation STK11/LKB1 germ, which normally acts as a suppressor gene (23).

5.4.4. Cowden syndrome is an autosomal dominant abnormality transmitted with high punch, also known as multiple hamartoamelor syndrome (gastrointestinal, skin, mucous membranes). Associated with various neoplasms (stomach, breast, thyroid, mucosal). (17) This syndrome occurs in succession a PTEN gene mutations located at 10q23, but has been shown (23) that has lost all gastrointestinal hamartoamele heterozigotivității in this locus.

5.4.5. Li-Fraumeni syndrome is a familial cancer syndrome that include various sarcomas, neoplasms of breast and other carcinomas, including gastric cancer, characterized by onset in childhood and frequent occurrence metacronă (29). It was first mentioned in literature in 1969 when revăzând medical records and death certificates of 648 patients with childhood onset rabdomiosarcoame, Li and Fraumeni have noticed the presence of various types of cancer in siblings and cousins of four patients. Over 70% of families with this syndrome have mutations in p53 gene. Another germinal heterozygous mutation identified by Bell et al. the CHK2 gene is also associated with Li-Fraumeni syndrome (23), but there seems to be responsible for the occurrence of gastric cancer in these families (18).

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GASTRIC CANCER – NEW PERSPECTIVE

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Keywords: *gastric cancer, biology, diagnosis, therapy*

Abstract: *The article aims to updatethe approaches of gastric cancer in both epidemiologyl and biology of this cancer and the modern diagnostic modalities useful in order to choose the best therapeutic solution. Article highlights the particular experience of Chinese medicine school. This studies benefit of substantial study groups, which are best able to draw relevant conclusions.*

Cuvinte cheie: *cancer gastric, biologie, diagnostic, terapie*

Rezumat: *Articolul îşi propune să aducă la zi perspectivele asupra cancerului gastric atât din punct de vedere epidemiologic cât şi cu privire la biologia acestui tip de cancer şi asupra modalităţilor de diagnostic modern util în alegerea celor mai bune soluţii terapeutice. Articolul evidenţiază în special experienţa şcolii de medicină din China, studiile acesteia beneficiind de loturi de studiu substanţiale, acestea fiind cele mai în măsură pentru elaborarea unor concluzii pertinente.*

SCIENTIFICAL ARTICLE OF BIBLIOGRAPHIC SYNTHESIS

Gastric cancer epidemiology

Gastric cancer incidence and mortality fell dramatically in the U.S. in recent decades. However, gastric cancer remains a major public health problem, being the 4th among the most common cancers and the second leading cause of cancer mortality (~800,000 per year) after lung cancer.

Demographic trends differ by tumor location and histology. While there has been a marked decline in distal, intestinal type gastric cancers, the incidence of proximal, diffuse type adenocarcinomas of the gastric cardia has been increasing, particularly in the Western countries.

Incidence by tumor sub-site also varies widely based on geographic location, race, and socioeconomic status. Distal gastric cancer predominates in developing countries, among blacks, and in lower socioeconomic groups, whereas proximal tumors are more common in developed countries, among whites, and in higher socio-economic classes. Diverging trends in the incidence of gastric cancer by tumor location suggest that they may represent two diseases with different etiologies.

The main risk factors for distal gastric cancer include Helicobacter pylori infection and dietary factors; whereas gastroesophageal reflux disease and obesity play important roles in the development of proximal stomach cancer. (1)

Scientists who have been following the health of more than 120,000 residents of the Netherlands for more than two decades have observed that smoking is linked to two forms of esophageal cancer as well as a form of stomach cancer, and that drinking alcohol is strongly associated with one form of esophageal cancer.

"The results of this study again confirm recommendations for a healthy lifestyle, namely not to smoke and to drink alcohol in moderation, but it also suggests that there must be other risk factors for EAC and GCA Smoking is a risk factor for both cancers, but since a decreasing part of the population smokes, this cannot explain why the incidence is rising so rapidly for both cancers in Western countries in recent decades." – Jessie Steevens, M.Sc., of the Department of Epidemiology at Maastricht University, in Maastricht.

Gastric hypoacidity and hypergastrinaemia are seen in several conditions associated with an increased risk of gastric malignancy. Studies using animal models can provide valuable information about risk factors and mechanisms in gastric cancer development as the models allow a high degree of intervention when introducing or eliminating factors possibly affecting carcinogenesis.

Animal models of gastric hypoacidity and hypergastrinaemia provide evidence hypergastrinaemia is a common causative factor in many otherwise diverse settings. In all species where sufficient hypoacidity and hypergastrinaemia have been induced, a proportion of the animals develop malignant lesions in the gastric oxyntic mucosa.

Gastric cancer like almost all other cancers has a molecular genetic basis which relies on disruption in normal cellular regulatory mechanisms regarding cell growth, apoptosis and cell division.

Growing evidence suggests that accumulation of multiple alterations such as activation of proto-oncogenes and inactivation of tumor suppressor genes is responsible for the development and progression of digestive system cancer. Genetic instability of oncogenes such as microsatellite instability (MSI) and loss of heterozygosity (LOH) is probably linked to mutations in genes responsible for tumor-genesis, and they play important roles in tumor clinical pathology. The studies of MSI and LOH of digestive system cancer have been focused on genetic instability of P53, P16 and FHIT, but few studies were seen in gene nm23H1.

The research team led by Prof. Li from Institute of Cell Biology, Zhejiang University used polymerase chain reaction-single strand conformation polymorphism (PCR-SSCP) to analyze MSI and LOH of nm23H1 gene, and immunohistochemistry was employed to check the expression of nm23H1 protein.

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Thus novel therapeutic approaches such as gene therapy promise to become the alternative choice of treatment in gastric cancer. In gene therapy, suicide genes, tumor suppressor genes and anti-angiogenesis genes among many others are introduced to cancer cells via vectors. Some of the vectors widely used in gene therapy are Adenoviral vectors.

In the article „FAT10 level in human gastric cancer and its relation with mutant p53 level, lymph node metastasis and TNM staging"(16) the role of FAT10 and mutant p53 in the pathogenesis, severity and prognosis of gastric cancer was revealed.

FAT10, mutant p53 mRNA and protein levels were measured by reverse transcription (RT)-PCR and immunohistochemistry in gastric cancer tissue (n = 62), tumor-adjacent tissue (n = 62) and normal gastric tissue (n = 62). Relation of FAT10 and mutant p53 expression with clinicopathological features and clinical outcomes of gastric cancer patients were analyzed. The FAT10, mutant p53 mRNA and protein levels were significantly higher in gastric cancer than in its adjacent and normal tissue. The FAT10 and mutant p53 levels in gastric cancer tissue were significantly correlated with lymph node metastasis and tumor, nodes, metastasis (TNM) staging. Moreover, the high FAT10 level was associated with the overall survival rate of patients. Multivariate Cox-proportional hazards model analysis showed that mRNA and protein levels of FAT10 and mutant p53, lymph node metastasis, distant metastasis and TNM stage were the independent prognostic factors for gastric cancer.

FAT10 may be involved in gastric carcinogenesis, and is a potential marker for the prognosis of gastric cancer patients.

„Influence of VEGF and Ki-67 expression on biological behavior of gastric cancer" (2) investigated the relationship between expression of vascular endothelial growth factor (VEGF) and proliferating cell nuclear antigen Ki-67 and the biological behavior of gastric cancer.

The Ki-67 labeling index (Ki-67-LI) and VEGF expression in tumors were analyzed by immunohistochemistry using specific antibodies. The relationship between each other and their prognostic significance were evaluated.

The Ki67-LI of VEGF positive group (562.8±118.3) was significantly higher than that of negative group (436.8±142.2)(P = 0.0 005). The prognosis of VEGF positive group was significantly worse than that of negative group. Ki67-LI was significantly correlated with lymph node metastasis (P = 0.027), tumor stage (P = 0.020) and prognosis (P = 0.036).

VEGF promotes tumor angiogenesis and development. High Ki67-LI reflects active proliferation of tumor cells. Both indicate an unfavorable prognosis.

The clinicopathological characteristics of patients with synchronous cancers and those of patients without synchronous cancers were compared in a retrospective study of the National Cancer Center, Korea from December 2000 to December 2004.

Multivariate analysis was performed to identify the risk factors for the presence of a synchronous cancer in gastric cancer patients.

111 of 3291 gastric cancer patients (3.4%) registered in the database had a synchronous cancer. Among these 111 patients, 109 had a single synchronous cancer and 2 patients had two synchronous cancers. The most common form of synchronous cancer was colorectal cancer (42 patients, 37.2%) followed by lung cancer (21 patients, 18.6%).

Multivariate analyses revealed that elderly patients with differentiated early gastric cancer have a higher probability of a synchronous cancer.

A study published in the World Journal of Gastroenterology in 21 May 2009 (Tsutomu Namikawa, Kazuhiro Hanazaki, Department of Surgery, Kochi Medical School, Japonia) that investigated the clinicopathological features of early gastric cancer with duodenal invasion demonstrated that the incidence of early gastric cancer with duodenal invasion is extremely low, although advanced gastric cancer that arises in the antrum occasionally invades the duodenum. Tumors > 60 mm in size invaded the duodenum more extensively, and the distance of duodenal invasion from the pyloric ring was further in the elevated type than in the depressed type of tumor. There was no significant difference between the length of duodenal invasion and the histological type of the tumor.

Gastric cancer located adjacent to the pyloric ring, even if cancer invasion was confined to the mucosa or submucosa, was more likely to invade the duodenum, thus highlighting the importance of identification of duodenal invasion and emphasysing that sufficient duodenal resection with a cancer-free distal surgical margin should be performed in cases of duodenal invasion.

The diagnosis of gastric cancer

In „**Diagnostic role of serum interleukin-18 in gastric cancer patients"** 68 patients were enrolled in a study at King Chulalongkorn Memorial Hospital during April 2003 to May 2005. Gastric cancer was histologically proven in 51 patients and gastric ulcer in 17 patients. Serum IL-6, IL-10, IL-12, and IL-18 levels were measured by enzyme-linked immunosorbent assay (ELISA). The findings of this study demonstrate that serum IL-6 and IL-18, but not IL-10 and IL-12 levels may be the useful biological markers of clinical correlation and prognostic factor in patients with gastric cancer. Moreover, IL-18 could serve as a diagnostic marker for gastric cancer with a high positive predictive value.

The study **Usefulness of endoscopic ultrasonography în preoperative TNM staging of gastric cancer"** (4) studied 41 patients with gastric cancer (12 early stage and 29 advanced stage) proved by esophagogastroduodenoscopy and biopsies, preoperatively evaluated with EUS according to TNM /UICC. Pentax EG-3630U/Hitachi EUB-525 echo endoscope with real-time ultrasound imaging linear scanning transducers (7.5 and 5.0 MHz) and Doppler information was used in the current study. EUS staging procedures for tumor depth of invasion (T stage) were performed according to the widely accepted five-layer structure of the gastric wall. All patients underwent surgery.

Diagnostic accuracy of EUS for TNM staging of gastric cancer was determined by comparing preoperative EUS with subsequent postoperative histopathologic findings and it was 68.3% (41/28) and 83.3% (12/10), 60% (20/12), 100% (5/5), 25% (4/1) for T1, T2, T3, and T4, respectively. The rates for overstaging and understaging were 24.4% (41/10), and 7.3% (41/3), respectively. EUS tended to overstage T criteria, and main reasons for overstaging were thickening of the gastric wall due to perifocal inflammatory change, and absence of serosal layer in certain areas of the stomach. The diagnostic accuracy of metastatic lymph node involvement or N staging of EUS was 100% (17/17) for N0 and 41.7% (24/10) for N+, respectively, and 66% (41/27) overall. EUS is a useful diagnostic method for preoperative staging of gastric cancer for T and N criteria. However, EUS evaluation of malignant lymph nodes is still unsatisfactory. The location and distribution of the tumour was predominatly in the antrum (20 patients) and in the small curvature (17 patients).3 cases were inoperable and were considered correctly diagnosed through EUS.

The treatment of gastric cancer

Surgery is currently the only potentially curative treatment for gastric cancer.

Since the inception of the gastrectomy for cancer of the stomach, there has been debate over the bounds of surgical therapy, balancing potential long-term survival with perioperative morbidity and mortality.

Laparoscopy has emerged as an essential staging modality prior to gastric resection, identifying unresectable disease in a significant number of patients deemed resectable by current radiographic and endoscopic modalities. The diagnostic given by laparoscopy has been improved by the addition of laparoscopic ultrasound and peritoneal cytology. Endoscopic mucosal resection (EMR) has been established as one of the treatment options for early gastric cancer (EGC). In Korea the gastric cancer represents the most frequent malignant affectionand the second cause of death through cancer.

Early gastric cancer (EGC) is defined as gastric carcinoma confined to the mucosa or submucosa regardless of the presence of regional lymph node metastases. The detection rate of EGC has been steadily increasing because of technical advances and awareness of benefit from early diagnosis, especially in eastern countries. Patients who undergo resection for EGC have an excellent prognosis, with a 5-year survival rate of over 90%. However, the quality of life after conventional surgical resection of gastric cancer is substantially impaired. Therefore, less invasive treatment options for EGC have been developed.

With technical advances of EMR, the size of a lesion which can be resected en bloc is becoming larger.One must be careful because EMR has a very important limitation that lymph nodes cannot be dissected. Data from Korea and Japan have shown that the incidence of lymph node metastasis in intramucosal EGC is about 2%-3% and the risks increase up to 20% when submucosal invasions are present. Because results of long-term controlled trials are not available, the current indications of EMR are based on the detailed analysis of pathology results from surgically resected gastric cancers._The ideal candidates for EMR are EGC patients who have no risk of lymph node metastasis. The problem is that there is no method that can definitely evaluate the status of lymph node without surgical dissection. Ideally, endoscopic ultrasound (EUS) should be useful for selecting patients without lymph node metastasis. However, clinical studies evaluating the role of EUS before EMR for EGC have shown unsatisfactory results._The current accepted indications of EMR for the treatment of EGC are as follows: (1) differentiated (well- and/or moderately differentiated adenocarcinoma and/or papillary carcinoma) type confined to the mucosa; (2) smaller than 2 cm for superficially elevated type lesions; (3) smaller than 1 cm for the flat and depressed type lesions; (4) without ulcer or ulcer scar; and (5) without venous or lymphatic involvement.

Recently, based on some clinical observation and surgical data, expanded criteria for EMR have been proposed. One report in which EMR indications included EGC lesions as large as 3 cm showed the disease free survival rates of 98% during a median follow-up of 38 mo when complete resections were performed. Recent large surgical data from Gotoda *et al* also provided supporting evidence for expanded criteria.

The list of EMR methods is quite long, but the basicsteps are in common: (1) delineation of the lateral margin with or without chromoendoscopy, (2) marking using brief burst of electrocautery or argon plasma coagulation, (3) submucosal injection to lift the lesion, and (4) resection of the lesion.

The complications of EMR include pain, bleeding, perforation, and EMR-induced ulcer. Pain after resection is typically mild and dull in nature. Pain can be controlled using a standard dose of proton pump inhibitor (PPI) twice a day with or without analgesics. Bleeding is the most common complication and most bleeding occurs during the procedure or within 24 h. Bleeding can be successfully treated in most cases through coagulation of the bleeding vessels, or placement of metallic clips.EMR-induced ulcer is reported to heal faster and to recurless often than noniatrogenic gastric ulcer and usually treated with antisecretory agents. Earlier experiences of EMR for EGC from 12 major institutions in Japan were reported by Kojima et al in 1998. En bloc resection rate was 75.8%, and complete resection rate was 73.9%. The follow-up period was from 4 mo to 11 years. Recurrence rate after histopathologically documented eradication was 1.9% and recurred lesions were treated with endoscopic retreatment or surgery. The disease-specific survival rate was 99.1%.

In the study „**Endoscopic mucosal resection of early gastric cancer: Experiences în Korea"** (5) *)* 283 patients with EGC have been treated by EMR from January 2000 to June 2005. The median age of the patients was 64 (range 26-85) years. The male to female ratio was 3.2:1. The median duration of follow-up was 21 (range 3-66) months from January 2000 to December 2002, The mean size of cancerous lesion was 1.38 cm. The overall rate of curative resection was 72.1%. The rate of curative resection was highest with ESD (80.2%), followed by EMR-P (70.3%). Submucosal invasion was found in 44 cases (15.5%). In patients with curative resection, local recurrence at EMR site was found in only one case (0.5%). In 51 cases who underwent surgical resection due to non-curative or non-evaluable resection, residual cancer was found in 13 cases (25.0%). Among 28 patients, who were followed up without surgery after non-curative or non-evaluable results, there were 13 recurrences (12 local recurrences and 1 hepatic metastasis) after a median follow-up of 7 mo. Five patients died during the follow-up period, but there was no death related to gastric cancer.

The effectiveness of endoscopic submucosal dissection using an insulation-tipped diathermic knife (IT-ESD) for the treatment of patients with over 20 mm early gastric cancer (EGC) is certain. A total of 112 patients with over 10 mm EGC were treated with IT-ESD at Sumitomo Besshi Hospital and Shikoku Cancer Center in the 5 year period from January 2002 to December 2006, including 40 patients with over 20 mm EGC. We compared patient backgrounds, the one-piece resection rate, complete resection (CR) rate, operation time, bleeding rate, perforation rate between patients with over 20 mm EGC (over 20 mm group (21-40 mm)) and the remaining patients (under 20 mm group). No significant difference was found between the 2 groups.

The study proves that IT-ESD is a feasible treatment for patients with over 20 mm mucosal gastric cancer although the long-term outcome should be evaluated in the future. The extent of gastric resection for distal lesions had been debated, and the traditional view that total gastrectomy (TG) is required for all gastric lesions have been challenged. Gouzi et al conducted a multicenter randomized trial comparing TG (with Roux en-Y esophagojejunostomy) to subtotal gastrectomy (distal gastrectomy and Billroth II gastrojejunostomy) enrolling 169 patients with resectable lesions of the gastric antrum.

Patients with macroscopic lymph node involvement of the cardioesophageal or splenopancreatic region were excluded from the study. Both procedures included a total omentectomy, and lymph node dissection extended to the pyloric, left gastric, hepatic, and cardiac nodes. Splenectomy was not routinely performed; however, the TG group had an unspecified higher splenectomy rate than the SG group. The authors concluded that TG or SG could be performed with equal morbidity and mortality, but that TG offered no added survival benefit. In a larger trial, Bozzetti et al also performed a randomized trial comparing TG to SG in 618 patients with resectable tumors at least 6 cm from the cardia. The authors concluded that SG was

the preferred operation for distal gastric cancer, provided that a proximal margin of at least 6 cm could be obtained, because it is technically less demanding, results in a lower splenectomy rate, and is associated with better quality of life.

The extent of resection needed to achieve cure in tumors of the gastroesophageal junctions has been a topic of much debate, Ito et al reviewed patients with Siewert type II (59) or III (23) carcinoma of the gastric cardia in an attempt to discern the optimal surgical approach.

The surgical approach varied, with 33% undergoing total esophagectomy, 29% undergoing extended gastrectomy with thoracotomy, and 38% undergoing extended gastrectomy without thoracotomy._There was no significant difference in post-operative mortality and survival rate; however, there was a higher post-operative morbidity associated with total esophagectomy as compared to extended gastrectomy with or without thoracotomy (33% vs 11%). There was a significantly higher incidence of microscopic residual disease at the proximal margin in the extended gastrectomy group with or without thoracotomy as compared to the total esophagectomy group (38% vs 7%).

Based on these results, showing R0 status and nodal status to be predictors of survival, the authors made the following recommendations: (1) A minimum proximal margin of 6 cm and distal margin of 4 cm should be obtained. (2) A minimum of 15 lymph nodes should be sampled. The type of surgical approach should be tailored to fit the individual patient with these goals in mind.TG is the traditional treatment for proximal gastric cancer; however, this has been recently challenged as well. Harrison et al reviewed 98 patients with proximal gastric cancer who underwent gastric resection via an abdominal approach, excluding all patients who underwent esophagogastrectomy of these 98 patients, 65 underwent proximal gastrectomy (PG), and 33 underwent TG. There was no difference in post-operative mortality, in time to recurrence or first site of recurrence and 5-year survival rate.

The article **„Distribution of solitary lymph nodes în primary gastric cancer: A retrospective study and clinical implications"** (6) investigated the distribution pathway ofmetastatic lymph nodes in gastric carcinoma as a foundation for rational lymphadenectomy. 173 cases with solitary or single station metastatic lymph nodes (LN) were investigated from among 2476 gastric carcinoma patients.

The location of metastatic LN, histological type and growth patterns were analyzed retrospectively.

The criteria used for patient inclusion was:

(1) D2 lymph node dissections had been performed;

(2) There were greater than 15 lymph nodes analyzed pathologically;

(3) Patients with pT4 and M1 stage were excluded;

(4) Patients' medical records were complete

Among the 173 cases, 88 had solitary lymph metastasis and 85 involved a single station lymph node. Sixty-four of the 88 patients were male and 24 female. The average age of the patients in this group was 57.6 ± 7.2 years (range 30-80). With respect to tumor location, the tumor was found in the upper third stomach area (U) in 8 cases, in the middle third (M) in 28, and in the lower third (L) in 52. With respect to tumor location, the tumor was found in the upper third stomach area (U) in 8 cases, in the middle third (M) in 28, and in the lower third (L) in 52. Amongst the patients with single station node metastasis, 60 were male and 25 female. The average age of the patients in this group was 58.2 ± 8.3 years (range 32-76). In respect of tumor location; the tumor was in the U in 23 cases, in the M in 12, and in the L stomach areas in 50. Among the 88 patients with a solitary metastatic lymph node, in 65 (73.9%) the lymph nodes involved were within N1, and 23 (26.1%) were over N1. In this study, transversal and skipping metastasis were found to be notable. Nodal metastases occur in a random and multidirectional process in gastric cancer and that not every first metastatic node is located in the perigastric region near the primary tumor. The rate of "jumping metastasis" in gastric cancer is much higher than expected, which suggests that the blind examination of the nodal area close to the primary tumor can not be a reliable method to detect the SLN and that a extended lymph node dissection (ELND) should be performed if the preoperative examination indicates submucosal invasion._ (7). D1 resection consisted of the removal of all lymph nodes within 3 cm of the tumor and D2 resection consisted of the standard resection of the omental bursa, the hepatoduodenal nodes for antral lesions and the splenic artery, splenic hilar, and retropancreatic nodes by distal pancreatectomy for middle and upper third lesions.

D2 curative resection, which includes gastrectomy and D2 lymphoadenectomy, required dissection of all the Group 1 and Group 2 nodes classified by anatomical location. However, with the development of D2 lymphoadenectomy, larger lymph nodes dissected may enable to fine larger metastatic lymph nodes, which induces a migration in the staging system.

The ratio of the number of metastatic lymph nodes over the total number of resected lymph nodes is introduced to prognosis evaluation.

It was reported that metastatic lymph node ratio (MLR) can minimize the stage migration effect caused by increasing total dissected lymph nodes, also can help refine the current TNM stage system.

Though many studies on the prognostic significance of MLR in gastric cancer have been carried out, relevant researches on advanced gastric cancer from the cardia and fundus are still rare. Therefore, the aim of the retrospective study „**Prognostic impact of metastatic lymph node ratio în advanced gastric cancer from cardia and fundus"** (8) was to discuss the clinical impact of MLR in patients with gastric cancer from the cardia and fundus, and provide further evidence for rational lymphoadenectomy.

Two hundred and thirty-six cases, diagnosed as primary gastric cancer from the cardia and fundus were treated with curative resection D2.

The correlations between MLR and the total lymph nodes, positive nodes and the total lymph nodes were analyzed respectively. The survival time of patients was influenced by MLR.

The MLR did not correlate with the total lymph nodes resected ($r = -0.093$, $P = 0.057$). The 5-year overall survival rate of the whole cohort was 3 7.5%.

Kaplan-Meier survival analysis identified that the following eight factors influenced the survival time of the patients postoperatively: gender ($\chi2 = 4.26$, $P = 0.0389$), tumor size ($\chi2 = 18.48$, $P < 0.001$), Borrmann type ($\chi2 = 7.41$, $P = 0.0065$), histological grade ($\chi2 = 5.07$, $P = 0.0243$), pT category ($\chi2 = 49.42$, $P < 0.001$), pN category ($\chi2 = 87.7$, $P < 0.001$), total number of retrieved lymph nodes ($\chi2 = 8.22$, $P = 0.0042$) and MLR ($\chi2 = 34.3$, $P < 0.001$).

Cox proportional hazard model showed that tumor size ($\chi2 = 7.985$, $P = 0.018$), pT ($\chi2 = 30.82$, $P < 0.001$) and MLR ($\chi2 = 69.39$, $P < 0.001$) independently influenced the prognosis. A linear correlation between MLR and the 5-year survival was statistically significant based on the multiple linear regression ($\beta = -0.63$, $P < 0.001$). Hypothetically, the 5-year survival would surpass 50% when MLR was lower than 10%. The MLR is an independent prognostic factor for patients with advanced gastric cancer from the cardia and fundus. The decrease of MLR due to adequate number of total resected lymph nodes can improve the survival. The best known trial to

evaluate lymphadenectomy was from the Dutch Gastric Cancer Group. Bonenkamp et al published the results from a randomized controlled trial comparing D1 and D2 gastrectomy in 80 Dutch hospitals over 5 years. D1 resection was defined as containing only the N1 (perigastric) nodes. D2 resection was defined as encompassing the N2 nodes. These authors reported statistically significant differences in post-operative mortality (4% *vs* 10%) and complication rate (25% *vs* 43%) for D1 *vs* D2 resection. The 5-year survival rate and the 5-year risk of relapse were not statistically signifi cant.D2 lymphadenectomy was associated with a higher morbidity and mortality without offering a long-term survival benefit, and thus it was not recommended A modified D2 lymphadenectomy, sparing the spleen and pancreas when possible, can be performed safely and may offer the best chance for long-term survival. To improve the long-term survival of patients with advanced gastric cancer located in the cardia and fundus, removing at least 20 LNs for stage II, 25 LNs for stage III, and 30 LNs for stage IV patients during D2 radical dissection is recommended. (9)

The following recommandations are made:

- Segmental/subtotal gastrectomy plus D1/D1+ No.7 should be performed for carcinoma (≤ 1.0 cm in diameter, protruded type and mucosa invasion).
- Subtotal gastrectomy plus D2 or D1 + No.7, 8a, 9 is the most rational operation, whereas No.11p, 12a, 14v lymphadenectomy should not be recommended routinely for poorly differentiated and depressed type of submucosa carcinoma (> 3.0 cm in diameter).

Total gastrectomy should not be performed in proximal, so does combined resection or D2+/D3 lymphadenectomy. (10)

Resection of adjacent organs in conjunction with gastrectomy can increase survival with minimal additional morbidity in a highly selected patient population.

Judicious use of en bloc PD and gastrectomy and strictly preventing postoperative complications may improve the long-term survival for advanced gastric cancer patients with pancreaticoduodenal region involvement. Well-differentiated histology and negative resection margin are the most important predictors of long survival. (11) **"Pancreaticoduodenectomy for advanced gastric cancer with pancreaticoduodenal region involvement"**

Given the very poor prognosis associated with positive margins, re-laparotomy may be justified in those patients with node-negative disease. A positive margin is more of an indication of advanced disease in patients with gastric adenocarcinoma of the cardia rather than an independent prognostic factor for survival. (12) **"Influence of a microscopic positive proximal margin in the treatment of gastric adenocarcinoma of the cardia"**

Since palliative gastrectomies are associated with significant perioperative morbidity and mortality, the authors recommend deliberate palliative resection only in carefully selected patients with severe symptoms.

The quality of life is a very hard to achieve goal. Comparing postoperative quality of life (QOL) in patients with gastric cancer treated by esophagogastrostomy reconstruction after proximal gastrectomy was the aim of „**Improved quality of life in patients with gastric cancer after esophagogastrostomy reconstruction"**(13). QOL assessments that included functional outcomes (a 24-item survey about treatment specific symptoms) and health perception (Spitzer QOL Index) were performed in 149 patients with gastric cancer in the upper third of the stomach, who had received proximal gastrectomy with additional esophagogastrostomy. Fifty-four patients underwent reconstruction by esophagogastric anterior wall end-to-side anastomosis combined with pyloroplasty (EA group); 45 patients had reconstruction by esophagogastric posterior wall end-to-side anastomosis (EP group); and 50 patients had reconstruction by esophagogastric end-to-end anastomosis (EE group). The EA group showed the best postoperative QOL, such as recovery of body weight, less discomfort after meals, and less heart burn or belching at 6 and 24 mo postoperatively. However, the survival rates, surgical results and Spitzer QOL index were similar among the three groups. Metastatic gastric cancer remains an incurable disease, with a relative 5-year survival rate of 7%-27%. Chemotherapy, which improves overall survival (OS) and quality of life, is the main treatment option. Metaanalysis has demonstrated that the best survival results obtained in earlier randomized studies were achieved with three-drug regimens containing a fluoropyrimidine, an anthracycline, and cisplatin (ECF). „**New perspectives in the treatment of advanced or metastatic gastric cancer"** (14)

A number of new combinations incorporating docetaxel, oxaliplatin, capecitabine, and S-1 have been explored in randomized trials. Some combinations, such as epirubicin-oxaliplatin-capecitabine, have been shown to be as effective as (or perhaps more effective than) ECF, and promising early data have been derived for S-1 in combination with cisplatin. One factor that might contribute to extending median OS is the advancement whenever possible to second-line cytotoxic treatments. However, the biggest hope for significant survival advances in the near future would be the combination of new targeted biological agents with existing chemotherapy first-line regimens. Preoperative intra-arterial infusion chemotherapy could increase the radical resection rate of advanced gastric cancer, but its effect on the long-term survival has not been assessed.

The article **„Clinical significance of preoperative regional intra-arterial infusion chemotherapy for advanced gastric cancer"** (15) illustrated the important role played by preoperative intra-arterial infusion chemotherapy in improving the prognosis of advanced gastric cancer. Clinicopathological data of 91 patients who underwent curative resection for advanced gastric cancer were collected. Among them, 37 patients undertaken preoperative intra-arterial infusion chemotherapy were used as the interventional chemotherapy group, and the remaining 54 patients as the control group. Eleven factors including clinicopathological variables, treatment procedures and molecular biological makers that might contribute to the long-term survival rate were analyzed using Cox multivariate regression analysis. The 5-year survival rate was 52.5% and 39.8%, respectively, for the interventional group and the control group ($P<0.05$).

A Pilot study was conducted to evaluate the efficacy and toxicity of postoperative adjuvant chemoradiation for advanced gastric cancer: Adjuvant 5-FU/cisplatin and chemoradiation with capecitabine. Thirty-one patients who had undergone a potentially curative resection for Stage III and IV (M0) gastric cancer were enrolled. Therapy consists of one cycle of FP (continuous infusion of 5-FU 1000 mg/m2 on day 1 to 5 and cisplatin 60 mg/m2 on day 1) followed by 4500 cGy (180 cGy/day) with capecitabine (1650 mg/m2 daily throughout radiotherapy). Four weeks after completion of the radiotherapy, patients received three additional cycles of FP every three week. The median follow-up duration was 22.2 months. The 3-year disease free and overall survival in this study was 82.7% and 83.4%, respectively. Four patients (12.9%) showed relapse during follow-up. Eight patients did not complete all planned adjuvant therapy. Grade 3/4 toxicities included neutropenia in 50.2%, anemia in 12.9%, thrombocytopenia in 3.2% and

nausea/vomiting in 3.2%. Neither grade 3/4 hand foot syndrome nor treatment related febrile neutropenia or death was observed.

These preliminary results suggest that this postoperative adjuvant chemoradiation regimen of FP before and after capecitabine and concurrent radiotherapy appears well tolerated and offers a comparable toxicity profile to the chemoradiation regimen utilized in INT-0116. This treatment modality allowed successful loco-regional control rate and 3-year overall survival.

In spite of the various therapeutical methods the prognostic of gastric cancer still remains a very poor one, being the second cause of cancer mortality worlwide.

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SOURCES OF DIAGNOSTIC AND THERAPEUTIC INACCURACY IN ACUTE CORONARY SINDROMES

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Keywords: *myocardial infarction, new definition, troponine, reperfusion*

Abstract: *A document adopted by a consensus between the European Society and the American College of Cardiology in 2000, redefines the acute myocardial infarction as any quantity of myocardial necrosis caused by ischemia. Together with the appearance of new, sensitive biomarkers of myocardial infarction, little quantities of necrotic myocardium started to be detected and recognized as literally. The recent definition has changed the diagnosis central role, focusing the attention towards the troponine levels and lowering the importance of the old criteria (clinical scenery and EKG changes), allowing a larger scale of interpreting these criteria. Even before been accepted, the new definition of the myocardial infarction was questioned: only half of the doctors accept the diagnosis in the presence of the symptoms and the high troponine levels (in the absence of the EKG changes or high levels of CK and CK-MB). The essential criteria in the fight with the time, regarding the decision of reperfusion, remains still the ST elevation. Regarding the decision for trombolysis, the EKG changes remain sovereign. Which doctor had never been confronted in the emergency room with the next situation: thoracic pain and un-interpretable electrocardiogram? In these particular situations, which can lead to diagnosis confusions, the interpreting of the troponine elevation can solve some problems. Moreover, the correct diagnosis of this cases can have serious therapeutic benefits. Even in the case of a correct and in time diagnosis, the percent of the eligible patients who do not receive any reperfusion form is unacceptable high (approximate 50%, after the data received from the European Congress 2008). The aim of this paper is to interpret from this point of view (of the new definition and recent indications of reperfusion), the data of the patients which were hospitalized during the last two years (January 2007 - October 2009) in the Cardiology Department of the Emergency Clinical County Hospital, having the diagnosis at admission of Acute Coronary Syndrome (ACS).*

Cuvinte cheie: *infarct miocardic, noua definiție, troponina, reperfuzie*

Rezumat: *Un document adoptat prin consens între Societatea Europeană şi Colegiul American de Cardiologie în 2000, redefineşte infarctul miocardic acut ca şi orice cantitate de miocard necrozat cauzat de ischemie. Odată cu disponibilitatea a noi şi sensibili biomarkeri de necroză miocardică, mici cantități de miocard necrozat pot fi detectate şi recunoscute ca atare. Definiția recentă a schimbat rolul central diagnostic, focalizând atenția asupra troponinei şi reducând greutatea vechilor criterii (scenariul clinic şi modificările ECG, permițând o plajă largă de interpretare a acestor criterii). Chiar înainte de a fi acceptată, noua definiție a infarctului miocardic este pusă sub semnul întrebării: doar aproximativ jumatate dintre doctori acceptă diagnosticul în prezența simptomatologiei şi a troponinei crescute (în absența modificărilor ECG sau a nivelurilor crescute de CK şi CK-MB). Cine nu s-a confruntat însă în regim de urgență, cu următoarea situație: durere toracică cu ECG ne- sau greu interpretabil? În aceste situații particulare, pretabile la confuzii diagnostice, interpretarea ascensiunii troponinei poate tranşa dilemele. Mai mult, încadrarea corectă, la timp, a acestor cazuri, poate avea serioase beneficii terapeutice. Dar chiar pentru situațiile „norocoase", ale unui diagnostic corect şi la timp efectuat, procentul de pacienți eligibili ce nu primesc nici o formă de reperfuzie este inacceptabil de înalt (aproximativ 50%, după datele culese la European Congress 2008). Scopul acestei lucrări este de a interpreta din acest punct de vedere (al noii definiții şi recentelor indicații de reperfuzie), datele pacienților internați pe perioada a aproape doi ani (2007- octombrie 2009), având diagnosticul de internare de Sindrom coronarian acut (SCA).*

INTRODUCTION

A document adopted by consensus between the European Society of Cardiology and American College in 2000, redefined myocardial infarction as any amount of necrotic myocardium caused by ischemia. With the availability of new and sensitive biomarkers of myocardial necrosis, small amounts of myocardial necrosis can be detected and recognized as such. Definition recent diagnosis changed the central role, focusing attention on reducing weight and cardiac troponin old criteria (clinical scenario and ECG changes, allowing a wide range of interpretation of these criteria). Even before it accepted the new definition of myocardial infarction is questionable: only about half of doctors accept the presence of symptoms and diagnosis of elevated cardiac troponin (in the absence of ECG changes or elevated levels of CK and CK-MB). The essential criterion in the fight time, in terms of the decision

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of reperfusion, remains supradenivelat ST. At least in terms of thrombolysis, ECG changes are not faced suverane.Cine but urgent, with following situation: chest pain with ECG interpretable us or hard?

In this particular situation, the price of diagnostic confusion, cardiac troponin rise can tranche interpretation dilemmas. Furthermore, correct classification at the time, these cases can have serious benefits for situations terapeutice.Dar even "lucky", the proper diagnosis and timely made, the percentage of eligible patients receive no reperfusion as unacceptable high (about 50%, after data collected at the European Congress 2008). The purpose of this paper is to interpret from this point of view (the new definition and recent indications of reperfusion), data of patients admitted during the nearly two years (2007 - October 2009), with admission diagnosis of acute coronary syndrome (ACS).

PURPOSE OF THE STUDY

The contents of this paper aims:

1. ACS, "false alarm"?
2. What is the use of cardiac troponin in ACS?
3. Angina with troponin positive - false diagnosis?
4. Vs. other biomarkers troponin
5. Troponin and other diagnostic criteria (compared to statistical indicators).
6. ACS and BRS: a controversial association.
7. Reperfusion therapy: underused?

Aborted MI or "masquerading" heart?

MATERIAL AND METHOD

Were considered in all patients admitted in the Cardiology Department of Hospital Clinic Sibiu County, in the period 01/01/2007 to 10/22/2009. This period was chosen purely pragmatic reasons, because cardiac troponin determination (and therefore the possibility of implementing new criteria for diagnosis) is made from early 2007. Among them were selected who presented at admission diagnosis of acute coronary syndrome. Respectively, from a total of 9633 patients hospitalized in this period, were selected from 734 patients with ACS, representing a rate of 7.62%.

RESULTS AND DISCUSSION

1. ACS, "false alarm"?

Of all patients hospitalized with suspected ACS, 65% dinagnosticul discharge of AMI was at 9% of hospital discharge diagnosis was angina, and 26% of cases (67 patients were discharged with diagnoses noncoronariene).

Of those 67 diagnoses "noncoronariene so-called" STEM is involved only in 19 cases (of which 8 were BRS). The remaining 48 cases were provided by non-stem.

Cases of "fake stem" were mostly covered by various forms of heart failure: left ventricular failure - 12 cases, acute pulmonary edema - 8 cases, congestive heart failure - 6 cases, followed by: dilative cardiomyopathy - 3 cases , pulmonary embolism - 2 cases, 2 cases of myocarditis, pericarditis 1caz, Takotsubo syndrome - a case.

2. What is the use of cardiac troponin in acute coronary syndromes?

In the literature, is that, for patients who have not received any dose of biomarkers of necrosis, an almost 10% and troponin in particular, this percentage increases to 60%. In our study group, troponin was measured in the 18.1% of patients admitted with a diagnosis of ACS. 9.8% were troponin positive and negative was 8.3%. Patients who have not received any dose of biomarkers are in number 61, representing 8.3%, percentage assimilated data. Discharge diagnosis of heart was at 376 patients in whom troponin was not wrapping. Therefore, this diagnosis is based on the old definition (WHO definition), which requires 2 / 3 criteria. If for Stem ECG remain sovereign, at least in terms of therapeutic decision for NSTEMI, biomarker test has become "the cornerstone". Low specificity of pain and ST-T changes and gives precedence biomarkers, specifically cardiac troponin. Of 379 patients only 58 were NSTEMI troponin wrapping. Of 48 patients with ACS and troponin BRS only seven were wrapping. However the percentage of NSTEMI patients without the biomarker dose is only 3.5%.

3.Angina with positive troponin-false diagnosis?

Troponin positive ACS is a combination which, as defined mean heart. Of 61 cases with positive troponin, only 53 were classified as stroke, the remaining eight being wrongly interpreted as an unstable majority.

Revising the diagnostic criteria under the new definition

- All patients were diagnosed with angina pain naturally,
- More than 3 were even supradenivelat ST
- One patient out of 8 with alternative diagnoses has noncoronariană pathology, pulmonary embolism respectively. Even this would be classified under the new criteria at least in category: MI type 2.

Given the reporting of cardiac troponin positivity in patients with admission diagnosis of ACS, it is reasonable not to perform cardiac troponin false positivity in the present batch (ultraselecționat).

4. Troponina vs. other biomarkers.

Protocols for the interpretation of cardiac biomarkers (American Association for Clinical Chemistry 2007 - Guidelines for use of biomarkers in ACS)

- Not suitable single marker.
- It is desirable to combine an early marker, sensitive (myoglobin) with one more specific and late (troponin).
- Excluding a timely diagnosis is a target variable depending on the probability per test, time from onset of pain
- Additional testing will be performed (or stress imaging) after MI was excluded.

The purpose of this chapter is to highlight the study group (734 patients with ACS) any differences between biomarkers in terms of statistici.S indicators were calculated sensitivity, specificity, positive predictive value, negative predictive value for each enzyme in parte.Comparația between the group diagnosed with myocardial infarction and the group without diagnosis at discharge, cardiac troponin is positive ($p < 0.01$), while for CK-MB and mioglobină could not establish such a correlation (for the present group, $p > 0.01$ for both biomarkers). Data obtained indicates troponin testing as the highest specificity. In terms of hierarchy, the result is not surprising. Biomarker troponin is the most specific and mioglobina has the highest sensitivity (data in agreement with the literature). Surprise result but in terms of value received. In literature, values reported for specific cardiac troponin does not fall below 90%. Although testing was performed on a batch ultraselecționat, with high probability of having the disease specificity of cardiac troponin is below the values reported in literature (about 78%). At least two explanations for this difference:

1. Este possible compliance at harvest (ie, a second dose at least 6h from onset) to reduce the number of false negative tests,
2. Diagnosticul discharge has not been reviewed on this lot. But there are eight cases with positive troponin, assigned to other diagnoses, most of the discharge diagnosis of angina pectoris.

Revision under the new definition would reduce the number of false positives, specificity reaşezând value, as

follows: sensitivity of cardiac troponin in the diagnosis of infarction is 57.7% while the specificity is 96.5%. Revised value for specificity is much closer to the literature by the correct classification of only 7 cases - 96.6%. Regarding other statistical indicators, that diagnostic accuracy, positive predictive value and negative - the comparison, even without revision is diagnostic for cardiac troponin. Therefore, it provides most of the cases correctly diagnosed (about 61%).

We studied two levels below significance of biomarkers in confirming or excluding the diagnosis of heart. Sure that the definition does not require the isolation of two biomarkers, but there is equivocal situations, the ECG or imaging criteria not working and the pain is low specificity. The purpose of cutting them would be good to know to what extent we can rely on positivity or negativity of the two biomarkers.

Therefore:

- + CK-MB positive troponin positive indicates a diagnosis of stroke in 99% ($p < 0.01$)
- + CK-MB negative troponin negative myocardial excluded in 95% ($p < 0.05$)
- + Mioglobina positive troponin positive indicates a diagnosis of heart in 95% ($p < 0.05$). Exclusion can not count on having two negative values of myocardial troponin and mioglobină. ($P > 0.05$). Mioglobinei Poor specificity probably justify this result.

5. Troponina versus other diagnostic criteria

The most common causes of ST supradenivelat are some statistics: SS, BRS, early repolarization and ventricular aneurysm in other STEM is third. SS and BRS keeps constant but instead on "the podium". Many of these conditions may be erroneously interpreted as myocardial infarction thrombolysis resulting in unwanted or inappropriate coronarografii emergency.

In our study group, observed that pain sensitivity is 89%, while specificity for diagnosis of chest pain of heart, a lot ultraselectionat with admission diagnosis of ACS is only 20% (one third of patients with pain and ACS are discharged without a diagnosis of heart). I tried to as a hierarchy of different ECG features in terms of performance testing. We calculated sensitivity and specificity of each element relative to the initial batch (ie those with ACS as the admission diagnosis). Although the calculation of performance testing for biomarkers was performed on different batches (only those on which the determination), at least indicative indicators can be compared to all elements involved in diagnosis.

In terms of diagnostic accuracy, ie the highest percentage of correct - provide ST elevation (66.8%), followed by pain and Q-wave (64%).

In subgroup with NSTEMI association: positive troponin + pain correlate with diagnosis of heart to the nearest 99% ($p < 0.01$). The subgroup with STEM correlation value is not as strong ($p = 0.05$), so be positive troponin correlated with the diagnosis of stroke with an accuracy of only 95%. If you do not take into account pain, virtually no correlation between troponin and diagnosis infarct.Pentru rest of the criteria for myocardial associations could not establish a statistical correlation ($p > 0.05$) for all these combinations.

6. SCA and BRS: a combination that can become problematic

Data from the literature argue that patients with MI and BRS were higher hospital mortality (22.6%) than patients without BRS (13.1%). This difference is due at least in part retention of reperfusion (drug or mechanically these patients). About half of patients with MI and BRS symptoms not typical (ie without chest pain are hospitalized). ST changes consistent (with QRS) and ST depression, V1-V3 on the merits of BRS were found to have high specificity (97%) confirmed the diagnosis of myocardial enzyme.

When new, BRS descending artery occlusion is related to previous infarction with a large quantity "jeopardized." Moreover, previous BRS is a powerful marker of LV dysfunction associated loss of myocardium so may result in shock cardiogen.Întrebarea entry that arises is whether the combination of MI and BRS is treated in accordance with the guidelines or not.

In group present with ACS as the admission diagnosis, BRS was present in 48 patients, representing 6.5% of the total. Of those, only 20 have received final discharge diagnosis of AMI. 20 patients received discharge diagnosis of angina and the remaining eight were assigned to diagnoses noncoronariene.

1. We compared the other two groups, namely: ACS and ACS without ST ST supradenivelat supradenivelat, ACS BRS, in terms of proportion of events ultimately interpreted as noncoronariene. The comparison provided significant results in "favor" BRS ($p < 0.01$ for both groups).
2. In terms of risk profile, group BRS is associated with a high risk profile that association with diabetes, hypertension and heart failure.
3. Given the difficulty of framing BRS as ACS, I tried reporting this kind of pathology (or BRS) in total 9632 patients admitted to the ward from 01/01/2007 to 10/22/2009.

In a number of 682 patients (7.07%) was diagnosed with left bundle branch block (BRS). Of all patients with BRS, 35 patients (5.13%) had troponin wrapping. 31 of these patients, cardiac troponin values were below the considered pathological. The remaining four patients had levels considered above normal upper limta. Of these, 3 patients were discharge diagnosis of acute myocardial infarction and one patient had the discharge diagnosis of acute myocardial infarction. Of all patients with BRS, 26 patients (3.81%) had CK wrapping. In 17 patients of them, CK-MB values were above the upper limit considered normal (4.5 ng / ml). The remaining nine patients had CK values considered normal. Of the 17 patients with BRS and elevated CK-MB, only three were made at discharge diagnosis of acute myocardial infarction. The remaining 14 cases were interpreted as acute myocardial infarction.

1. No patient with ACS and BRS was not thrombolysed, although 20 of 48 were diagnosed with AMI at discharge. BRS is therefore included a significant proportion of cases among nontromboliză reasons.
2. In terms of evolution, there is also a higher percentage of patients with adverse developments in the group with ACS and BRS, lots to type stem or NSTEMI ACS.
3. Terapia reperfusion - underused?

In our study group 42.2% of patients with myocardial STEM as discharge diagnosis were thrombolysed. Sure that the percentage may reflect greater label, by adjusting the lot on the time of onset, age, contraindications thrombolysis.

Relationship with age: 66.70% of patients between 31-40 years with an indication of thrombolysis were thrombolysed; remaining percentages are as follows: 30% (41-50) 18.50% (51-60 years), 16 80% (61-70 years), 7.90% (71-75 years), 9.5% (76-80 years), 1% (81-90 years). But we found that age was not a major impediment to initiate thrombolysis. There were 10 patients, representing approximately 10% over 75 years, who were thrombolysed.

Relation to Sex: 68% of female patients were not thrombolysed, 51% of male patients were thrombolysed. Percentage of female patients who were not thrombolysed significantly higher than in male patients ($p < 0.01$). Tromboliticele used, in order of frequency were: streptokinase (58.75%), Alteplase (28.75 %), Tenecteplase (10%), Reteplase (2.5%). The percentage of patients sent for PCI in particular

reflect the reality of logistical limitation in implementing this therapy. We calculated, however, and the percentage of patients who received reference purposes invasive revascularization: 15.4% of patients with AMI as discharge diagnosis and 6 2% of patients with angina, the diagnosis of extrenare. Of the 73 patients with AMI sent for PCI, 31 were previously thrombolysed.

In our study group, the presence of the following factors proved to have statistical significance in the netrombolizați group ($p < 0.01$) heart failure, hypertension, diabetes, BRS.Există several potential reasons for failure of thrombolysis in these patients, and lack of knowledge that reperfusion indications were extended to more complex groups (less studied in trials). For example, doctors hesitate to prescribe reperfusion in patients with atypical symptoms (shortness of breath instead of classic retrosternal pain). Patients with old myocardial infarction or CABG are also less subject to difficulties in interpretation supradenivelării reperfusion ST (old or new?). Patients with heart failure or diabetes symptoms are not typical, resulting in no further investigation ECG.

CONCLUSIONS

1. There is a "restraint" from physicians in the diagnosis of AMI according to new criteria.
2. Underspending cardiac troponin and CK-MB, and biomarkers of necrosis recommend the new definition is relevant to the lack of implementation.
3. One (or more than two determinations) may amount calculations "complicated" mutivariabile used in prognostic assessment.
4. Underestimated the true incidence of AMI is the correct diagnostic inconsistency. The percentage of "false ACS (ie, cases that were not completed in coronary diagnosis) is only 9%. Various forms of heart failure is the major manifestation in these patients.
5. Positive troponin correlates with the diagnosis of stroke with an accuracy of 99% ($p < 0.01$), which could not be found for other biomarkers ($p > 0.05$). The diagnostic review (ie, using new criteria), the specificity of cardiac troponin is similar to the literature (96.5%).
6. Findings combination of two values of biomarkers in confirming, excluding diagnosis of heart that is in favor: troponin + CK. Mioglobina in combination with troponin can be used for confirmation ($p < 0.05$), but can not be used for exclusion ($p > 0.05$).
7. Comparison in performance between elements ECG testing indicates that the component BRS provides the fewest false-positive cases, followed by ST depression and ST supradenivelat (89% vs.75.4 vs.66.5). Highest percentage of correct results it provides ST elevation (66.8% accuracy).
8. In the group with troponin wrapping, its positive predictive value was superior to other clinical and ECG evidence for both STEM and for NSTEMI.
9. Combination pain - troponin is superior to other combinations in the diagnosis of infarction ($p < 0.01$), probably by cross-fertilization (for pain, showed 89% sensitivity, while only 20% specificity).
10. The presence of BRS in patients with ACS is associated with an increased risk profile, with high probability of conservative treatment ($p < 0.01$) and highest proportion of hospital deaths (compared to the group with ST supradenivelat and NSTEMI).
11. Reperfusion was performed as follows: drug to 24.6%, invasive 16.9% to 7.2% combined. 65.6% following conservative treatment (group considered include both STEM and NSTEMI patients, but the hospital had AMI). This diagnosis was considered a substitute for NSTEMI risk (as they would be guidelines only indication of revascularization).
12. Reported only in patients with STEM, these data are encouraging, that are similar to those in literature - 71% of patients with revascularized STEM.

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THE DOWN SYNDROME, TETRALOGY OF FALLOT AND THE LEFT-TO-RIGHT SHUNT

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Keywords: *statistics, genetics, cardiac malformations*

Abstract: *The cardiac malformations are frequently seen at children with chromosomal disorders. The percentage of the cases with the Down syndrome out of the lot of study represents 8,2%. In the lot of study we also introduced 6 cases (5,5%) presenting tetralogy of Fallot. The herein paper embodies descriptive statistics results measured for each of the variables.*

Cuvinte cheie: *statistică, genetică, malformații cardiace*

Rezumat: *Malformațiile cardiace sunt frecvent întâlnite la copiii cu aberații cromozomiale. Procentul cazurilor cu sindrom Down din lotul de studiu reprezintă 8,2%. În lotul de studiu am introdus şi 6 cazuri (5,5%) cu Tetralogie Fallot. Această lucrare conține rezultatele de statistică descriptivă obținute pentru fiecare variabilă în parte.*

Descriptive statistics

This part embodies descriptive statistics results measured for each of the variables. The bivariat relationships are studied using tables of association, grouped bar diagrams.

Table no. 1. Descriptive statistics for the variables: sex, background, weight curve, age

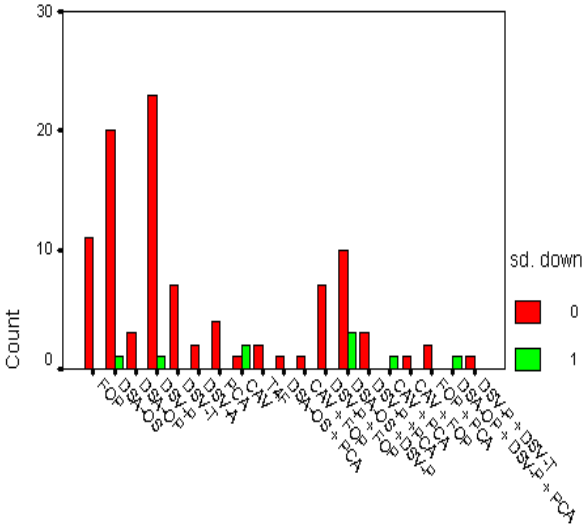
Variable	N	%
Sex		
Masculine	54	49.1
Feminine	56	50.9
Background		
Urban	58	52.7
Rural	52	47.3
Weight		
Normal	65	59.1
In stagnation	45	40.9
Age		
Average (SD)	2.6(3.8)	

The data basis consists of approximately an equal number of women (49%) and men (51%), the persons coming from the urban environment (52,7%) being more numerous than the ones having a rural background (47,3%). In 66% of the cases the age of the children is under 1 year; approximately 6% between 1 and 2, and the rest are children over 2 years.

During the study 59,1% of the children maintained a normal body weight while 40,9% of them presented a loss or stagnation of weight.

The cardiac malformations are frequently seen at children with chromosomal disorders. The main chromosomal disorders present in the lot of study were Down Syndrome – trisomies (9 cases), are associated as cardiac malformations with left-to-right shunt: DSA-OS + DSV-P, CAV, CAV+PCA, DSA-OP+DSV-P+PCA, DSA-OS, DSV-P.

Figure no. 1. Down Syndrome and the type of malformation



Out of the 9 cases with Down syndrome 2 of them (22,2%) closed naturally, in the rest of the cases, 7 (77,8%), the closure was performed by surgery in 3 cases (33,3%) which represents 10,3% of the total of cases subject to surgery within the lot of study, the other 4 being monitored at present, the further evolution directing the case towards the type of therapy.

The percentage of the cases with Down syndrome within the lot of study represents 8,2% of the total number of cases. In the lot of study, the karyotype was performed in Sibiu at the genetics laboratory, and the type of trisomy presented as a result was of trisomy 21=100%. The 21 trisomy frequently associated malformative cardiopathy: atrioventricular canal (AVC), interventricular septal defect (VSD), interatrial septal defect (ASD), or associations between these defects.

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Table no. 2. Table of association for the Down syndrome's variables and the self closure of the defects

			inchis singur		
			0	inchis	Total
sd. down	0	Count	56	45	101
		% within sd. down	55.4%	44.6%	100.0%
		% within inchis singur	88.9%	95.7%	91.8%
		% of Total	50.9%	40.9%	91.8%
	1	Count	7	2	9
		% within sd. down	77.8%	22.2%	100.0%
		% within inchis singur	11.1%	4.3%	8.2%
		% of Total	6.4%	1.8%	8.2%
Total		Count	63	47	110
		% within sd. down	57.3%	42.7%	100.0%
		% within inchis singur	100.0%	100.0%	100.0%
		% of Total	57.3%	42.7%	100.0%

Table no. 3. Table of association for the Down syndrome's variables and the surgical closure of the defects

			operat		
			0	operat	Total
sd. down	0	Count	75	26	101
		% within sd. down	74.3%	25.7%	100.0%
		% within operat	92.6%	89.7%	91.8%
		% of Total	68.2%	23.6%	91.8%
	1	Count	6	3	9
		% within sd. down	66.7%	33.3%	100.0%
		% within operat	7.4%	10.3%	8.2%
		% of Total	5.5%	2.7%	8.2%
Total		Count	81	29	110
		% within sd. down	73.6%	26.4%	100.0%
		% within operat	100.0%	100.0%	100.0%
		% of Total	73.6%	26.4%	100.0%

The tetralogy of Fallot associates, from a historical point of view, an interventricular communication, a pulmonary stenosis, dextroposition with aorta dilatation and right ventricular hypertrophy. In fact the only important ones are the interventricular communication and the pulmonary stenosis, the other two being the consequences of the first. The tetralogy of Fallot is one of the cardiac malformations frequently associated with extracardiac anomalies.

We introduced 6 cases (5,5%) in the lot of study, and none of them presented a self closure of the shunt from the interventricular communication level which confirms the fact that the malformation is complex and the hemodynamics of these malformations does not allow its closure.

Tabele no. 4. Table of association for the tetralogy of Fallot's variables and the self closure of the defects

			inchis singur		
			0	inchis	Total
t4f	0	Count	57	47	104
		% within t4f	54.8%	45.2%	100.0%
		% within inchis singur	90.5%	100.0%	94.5%
		% of Total	51.8%	42.7%	94.5%
	1	Count	6		6
		% within t4f	100.0%		100.0%
		% within inchis singur	9.5%		5.5%
		% of Total	5.5%		5.5%
Total		Count	63	47	110
		% within t4f	57.3%	42.7%	100.0%
		% within inchis singur	100.0%	100.0%	100.0%
		% of Total	57.3%	42.7%	100.0%

There were 4 cases resolved by surgical means, namely 13,8% of the total number of children subject to surgery from the lot of study, with left-to-right shunt.

As the study shows, there was only one case of death and that belonging to the tatralogy of Fallot's group, representing 16,7% of the cases with tetralogy of Fallot and 9% of the total number of cases subject to the study.

Table no. 5. Table of association for the tetralogy of Fallot's variables and cases of death

			operat		
			0	operat	Total
t4f	0	Count	79	25	104
		% within t4f	76.0%	24.0%	100.0%
		% within operat	97.5%	86.2%	94.5%
		% of Total	71.8%	22.7%	94.5%
	1	Count	2	4	6
		% within t4f	33.3%	66.7%	100.0%
		% within operat	2.5%	13.8%	5.5%
		% of Total	1.8%	3.6%	5.5%
Total		Count	81	29	110
		% within t4f	73.6%	26.4%	100.0%
		% within operat	100.0%	100.0%	100.0%
		% of Total	73.6%	26.4%	100.0%

Table no. 6. Table of association for the tetralogy of Fallot's variables and cases of death

			decedat		
			nu	da	Total
t4f	0	Count	104		104
		% within t4f	100.0%		100.0%
		% within decedat	95.4%		94.5%
		% of Total	94.5%		94.5%
	1	Count	5	1	6
		% within t4f	83.3%	16.7%	100.0%
		% within decedat	4.6%	100.0%	5.5%
		% of Total	4.5%	.9%	5.5%
Total		Count	109	1	110
		% within t4f	99.1%	.9%	100.0%
		% within decedat	100.0%	100.0%	100.0%
		% of Total	99.1%	.9%	100.0%

Table no. 7 a,b. Table of association between the variables – Down syndrome and tetralogy of Fallot - and the evolution

			t4f		
			0	1	Total
evolutie	favorabila	Count	64		64
		% within evolutie	100,0%		100,0%
		% within t4f	61,5%		58,2%
		% of Total	58,2%		58,2%
	nefavorabila	Count	40	6	46
		% within evolutie	87,0%	13,0%	100,0%
		% within t4f	38,5%	100,0%	41,8%
		% of Total	36,4%	5,5%	41,8%
Total		Count	104	6	110
		% within evolutie	94,5%	5,5%	100,0%
		% within t4f	100,0%	100,0%	100,0%
		% of Total	94,5%	5,5%	100,0%

			sd. down		
			0	1	Total
evolutie	favorabila	Count	63	1	64
		% within evolutie	98,4%	1,6%	100,0%
		% within sd. down	62,4%	11,1%	58,2%
		% of Total	57,3%	,9%	58,2%
	nefavorabila	Count	38	8	46
		% within evolutie	82,6%	17,4%	100,0%
		% within sd. down	37,6%	88,9%	41,8%
		% of Total	34,5%	7,3%	41,8%
Total		Count	101	9	110
		% within evolutie	91,8%	8,2%	100,0%
		% within sd. down	100,0%	100,0%	100,0%
		% of Total	91,8%	8,2%	100,0%

In what concerns the Down syndrome cases, the evolution was favorable in 11,1% of cases and not favorable in 88,9% of cases.

In these groups of study the evolution was different because of the more complex malformations with shunt and

associated chromosomal disorder (Down syndrome).

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THE PEDIATRIC ECHOCARDIOGRAPHY AND THE FUNCTION OF THE LEFT VENTRICLE

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Keywords: *pediatric echocardiography, left-to-right shunt, cardiology*

Abstract: *A left-to-right shunt is when blood from the left side goes to the right side and affects the pulmonary circulation. The shunt is recognized by clinical pulmonary and cardiac signs, pulmonary hypervascularity and echocardiographic signs. In order to determine the function of the left ventricle, the echocardiography is the most common method of study, the most available and easy to use within the pediatric cardiology. The great advantage of the echocardiography is its availability and possibility of usage by all cardiologists even if the patient is in bed.*

Cuvinte cheie: *Echocardiografiegrafie pediatrică, shunt stânga – dreapata, cardiologie*

Rezumat: *Un shunt stânga-dreapta este o cantitate de sânge saturat ce trece de la stânga la dreapta şi încarcă circulaţia pulmonară. Shuntul este recunoscut prin semne clinice pulmonare şi cardiace, o hipervascularizaţie pulmonară şi semne echocardiografice. Pentru determinarea funcţiei ventriculului stâng echocardiografia este cea mai practicată metodă de studiu, cea mai disponibilă şi simplu de realizat în cardiologia pediatrică. Avantajul major al echocardiografiei este disponibilitatea sa şi posibilitatea utilizării sale de către toţi cardiologii dacă este necesar şi la patul bolnavului.*

SCIENTIFICAL ARTICLE OF BIBLIOGRAPHIC SYNTHESIS

Left ventricular insufficiency

The description on segments of how to perform an echocardiography is in fact the way of approaching the heart and its different structures.

a) Abdominal situs: or the position of abdominal organs;
b) Position of heart in the thorax: to the left, to the right, centered;
c) Atrial situs (auricular): or the position of the left and right atriums;
d) Atrio-ventricular relationship;
e) Ventricular-arterial relationship.

The evaluation of the systolic function of the left ventricle (LV) is of paramount importance, crucial for taking under observation and monitoring patients that present congenital cardiopathy with left-to-right shunt. The function of the left ventricle, seen by measuring the fractional shortening (FS) of the LV, represents a major prognostic factor for cardiopathies with left-to-right shunt. The limit value of FS of LV is proposed in different recommendations, in cardiac insufficiency, for the most efficient current therapeutic indications (medical treatment). Thus, the determination of the fractional shortening has to be specified and the echocardiography represents the most common method.

The children subject to the study presented cardiac malformations with left-to-right shunt: clinical pulmonary and cardiac signs, namely pulmonary hypervascularity and echocardiographic signs.

Unlike the adult, the child offers an excellent transthoracic echogenity, the problem is given by its compliance during the examination.

The TM (fractional shortening, ejection fraction, ventricle wall thickness) allows an evaluation of the LV function. The bidimensional echocardiography (2D) has become the most frequently used echocardiographic technique. It uses pulsed ultrasounds in order to immediately supply correct images in space of the cord. In addition to this, the 2D echocardiography allows the numerous heart sections and major vessels to be visualized.

The Doppler echocardiography uses ultrasound technology to measure the velocity, direction and type of blood flow within the cardiovascular system. The color Doppler echocardiography represents a bidimensional Doppler echocardiography in which the signal is encrypted in color in order to point the direction of the blood flow (red is the color that approaches the transductor and blue is moving away).

From a clinical point a view, the cardiac insufficiency is stressed by a tachycardia induced by effort, or in what the newborns are concerned, while being fed, and associated with weight stagnation and respiratory distress.

With the help of the echocardiography we can see the hyporkinetic of the left ventricle, its dilution, the septal curve becomes flat (rectilinear), the fractional shortening measured in the TM mode begins to drop towards the minimum value or below it (30-45%).

The left ventricular function is usually studied in the TM mode. The bidimensional study of the left ventricle is not indispensible unless it has a diskinetic contractility.

The population subject to this study was represented by 110 children having cardiac malformations with left-to-right shunt, from the moment of birth until the age of 18. These children were selected out of the total number of approximately 2906 children with cardiac symptomatology: cardiac soufflé, loss of weight or weight stagnation, cyanosis, precordial pains, dyspnoea at effort or repose, examined in our clinic in this period of 6 years.

There is accordance between the clinic and the

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echocardiographic study in what concerns the left ventricular insufficiency, and this fact is outlined by the results of the study on the correlation between the weight curve and the fractional shortening. When the body weight is growing, the fractional shortening values are within normal limits, whereas in the presence of a loss or stagnation of weight the fractional shortening is below the normal values (p=0,001).

Tabele no. 1. Study on the correlation between weight and FS

		greutate (curba ponderala)	FS%
greutate (curba ponderala)	Pearson Correlation	1.000	-.308**
	Sig. (2-tailed)	.	.001
	N	110	110
FS%	Pearson Correlation	-.308**	1.000
	Sig. (2-tailed)	.001	.
	N	110	110

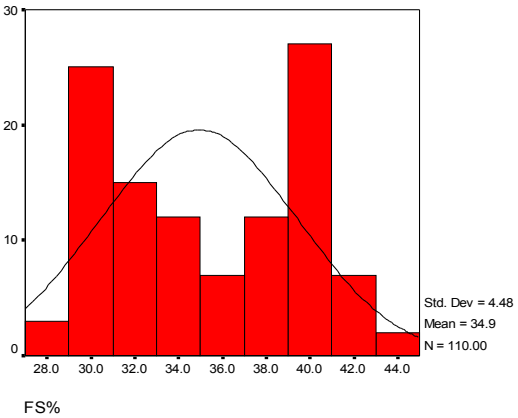
The fractional shortening measured in the TM mode goes below the minimum value (30%) in 13,6% of the cases, in the rest of 86,4%, its value remains within the normal values (30-45%), thus it does not present left ventricular insufficiency. The aforementioned results are drawn from the next table of frequency and the histogram graphic, the latter mentioning also the fractional shortening values within the lot of study, this being of 34,9% (SD=4,48).

Table no. 2. Tabel de frecvenţa FS

FS%

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	28	3	2.7	2.7	2.7
	29	12	10.9	10.9	13.6
	30	13	11.8	11.8	25.5
	31	5	4.5	4.5	30.0
	32	10	9.1	9.1	39.1
	33	5	4.5	4.5	43.6
	34	7	6.4	6.4	50.0
	35	5	4.5	4.5	54.5
	36	2	1.8	1.8	56.4
	37	5	4.5	4.5	60.9
	38	7	6.4	6.4	67.3
	39	11	10.0	10.0	77.3
	40	16	14.5	14.5	91.8
	41	5	4.5	4.5	96.4
	42	2	1.8	1.8	98.2
	43	1	.9	.9	99.1
	44	1	.9	.9	100.0
	Total	110	100.0	100.0	

Figure no. 1. Histograma FS



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PRIMARY NON ALCOHOLIC FATTY LIVER DISEASE IN HYPERTENSIVE PATIENTS

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Keywords: *essential hypertension, primary non alcoholic fatty liver disease, circadian blood pressure rhythm, insulin resistance*

Abstract: *The aim of the present study was to investigate the prevalence of NAFLD and the relationship between insulin sensitivity and NAFLD in grade III high and very high cardiovascular additional risk essential hypertensive patients according to the circadian blood pressure (BP) rhythm. This four years prospective study conducted at the Departament of Internal Medicine from the Diagnosis and Treatment Center from Cluj-Napoca. The study included grade III essential hypertensive patients. Hypertensive patients were divided into four groups: dipper(D), non-dipper (ND), reverse-dipper (RD), extreme-dipper (ED) according the diurnal index (DI) from ABPM monitoring. All hypertensive patients underwent 24 hour ambulatory blood pressure monitoring (ABPM) (for systolic and diastolic blood pressure evaluation), blood tests and abdominal ultrasonography for the diagnosis of fatty liver disease. Thirty five hypertensive patients were included in the study, a number of 31.42% ND, 11.43% RD, 8.57% ED and 48.57% D. The prevalence of NAFLD was significantly higher in ND, RD, ED compared to D. When compared to dipper group of hypertensive patients a statistically significantly higher level of plasma insulin was observed in the group of non-dipper (86.3±17.9pmol/l vs. 62.2±203pmol/l, p<0.05), in reverse dipper (88.3±18.6pmol/l vs. 62.2±20.3pmol/l) in extreme-dippers (86.7±16.88pmol/l vs. 62.2±20.3 pmol/l, p<0.05). The altered dipping status (ND, RD, ED) of hypertension associated a higher insulin resistance that could be the pathogenetic link between the NAFLD and altered blood pressure status. Altered blood pressure status could be a marker of NAFLD in hypertensive patients.*

Cuvinte cheie: *hipertensiune arterială esenţială, steatoza hepatică non alcoolică primară, ritmul circadian tensiunii arteriale, rezistenţa la insulină*

Rezumat: *Obiectivul acestui studiu a constat în investigarea prevalenţei steatozei hepatice non-alcoolice (NAFLD) şi relaţia dintre sensibilitatea la insulină şi NAFLD în hipertensiunea arterială (HTA) de grad III risc adiţional mare şi foarte mare în conformitate cu ritmul circadian al tensiunii arteriale. Acest studiu prospectiv a fost efectuat pe o perioadă de patru ani la Departamentul de Medicină Internă de la Centrul de Diagnostic şi Tratament din Cluj-Napoca. Studiul a inclus pacienţi cu HTA esenţială gradul III. Pacienţii hipertensivi au fost împărţiţi în patru grupe: dipper (D), non-dipper (ND), reverse-dipper (RD), de extreme dipper (ED), potrivit indexului diurn (DI) de la monitorizarea ambulatorie automată (MATA). Toţi pacienţii hipertensivi au fost monitorizaţi MATA timp de 24 de ore pentru presiunea sistolică şi diastolică, li s-au efectuat analize de sânge şi ecografie abdominală pentru diagnosticarea afectării hepatice. Treizeci şi cinci de pacienţi hipertensivi au fost incluşi în studiu, un număr de 31.42% ND, 11.43% RD, 8.57% ED şi 48.57% D. Prevalenţa NAFLD a fost semnificativ mai mare în ND, RD, ED, comparativ cu D. Când au fost comparaţi cu grupul cu profil dipper s-a observat un nivel statistic semnificativ mai mare de insulină plasmatică în grupul de non-dipper (86.3 ± 17.9pmol / l vs 62.2 ± 203pmol / l, p <0,05), în reverse dipper (88.3 ± 18.6 pmol / l vs 62.2 ± 20.3pmol / l) în extreme-dippers (86.7 ± 16.88pmol/lvs.62.2±20.3pmol/l,p<0,05). Alterarea statustului dipper (ND, RD, ED) al hipertensiunii arteriale asociază o rezistenţă la insulină mai mare care ar putea fi legătura dintre patogenetice NAFLD şi modificarea statusului tensiunii arteriale. Alterarea statustului tensiunii arteriale ar putea fi un marker al NAFLD la pacienţii hipertensivi.*

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) represents a spectrum starting from fatty liver, fatty liver and inflammation to evidence of damage to hepatocytes and can progress to cirrhosis or in the most extreme form of NAFLD can progress to hepatocellular carcinoma or liver failure (1).

Non-alcoholic fatty liver disease is considered the most common liver disease affecting 15–25% of the general population (2). Primary NAFLD results from insulin resistance and NAFLD is considered as part of the metabolic syndrome (3-6).

Essential hypertension is considered an insulin resistant state (7,8) and through the basis of insulin resistance mechanisms recent studies consider NAFLD as an early mediator of atherosclerosis (9,10) and an increased cardiovascular risk factor (11).

The aim of the present study was to investigate the prevalence of NAFLD in grade III high and very high cardiovascular additional risk hypertensive patients according to circadian blood pressure (BP) rhythm and to investigate the relationship between insulin sensitivity and NAFLD in essential hypertensive patients according to the circadian blood pressure (BP) rhythm.

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MATERIAL AND METHOD

Study population

From November 2005 to December 2009 a prospective study was conducted. The study included consecutive eligible adult hypertensive patients attending at the Departament of Internal Medicine from the Diagnosis and Treatment Center from Cluj-Napoca.

The study included patients of either sex with grade III essential hypertension and additional high and very high global cardiovascular risk. Essential hypertension was defined according to the ESC/ESH 2007 Guideline European Society of Hypertension (12) as office sitting systolic BP (SBP) of ≥180 mmHg and/or office diastolic blood pressure (DBP) ≥110mmHg measured by mercury sphygmomanometer, at rest in a sitting position in at least three separate casual measurements within the last month.

Patients with mild or moderate essential hypertension or suspected secondary hypertension were excluded. Also patients with chronic alcoholism, diabetic mellitus, evidence of cardiovascular, pulmonary, renal, hepatic disease, patients with previous drug induced fatty liver treatment (corticoids,chronic salicylates,tricyclic antidepressants, tamoxifen, tetracyclines, synthetic oestrogens and amiodarone) (13,14) were excluded from the study.

Thirty five hypertensive patients gave their informed consent before taking part in the study, completed the inclusion criteria and were therefore enrolled in the study.

All hypertensive patients underwent 24 hour ambulatory blood pressure monitoring (ABPM) (for systolic and diastolic blood pressure evaluation), blood tests and abdominal ultrasonography.

The ambulatory blood pressure (ABPM) was monitored with ABPM-04, 99/BP411 - Medibase. Before the beginning of ABPM, blood pressure was measured with a mercury sphygmomanometer, with the patient seating for at least 10 minutes.

The arm with higher BP values at sphygmomanometer evaluation was chosen for ABPM. In order to reduce errors during the day all patients were asked to ensure that the arm was always parallel to the trunk when the cuff was inflated. Readings were obtained automatically at 15 minutes interval from 7:00 am to 22:00 pm and 30 minutes interval from 22:00 pm to 7:00 am. All the measurements were performed by the same investigator, using the same equipment, both at the beginning of the study and during the follow up.

Hypertensive patients were divided into four groups: dipper, non-dipper, reverse-dipper, extreme-dipper according the diurnal index (DI) from ABPM monitoring. Dipper patients were defined as 10%≤DI<20%, non-dipper defined as 0 ≤DI<10%, extreme-dipper defined as DI≥20%, reverse-dipper defined as DI<0 (15).

The diagnosis of fatty liver, was established using the noninvasive method of abdominal ultrasound followed by the exclusion of the secondary causes of hepatic steatosis: a history of another known liver disease, alcohol intake of 30g/day or more for males and 20g/day or more for females, a positive serology for hepatitis B or C virus or ingestion of drugs known to produce hepatic steatosis.

The liver ultrasonography scanning was performed by standard criteria (16,17) by the same investigator, in all patients in the morning , after overnight fasting, using the same equipment (ESAOTE MyLab,with a 3.5-MHz transducer). The presence of liver steatosis was graded semiquantitatively according to a previously reported scale (18): 0 - absent, 1 - mild, 2 - moderate, and 3 - severe steatosis.

In all hypertensive patients who fasted overnight for biochemical and metabolic profile, blood samples were evaluated by standardised routine laboratory techniques.
Serum triglycerides, total, and HDL cholesterol, glucose, insulin, alanine amino transferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT) levels were measured, using routine automated assay methods. Reference range of values, are 0–40 IU/l for ALT, 0–37 IU/l for AST, 6–20 mIU/ml for insulinaemia, 0–50 IU/l for cGT, 70–170 mg/dl for triglycerides, 60–110 mg/dl for glucose, and up to 200 mg/dl for total cholesterol.

Insulin resistance was calculated by the homeostasis monitoring assessment (HOMA) formula. The HOMA index was calculated as the product of the fasting plasma insulin level (μU/mL) and the fasting plasma glucose level (mmol/L), divided by 22.5. (19,20).

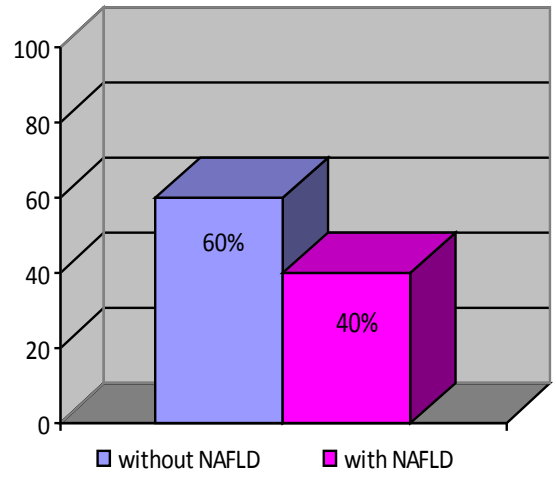
Statistical analysis.

Descriptive statistics, including means, SD, ranges and percentages, were used to characterize the study subjects. Statistical significance between groups was assessed by Student‘s t test in normally distributed for independent samples. A p-value < 0.05 was considered statistically significant. Statistical analyses were performed using SPSS and Statistica 8 programe.

RESULTS

NAFLD was present in 14 hypertensive patients (40%) with grade III essential hypertention with high and very high additional cardiovascular risk as reported in figure 1.

Figure no. 1. The prevalence of NAFLD in hypertensive patients



According to diurnal index from ABPM the thirty five hypertensive patients were devided into four groups as following: 48.57% (n=17) patients as dippers, 31.42% (n=11) patients as non-dipper, 11.43% (n=4) pacients as reverse dippers and 8.57% (n=3) patients as extreme dippers.

No statistically significant differences, between the four groups of patients in demographic baseline characteristics (p>0.05) were observed.

Baseline demographic, clinical and laboratory characteristics of the study population are presented in Table 1.

The prevalence of NAFLD was significantly higher in non dipper patients group 54.54% (n=6), reverse dipper hypertensive groups 50% (n=2) and extreme-dipper hypertensive patients 33.33% (n=1) compared to dipper hypertensive patients group 29.41% (n=5)(p<0.05).

The prevalence of liver steatosis grades according to diurnal status of dipper, non dipper, reverse-dipper,extreme dipper was observed as presented in figure 3.

Table no. 1. Baseline Demographic and Clinical Characteristics by Blood Pressure circadian rhythm

Variable	Dippers (n=17)	Nondippers (n=11)	Reverse dippers (n=4)	Extreme dippers (n=3)	p value
Gender: absolute frequency (percentage)					
Male	8 (47.05%)	7 (63.63%)	1(25%)	1(33.33%)	ns
Female	9 (52.95%)	4(36.37%)	3(75%)	2(66.67)	ns
Age: means±SD					
Male (years)	51.6±11.3	53.8±12.22	54.21±12.02	53.87±11.62	ns
Female (years)	50.2±9.78	52.2±10.84	54.66±8.99	52.33±9.79	ns
BMI (kg/m²)	32.42±3.99	35.32±4.55	36.3±7.77	35.5±3.87	ns
Mean 24h SBP (mmHg)	143.5±14.88	143.5±14.75	144.3±17.44	145.8±15.5	ns
Mean 24h DBP (mmHg)	88.7±11.05	86.3±12.06	87.5±12.41	85.3±12.77	ns
Triglycerides (mg/dl)	108.5±33.42	111.5±35.21	110.8±30.77	107.3±32.45	ns
Total cholesterol (mg/dl)	220.3±45.2	205.66±44.31	208.5±41.02	210.8±42.03	ns
HDL cholesterol (mg/dl)	47.5±3.22	46.8±4.04	46.2±3.71	48.3±4.57	ns
ALT (U/l)	19.4±7.77	22.4±8.31	23.9±6.98	24.5±8.87	ns
AST (U/l)	22.8±8.75	20.4±8.53	22.3±7.93	20.6±8.35	ns
GGT (U/l)	23.9±11.1	25.4±12.3	25.5±10.7	20.8±8.33	ns

SD = standard deviation, SBP= systolic blood pressure,DBP= diastolic blood pressure, LDL=low-density lipoprotein, HDL=high-density lipoproteins,ALT=alanine amino transferase, AST=aspartate aminotransferase, GGT= gamma-glutamyl transferase

Figure no. 2. The prevalence of NAFLD in hypertensive patients

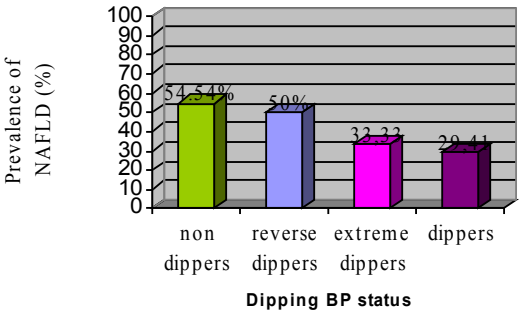
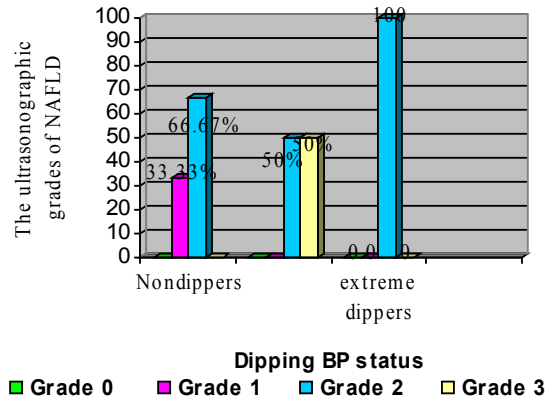


Figure no. 3. The ultrasonographic grades prevalence of NAFLD in hypertensive patients



A statistically significantly higher level of plasma insulin was observed in the group of non-dipper when compared to the dipper group of hypertensive patients (86.3±17.9pmol/l vs. 62.2±203pmol/l, p<0.05) in reverse dipper when compared to dipper hypertensive patients (88.3±18.6pmol/l vs.62.2±20.3 pmol/l) in extreme-dippers versus dipper hypertensive patients groups (86.7±16.88pmol/l vs. 62.2±20.3 pmol/l, p<0.05). In the group of non dipper, reverse dipper, extreme-dipper a significantly higher level of HOMA index were observed when compared to the dipper group of hypertensive patients (in non dipper vs. dipper: 3.7±1.03 vs.2.2±0.88, p<0.05), (in reverse dipper vs. dipper 4±0.99 vs. 2.2±0.88,p<0.05) and (in extreme dipper vs. dipper 3.6±0.97 vs.2.2±0.88, p<0.05).

DISCUSSIONS

This study revealed a significantly statistical difference of the NAFLD prevalence, between altered dipping status (non-dipper, reverse-dipper, extreme-dipper) and normal dipping status of hypertensive patients. A higher prevalence of the NAFLD was observed in nondipper hypertensive patients, followed by reverse-dipper and extreme-dipper when compared with dipper hypertensive patients. The liver steatosis grade was more severe in reverse dipper group of hypertensive patients who presented a grade 2 and 3 of NAFLD. All extreme-dipper hypertensive patients presented a grade 2 of disease.

Grade III essential hypertensive patients with altered dipping profile (ND, RD, ED) revealed a statistically significant higher level of plasma insulin when compared to dipper group of hypertensive patients suggesting that insuline resistance could play a role in the tendency of a greater end organe damage in hypertensive patients with an altered circadian rithm (non-dipper, reverse-dipper, extreme-dipper) (21,22).

The association between the nondipper status and insuline resistance, that was observed in the present study has already been demonstrated (23,24).

Altered dipping status (non-dipping, reverse-dipping, extreme-dipping) have been demonstrated in population based studies to correlate with target organe damage, including cardiovascular morbidity and mortality (25-28) progression of preexisting renal disease (29,30) and cerebrovascular disease (31).

Because the altered blood pressure status of hypertension associated both a higher insulin resistance and a higher prevalence of NAFLD brings us to the conclusion that insulin resistance could be the pathogenetic link between the NAFLD and altered blood pressure status. Altered blood pressure status could be a marker of NAFLD in hypertensive patients.

Acknolegements:

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ASSESSMENT OF CARDIOVASCULAR RISK IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE

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Keywords: *nonalcholic fatty liver disease, cardiovascular risk, metabolic syndrome*

Abstract: *Non-alcoholic fatty liver disease falls into a spectrum of liver diseases characterized mainly by macrovesicular fatty degeneration that occurs in the absence of significant alcohol consumption (20-30 g pure alcohol per day or under 200g pure alcohol / week.). We studied the cardiovascular risk of 125 patients with ultrasound appearance of fatty liver, using 4 different metods: Framingham cardiac risk score, SCORE system, Hypertensive waist, Hypertriglyceridemic waist. Prevalence of cardiovascular risk factors was high in patients with fatty liver, particularly in patients with type 2 diabetes, association of more than three risk factors increasing with age. Framingham cardiovascular risk score and SCORE system increased with age. The risk was lower in female sex and, as expected, higher in individuals presenting obesity, hypertensive waist or metabolic syndrome*

Cuvinte cheie: *ficat gras non-alcoolic, risc cardiovascular, sindrom metabolic*

Rezumat: *Ficatul gras non-alcoolic (FGNA) sau hepatopatia adipoasă non-alcoolică se încadrează într-un spectru de boli hepatice caracterizate în principal prin degenerescența grăsoasă macroveziculară ce apare în lipsa consumului semnificativ de alcool, respectiv sub 20-30 g alcool pur/zi sau sub 200 g alcool pur/săptămână. Am evaluat 125 pacienți cu FGNA din punct de vedere al riscului cardiovascular utilizând mai multe metode: Riscul Framigham, Riscul SCORE, talia hipertensivă şi talia hipertrigliceridemică. Pacienții cu FGNA au avut un risc cardiovascular mai mare decât cei de aceeaşi vârstă şi sex fără afectare hepatică, riscul crescând odată cu vârsta şi fiind de asemenea, mai mare la pacienții cu obezitate, talie hipertensivă sau sindrom metabolic.*

INTRODUCTION

Non-alcoholic fatty liver (NAFLD) fits into a spectrum of liver diseases characterized mainly by fatty macrovesicular degeneration that occurs in the absence of significant alcohol consumption, respectively under 20-30 grams of pure alcohol per day or under 200g pure alcohol / week.(1)(2)(3)

Disease spectrum is composed of three clinical-pathological entities:

1. Hepatic steatosis: is characterized by predominant in hepatocytes of macrovesicules with fatty acids and triglycerides
2. Steatohepatitis: hepatic steatosis associated with necro-inflammatory process, Mallory bodies and early fibrosis
3. Cirrhosis: liver architecture characterized by fibrosis and inflammatory infiltration associated with fatty liver. (4) (5)

Non-alcoholic steatosis is caused by multiple factors and variations, of which most frequent in practice are: nutritional causes; drugs; metabolic or genetic diseases; insulin resistance syndromes; exposure to toxins.

PURPOSE OF THE STUDY

Increasing prevalence of metabolic syndrome and diabetes mellitus among patients in conjunction with tight connections between these diseases and non-alcoholic fatty liver allow the assumption that there is a rather large mass of undiagnosed patients who have this disease.

Clinical diagnosis of metabolic syndrome is not sufficient to assess the risk of cardiovascular disease. In order to appropriate assessment and management of overall cardiovascular risk in clinical practice, it is important to take into account traditional risk factors and the additional contribution brought by abdominal obesity / insulin resistance and their related complications.

The overall risk resulting from this traditional risk factors with abdominal obesity is called global cardiometabolic risk. (6)

MATERIAL AND METHOD

We aimed to evaluate the cardiovascular risk of patients with non-alcoholic fat liver. We calculated cardiovascular risk to all those 125 patients with NAFLD (group A) and 34 subjects considered as a control group using two forms of assessment in clinical practice - Framingham risk score and SCORE scale(the HeartSCORE ® formula)

We also evaluated patients in terms of two new combinations of clinical and laboratory factors predictive of increased cardiovascular risk: hypertriglyceridemic waist and hypertensive waist.

RESULTS AND DISCUSSION

A. Hypertriglyceridemic waist

Hypertriglyceridemia size is defined as simultaneous presence of above the normal waist circumference associated with triglyceride levels above 150 mg%.

Because metabolic syndrome increases the risk of type 2 diabetes and cardiovascular disease, several organizations have proposed this screening approach to identify patients with metabolic syndrome features. Based on the consideration that waist circumference and triglyceride levels may be as important as other more demanding approaches, such as NCEP-ATP III criteria, hypertriglyceridemic waist may be the simplest tool

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available for rapid initial screening assessment of the metabolic syndrome in clinical practice. (7)

Patients in group A had a prevalence of hypertriglyceridemic waist in men of 43.2% (n = 16) and 46.6% in women (n = 41), with an overall prevalence of 45.5% (n = 57), unlike the control group, where this condition was present in 2 women (5.8%) and no man.

B. Hypertensive waist

Hypertensive waist is defined as simultaneous presence of above the normal waist circumference associated with systemic hypertension (SBP> 140mmHg or antihypertensive treatment).

Many studies consider the method to have a high sensitivity and specificity, very useful in screening for metabolic syndrome because of the ease of measuring the two parameters. Subsequently, patients with hypertensive waist will need further determinatin of other elements necessary to define the syndrome (blood glucose, triglycerides, HDL-cholesterol). (8)

In hypertensive patients of group A we detected at a size of 48 (54.5%) in women and 19 (51.3%) in men, with an overall prevalence of 67 patients (53.6%).

C. Framingham cardiac risk score

The absolute risk of developing cardiovascular disease is defined as the probability of a clinical event (in this case cardiovascular death) that will occur to a person in a period of time. In this case, the prediction interval is set at 10 years.

Over 15 years ago, the Framingham Heart Study, which followed 3 generations of men and women from Framingham, Massachusetts, revolutionized the evaluation of cardiovascular pathology in terms of treatment and especially of its prevention. Framingham risk score is being used today in clinical evaluation, taking into account a number of personal factors - age, sex, cholesterol, smoking, hypertension, diabetes mellitus - and establish the risk of developing either myocardial infarction or cardiovascular death in the next 10 years. A risk of 10% means that 10 of the 100 people who will develop heart disease or die of cardiovascular disease in the next 10 years. (9)

We calculated the risk in patients aged 30-74 years in the 2 groups and obtained these results: a total of 113 patients in group A were framed in terms of age and we calculated an average risk of 12.21239%, with a statistically significant difference compared to score of the population at the same age and sex (p = 0.000515).

Risk in the control group was 3.473684%, calculated from the 19 subjects who fit the age criteria.

We also found weak positive linear correlation between waist circumference (r = 0.137) respectively mean blood pressure (r = 0.238) and Framingham risk, signifying that patients with elevated waist circumference and blood pressure have a high average 10 years risk to suffer a major cardiovascular pathology. D. SCORE Cardiovascular risk

European Society of Cardiology has initiated development of a risk estimation (SCORE) using data from 12 European cohort studies (N = 205,178) covering a wide geographic area, at different levels of cardiovascular risk. To calculate cardiovascular risk according to SCORE system we used the formula HeartSCORE ®, which is a web program of management and risk prediction in order to assist clinicians in optimizing individual cardiovascular risk reduction. (10)

In patients of group A which were included in the age criteria for calculating cardiovascular risk according to HeartSCORE ® (n = 101), we obtained an average of 3.03%, statistically significant higher than the people of the same age and sex (1.88 %) - p = 0.001739.

A total of 20 patients in group A showed an increased cardiovascular risk (≥ 5) quantified by SCORE system and many were men (n = 13).

Cardiovascular risk score estimated using Framingham and SCORE systems increased with age (Spearman coefficient r = 0.64, r = 0.47 respectively).

The risk was lower in women and greater in those presenting obesity, hypertensive waist or metabolic syndrome.

CONCLUSION

Cardiovascular risk of subjects with liver fat is extremely large and often overlooked by the treating physician that is generally concerned only with digestive pathology. Information and involvement of professionals from all levels of health care is unfortunately not enough supported, while addressability, adherence and compliance to lifestyle changes of patients is too far from an acceptable threshold.

In response, many patients with cardiovascular disease are neglected in terms of existence for other associated pathologies which reiterates the assertion that non-alcoholic fatty liver can be considered as hepatic component of the metabolic syndrome.

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LIVER FIBROSIS IN CHRONIC VIRAL HEPATITIS C

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Keywords: *chronic hepatitis C, cirrhosis, liver fibrosis*

Abstract: *Chronic hepatitis C is an inflammatory liver disease caused by infection with hepatitis Cvirus, potentially evolving to cirrhosis, hepatocarcinoma, death. HCV infection in Romania is responsible for 64% of chronic hepatitis and 55.8% of liver cirrhosis. To establish the treatment needs should be staging the disease, the liver fibrosis caused by viral action constitutes an important means of assessing the severity of liver injury.*

Cuvinte cheie: *hepatită cronică virală C, ciroză hepatică, fibroză hepatică*

Rezumat: *Hepatita cronică virală C este o boală inflamatorie hepatică determinată de infecţia cu virusul hepatitic C, cu potenţial evolutiv spre ciroză hepatică, hepatocarcinom, deces. În România infecţia VHC este responsabilă de 64% din hepatitele cronice şi 55,8% din cirozele hepatice. Pentru stabilirea necesităţilor de tratament se impune stadializarea bolii, nivelul fibrozei hepatice determinate de acţiunea virală reprezentând un important mijloc de apreciere a gravităţii afectării hepatice.*

PURPOSE OF THE STUDY

To establish the treatment needs should be staging the disease, the liver fibrosis caused by viral action constitutes an important means of assessing the severity of liver injury.

MATERIAL AND METHOD

We have studied 184 patients diagnosed with chronic hepatitis C who were admitted between January 2002 - March 2009, in the Emergency Clinical Hospital Sibiu and Military Emergency Hospital Sibiu.

Inclusion criteria

Diagnosis of chronic hepatitis C was made on clinical criteria, ultrasound, laboratory- persistent changes in liver enzymes more than six months (although they were minimal), the presence of HCV antibodies.

Quantitative determination of viremia in most patients was performed after liver biopsy, if the histological changes were entered into treatment protocols.

Exclusion criteria

Exclusion criteria were established in the failure of patients to perform liver puncture and the presence of contraindications bios points.

For determination of contraindications for biopsy in all patients were performed:

- ultrasound evaluation (to rule out the presence of ascites, the expansions of bile canaliculi, the presence of hemangiomas)
- chest radioscopy

Biological evaluation excluding mainly of haemostasis disorders, severe anemia, severe cholestasis.

Punctures were made with these Menghini needles of 1.6 mm diameter (16 gauge) by transthoracic approach, with local anesthesia prior to post-expiratory apnea.

All fragments analyzed had lengths greater than 15 mm. In very few situations where we extracted a smaller piece we repeated extraction of a representative excerpt. Histopathology of liver fragments obtained was performed by the pathological laboratory of the Clinical Hospital of Emergency. Histopathological examination results were quantified using the Ishak score, the need for uniform analysis of cases.

Statistical analysis

Statistical analysis of results was done on several variables, the distribution by age, sex, profession, type of work, living environment, possible sources of infection, alcohol abuse or the presence of diabetes correlated with changes detected in biopsy fragments necroinflamatory-activity, fibrosis, presence of steatosis.

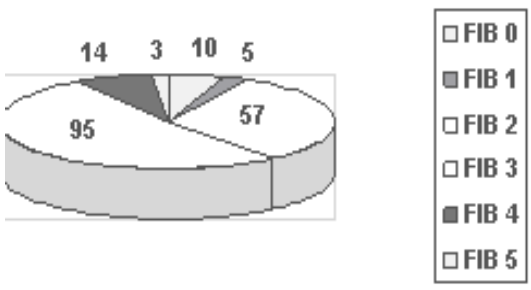
RESULTS AND DISCUSSIONS

Fibrosis

The entire group of 184 subjects on key values Ishak fibrosis index had the following distribution (fig.1):

- Fibrosis 0 = 10 subjects (5.43%)
- Fibrosis, 1 = 5 subjects (2.71%)
- Fibrosis, 2 = 57 subjects (31%)
- Fibrosis, 3 = 95 subjects (51.6%)
- Fibrosis 4 = 13 subjects (7%),
- Fibrosis 5 = 3 subjects (1.6%)

Figure no. 1. The repartition of the fibrosis levels in the studied group



Fibrosis were considered significant higher values than 3.

Thus group consisted of 72 (39.1%) patients with insignificant fibrosis, 109 (59.2%) patients with significant

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fibrosis and three subjects with cirrhosis (1,6%) (fig.1)

Distribution by sex

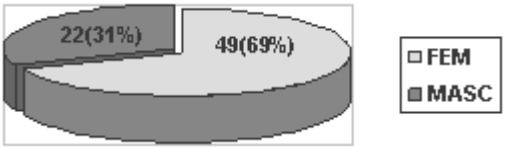
Sex distribution in the whole group was as follows (fig 2): 121 females (65.8%);63 mens (34.2%)

In the group with fibrosis below 3, the distribution by sex was: Female 49 (69%), male 22 (31%) (Fig. 3)

In the group with fibrosis more than 3 distribution by sex was: Female 72 (69%);males 41 (31%)

Figure no 2. The repartition on gender in the studied group

Figure no. 3. The repartition on gender in the group with non-significant fibrosis



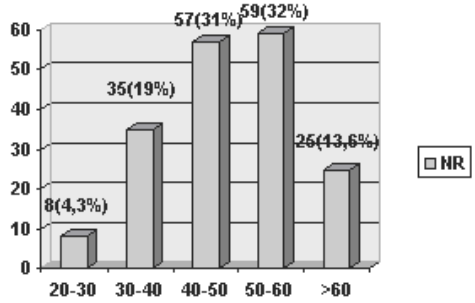
Age

The average age of patients studied was 48.45 years, with limits between 22 and 65 and a standard deviation of 10.18.

Structuring by age group was as follows (fig. 4):

- In group 20-30 years were enrolled 4.3% of subjects (8).
- The group 30-40 years, 19% (35).
- The group 40-50 years, 31% (57).
- The group 50-60 years, 32% (59).
- Over 60 years, 13.6% (25).

Figure no. 4. The repartition on age groups



Note that most of the subjects (63%) were aged between 40 and 60 years.This distribution can be explained by the presence of virus need for a long period required for establishment of chronic hepatitis amendments requiring virus persistence and its action in the body (1, 2, 3).

In the group average age of female subgroup was significantly lower compared to male subgroup, which is not found in the detailed analysis on the group index of fibrosis (Ishak) <3 or> 3.

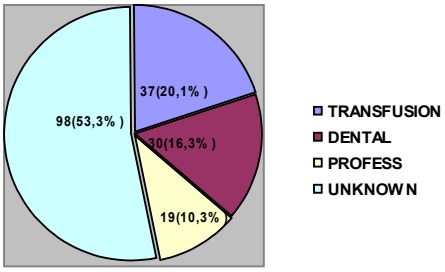
This could be explained by the general trend of more severe hepatitis C virus in males, which could cause symptomatic disease earlier than in females, leading to presentation to a medical service and investigation.

Source of infection (fig.5)

Given the long duration of infection until diagnosis, source of infection could be suspected in a small number of patients, many remain unknown (6,9). (fig. 5)

Thus, of the 184 patients 37 (20.1%) had undergone blood transfusions, the most likely source of infection is that, with a mean age of 47.59 years and a standard deviation of 9.7630 (16.3%) of them underwent dental treatment more frequently than others, with an average age of 48.5 years and a standard deviation of 10.69. 19 (10.3%) were medical workers, most likely cause of infection was occupational exposure (4, 5-8), with an average age of 47 years, standard deviation of 11.25. With all information requested on 98 patients in group (53.3%) source of infection could not be established, with a mean age of 49.04 years and a standard deviation of 10.08. Between the ages of four groups there was no significant difference, p = 0.764.

Figure no. 5. The repartition of the group by the way of infection



Living environment

Patients in the study came from rural areas at a rate of 24.5% (45 subjects) and urban areas at a rate of 75.5% (139 subjects) .This can result in better informing patients about the disease in urban areas, with their increased addressability to the family physicians in urban areas. The physicians are more informed about the risk of long-term development of the illness, about the epidemiological conditions, they have increased opportunities to participate in symposiums, conferences, or accessibility to the Internet.

Figure no. 6. Distribution according to lifestyle

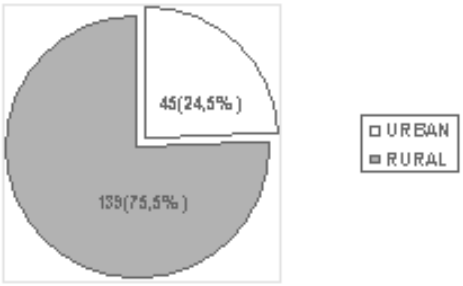
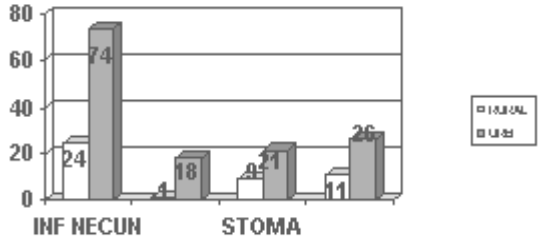


Figure no 7. The correlation between the way of living and the way of infection

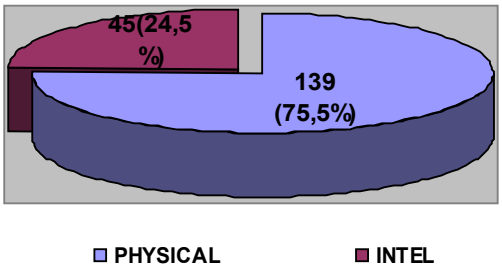


Also, there was not a significant correlation between the environment of origin of subjects and the ways of getting infected.

Type of activity

In group the proportion of subjects in the study to provide physical labor was 75.5% of them (139), and those who perform intellectual work 24.5% (45)

Figure no. 8. The type of performed work



There is a significant correlation between the type of activity and the source of infection both in the overall group and the fraction with significant degree of fibrosis.

In patients who performs physical work the number of unknown source of infections was significantly higher than those who provide intellectual work. Cases of occupational infection occurred less frequently in situations of occupation based on physical labor, because they are less exposed to contamination with HCV.

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NON-INVASIVE MARKERS OF LIVER FIBROSIS IN CHRONIC VIRAL HEPATITIS C

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Keywords: *liver biopsy, hepatic fibrosis, non-invasive markers*

Abstract: *In assesing liver fibrosis liver biopsy is still considered "gold standard" but since the process of hepatic fibrosis is governed by a series of mediators tried to find non-invasive methods for assessment of hepatic fibrosis, which is devoid of risks and repeated at different stages of disease and treatment.*

Cuvinte cheie: *puncție biopsie hepatică, fibroză hepatică, markeri neinvazivi*

Rezumat: *În evaluarea fibrozei hepatice puncția biopsie hepatică se consideră încă "standardul de aur" dar având în vedere că procesul de fibroză hepatică este guvernat de o serie de mediatori s-a încercat găsirea unor metode de apreciere neinvazivă a fibrozei hepatice, care să fie lipsite de riscuri şi repetitive în diferite stadii de boală şi tratament.*

INTRODUCTION

Conditions should be met by serological marker would ideally be:

1. be specific for liver
2. have adequate statistical value
3. its levels are not influenced of comorbidity (eg. renal disease)
4. measuring one or more of the following:
   - Fibrosis stage,
   - Activity of extracellular matrix deposition,
   - The activity of extracellular matrix degradation.
5. be easily performed
6. have a low cost price
7. be reproductible

POURPUSE OF STUDY

Comparing the results obtained on the degree of fibrosis by liver biopsy and obtained by calculating several noninvasive markers in a group of patients with chronic hepatitis C.

MATHERIAL AND METHOD

We have studied patients with chronic hepatitis C, hospitalized in January 2002 - March 2009, in Sibiu County Emergency Hospital and Emergency Military Hospital Sibiu. All patients were biopsy using Menghini needles of 16 G, which were extracted fragments minim15 mm.

Analysis of liver fragments was made after the score Metavir considering the significant fibrosis ≥ F2 values.

Our study took place in two distinct groups: first group included 184 subjects who fibrosis index compared with values obtained by biopsy obtained by calculating the scores priori FORNS, FIBROINDEX, FIB-4 and a total of 30 subjects was applied and FIBROTEST.

We intend to make partial batch analysis of 30 subjects.

RESULTS AND DISCUSSIONS

It was composed of 22 women (73%) and 8 men (37%).

Distribution of age groups was: 20-29 years 2 subjects (6.66%), 30-39 years 10 subjects (33,33%), 40-49 years four subjects (13.33%), 50-59 years, 11 patients (36.66), 60-65 years three subjects (10%).

Of the entire group to analyze biopsy fragment scale Metavir 4 subjects had F1 fibrosis, 21- F2 and 5 subjects had fibrosis F3. Were considered significant values of the fibrosis ≥ 2.

APRI score (1)

APRI = (AST (/ upper limit of normal) x100) / number of platelets (10^9 / l)

Cut off values used were:

Value ≤ 0.5 = no significant fibrosis.

Value of 1.5 = presence of significant fibrosis.

Values ≥ 2 = cirrhosis

Have been classified a total of 17 subjects (56.6%).

The following parameters were recorded:

Table no. 1. Results obtained at the APRI analysis

SCOR	SENS	SPEC	PPV	NPV	ACC
≤ 0,5	0,85	0,1	0,65	0,25	0,6
> 1,5	1	0,15	0,16	1	0,23

Note that there have been good sensitivity values for both the absence of fibrosis (0.85), and for the presence of fibrosis (1), the NPV for the presence of fibrosis (1), but lower scores for other parameters.

AUROC for detection of significant fibrosis was 0.56.

No significant values were recorded for liver cirrhosis.

Wai's in the original study were obtained as follows:

Table no. 2. Values obtained in the WAI original study

SCOR	SENS	SPEC	PPV	NPV
≤ 0,5	0,91	0,47	0,61	0,86
> 1,5	0,41	0,95	0,88	0,64

AUROC value for detection of significant fibrosis was 0.88.

While numerous studies have been conducted that have examined only APRI score or combination of this and other scores (2-6).

Forns score

FORNS score = 7.811 to 3.131 x ln (no count) + 0.781 × ln (GGT) + 3.467 x age-0.014 x ln (cholesterol).

Values less than 4.2 certify the absence of fibrosis

Higher values of 6.9 signifies the presence of significant fibrosis (7).

They recorded the following results:

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Have been classified a total of 10 subjects (33.3%).

Table no. 3. Results obtained in the FORNS analysis

SCOR	SENS	SPEC	PPV	NPV	ACC
<4,2	0,95	0,27	0,69	0,75	0,7
> 6,9	1	0,18	0,31	1	0,4

AUROC for the detection of significant fibrosis was 0,63.

The original Forns study was obtained AUROC 0.94.

Have been developed and other studies that have found lower results in patients with genotype 3, which call lower cholesterol values (8, 9).

FIB-4

4 FIB score combines the following elements: **age (years) x AST (U / l) / platelets (10^9 / l) x √ ALT (U / l)**

Values **<1.45** excluded the presence of significant fibrosis.

Values> **3.25** confirms the presence of significant fibrosis (10).

They obtained the following results:

Could not be classified a total of 10 subjects (33.3%).

Table no. 4. Results obtained in the FIB-4 analysis

SCOR	SENS	SPEC	PPV	NPV	ACC
<1,45	0,92	0,18	0,46	0,75	0,5
> 3,25	1	0,15	0,16	1	0,23

AUROC value for detection of significant fibrosis was 0.59.

FIBROINDEX

Formula: 1.738 to 0.064 (Tr x 10^4 / mm $^{3)}$ + 0.005 (AST (U / l)) + 0.463 (gamma globe. (G / dl))

Values **<1.25** are representative of the absence of significant fibrosis.

Values> 2.25 are representative of the presence of significant fibrosis (11).

They obtained the following results:

Could not be classified a total of 19 subjects (63.3%)

Table no. 5. Results obtained in the FIBROINDEX analysis

SCOR	SENS	SPEC	PPV	NPV	ACC
<1,25	1	0,4	0,77	1	0,8
> 2,25	1	0,14	0,04	1	0,17

AUROC value for detection of significant fibrosis was 0.55.

Fibro Test team imagined Imbert-Bismuth and associates in 2001 met several determinations of markers, much less used in practice (12).

Index calculation is made according to a formula, after determining the following components:

- Alpha 2-macroglobulin;
- Total bilirubin;
- Gamma-GT;
- A1 apolipoprotein;
- Haptoglobin

combined with age and sex of the patient, a computer algorithm (USPTO 6,631,330). This test has not let quality unclassified subjects.

They obtained the following data:

Tabelul nr. 6. Results obtained in the FIBROTEST analysis

SCOR	SENS	SPEC	PPV	NPV	ACC
	1	0,31	0,65	1	0,7

AUROC for significant fibrosis detection: 0,66. The initial studies were obtained range from 0,84 to 0,87.

While comparative studies have been conducted on large groups of patients with high PPV affirming significant fibrosis, especially in subjects with elevated values of Fibrotest (13, 14).

APRI score is the quality that uses routine determinations in clinical practice and is easy to calculate, with good results in the original study, AUROC 0,88 for detection of significant fibrosis in our study were much lower values are obtained-0,56. Forns index also uses the usual laboratory tests, mentioning the possibility of results due to the high values of GGT change (alcohol) or cholesterol which may be dependent on genotype (3). AUROC for detection of significant fibrosis was the study's original Forns 0,94. In our study had a value of only 0,66. They won, but good values of both sensitivity and excluding significant fibrosis in affirming it. FIBROINDEX and Fib-4 used in calculation routine determinations in clinical practice, but in our study were obtained low values for AUROC affirmation fibrosis, significant increased sensitivity to both assertion and the absence of this fibrosis.

A negativ element in the use of these scores is that they show a range of values that do not qualify subjects, this limiting their use. In our study, remained unclassified 56.6% (APRI), 33.3% (Forns), 33.3 % (Fib-4) and 63.3% (FIBROINDEX).

Fibrotest-has the advantage that it can classify all patients, with sensitivity in the detection of fibrosis, but the PPV of moderate value.

Shows the important disadvantage of cost, using determinations are not routinely performed and a particular algorithm.

Clearly very different values obtained in subgroup analysis presented is also due to small number of subjects analyzed, the impossibility of analyzing using Fibrotest a more representative group.

CONCLUSIONS

Using non-invasive markers for assessing liver fibrosis in chronic hepatitis C can be used in a limited number of cases; are frequent cases when subjects can not be classified, some of them shows the high cost price. It is possible that a conjunction of several tests to ensure more correct classification of a larger number of patients, in this sense there is more and more studies.

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NON-INVAZIVE METHODS FOR HEPATIC FIBROSIS EVALUATION

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Keywords: *non-alcoholic fatty liver disease, liver fibrosis, non-invasive markers*

Abstract: *Since it is known that patients with fatty liver and advanced fibrosis are prone to evolution to the final stages of the disease- cirrhosis and liver biopsy is invasive, expensive and marked by multiple complications, there is currently a concern increasingly higher by finding reliable methods of non-invasive diagnosis of the degree of inflammation and liver fibrosis. We evaluated 125 patients with non-alcoholic fatty liver using 7 non-invasive method of calculating the degree of liver fibrosis currently available: AST / ALT ratio, Forns fibrosis score, FIB 4, API, ASPRI, APRI and Fatty Liver Index.*

Cuvinte cheie: *ficat gras non-alcoolic, fibroza hepatică, evaluare non-invazivă*

Rezumat: *Deoarece se ştie că pacienţii cu ficat gras şi fibroză avansată sunt predispuşi la evoluţia spre stadiile finale ale bolii, respectiv spre ciroză, iar biopsia hepatică este invazivă, scumpă şi marcată de multiple complicaţii, există în prezent o preocupare din ce în ce mai mare către găsirea unor metode fiabile de diagnostic non-invaziv al gradului de inflamaţie şi fibroză hepatică. Am evaluat 125 pacienţi cu hepatopatie adipoasă non-alcoolică utilizând 7 metode de calcul non-invaziv al gradului de fibroză hepatică disponibile în prezent, şi anume: raportul ASAT/ALAT, scorurile de fibroză Forns, FIB 4, API, ASPRI, APRI şi evaluarea Fatty Liver Index.*

INTRODUCTION

Considering the quite low predictivity of ALT, GGT and ultrasound as well as risk and variability of liver biopsy results, non-invasive assessment of fibrosis using batteries of biochemical tests seems to be one pertinent solution for correct future assesment of non-alcoholic steatohepatitis. Costs are likely to be similar to those of Fibro Test (about € 100), much cheaper than a liver biopsy or MRI. Patients with high score SteatoTest-imagined by Poynard, Ratziu et al. , showed increased age, BMI, ALT, AST, GGT, glucose, triglycerides but also of haptoglobin, apolipoprotein AI (ApoA1), α2-macroglobulin, bilirubin and cholesterol. (1)

Independent predictor of advanced fibrosis were age, BMI, hyperglycemia, platelet count, albumin level, AST / ALT ratio. A scoring system that uses these 6 parameters obtained an AUC of 0.88 in the estimation group and 0.82 in validation group.A lower cut-off score (-1,455) could exclude fibrosis with relatively high accuracy and negative predictive value of 93% for the estimation group and 88% in the validation group. (2)

Intra-individual variation of biochemical markers proved to be very small and food intake did not significantly affected the results of FibroTest or ActiTest, so this tests allows a very affordable and effective evaluation of patients with chronic liver disease. (3) In this study it was not possible an histological assessment of liver fibrosis by liver biopsy puncture because the patients refused intervention. Therefore we decided to assess the degree of liver fibrosis by non-invasive methods, using clinical data and serum markers.

PURPOSE OF THE STUDY

We aimed to assess the degree of liver fibrosis by non-invasive methods using clinical data and serum markers in 125 patients with non-alcoholic fatty liver.

MATERIAL AND METHODS

We used 7 non-invasive methods of calculating the degree of liver fibrosis that are currently available, in order to assess all the 125 patients, namely: AST / ALT ratio , Forns index , FIB 4, API, ASPRI, APRI and Fatty Liver Index.

RESULTS

Table no. 1. Liver fibrosis Scores of patients (average / std. dev)

INDEX FORNS	3.9	±1.5733
Fib 4	0.00047	±0.00033
SCOR APRI	0.0034	±0.0022
SCOR ASPRI	3.10804	±1.21032
ASAT/ALAT	1.032	±0.622

- **FIB 4 SCORE**

To optimize management of patients with chronic HCV liver disease, were developed more non-invasive tests to determine the degree of liver fibrosis. A study by Vallet-Pichard et al. validated non-invasive simple and cheap test called FIB- 4 that combines standard biochemical values (platelets, AST, ALT) and age in a series of 847 liver biopsies performed on patients with VHC infection.The authors compared results of 592 patients in whom determinations were made of FIB-4 and FibroTest in the same day. It was found that FIB-4 test allowed correct identification of patients with severe fibrosis (F3-F4) and cirrhosis with an AUC of 0.85 and 0.91 respectively.

An index <1.45 had a negative predictive value of 94.7% to exclude severe fibrosis with a sensitivity of 74.3%, while a score greater than 3.25 showed a positive predictive value of 82.1% to confirm significant fibrosis (F3- F4) with a specificity of 98.2%. Using these limits, 72.8% of 847 biopsies were correctly classified. Also, Fib-4 was correlated closely with results FibroTest for scores <1.45 or> 3.25 (kappa = 0.561, P <0.01). In conclusion, for values outside the range 1.45-3.25, FIB-4 score is a simple, reliable and cheap to assess liver fibrosis, proving consistent with results of FibroTest. (4)

Fib-4 = (age (years) x AST (U / L)) / (count (109 / L) x ALT (U / L) / 2) (5)

We calculated FIB-4 and found that 124 cases (99.2%) had values <1.4, which suggests absence of severe fibrosis

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(median of 0482), and only one case shows the index of 1.8 (not fitting into evaluation).

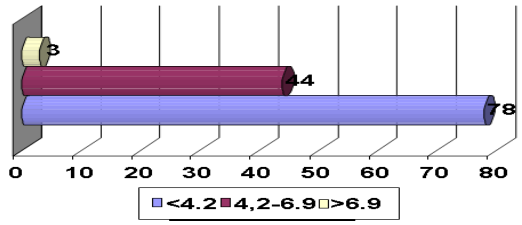
➢ **FORNS Fibrosis Score**

In a 2006 study published in Gut, the authors used more non-invasive scores of liver fibrosis evaluation in patients with chronic HCV liver disease, Forns score being assessed as the best predictor of non-invasive liver fibrosis. (6)

Forns score = 7.811–3.131 ln (plt (10^9/l)) + 0.781 ln(GGT(UI/l)) + 3.467 ln (age (yrs)) – 0.014x (cholesterol (mg/dl)(6)

They used cut off levels of <4.2 to rule out liver fibrosis. We calculated the Forns score obtaining a mean (average) of 3.78097 (± 1.573306). A total of 78 patients (62.4%) were scored Forns <4.2, 44 patients (35.2%) had a score between 4.2 and 6.9, while only 3 patients scored more than 6.9 suggesting significant liver fibrosis .

Figure no. 1. Distribution of patients according to the score FORNS

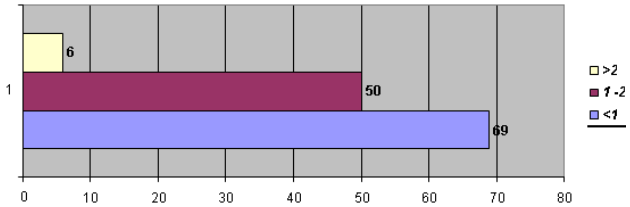


➢ **AST / ALT RATIO**

Several recently published studies have shown that patients with non-alcoholic steatohepatitis (NASH) and normal transaminases may have liver fibrosis or cirrhosis. In a study on 36 patients with type 2 diabetes and NASH, diabetes was the only factor independently associated with liver fibrosis, the aim being to detect predictors of cirrhosis in patients with NASH and diabetes. In these patients , AST: ALT ratio ranged from 0.41 to 1.85 with an average of 0.98 ± 0.26. Stronger statistical methods that used multiple regression calculations found statistically significant differences between patients with and without fibrosis on AST, ALT and AST / ALT> 1 in approx. 80% of cases, with a sensitivity of 55% and a specificity of 92%, concluding that these parameters can be useful in predicting liver fibrosis in diabetic patients with non-alcoholic steatohepatitis. (7)

In patients with liver steatosis we found an average AST: ALT ratio of 1.087252742. More specifically, 69 patients had a score <1 (55.2%), 50 patients had a score between 1-2 (40%) and 6 patients scored above 2.

Figure no. 2. Distribution of patients according to the AST/ALT ratio



➢ **APRI SCORE**

Score APRI (AST to Platelets index ratio) was initially described by Wai et al, calculated as **APRI = ((AST / upper limit of normal) / platelet count (10^9 / L)) × 100)**

It is a very simple test using laboratory parameters of wide accessibility and very easy to calculate. Several studies have demonstrated the accuracy of this test to identify significant fibrosis and cirrhosis of liver, so it is considered that using cut-off limits proposed by authors can be classified approximately 50% of patients with chronic liver diseases, especially those without HCV chronic hepatitis, without the need to conduct liver biopsy. (8) It appears that in patients with HCV hepatitis, but also in patients with liver transplant, the APRI value> 1.4 has a sensitivity of 91% and specificity of 75% in the detection of fibrosis F> 2. (9) All of our subjects had values of APRI <1.4, with an average of 0.341, suggesting the absence of hepatic fibrosis F> 2 in this group of patients.

➢ **API SCORE**

Originally studied in order to evaluate the degree of non-invasive liver fibrosis in patients with viral hepatitis HBV, API score (Age / Platelets Index) has demonstrated statistic viability, showing a significant correlation with the the degree of liver fibrosis proven by liver biopsy. (r = o.669, p <0.001). **Cut off limit is <1.5,** and a higher API score (eg 4, 6, 8) is considered to prove an even more severe degree of liver fibrosis. (10)

Table no. 2. API score calculation method

API	Age(years) <30=0; 30-39=1; 40-49=2; 50-59=3; 60-69=4; ≥70=5
	Platelets (10^9/l): ≥225=0; 200-224=1; 175-199=2; 150-174=3; 125-149=4; <125=5
	AP index(API) is the sum of the above (possible values = 0-10)

In our study we found an API score > 1.5 in 119 patients (95.2%) with values predominantly between 4 and 8.

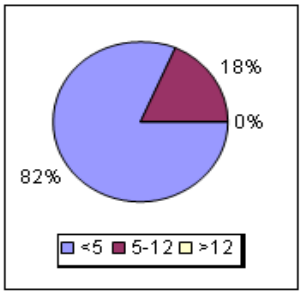
➢ **ASPRI SCORE**

Three independent factors: age, the long axis of the spleen and platelet count were used in designing this score. To exclude the effect of fluctuations in transaminases (as the case of AST in the APRI score, widely accepted as a non-invasive test) this parameter was replaced with spleen size.

Regarding the age factor, a score was calculated a gravity score as follows:<30 years-0 points., between 30-40 years-1 pt., 40-50ani-2pt, 50-60 years-3pt., 60-70 years-4pt. Over 70 years-5 points

SPRI = spleen diameter (cm) / platelets count (10^9 / l) x 100 ASPRI = age score + SPRI

Figure no. 3. Distribution according to the ASPRI score



In a study published in 2007 were demonstrated statistical significant correlation with liver fibrosis using all the tests: APRI, API, SPRI and AST / ALT , but ASPRI showed the highest correlation with fibrosis (r = 0.703, P <0.001). Using a cutoff score> 12 , the cirrhosis was identified correctly by 96.3% positive predictive value and a score below 5 this was of 100% negative predictive value. (10)

Our patients had the following ASPRI scores:ASPRI <5 = 102 patients - 81.6%, ASPRI> 12 = 0 patients, ASPRI between 5 and 12 = 23 patients - 18.4%.

➢ **FATTY LIVER INDEX**

Fatty Liver Index (FLI) or steatosis prediction index is presented by Italian researchers using a simple formula including triglycerides levels (mg / dl), BMI (kg/m2), GGT (U /

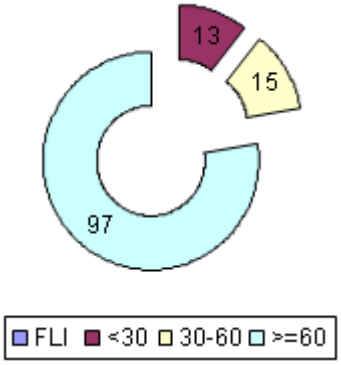
L) and waist circumference (cm) resulting in a numerical value.

One result of FLI over 60 signifies a 85% possibility of having steatosis while a FLI value below 30 means more than 86% probability of not having fatty liver. (11)

$$FLI = (e^{0.953*\log(\text{triglycerides}) + 0.139*IMC + 0.718*\log(GGT) + 0.053*\text{waist} - 15.745}) / (1 + e^{0.953*\log(\text{triglycerides}) + 0.139*BMI + 0.718*\log(GGT) + 0.053*\text{waist} - 15.745}) * 100$$

FLI calculation showed that only 13 subjects had levels of FLI score below 30, but these patients demonstrated mild steatosison liver ultrasound with posterior attenuation, most patients - 77.6% (n = 97) having FLI values> 60, confirming thus also by this method the presence of fatty liver.

Figure no. 4. Distribution of patients according to FLI



DISCUSSIONS

- Non-invasive calculation of the degree of liver fibrosis using proprietary formulas for other chronic liver diseases had slightly different results depending on the formula used: no patient with severe fibrosis (APRI and FIB- 4), 3 patients with severe fibrosis (Forns score), 44.8% - liver fibrosis (AST / ALT ratio > 1), 102 patients (81.6%) in whom can be surely excluded hepatic cirrhosis –according to ASRI score, 119 patients with API score values> 1.5 , which signifies the existence of a degree of liver fibrosis.
- Calculation of FLI (Fatty Liver Index) confirm the applicability of this assay based on triglyceride levels, BMI, GGT and waist circumference in the prediction of fatty liver, most patients (n = 97) having FLI values> 60, confirming the existence of fatty liver.
- In patients with non-alcoholic fat liver, non-invasive assessment of liver fibrosis by the methods described above may be a step up in the diagnostic algorithm, following that in subjects with elevated or inconclusive results to perform a biopsy liver.

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CORRELATION BETWEEN THE SERUM LEVELS OF TRANSAMINASES AND THE FIBROSE STAGE OF THE LIVER IN CHRONIC HEPATITIS

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Keywords: *chronic hepatitis, liver fibrosis, percutaneous liver biopsy, ALAT, ASAT*

Abstract: *Fibrogenic reaction is a consequence of immunological mechanisms that have developed in the presence of the virus influencing fibrogenesis. The aim of this study is to observe whether there is any correlation between histological changes and high ALAT and ASAT values. All patients included in our study presented some degree of fibrosis, a fact that may be explained by the easy subjective symptomatology of the disease and the lack of reliable tests, except liver biopsy, for the detection of fibrosis. The ASAT / ALAT report has been <1 in all cases. According to the results we have obtained, the histological activity index may be correlated with the degree of fibrosis, and the ASAT and ALAT serum values are significant in relation to the degree of fibrosis; therefore they may be used for the purpose of monitoring the treatment of fibrosis regression during therapy.*

Cuvinte cheie: *hepatita cronică virală, fibroza hepatică, puncție biopsie hepatică, ALAT, ASAT*

Rezumat: *Reacția fibrogenică este consecința mecanismelor imunologice desfășurate în prezența virusului care are influență asupra fibrogenezei. Scopul studiului a fost de a observa dacă există o legătură între modificările histologice şi valorile crescute ale ALAT şi ASAT. În acest studiu toți pacienții au avut un anumit grad de fibroză, fapt explicat prin simptomatologia subiectivă uşoară a bolii şi lipsa unor teste fiabile pentru descoperirea fibrozei în afară de biopsia hepatică. Raportul ASAT/ALAT a fost <1 la toate cazurile. Conform rezultatelor obținute indicele de activitate histologică este în corelație cu gradul de fibroză, valorile serice ASAT şi ALAT sunt semnificative în raport cu gradul de fibroză, ele putând fi recomandate în urmărirea tratamentului de regresie a fibrozei sub tratament.*

INTRODUCTION

Hepatic viral infections are one of the major causes for the development of liver fibrosis. It is still uncertain why human beings are not able to eliminate the infection with B and C hepatitis viruses (1). Once in the body, 40-50% of the hepatic viruses latently evolve towards a chronic form; in a relatively long period, of 20 to 30 years, 20% of these viruses evolve to cirrhosis. 1-4% of the patients with cirrhosis will present hepatocellular carcinoma.

Fibrosis is a dynamic process, which depends on the transcriptional gene and the extra-cellular matrix that synthesizes the proteoglycans and organizes them into a three-dimensional structure.

Experimental models (2) contributed to defining the mechanisms whereby hepatic fibrosis is induced. Fibrogenic reaction is a consequence of immunological mechanisms that have developed in the presence of the virus influencing fibrogenesis.

PURPOSE OF THE STUDY

The purpose of this study is to investigate the correlation between the histological activity index (HAI) and the degree of fibrosis to the serum levels of alanin-aminotransferase (ALAT) and aspartatamino-transferase (ASAT), in patients with chronic hepatitis of B and C viral etiology, taking as reference standards the histological results obtained from the material collected by liver biopsy.

MATERIAL AND METHOD

This study is based on the observation of 140 patients with chronic viral hepatitis (type B, C and B + C) at whom percutaneous liver biopsy (PLB) was performed in Oradea County Hospital, between March 2009 - March 2010.

The criterion for inclusion in the study was the absence of antiviral therapy in patients with chronic hepatitis.The distribution of cases by sex, age and etiology is shown in Table I

The histological diagnosis was based on the material obtained by liver biopsy. Tissue samples were placed in 10% formaldehyde solution.

The processing was performed in paraffin blocks of which 5µ slices were cut and colored in standard hematoxylin and eosin staining, Masson Trichrome staining and the reticulin method.

The histopathological changes observed were the parenchymal lesions of the liver, as well as the size and composition of the port space, the changes in Kupffer cells, biliary canalicula and others.

The liver lesions were categorized and scored using the Metavir and the Knodell scores (3.4). Such forms of evaluation are essential for diagnosing, treatment choice, prognosis estimation, and the clinical observation of these pathologies.

The serum levels of ALAT and ASAT were obtained by kinetic method using a Hitachi 902 Cobas-Mira device type (normal values: ASAT <38 U/L in men and <32 U/L in women, ALAT <41 U/L in men and <31 U/L in women).

For the statistical interpretation of data, the SPSS, version 17, was used for calculating the averages of parameters, the standard deviations, the median, the coefficient of variations, the variation range (min-max) and the quartila variation (5).

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Table no. 1. The distribution of subjects in relation to etiology, sex and age groups

ETIOLOGY																	
HCV						HBV						HBV+HCV					
<40 years old		40-60 years old		>60 years old		<40 years old		40-60 years old		>60 years old		<40 years old		40-60 years old		>60 years old	
M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
FREQUENCY																	
12	18	35	45	2	2	5	7	5	3	1	0	2	0	1	1	1	0
Total: 114 cases						Total: 21 cases						Total: 3 cases					
PERCENT																	
24.5	27.7	71.4	69.2	4.1	3.1	45.5	70	45.5	30	9.1	0	50	0	25	100	25	0

Table no. 2. Mean values of transaminases in chronic viral hepatitis, in relation to etiology and sex

SEX	ETIOLOGY		ALAT	ASAT
MASCULINE	HVC	Mean	94.43	82.29
		N	49	49
		Std. Deviation	18.753	18.677
	HVB	Mean	94.45	79.45
		N	11	11
		Std. Deviation	9.310	16.121
	HVC+HVB	Mean	92.25	74.00
		N	4	4
		Std. Deviation	13.817	14.213
FEMININE	HVC	Mean	90.75	77.85
		N	65	65
		Std. Deviation	21.091	15.733
	HVB	Mean	104.50	90.30
		N	10	10
		Std. Deviation	20.845	22.774
	HVC+HVB	Mean	102.00	67.00
		N	1	1
		Std. Deviation	.	.

The Student Test was used to compare the average values with the normal distribution.

RESULTS

Laboratory results were compared with the results obtained after performing liver biopsy, which constituted the reference standard for the diagnosing of liver fibrosis.

The mean values of serum transaminases (ALAT, ASAT) (see Table II) were significantly increased statistically ($p < 0.001$), as compared to normal values in both chronic hepatitis B (HBV) and in chronic hepatitis C (HCV). The highest values of ASAT and ALAT, as compared to the normal ones, were recorded in HBV, with a mean value of 84.62 U/L, respectively 99.24 U/L.

Mean transaminase values are higher in males as compared to those in females, though the differences are not statistically significant ($p > 0.05$) for both ALAT and for ASAT).

Depending on the value of the necrotic inflammatory index, the hepatitis activity was considered minimally active (METAVIR score A1F1-A1F2), moderately active (METAVIR score A2 or 3F2 or 3) and severely active (METAVIR score A3F3 or 4) (Table III)

ASAT Values

- were higher in the first category, the one with minimum active hepatitis (A1F2);
- were increased in patients with A1F2 METAVIR score (78.25±17.06)
- were higher in moderately active hepatitis, at those with A3F3 (88) activity – having no statistical significance for the present study, as there is only one case.

ALAT values:

- the highest values were recorded in the first category (minimum active hepatitis A1F2) (78.25±17.06);
- in terms of age groups, a higher value was obtained at the age group of people over 60 years old, in those with hepatitis C (117±31003), as compared to other etiological categories.

ASAT and ALAT values were consistently higher in patients with viral hepatitis C, as compared to the other categories, presenting an average value of 79.25 ±17 125 ASAT and of 92.33± 20 116 ALAT.

Table no. 3. The inflammatory necrotic index and the serum levels of the transaminases

ACTIVITY	SCORE		ASAT	ALAT
MINIMALLY ACTIVE	AOF1	Mean	68.00	74.00
		N	2	2
		Std. Deviation	.000	1.414
	A1F0	Mean	71.83	87.00
		N	12	12
		Std. Deviation	11.769	17.220
	A1F1	Mean	70.55	86.65
		N	20	20
		Std. Deviation	10.570	16.516
	A1F2	Mean	78.25	94.80
		N	20	20
		Std. Deviation	17.060	22.336
MODERATELY ACTIVE	A2F1	Mean	67.00	77.60
		N	5	5
		Std. Deviation	3.317	14.153
	A2F2	Mean	84.96	94.53
		N	51	51
		Std. Deviation	18.702	18.196
	A2F3	Mean	87.20	100.92
		N	25	25
		Std. Deviation	19.205	21.629
	A3F3	Mean	88.00	116.00
		N	1	1
		Std. Deviation	.	.
	A3F4	Mean	87.00	115.00
		N	1	1
		Std. Deviation	.	.
SEVERELY ACTIVE	A2F3	Mean	70.50	99.50
		N	2	2
		Std. Deviation	3.536	4.950
	A3F3	Mean	94.00	98.00
		N	1	1
		Std. Deviation	.	.

The majority of patients included in the study presented moderately active activity, the histological activity index (HAI) ranging between 9 and 12 points, while at the 55 patients with minimally active activity, 2-7 points were obtained. The Spirman correlation coefficient was of 0.79 ($p < 0.01$) for patients with chronic hepatitis C, indicating a correlation between the HAI score and the fibrosis stage.

Table no. 4. Serum transaminase values by etiology types

Etiology/ Transaminase		No. of cases	Minimum	Maximum	Mean	Std. Deviation
HCV	**ALAT**	114	46	149	92.33	20.116
	ASAT		60	131	79.75	17.125
HBV	**ALAT**	21	76	141	99.24	16.288
	ASAT		63	135	84.62	19.853
HCV+HBV	**ALAT**	5	72	103	94.20	12.736
	ASAT		61	94	72.60	12.700

DISCUSSIONS

Several studies (6,7,8,9,10) have discussed the values of serum markers (ALAT, ASAT) in chronic viral hepatitis, especially at cases of infection with the C virus; however, the fluctuations in serum transaminase levels and their connection to inflammatory activity and the degree of fibrosis is still uncertain. Among the cases of hepatitis that have been studied so far, the ones caused by virus C raise special problems, as 20% of the cases evolve to cirrhosis and 1-4% of them develop liver-cell carcinoma each year.

The control of infection, of fibrosis progression and the therapeutic trials for the remission of fibrosis have been actively investigated lately. Recent years research on the factors that initiate and influence the development of extra-cellular matrix towards fibrosis show that these processes may be reversible (11,12,13,14).

Our aim has been to observe whether there is a correlation between histological changes and high ALAT and ASAT values. All patients included in our study presented some degree of fibrosis, a fact easily explained by the easy subjective symptomatology of the disease and lack of reliable tests for the detection of fibrosis, except liver biopsy. Although there are systems to detect serum parameters indicating liver fibrosis, these are not reliable enough and therefore are not used extensively (15), biopsy remaining the main method for detecting liver fibrosis. Performing percutaneous liver biopsy in patients with normal levels of serum transaminases is still under study (16,17,18). Our results indicate a significant correlation between the degree of fibrosis and the serum values of ALAT and ASAT. The ASAT / ALAT report is <1 in all cases, being consistent with the results of some authors (19) and inconsistent with the results of others (20). Some authors consider that increased ALAT levels might be correlated with a high degree of fibrosis progression, while the normal values of this parameter are not frequently associated with it (17.21).

CONCLUSIONS

According to the results we have obtained, the histological activity index may be correlated with the degree of fibrosis, and the ASAT and ALAT serum values are significant in relation to the degree of fibrosis; therefore they may be used for the purpose of monitoring the treatment of fibrosis regression during therapy.

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ENDOTHELIN 1-21 SERUM LEVEL IN PATIENTS WITH LIVER CIRRHOSIS

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Keywords: *liver cirrhosis, pulmonary arterial hypertension, Doppler transthoracic echocardiography, ET1-21*

Abstract: *Background: Endothelin plays a role in the pathology and severity of pulmonary hypertension which affects liver cirrhosis patients, but its importance in the context of other physiopathological modifications is not yet well defined.Objective: The assessment of the relationship between Endothelin 1-21 serum level and the presence and severity of pulmonary hypertension in patients with liver cirrhosis. Materials and methods: Between January 2007 and December 2008, 37 patients with liver cirrhosis (25 men), with an average age of 58.54 ± 9.01 years, diagnosed at Medicala III Clinic from Cluj-Napoca by liver enzymes, immunologic and viral markers, abdominal ultrasound, superior digestive endoscopy and/or liver biopsy, and a control group of 14 healthy subjects (4 men), with an average age of 59 ± 9.85 years were included in the study. The etiology of liver cirrhosis was hepatitis C for 29.73 % of the patients (11p) and alcohol for 45.94% (17p). Sixty seven percent of the patients were part of Child-Pugh class A (25p). The evaluation of pulmonary hypertension (PAH) was done using clinical examination, electrocardiogram and Doppler transthoracic echocardiography, performed in the Cardiology-Rehabilitation Clinic from Cluj-Napoca. A single parameter was assessed using Doppler transthoracic echocardiography – the systolic pressure in the pulmonary artery (PAPSs). PAPs value ≥ 30 mmHg was considered suggestive for the diagnosis of PAH. According to PAPs value, the patients were divided into 3 groups of pulmonary hypertension, as follows: mild PAH = 30 – 44 mmHg (14 patients); average PAH = 45 – 70 mmHg (12 patients); severe PAH > 70 mmHg (0 patients). Eleven patients did not have PAH (PAPs < 30 mmHg). The serum level of 1-21 endothelin (ET1-21) was measured for the all the patients in the cirrhosis and the control group, using the ELISA method (NV: 0.02 fmol/ml). For the statistical analysis, the t-Student test, χ^2 test and the Pearson correlation test were used. Results: In the liver cirrhosis group, the average values of ET1-21 were significantly higher than those in the healthy subjects group (1.90 ± 0.96 fmol/ml vs. 0.9 ± 0.07 fmol/ml, p<0.0001). The average serum values of ET1-21 were higher for the patients with liver cirrhosis and PAPs> 45 mmHg compared with those without pulmonary hypertension (2.02 ± 0.85 fmol/ml vs 1.92 ± 1.32 fmol/ml, p=0.41), but the difference was statistically significant (2.02 ± 0.85 fmol/ml vs 0.9±0.07 fmol/ml, p=0.0004) when compared to the values for the healthy subjects. In what concerns the severity of liver cirhhosis, the distribution of ET1-21 values was as follows: Child-Pugh class A 1.87 ± 0.87 fmol/ml, Child – Pugh class B 1.74 ± 0.26 fmol/ml, Child – Pugh class C 2.35 ± 1.89 fmol/ml. Conclusion: ET1-21 serum levels were significantly higher in patients with liver cirrhosis, the highest values being recorded in women. ET1-21 serum level was significantly higher in patients with liver cirrhosis and PAH compared to healthy subjects, supporting the role of the endothelin in the pathogenesis of PAH.*

Cuvinte cheie: *ciroză hepatică, hipertensiune arterială pulmonară, ecocardiografie transtoracică Doppler, ET1-21*

Rezumat: *Endotelina este incriminata in patogeneza si severitatea hipertensiunii pulmonare aparute la bolnavii cu ciroza hepatica, dar importanta sa in contextul altor modificari fiziopatologice nu este inca clar definita. Obiective: Studiul nivelului seric al endotelinei 1-21 in relatie cu prezenta si severitatea hipertensiunii pulmonare la bolnavii cu ciroza hepatica. Material şi metodă: În perioada ianuarie 2007 – decembrie 2008 s-au luat în studiu 37 pacienţi cu ciroză hepatică (25 bărbaţi), cu vârsta medie de 58,54±9,01 ani, diagnosticaţi la Clinica Medicală III Cluj - Napoca prin probe hepatice, imunologice, markeri virali, ecografie abdominală, endoscopie digestivă superioară şi/sau puncţie biopsie hepatică, şi un lot de 14 subiecţi sănătoşi (4 bărbaţi), cu vârsta medie 59±9.85 ani (martori). 29,73 % din pacienţii cu ciroză hepatică au avut etiologie virală C (11 p), 45,94 % etiologie etanolică (17 p). 67,56% din pacienţi au fost în clasa Child - Pugh A (25 p). Evaluarea hipertensiunii pulmonare (HAP) s-a făcut prin examen clinic, electrocardiografie, ecocardiografie transtoracică Doppler în Clinica de Cardiologie-Recuperare, Cluj-Napoca. Ecocardiografic s-a evaluat un singur parametru - presiunea sistolică în artera pulmonară (PAPs). Valoarea PAPs ≥ 30 mmHg a fost considerată sugestivă pentru diagnosticul de HAP. În funcţie de valoarea PAPs pacienţii au fost împărţiţi în trei grupe de hipertensiune pulmonară, după cum urmează: HAP uşoară = 30 – 44 mmHg (14 pacienţi); HAP medie = 45 – 70 mmHg (12 pacienţi); HAP severă > 70 mmHg (0 pacienţi).11 pacienţi nu au avut HAP (PAPs<30 mmHg). La toţi pacienţii şi subiecţii martori s-a determinat endotelina 1-21 serică (ET1-21),*

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utilizând metoda ELISA (VN: 0,02 fmol/ml). Pentru analiza statistică s-a folosit testul t-Student, testul χ^2 şi testul de corelaţie Pearson. Rezultate: La pacienţii cu ciroză hepatică valorile medii ale ET1-21 au fost semnificativ crescute faţă de cele ale lotului martor (1,90±0.96 fmol/ml vs 0,9±0,07 fmol/ml, p<0,0001). Valorile serice medii ale ET1-21 au fost mai mari în cazul pacienţilor cirotici cu PAPs > 45 mmHg faţă de cei fără hipertensiune pulmonară (2,02±0,85 fmol/ml vs 1,92±1,32 fmol/ml, p=0,41), dar comparativ cu subiectii sanatosi diferenta a fost semnificativa statistic (2,02±0,85 fmol/ml vs 0,9±0,07 fmol/ml, p=0,0004). În ceea ce priveşte severitatea cirozei hepatice, distribuţia valorilor ET-1-21 a fost următoarea: clasa Child-Pugh A 1,87±0,87 fmol/ml, clasa Child – Pugh B 1,74±0,26 fmol/ml, clasa Child – Pugh C 2,35±1,89 fmol/ml. Concluzie: Nivelele serice ale ET1-21 au fost semnificativ crescute la pacientii cu ciroza hepatica, valorile cele mai crescute inregistrandu-se la sexul feminin. De asemenea nivelul seric al ET1-21 a fost semnificativ mai mare la cei cu ciroza hepatica si HAP fata de subiectii sanatosi sustinand astfel rolul si interventia endotelinei in patogeneza HAP.

INTRODUCTION

Portopulmonary hypertension (PPH) is one of the complications described in liver cirrhosis patients, its pathology being insufficiently elucidated. Several studies showed that in liver cirrhosis, endothelin 1 (ET1) levels were increased, both by an augmented synthesis and by a reduced clearance (1,2,3), offering the premises for PAH development, and in the meantime, that ET1 levels are higher in patients with PPH, supporting its implication in the pathogenesis of PAH.

ET1 is the strongest vasoconstrictor in the endothelin family, having 3 isopeptides: ET1, ET2, ET3. Their precursor is represented by pre-pro-endothelin (pre-pro-ET1 – 203 aminoacids), which, under the action of certain endopeptidases, is transformed in big endothelin (big ET – 38 aminoacids), an inactive compound. Under the action of the endothelin conversion enzyme, big ET is transformed in ET1-21 (21 aminoacids), the mature form of endothelin. There are 2 types of endothelin receptors, ETA and ETB, which mediate the biological actions if ET1-21, more importantly vasoconstriction and cellular proliferation.

The purpose of this study was to evaluate ET1-21 serum level, the most powerful natural vasoconstrictor known to date, in relationship with the presence and the severity of PAH (echocardiographically determined) in patients with liver cirrhosis, due to the fact that this aspect was little studied in Romania.

MATERIAL AND METHOD

Between January 2007 and December 2008, 37 patients (25 men), with an average age of 58.54 ± 9.01 years, diagnosed at Medicala III Clinic from Cluj-Napoca with liver cirrhosis by clinical evaluation, liver enzymes – ALT, AST, γ-GT, alkaline phosphatase, total and direct bilirubin, protrombine time, total protein and albumin level; abdominal ultrasound, superior digestive endoscopy and/or liver biopsy. The etiology of liver cirrhosis was determined using viral markers: HbsAg, Anti HCV Ab, and immunological markers: ANA, AMA, SMA anti LKM. The severity of liver cirrhosis was evaluated using the Child-Pugh classification (Child class A = 5-6 points, Child Class B = 7-9 points, Child class C = 10-15 points).

A group of 14 healthy subjects (4 men) with an average age of 59 ± 9.85 years (47-73 years old) were also included in the study. Other possible causes of PAH were excluded from the study.

The evaluation of pulmonary hypertension was done using the clinical exam, electrocardiography, chest X-Ray, transthoracic echocardiography and Doppler ultrasound. The echocardiographic examinations were performed in the Cardiology-Rehabilitation Clinic from Cluj-Napoca, using an Esaote MyLab 50X Vision system, with a 3.5 MHz frequency transducer. For the diagnosis of pulmonary hypertension, the systolic pressure in the pulmonary artery (PAPs) was measured, quantifying the maximum velocity of the tricuspid regurgitation (VRT) in continuous Doppler mode, from the right ventricular inflow tract (RVIT) - modified parasternal long axis, parasternal short axis at the base of the great vessels, apical 4 chambers and subcostal incidences. The trans-tricuspid pressure gradient was calculated using Bernoulli's simplified equation, to which the right atrial pressure (PAD) was added, evaluated by the inspiratory collapse of the inferior vena cava from the subcostal view. PAPs value ≥ 30 mmHg was considered suggestive for the presence of PAH. According to PAPs value, the patients were divided into 3 groups of pulmonary hypertension, as follows: mild PAH = 30 – 44 mmHg (14 patients); average PAH = 45 – 70 mmHg (12 patients); severe PAH > 70 mmHg (0 patients). Eleven patients did not have PAH (PAPs < 30 mmHg). The serum level of 1-21 endothelin (ET1-21) was measured for the all the patients in the cirrhosis and the control group, using the ELISA method (NV: 0.02 fmol/ml). With the patients in a fasting state, 5 ml of blood was drawn, and after blood coagulation, the serum was separated by centrifugation at 3000G for 10 minutes. The serum was conserved at a temperature of -20°C.

In what concerns the etiology of liver cirrhosis, in 45.94% of the patients (17p) alcohol was incriminated and in 29.73% (11p) hepatitis C. Other causes were as follow: 2.7% (1p) hepatitis B, 8.1% (3p: viral B + alcohol - 2p, viral C + alcohol – 1p) mixed etiology, 2.7% (1p) primitive biliary cirrhosis (CBP), 2.7% (1p) autoimmune, 2.7% (1p) Wilson's disease and 5.4% (2p) cryptogenic origin. Hepatitis C virus-associated liver cirrhosis was more common in women (58.33% = 7p), while alcohol-associated liver cirrhoses was more common in men (64%=16p).

According to the severity of liver cirrhosis, evaluated by the Child-Pugh class, 67.56% of patients were in Child-Pugh class A (25p), 18.92% in Child-Pugh class B (7p) and 13.52p in Child-Pugh class C (6p).

For the statistical analysis, the t-Student test, χ^2 test and the Pearson correlation test were used. Data is presented as average ± standard deviation for continuous variables and percentage (%) for categorical variables.

RESULTS

ET1-21 serum level was significantly higher in the liver cirrhosis group compared to the healthy subjects group (1.90 ± 0.96 fmol/ml vs. 0.9 ± 0.07 fmol/ml, p<0.0001) (figure 1).

ET1-21 serum levels were also significantly higher in women with liver cirrhosis compared to men with liver cirrhoses. (2.5 ± 1.47 fmol/ml vs 1.6 ± 0.36 fmol/ml, p=0.03) (figure 2)

In patients with liver cirrhosis, a statistically significant inverse variation relationship between ET1-21 serum level and age was obtained (r=-0.02, p=0.0002) (figure 3).

The statistical analysis of the ET1-21 serum level according to the etiology of the liver cirrhosis did not show significant differences, but the highest ET1-21 serum levels

were obtained in the patients with primitive biliary cirrhosis and autoimmune cirrhosis (2.32 ± 0.79 fmol/ml).

In what concerns the severity of the liver disease, the patients with liver cirrhosis in Child-Pugh class A had an average ET1-21 serum level of 1,87±0,87 fmol/ml, those in Child – Pugh class B 1.74 ± 0.26 fmol/ml, and those in Child – Pugh class C 2.35 ± 1.89 fmol/ml, but these results were not statistically significant (p>0.05).

Figure no. 1. Comparison of ET1-21 serum levels in patients with liver cirrhosis vs. healthy subjects

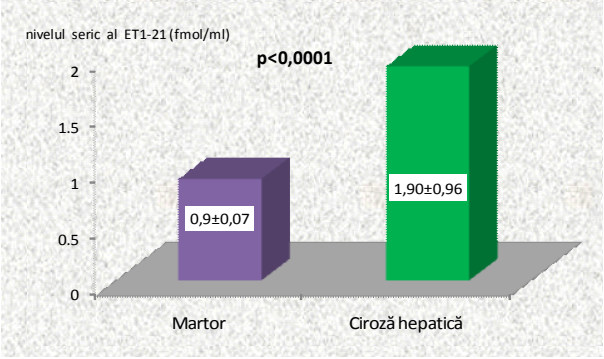


Figure no. 2. ET1-21 serum level sex distribution in patients with liver cirrhosis

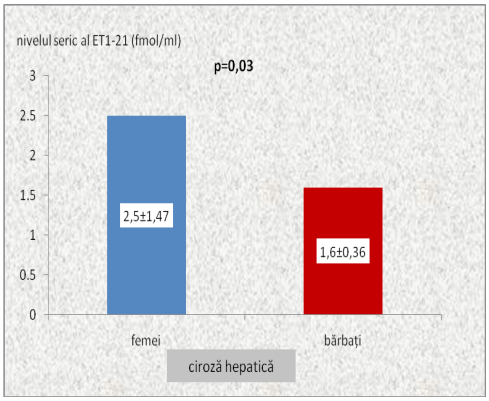
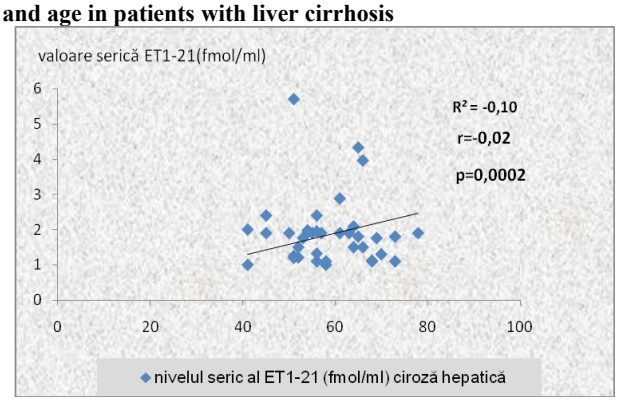


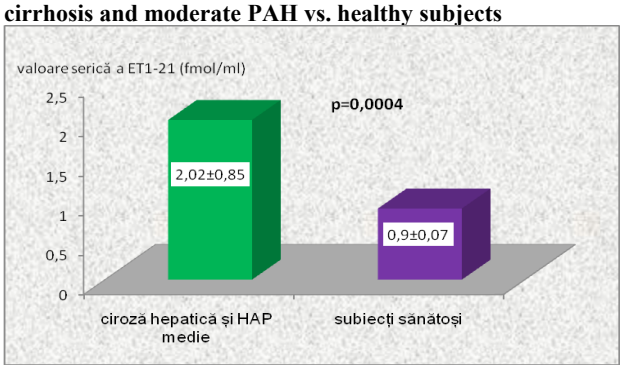
Figure no. 3. The relationship between ET1-21 serum level and age in patients with liver cirrhosis



According to the presence and the severity of PAH, higher serum values of ET1-21 were obtained in patients with moderate PAH compared to patients without PAH (2.02 ± 0.85 fmol/ml vs 1.92 ± 1.32 fmol/ml, p=0.41), with no statistical significance, but the difference was statistically significant when these data were compared to the healthy subjects group (2.02 ± 0.85 fmol/ml vs 0.9 ± 0.07 fmol/ml, p=0.0004) (figure 4).

From the 37 patients enroled in the study, 32.43% had echocardiographically diagnosed ascites (12p). These patients had a higher average ET1-21 serum level compared to those without ascites, but the data had no statistic significance (1.98 ± 1.21 fmol/ml vs. 1.86 ± 0.84 fmol/ml, p=0.38).

Figure no. 4. ET1-21 serum values in patients with liver cirrhosis and moderate PAH vs. healthy subjects



DISCUSSION

ET1 is a vasoactive peptide derived from the endothelia that plays a key role in the modulation of the vasomotor tone in healthy individuals, but with multiple other important roles in pathology, such as the stimulation of cell growth and fibrogenesis (8,9). In the last decade, a great intereset was accorded to the role of ET1 in the pathogenesis of liver cirrhoses. In patients with liver cirrhoses, the serum level of ET1 is increased, espiecially in those patients with advanced liver disease (1,2,3), and apparently the level increases with the severity of the liver function alteration, evaluated by the Child-Pugh score (3,10).

The patients usually have a hyperdinamic circulation, characterised by low arterial blood pressure, high cardiac output and low peripheral vascular resistance (11,12,13). Therefore, it has been suggested that in advanced liver cirrhoses, the peripheral arterial vasodilation with secondary neurohumoral activation represents the major stimulus for the synthesis of ET1 (14). But it has also been proved that the administration of isotonic saline solutions or iv albumine, which determines a rise in plasma volume, reduces the activity of plasma renin and aldosterone while the level of ET1 does not change, which contradicts the theory according to which arterial vasodilation influences the synthesis of ET1 (15).

The hepato-splanchnic circulation represents the major source for the increased secretion of ET1 (3,16,17,18). While in healthy subjects the most part of ET1 is synthetised at the level of vasculat endothelia, in the cirrhotic liver ET1 is produced by the activated hepatic stellate cells (18). Pinzani and co. demonstrated that mRNA ET1 and the expression of the protein in the liver are increased (17).

Experimental studies have showed that the endothelin contributes to the modulation of the intrahepatic vascular tone in cirrhosis. Also, it was showed that the alterated response to ET1 can contribute to the modifications in the systemic and mesenteric circulation (19). Despite the elevated circulating level of ET, of vasopressin, of the activation of the renin-angiotensin system and of the central nervous system, the systemic and mesenteric vascular tone are decreased in patients with advanced liver disease, the degree of activation of vasoconstrictor response being higher in those in which vasodilation is predominant (20). Therefore, it is sugested that the vascular response to these endogenous vasoconstrictors is altered.

For patients with liver cirrhosis who have associated pulmonary hypertension, the studies have showed that the endothelines system is overexpressed (21,22), and ET1 is

substantially involved in the pulmonary vasomotor tonus changes and in the pulmonary vascular remodeling. The precise sequence of events is less well understood. Initially, the increased levels of ET1 in the pulmonary circulation, resulted form the hepato-splanchnic circulation and from the local synthesis due to parietal stress, induce pulmonary vasocontriction and proliferation of smooth muscle cells. Subsequently, the vascular stretching resulted from the elevated pressure in the pulmonary artery determines supplementary structural adaptative responses, which leads to vascular obliteration (23).

But because only a little proportion of the patients with liver cirrhosis develop pulmonary hypertension, this suggests the involvement of aditional factors and/or genetic factors in this condition. This concept also explains why only a part of the patients with liver cirrhosis develop moderate PAH, while others develop a rapid progression of the disease (23).

In the present study the serum ET1 levels were two times higher in the patients with liver cirrhosis compared to healthy individuals, the difference being statistically significant, which allows us to say that ET1-21 is a marker of liver cirrhosis. We also observed that in the patients with liver cirrhosis, the serum levels of ET1-21 are influenced by sex (significantly higher serum levels for women, p=0.03) and by age (with an inverse variation existing between age and ET1-21 levels). The data from the existing literature are contradictory in this aspect.

The etiology does not seem to influence the serum level of ET1-21, although the hghest values of ET1-21 were seen in patients with primitive biliary cirrhosis, autoimmune cirrhosis and PAH, but which were not statistically significant. These results would suggest that women are more predisposed to developing PAH, because they have elevated serum levels of ET1-21, and are in concordance with the results published by Kawut and co., who found women to be at a greater risk of developing PAH and autoimmune hepatitis (24).

Even though in the present study the differences between the patients with liver cirrhosis without PAH who had an elevated serum level of ET1-21 and the patients who had already developed PAH were not statistically significant, the difference between the patients with PAH and healthy subjects strongly indicate the endothelin's role and implication in the pathogenesis of PAH. These results can probably be explained by the absence of patients with severe PAH in the present study and by the small number of patients included. It is also known that in patients with PAH, 40% of ET1-21 is eliminated by the lungs via ET-B receptors, which explains the short half-life and the reduced serum level and, on the other hand, that the level of ET1-21 is sensible to physiological and pathological fators such as clino- and orthostatism, venous stasis, systemic atrerial hypertension. In the patients with mild PAH the serum level of the endothelin were lower than in those without PAH, which suggests the contribution of the hyperdynamic circulation and the elevated plasma volume in this stage of the disease.

It is also known that the patients with liver cirrhosis with refractory ascites (defined by ascites which does not responde to maximal diuretic treatment: 160 mg of Furosemide + 400 mg of Spironolactone daily, for two weeks) have elevated plasma ET1 levels, because these patients have a more pronunced hyperdinamic circulation (25). In our study, only 32.43% of the patients with liver cirrhosis had ascites. And even though the patients with ascites had higher ET1-21 levels compared to those without ascites, the statistical analysis did not show significant differences (p=0.38). The patients in the present study had small/medium quantity ascites, easily influenced by diuretic treatment, and, on the other hand, there was no patient with liver cirrhosis and refractory ascites. These results can also be influenced by the fact that the analysis of the relationship between the high levels of ET1-21 and ascites was performed on a small number of cases and that it ws not quantitatively evaluated. In the present study we did not evaluate the relationship between the presence of ascites, diuretic treatment and ET1-21 serum level.

Limits of the study: The absence of severe PAH; the small number of Child-Pugh class C cases; the low number of patients with ascites (no cases of refractory ascites); The PAH was not confirmed by catheterisation; the imposibility of long-term follow-up.

In conclusion, ET1-21 serum levels are significantly higher in patients with liver cirrhosis, the highest values being recorded in women. ET1-21 serum level is significanlty higher in patients with liver cirrhosis and PAH compared to healthy individuals, supporting the role of endothelin in the pathogenesis of PAH.

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CLINICAL FEATURES IN CROHN'S DISEASE - A RETROSPECTIV BICENTRYC STUDY (BUCHAREST, TIMISOARA) DURING 2005-2009

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Keywords: *inflammatory bowel disease, Crohn's disease, Montreal classifications*

Abstract: *The aim of our study is the characterization of Crohn's disease (CD) in terms of clinical onset, the degree of activity, the appearance and the topographical distribution of the lesions and the clinical and the pathological behavior of the disease. Materials and Methods The study group consists of adults (> 18 years) with newly diagnosed CD investigated in The Fundeni Institute, The Center of Gastroenterology and Hepatology and in the Department of Gastroenterology and Hepatology, of The Emergency County Hospital Timisoara during the period 2005-2009. Results The major signs and symptoms at admission were: chronic diarrhea in 59.4% of the cases, abdominal pain in 45%, weight loss (below 10% of the ideal weight) in 39.4% of the cases. By correspondingly Harvey-Bradshaw index, 27.2% of the cases were classified as having mild activity, 43.3% of the cases as moderate activity, 3.9% engaged in severe activity; 25.6% of the patients were classified as inactive clinicaly and biologicaly. Typical findings on endoscopy were: ulcers in 70.6% of the all cases, strictures in 14.5%, cobblestone pattern 18.3%, "skip lesions" in 11.1%, non-perineal fistulas in 1% of cases. By Montreal phenotype classification, patients are grouped in relatively equal proportions from 17 to 40 years and over 40 years; 56.6% of the cases were colonic disease, 32.2% ileocolonic disease and 11.2% small bowel disease; 72.2% of the cases were non-penetrating/non-stricturing, 14.5% stricturing, and penetrating 13.3%; perineal disease was present in 10% of the cases (56% fistulas and 44% abscesses). Conclusions: Although symptoms and signs at onset and endoscopic lesions are similar to those described in literature, the Montreal phenotype classification results confirm the previous studies that attest in Romania a late onset, a predominance of colonic disease and of non-penetrating/non-stricturing behavior and a reduced incidence of perianal disease. Most cases are moderately active CD, followed in relatively equal proportions by cases with mildly active and inactive CD. Percentage of severely active CD was very low compared with literature data. These data confirm the existence of a particular phenotype of CD in Romania.*

Cuvinte cheie: *boli inflamatorii intestinale, boala Crohn, clasificarea Montreal*

Rezumat: *Scopul studiului nostru constă în caracterizarea cazurilor de boală Crohn (BC) din punct de vedere al debutului clinic, al gradului de activitate, al aspectului şi distribuţiei topografice a leziunilor şi al comportamentului clinico-patologic al bolii. Material şi metodă Lotul de studiu este alcătuit din pacienţii adulţi (>18 ani) cu BC nou diagnosticată investigaţi în Institutul Clinic de Gastroenterologie şi Hepatologie Fundeni şi în Clinica de Gastroenterologie şi Hepatologie Timişoara, în intervalul de timp 2005-2009. Rezultate Principalele semne şi simptome la internare au fost: diareea cronică în 59,4% din cazuri, durerea abdominală în 45%, scăderea ponderală (sub 10% din greutatea ideală) în 39,4%. Corespunzator indicelui Harvey-Bradshaw, 27,2% cazuri au fost încadrate ca având activitate uşoară, 43,3% din cazuri ca activitate moderată şi 3,9% ca activitate severă; 25,6% din pacienţi au fost clasificaţi ca fiind inactivi clinico-biologic. Din punct de vedere endoscopic au fost descrise ulceraţii în 70,6% din cazuri, stenoze în 14,5%, aspectul de „piatră de pavaj" în 18,3%. Distribuţia discontinuă a leziunilor a fost menţionată la 11,1% din pacienţi, fistule non-perineale în 1% din cazuri. Privind clasificarea Montreal, pacienţii s-au încadrat în proporţii relativ egale între 17-40 de ani şi peste 40 de ani. În 56,6% din cazuri localizarea a fost colonică, în 32,2% ileo-colonică şi în 11,2% ileală; în 72,2% din cazuri patternul bolii a fost non-penetrant/non-stenozant, în 14,5 % din cazuri stenozant şi 13,3% penetrant, afectarea perineală fiind prezentă în 10% din cazuri, dintre care 56% fistule şi 44% abcese. Concluzii Deşi simptomele şi semnele la debut, precum şi leziunile endoscopice, sunt similare celor din literatură, aspectele clinice identificate confirmă rezultatele studiilor româneşti anterioare care atestă debutul mai tardiv, localizarea colonică şi categoria non-penetrantă non-stenozantă a bolii mai frecvente precum şi incidenţa redusă a afectării perianale. Majoritatea cazurilor noi internate au prezentat forme moderate de BC, urmate în proporţii relativ egale de cazurile cu activitate uşoară şi în remisiune. Procentul formelor severe de BC a fost foarte redus comparativ cu datele din literatură. Aceste date confirmă existenţa unui tip particular al BC în România.*

INTRODUCTION

Crohn's disease (CD) is a complex clinical entity, due to the variability in the anatomical distribution, which causes a variety of the clinical presentation, severity degrees, natural

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history and therapeutic options.

PURPOSE OF THE STUDY

The aim of our study is to analyze the emerging CD cases in terms of the clinical onset, the Montreal classification, the disease severity and the type of the described endoscopic lesions.

MATERIAL AND METHOD

The study group consists of 180 adult patients with newly diagnosed CD, investigated in the Clinical Institute of Gastroenterology and Hepatology Fundeni (152 patients) and in the Department of Gastroenterology and Hepatology Timisoara (28 patients), between 2005 - 2009.

For each new cases there were studied the main symptomes and signs at onset, the location and disease behavior and the degree of the disease activity.

The diagnosis was confirmed by endoscopic, radiological and histological examination in the settings of the clinical manifestations.

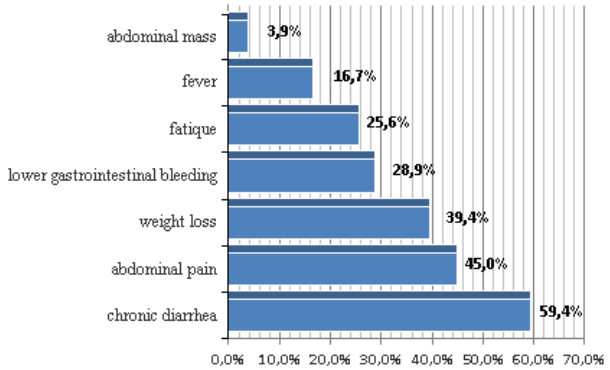
Each case was classified according to age (A), location (L) and disease behavior (Montreal classification).

For assessmant of the disease activity we used the Harvey-Bradshaw index (activity index: general well-being 0 = best, 1 = slightly impaired, 2 = very impaired, 3 = severe; abdominal pain: 0 = absent, 1 = mild, 2 = moderate , 3 = severe; number of liquid stools; abdominal mass: no= 0, qustionable=1, definite= 2; definite and firm= 3; complications: arthritis/arthralgia, iritis/uveitis, erythema nodosum, pyoderma gangrenosum, aphtous stomatitis, anal fissure/fistula/abscess = 1).

RESULTS

Patients with CD were admitted in the gastroenterology departments with the following signs and symptoms: chronic diarrhea in 59.4%, abdominal pain in 45%, weight loss (less than 10% of ideal weight) in 39.4% and lower gastrointestinal bleeding in 28.9% of cases.

Figure no. 1. The percentage of the main symptoms and signs at onset (N=180 cases)



Diagnosis was confirmed by colonoscopy, performed in most cases (83.9%), by esophagogastroduodenoscopy performed in 35.6%, by conventional radiology in 37.8%, abdominal computed tomography in 6.7%, abdominal MRI in 2.8%, wireless capsule endoscopy in 0.6% of cases. The frequency of the procedures used in the diagnosis of CD is shown in figure nr. 2.

Regarding the typical endoscopic features we found: ulcers in 70.6% of cases, stenosis in 19.4%, the "cobblestone" pattern in 18.3%, "skip lesions" in 11.1% of cases, non-perineal fistula in 1% of cases. The frequency of the endoscopic aspects is depicted in the figure nr. 3.

Figure no. 2. The percentage of recommended procedures used for CD diagnosis

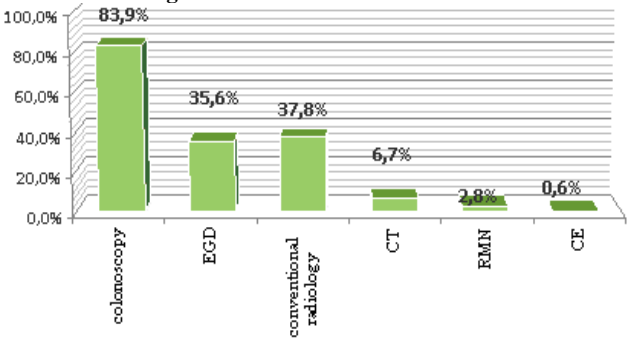
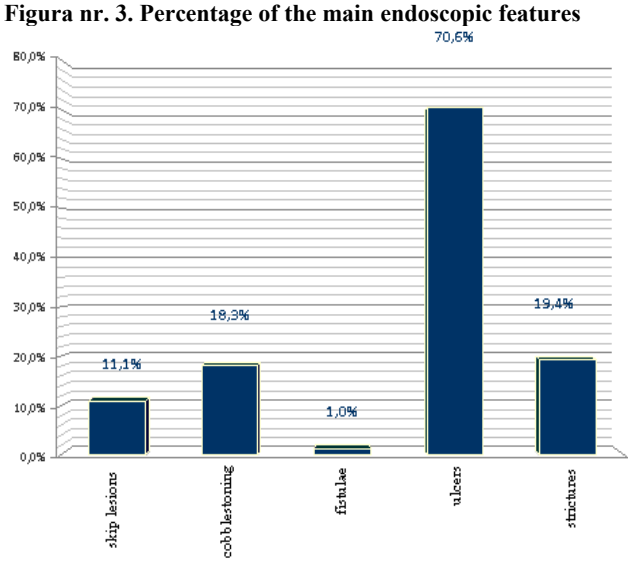
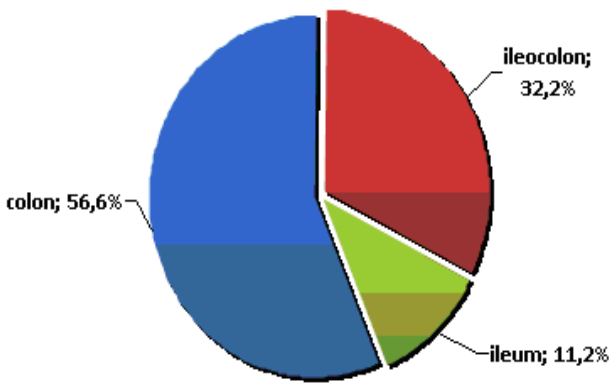


Figura nr. 3. Percentage of the main endoscopic features



According to the Montreal classification, 51.7% of patients were aged between 17-40, and 48.3% were over 40; in 56.6% of the cases the colon was affected, the ileocolon in 32.2% of the cases and 11.2% of the cases showed only ileal involvement, the disease behavior was non-sticturing-type/non-penetrating (B1 inflammatory) in 72.2% of cases, stricturing (B2) in 14.5% of cases and penetrating (B3) in 13.3% of cases; perianal disease was present in 10% of the patients (56% fistulas and 44% abscesses). Most common combinations that we have found are: A2L2B1 (23.8%) and A3L2B1 (19.4%) followed by A2L3B1 (8.8%).

Figure no. 4. The classification of the cases by location



By using the Harvey-Bradshaw index for assessment of the disease activity, we found 43.3% of the cases moderately active CD, 27.2% of the cases mildly active CD, 3.9% of the cases severely active CD, and 25.6% inactive CD.

Figure no. 5. The classification of the cases by behavior

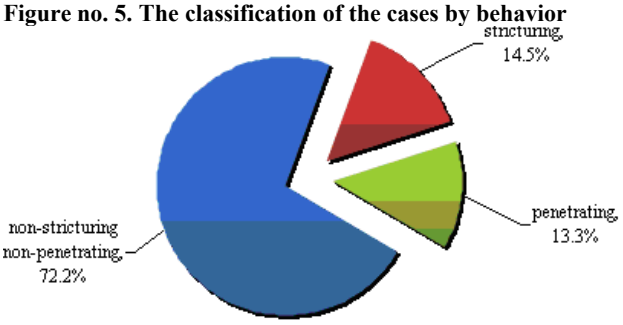


Figure no. 6. The perianal involvement

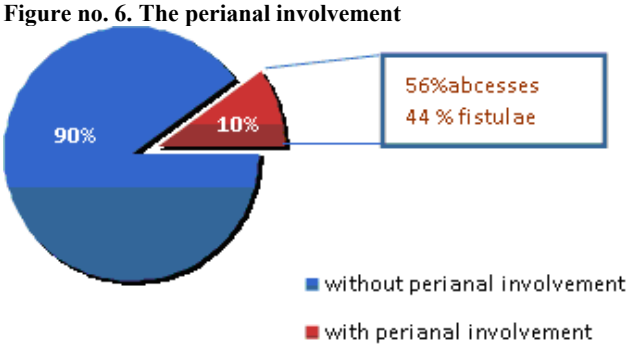
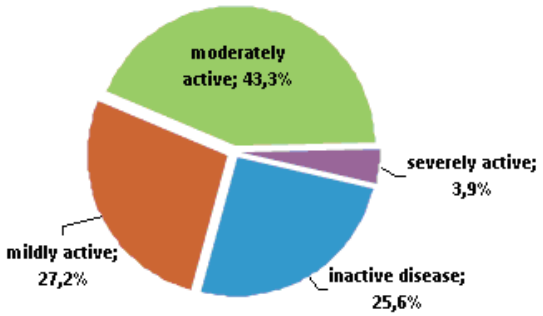


Figure no. 7. Disease activity by Harvey-Bradshaw Index



DISCUSSIONS

The diagnosis of CD was based on the combination of the following criteria: 1. clinical features: abdominal pain, diarrhea, weight loss (more thean 10% from ideal weight) 2. macroscopic features: aphthoide ulcers, depp linear ulcers, ileal disease, rectum typicaly spared, deep fisures, skip lesions, fistulae, cobblestoning, thickening of the intestinal wall, strictures; 3. radiology: ulcers, fistulae, strictures, cobblestoning; 4. laparoscopic examination: bowel wall thickening, mesenteric limphadenopathy 5. histopathological examination: focal chronic and patchy inflammation, focal crypt irregularity, granulomas .(1, 2)

In our study the main symptoms were present in a variable rate: chronic diarrhea (59.4%) abdominal pain (45%), weight loss (39.4%), lower gastrointestinal bleeding (28 9%); the frequency of the clinical signs was relatively low, confirming that physical examination may be unnoticed at the onset of the disease in mild forms or during the periods of inactive disease.

According to the literature, chronic diarrhea is the most common presenting symptom of CD, being present in 85% of cases, followed by abdominal pain in 70% of cases and weight loss in 60%.(3, 4)

In this regard, the relatively low frequency of the symptoms in the study group is explained by the high proportion of midly or inactive CD. Although lower gastrointestinal bleeding is less common in CD than ulcerative colitis, it is described in literature in 40-50% of colonic CD, explaining the high frequency of this symptom in our study in which the colon was involved in 56,6% of the cases. (2)

Compared with the literature, in our study group the small bowel follow- through was performed in a significantly lower number of cases, while colonoscopy was the gold standard for the diagnosis.(5) Thus, colonoscopy was performed in most cases, esophagogastroduodenoscopy was performed in 34.9% of the cases and small bowel follow through in 39.5% of cases; other imaging techniques (computed - tomography, MRI, capsule endoscopy) were rarely used.

The value of the imaging techniques is high when an extramural complication is suspected (fistulas, abscesses), in the assessment of stricturing, establishing the location and the extent of the disease on the small bowel when endoscopic changes were identified, or the terminal ileum intubation can not be perform. For assessment of the location and of the extension of CD in the small bowel, most centers perform enteroclysis and small bowel follow through; only a few gastroenterology department are performing enteroclysis CT / MRI. (2)

In Romania the dominant phenotype of CD is inflammatory non penetrant/non stricturing, with mildly and moderately active disease; so, it seems rational that such investigations need to be used with lower frequency when compared with international data. On the other hand, we can speculate that in these conditions, a number of cases with CD with small bowel involvment remain undiagnosed; in the future the more frequent use of CT/RMN techniques will help to refine the CD extension and will change the existing phenotypes.

In our study group the most frecquent endoscopic finding was, unsurprisingly, the ulcers (70.6%), followed by "skip lesions", cobblestoning, inflammatory polyps and stricturing.

The initial establishment of the disease location is particularly important since it was described a stability of the anatomical location during the disease evolution in the adult patients, while the disease behavior is dynamic in time. Thus, young patients with ileocolonic location and/or perianal disease who requires corticosteroids treatment for the first atac have a high risk of disabling disease in 5 years from the onset; for these patients the early initiation of immunosuppressant or biological therapy is wholesome. The upper gastrointestinal involvement is encumbered by a more severe prognosis.(6, 7) CD diagnosed under the age of 40 is most commonly associated with ileocolonic involvement, while the incidence of the colonic location increases after 40 years. (8)

The data obtained in our study group is significantly different from those from literature, the ileal location being the most frequent (45%) followed by ileocolonic involvement (25%) and colonic location (25%); the perianal involvement is found in over 50% of the cases, usually in combination with colon locations. (9, 10)

These differences may reflect the particular type of the Romanian patients, but we can not rule out the possibility of underestimating the ileal location because of the lower sensitivity of the conventional radiology in detecting early ileal lesions or merely the more sparsely use of CT/MRI and capsula endoscopy. From this point of view the ileal involvement is likely to be underestimated.

The colonic location was found in similar percentages between 17-40 and after the age of 40, while ileocolonic location was more frequent in patients under 40.

Behavior of CD in the study group was B1 (non-stricturing/ non-penetrating) in 72.2% of cases, B2 (stricturing) in 14.4% of cases and B3 (penetrating) in 13.3% of cases; the perineal disease was present in 10 % of cases. These results are

consistent with previous romanian studies which also indicated, the non-penetrating/non-stricturing behavior as the most frequent and a reduced incidence of the perianal disease compared with international studies. (11)

The disease activity was assessed by Harvey-Bradshaw index, validated in the pilot and the cohort studies and easier to apply than CDAI score, to which it correlates to 90%. Harvey-Bradshaw Index <5 indicates a clinical remission, between 5-7 mildly active, between 8-16 moderately active and > 16 severely active CD .(12, 13)

In our study group, most cases were moderately active CD (43.3%) and a relative similar percentage being mildly active (27.2%) and inactive disease (25.6%); a low number of patients had severely active CD (3.9%).

Our study confirms previously published date on CD peculiarities in Romania and suggests a mildly onset, non-penetrating pattern/non-stricturing dominant type and the low incidence of the perianal disease.(14)

As the overall incidence of inflammatory bowel disease is increasing in our country, it is expected that, due to lifestyle modification and its proximity to the European Union, the clinical aspects will modify and the cases will be more and more severe.

CONCLUSIONS

- the main symptoms at onset were diarrhea, abdominal pain, weight loss;
- the gold standard for diagnosis was colonoscopy, performed in 83,9% of the cases;
- the imaging techniques (MRI, CT scan, capsule endoscopy) had a low share in diagnosis;
- the main endoscopic features were ulcers, cobblestoning and “skip lesions”;
- the age distribution of the cases was relatively balanced, attesting the late onset of CD compared with literature;
- the disease location was predominantly colonic, followed by ileocolonic and ileal involvement;
- most common behavior was B1, non-stricturing-non-penetrating, with a low incidence of stricturing and penetrating behavior and of the perianal disease;
- most cases were moderately active, followed by midly active and clinically inactive disease, whereas severely active cases were very low compared with literature data;
- there are still needed extensive multicenter studies for better characterization of phenotype and the evolution peculiarities of CD in Romania.

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AMYAND HERNIA CASE PRESENTATION

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Keywords: ***Amyand Hernia,*** *treatment, diagnosis*

Abstract: *We present the case report of a patient for 36 years, admitted through Emergency Unit with the diagnosis of right inguinal strangled hernia. After surgical intervention, the case analysis reveals some particuliarities: the relatively recent right inguinal hernia; strangulation under four hours with easz reduction in taxis and rapid resumption of bowel movements, the persistence of spontaneous pain and endured feeler with finding a formation stretched to cover the entire canal, erroneously interpreted as acceding endured epiploic fringe bag, bag adherence raises the issue of an older recruitment, silent development of acute appendicitis with unchanged biological values, the etiopathogenic factors of the acute appendicitis were the adherence to the bag the hernial strangulation which lead to appendix ischaemia and secondary circulatory alterations. In conclusion, although extensive medical literature describs the symptoms and development of acute appendicitis in hernial bag, Amyand hernia constitutes an intraoperative surprise.*

Cuvinte cheie: *hernia Amyand, diagnostic, tratament*

Rezumat: *Se prezintă un cazul unui pacient de 36 ani, internat prin Urgență, cu diagnosticul hernie inghinală dreaptă ştrangulată. După intervenția operatorie, analiza cazului relevă anumite particularități: hernie inghinală dreaptă relativ recentă; ştrangulare mai recentă de patru ore cu reducere uşoară la taxis şi reluarea rapidă a tranzitului intestinal; persistența unei dureri spontane şi palpatorie cu constatarea unei formațiuni indurate alungite ce cuprinde întreg canalul inghinal, eronat interpretată ca franj epiploic indurat aderent la sac; aderența la sac a apendicelui ridică problema unei angajări mai vechi; evoluția silențioasă a apendicitei acute, cu constantele biologice nemodificate; aderența la sac şi ştrangularea herniară prin ansă ileală au fost factorii etiopatogenici ai declanşării apendicitei acute prin ischemierea apendicelui şi modificările circulatorii secundare. În concluzie, deşi literatura medicală descrie pe larg clinica şi evoluția apendicitei acute în sacul herniar, hernia Amyand reprezintă o sursă de surpriză intraoperatorie.*

INTRODUCTION

Claudius Amyand described, in 1736, the Amyand hernia is an abdominal wall hernia containing an inflamed vermiform appendix, being excluded from definition the free and mere presence of an appendix in a hernial sac. Inguinal hernias, both the external oblique and direct ones, but especially neglected scrotal inghino-old may engage in various abdominal viscera hernial sac, herniated organs may develop in the various pathologies specific to each bag. Azand herni's incidence varies from 0.13% (upon Ryan quoted by (7)) at 0.67% (upon Burger and D'Alia, ibidem). The vast majority of Amyand hernia is fount in the right inguinal hernia, but may also occur in the left umbilical eventration. The etiopathogenesis of intrasaculare hernial strangulated appendicitis raised the discussion of a possible concomitant disease, local trauma and other mechanisms that increase abdominal pressure and ischemic disorders that induce inflammation followed by appendicitis.

CASE REPORT

J.S., male, 36 years of old, unemployed, from rural area came at the Emergency Unit showing a right inguinal strangled hernia more recent than 4 hours. The hernia is easily reduced by gentle taxis. Preoperative preparation. After about an hour, bowel transit appears, but the patient complains of a slight sore groin, spontaneous and iat effort. To palpation in the right groin develops a endured painful formation in diameter of about 0.5 cm, flat, occupying the whole inguinal canal. Given the recent strangulation, we consider the formation as an epiploic congested fringe adhering to the bag.

Laboratory investigations eveal normal values: ESR 2 / 4, 4.42 million red cells, white cells 5570, Haematocrit 39.36, 33.3% Urea, Creatinine 1.10 mg., Blood sugar 90.3 mg / %, platelets 220 000, TQ 17 and INR 1.3, Exam-negative urine.

We demerced the surgical intervention in rahianestesia. When opening the hernial sac, we discovered the presence of an acute appendicitis with appendix closely acolyted at the back to to the bag back to its full length, especially in the package, which partly adherenced of the check, easily congestive and serous infiltrated. We proceeded the careful lysis of adhesions, appendix and issuing checks, followed by appendectomy without clogging with intraperitoneal stump grinding and abandonment and control haemostasis. We prepare the bag to package the ligation and resection. We sprained the spermatic cord from his situs and we restored the inguinal wall by retrofunicular procedure, with subcutaneous suture and Cooper drainage. Postoperatively, we administrated antibiotics, analgesics, anti-inflammatory (NSAID) suppositories, local ice, restrooms, dressing, daily supervision.

Simple postoperative evolution, bowel transit resumes after 24 hours, after 2 days we spained the drain tube, at 7 days we

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removed the skin stitches and the patient left hospital with appropriate recommendations, surgically cured.

The case analysis highlights some features:

- Relatively recent right inguinal hernia, under two years of evolution;
- Strangulation under four hours with slight reduction in taxi and rapid resumption of bowel transit;
- Persistence of spontaneous pain and endured feeler, an elongated formation which covers the entire inguinal canal, erroneously interpreted as acceding endured epiploic fringe bag;
- Adherence to bag the appendix, relatively close, raises the question of an older hiring;
- Quiet evolution of the acute appendicitis, with unchanged biological values;
- Adherence to the bag and hernial strangulation through intestinal loop are the etiopathogenic factors of the acute appendicitis through appendix ischemia and secondary circulatory alterations;
- Surgical treatment of both diseases assured the clinical recovery. A patient's refuse of the surgical intervantion leads to the complication of the acute intrasaculare appendicitis.

CONCLUSIONS

Although extensive medical literature describes the clinical sygns and development of acute appendicitis in the hernial sac, with all modern facilities paraclinical diagnosis, Amyand hernia is always a source of intraoperative surprisea, as for Claudius Amyand during its surgical intervention on 6 December 1736 St. George's Hospital in London.

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FROM ORAL CANDIDOSIS TO HASHIMOTO THYROIDITIS

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Keywords: *oral candidiasis, Hashimoto thyroiditis*

Abstract: *The present article intends to demonstrate the raise in reception of the micotic infection of the oral cavity on the patients suffering from hypothyroidism. The Hashimoto thyroiditis is one of the most frequent cause of the hypothyroidism. The thyroid substitution treatment ameliorates the state of health of those patients and exercises favouring effects on the micotic infection.*

Cuvinte cheie: *candidoză orală, tiroidita Hashimoto*

Rezumat: *Prezentul articol își propune să demonstreze creşterea receptivității la infecția micotică a cavității orale a pacienților suferind de hipotiroidism. Tiroidita Hashimoto este una dintre cele mai frecvente cauze ale hipotiroidismului. Tratamentul substitutiv tiroidian ameliorează starea de sănătate a acestor pacienți şi exercită efecte favorabile asupra infecțiilor micotice.*

INTRODUCTION

The microscopic uni-cells levures are ubicitare. The biggest part of them is inoffensive, even useful to the organism, some of them commensal, including those from the buccal cavity (1). Nevertheless a small percentage of fungi are pathogen and can cause severe infections of the buccal cavity mucosa, of the oesophagus, the gastrointestinal tract, the vagina, the lungs, the teguments and even system infections when the pathogen agents spreads on haematogenous way (2).

The main factors of risk for fungi infections are the lowering of the immunity, the solutions of continuity of the mucosa and of the skin (3).

The oral candidosis is an opportunist infection of the buccal cavity. Among the human candidosis, the oral one prevails (4). Its cause is usually (80%) the Candida albicans. The population is usually the asymptomatic host of Candida, in a proportion of 20 to75%, intervals varying reported to different studies (5,6).

When oral candidosis is manifested, the patient accuses local discomfort, presents modifications of the taste, the sensation of burning at the level of the tongue, dysphasia.

The predisposing factors of the oral candidosis are multiple. (5). Generally speaking they induce disequilibrium of the normal flora of the buccal cavity. More frequently the oral candidosis appears at immune – depressed persons, at holders of complete or edentate dental prosthesis. The micro-lesions of the epithelia caused by the chronic irritation allow the access of pathogen fungi that is in greater number in the saliva of the holders of prosthesis and edentations. The tabagism is a favouring factor (7).

The medical treatments are factors favouring the oral candidosis through many mechanisms (8). The antibiotics with large spectre favour the disequilibrium of the normal buccal flora. Xerostomia is a secondary effect of many medications (anticolinergics, sympatomimetics, muscles relaxing, anti-migraine, benzodiazepines, hypnotics, opiates, cytotoxics). Radiotherapy on the cervical-facial region destroys the salivary glands favouring candidosis (9).

Manu more endocrinopatia among which the diabetes, acromegalia, Cushing syndrome and, more especially, hypo-thyroids are factors of risk for oral candidosis (10, 11).

The mucous – cutanate chronic candisosis is a clinic - biologic entity summing up many endocrine insufficiencies (thyroid, para – thyroid, ovarian, pancreatic, cortical – super – renal) and oral candidosis, of the tegument and of the fanere.

The buccal cavity is affected in 90% of the cases. The biggest part of the patients suffering of this affection has a selective cell immune deficit for Candida albicans. Among the endocrine insufficiencies, the most frequent is the hypo-thyroids due to Hashimoto thyroiditis (12).

CASE PRESENTATION

The patient, aged 43, from urban environment, has been suffering from 2 years, of allergic conjunctivitis, treated without satisfying results, with local and oral antihistaminic, is sent, by the ophthalmologist, for a stomatologic check-up in order to exclude some possible dental hotbed that could entertain the conjunctiva reaction.

The stomatologic checking-up doesn't find clinical signs of dental decay, but notes that the buccal mucosa is hyperaemic, with pointed white deposits on the tongue and on the posterior side of the palace. More than that, it finds out the presence of a small goitre, facies with carotene tint and discrete palpebrale oedema.

The stomatologist recommends: 1) dental panoramas radiography, 2) endocrinology check-up, 3) and sends her to the lab for a test from the deposits on the tongue, for mycological exam.

The dental panoramic radiography detects dental decays.

The lab confirms the diagnosis of oral candidosis.

The endocrinologist retains from the anamnesis: asthenia, focus difficulties, oligoraromenoree, cold intolerance. It is objectively noted: overweight (indices of corporate mass 27kg/mp), pale, dry, cold teguments, palpebrale oedema, goitre II-nd grade with firm consistency, with irregular surface, un-painful at palpation, mobile at swallowing, without side – cervical palpable ganglions. The thyroid ecography shows an

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aspect of chronic thyroid.

Hormone dosage: TSH: 6.4 μUI/ml (normal values 0.4-4.0 μUI/ml), FT3 2.1 mg/ml (normal values 1.5-4.1 mg/ml), T4 1.3 mg/dl (normal values 0.8-1.9 mg/dl), TPO 460 UI/ml (normal values under 12 UI/ml).

Based on the symptoms, objective signs and para-clinical investigations (the thyroid echographic aspect, TSH with raised values, T3, T4 with normal values and TPO with raised values) it is establishing the diagnosis.

After 2 months of thyroid substitutive treatment (25 μg LT4 / day), the general aspect of the patient gets very well, the objective symptoms and signs of conjunctivitis disappeared.

DISCUSSIONS

The Hashimoto thyroiditis is the most frequent cause of the hyper-thyroids after iatrogenic thyroidal insufficiencies (post – thyroidectomy and radiotherapy). The beginning of the affection is progressively lent, being necessary many years until putting the diagnosis. It is more frequent on women, especially those with antecedents of thyroid affections in the family. The prevalence of the Hashimoto thyroiditis is inside the general population between 1 and 5% (13, 14).

The Hashimoto thyroiditis is a self-immune affection, due to a dysfunction of the suppressor T-cells, the B-cells producing self – antibodies against thyroid antigens – thyreoglobulina and thyroperoxidasa (15).

In the initial stage of the affection, the anti - thyreoglobulina anti – bodies prevail, than they may disappear while the anti – thyroperoxidosis anti – bodies raises, staying like that for many years (16).

From the histopathology point of view, the lymphocytes infiltrate the thyroid, destroying the thyroid parenchyma, forming lymphoid follicular and germinate centres. The epithelia follicular cells are bigger on volume and contain basophile cyto-plasma (Hurthle cells).

The destroying and replacing of the normal thyroid tissue has as a result the lowering of the circulating level of the thyroid hormones and, through the desinhibition of the thyreopropus hypophisis the increase of the TSH takes place. For a while, TSH stimulating the restant functional tissue, succeeds to maintain the normal - thyroids, but afterwards, when the gland is partially or totally destroyed, the hyperthyroidism is installed, at first, sub - clinically, than, frankly manifest (mix oedema).

The signs of the thyroid insufficiency appear, generally, in some years, as asthenia, cold intolerance, overweight, constipation, bradicardia, concentration troubles, depression.

The Hashimoto thyroiditis is part of the self-immune thyroid affections group: Graves-Basedow affection, endocrine ophtalmopathia, idiopathic oedema. It can be associated to other self-immune affections: pernicious anaemia, primary cortical – suprarenal insufficiency, hyperparathyroidism, myasthenia gravis, vitiligo (20).

The Schmidt syndrome includes the Hashimoto thyroiditis and the primary cortical – suprarenal insufficiency with self-immune etyology.

The self – immune poli -endocrine syndrome contains, besides the Schmidt syndrome: the hypoparathyroidism, the diabetes, the ovarian insufficiency and the Candida infections.

Usually, clinically the patient presents a middle volume goitre, with raised consistency (rubber goitre) with uneven surface (boselata), spontaneously or palming unpainful. At the beginning the patient is normal – thyroidal, than he becomes hypo – thyroidal. The affection is 5 times more frequent on women than on men.

The main symptoms are cold intolerance, overweight, fatigue, constipation, dry teguments, deregulation of the menstrual period, infertility, difficulties in concentration, palpebrale oedema, osseous - tendons reflexes, bradicardia.

Para clinically, the radioiodecaptation can increase, or be normal or low. The circulating thyroid hormones can be normal in the first phase of the affection, than lower. The TSH is increased since the sub clinic hypo-thyroid phase. The Hashimoto thyroid markers are the anti – thyreoglobulina and anti – thyroperoxidase antibodies in very big concentrations.

The decisive test of diagnosis is the punction with a thin needle followed by a cytological exam emphasizing the rich lymphocyte infiltrate and the Hurthle cells.

The major complication of the affection is the progressive hyperthyroidism. Other two complications can be the lymphoma of the thyroid and the thyroid adenocarcinoma, more frequent on patients with Hashimoto thyroiditis.

The treatment is of substitution with thyroid hormones, when a thyroid insufficiency is found (21).

Without a treatment, the Hashimoto thyroiditis evolves through mixedem.

The Hashimoto thyroiditis can pass through periods of hyperthyroidism (hashitoxicose). This hyperthyroidism is reversibly spontaneous, the treatment being symptomatic or with small doses and for short periods with antithyroids of synthesis.

The patients with Hashimoto thyroiditis can develop eye (thyroidal ophtalmopathia) or skin (pre-tibia mix oedema) complications, without thireotoxicose, syndrome that is called Graves euro thyroid affection.

CONCLUSIONS

1. The case we presented emphasizes two important medical aspects: a) the oral candidosis can cause allergic manifestations; b) the sub clinic hypothyroidism, without clinical symptoms or with discrete clinical symptoms and signs, is the factor of risk for oral candidosis.
2. The early diagnosis of the hyperthyroidism associated with the Hashimoto thyroiditis and the initiation, as soon as possible, of the treatment with thyroid hormones, ameliorates the quality of the patient's life and prevents the installation of the complications, including the oral candidosis.
3. The thyroid substitution treatment in the Hashimoto thyroids (affection with insidious installation, often with late diagnosis) is simple and without secondary effects.

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OLECRANON OSTEOTOMY FOR DISTAL HUMERUS FRACTURES

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Keywords: *distal humerus fractures, ORIF, olecranon osteotomy*

Abstract: *In this study we will analize the olecranon osteotomy approach for distal humerus fractures. For olecranon osteosynthesis were used AO tension band or a sponge screw 6.5 mm with extra washer or a screw 6.5 mm and additional wire. Following observations and measurements were recorded following imperfections of the olecranon osteotomy osteosynthesis: angulation of the fragment in the tranche of osteotomy, displacement of the osteotomy fragments, diastasis of the fragments in the osteotomy tranche. Olecranon osteotomy is a gesture which should be evaluated very carefully in traumatic surgery of the distal humerus. Therefore, when is absolutely necessary, the olecranon osteotomy can be done in V-shaped, with a thin blade saw, so loss of the bone in the tranche of osteotomy to be the smallest.*

Cuvinte cheie: *fractura humerusului distal, tratament chirurgical, osteotomia olecranului*

Rezumat: *În acest studiu se va analiza oportunitatea osteotomiei olecranului în abordarea fracturilor humerusului distal. Pentru osteosinteza olecranului s-au folosit fragmente de broşă Kirschner şi fir metalic cu efect de hobană sau un şurub de spongie 6,5 mm cu şaibă adiţională sau un şurub de spongie 6,5 mm şi fir metalic cu efect de hobană. În urma observaţiilor şi măsurătorilor efectuate au fost constatate următoarele imperfecţiuni ale osteosintezei tranşei de osteotomie a olecranului: angulaţia fragmentelor, decalajul fragmentelor, diastazisul fragmentelor la nivelul tranşei de osteotomie. Osteotomia olecranului este un gest care trebuie evaluat foarte atent în chirurgia traumatică a humerusului distal. Prin urmare, atunci când este absolut necesară, osteotomia transarticulară a olecranului trebuie făcută în forma literei V, cu o lamă cât mai fină, în aşa fel încât pierderea de substanţă osoasă la nivelul tranşei să fie cât mai mică.*

INTRODUCTION

In this study we will analize the olecranon osteotomy approach for distal humerus fractures. We will review especially the status after osteosynthesis of the olecranon and the anatomy changes of the section and the impact to the joint congruency.

MATERIAL AND METHOD

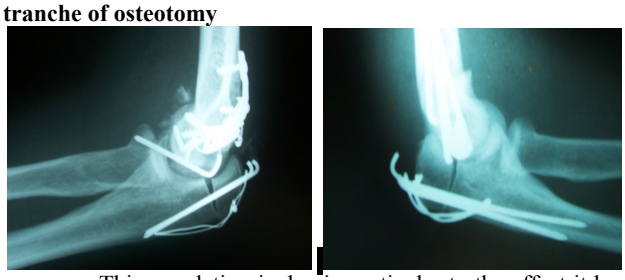
This study includes a group of 50 patients aged between 20 years and 60 years with an average age of 49,7 years. The study is carried out retrospectively. At all patients was performed the olecranon osteotomy to approach the distal humerus fractures. The osteotomy was performed with oscillating saw with blade of 1 mm or 2 mm thick or with Gigli saw. In cases where the osteotomy was made with oscillating saw, the section was made right for 16 cases and V-shaped for 20 cases. Last portion of the olecranon section was fractured as AO (Arbeitsgemeinschaft für Osteosynthesefragen) technique. For internal fixation of the humeral fracture was used a posterior plate, Y-plate or two perpendicular plates as is customary AO (posterior for external column, internal for the internal column), wire fragments, wire fragments and screws for intercondilar fixation, Herbert screws or a combination of materials previously maintained according to intraoperative conditions, quality of bone or surgeon preference. For olecranon osteosynthesis were used AO tension band or a sponge screw 6.5 mm (1,4) with extra washer or a screw 6.5 mm and additional wire. After surgery, in two days was made radiological control. Radiographs from these controls were used for radiological assessment of distal humerus fixation and evaluate osteosynthesis of olecranon osteotomy tranche.

RESULTS AND DISCUSSIONS

Following observations and measurements were recorded following imperfections of the olecranon osteotomy osteosynthesis:

- Angulation of the fragment in the tranche of osteotomy (Fig.1. a, b)..

Figure no. 1. a and b. Angulation of the fragment in the tranche of osteotomy



This angulation is due in particular to the effect it has the AO tension band on the posterior surface of the olecranon. Basically, because of the tension and compaction force that are engaged in the posterior cortex of the olecranon, combined with anterior cortical bone integrity (which was fractured) (Fig.2.a), appear this angulation (Fig.2.b), angulation, which is directly proportional with defect size produced by oscillating saw and metal wire tension. This angle is inversely proporţinal with ulna size, respectively as the distance between the two cortical of the

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olecranon is less, the angle is greater after the osteosynthesis. Also, the angle can increase by excessive tension in metal wire, by spongious bone compacting and corticals superposition. If the osteotomy cuts is straight, the angulation results from the residual defect of the olecranon cortex after osteotomy. This defect may be important when the osteotomy is done improper (very thick blade saw, Gigli increased diameter).

- Displacement of the osteotomy fragments (Fig. 3.)

Figure no. 2. a. Defect formed by osteotomy, b. Angle formed by osteosynthesis

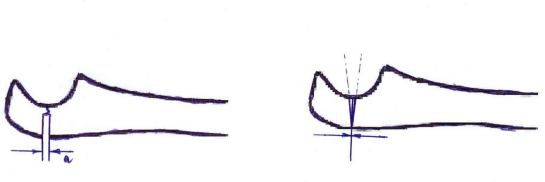
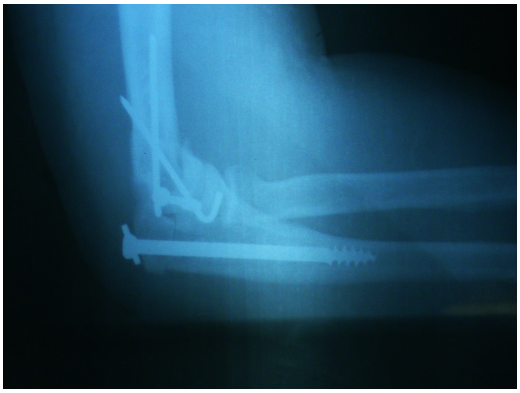


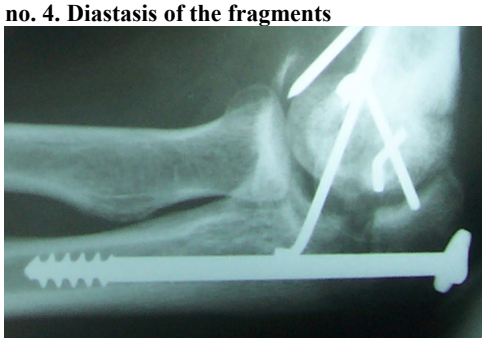
Figure no. 3. Displacement of the osteotomy fragments in a screw osteosinthesis



Displacement of the fragments appear particularly when the osteotomy tranche is right and the osteosynthesis is done with screw, because when the screw engages in the channel, it will turn along ulna channel (2,5,6), resulting the displacement of the proximal fragment, cause exists a natural angulation of the proximal part of ulna. This displacement will create a step in the joint, which if is important will reduce significantly the cubital articular surface that comes into contact with articular surface of the distal humerus. This will lead to changes in components of reaction forces that occur in the joint during flexion-extension cycle.

- Diastasis of the fragments in the osteotomy tranche (**Fig.4**.)

Figure no. 4. Diastasis of the fragments



Interfragmentar diastasis may have two causes: either a very large tranche of the osteotomy or cubits wide channel, where the screw has no stability. When the channel is wide, diastasis can be corrected by adding a wire with tension effect. This can translate diastasis evolving through the development of a close pseudarthrosis (3) to the olecranon, pseudarthrosis, which generally is well tolerated. Healing is slower outbreak olecranon diastasis interfragmentar and this will interfere with functional rebilitation program and progress are modest recovery of elbow function in this case.

CONCLUSIONS

Olecranon osteotomy is a gesture which should be evaluated very carefully in traumatic surgery of the distal humerus. Any osteotomy, regardless of how it is achieved, by osteosynthesis, induces unwanted changes in the olecranon geometry. These changes are important as both can lead joint non-congruency, mismatch can have a devastating impact on the subsequent function of the elbow (3). Therefore, when is absolutely necessary, the olecranon osteotomy can be done in V-shaped, with a thin blade saw, so loss of the bone in the tranche of osteotomy to be the smallest.

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THE ISCHEMIC NEUROPATHY OF THE LOWER LIMBS – INVOLVEMENT OF THE MOTOR FIBRES

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Keywords: *ischemic neuropathy, multiplex mononeuropathy*

Abstract: *Secondary affection of the peripheral nerves of lower limbs during the chronic obliterative arteriopathy stands for ischemic neuropathy. The aim of this article is to establish the involvement degree of the peripheral nervous system and the muscle fiber in the ischemic pathology, by comparing the functional / clinical aspects and also to set an electroneurographic and electromyographic investigation grid for patients with ischemic pathology. The study results showed that the decrease of the motor potential amplitude is much more common in comparison with the decease of conduction velocity, suggesting a predominantly axonal impairment of the motor nerves. Both the motor potential amplitude as well as the motor velocity decrease differently on the studied nerves, fact that suggests the presence of multiplex mononeuropathy. A significant proportion of the studied nerves are normal, sustaining the predominantly inhomogeneous effect on the peripheral nerves in ischemic neuropathy. The most commonly encountered electromyographic aspect is the chronic neuropathic type, more rarely with the presence of active denervation signs.*

Cuvinte cheie: *neuropatie ischemică, mononeuropatie multiplex*

Rezumat: *Articolul are ca scop evaluarea gradului de interesare a sistemului nervos periferic şi a fibrei musculare în patologia ischemică, comparând aspectele funcţional/clinic şi îşi propune să stabilească o grilă de explorare electroneurografică şi electromiografică la pacienţii cu patologie ischemică a membrelor inferioare. Rezultatele studiului au pus în evidenţă faptul că scăderea amplitudinii potenţialului motor este mult mai frecvent întâlnită comparativ cu scăderea vitezei de conducere, ceea ce sugerează o afectare predominant axonală a nervilor motori. Atât amplitudinea potenţialului motor cât şi viteza de conducere motorie scad în mod diferit pe nervii studiaţi, aspect care sugerează prezenţa mononeuropatiei multiplex. Un procent semnificativ din nervii studiaţi sunt normali, susţinând afectarea predominant inomogenă a nervilor periferici în neuropatia ischemică. Aspectul electromiografic cel mai des întâlnit este traseul de tip neurogen cronic, mai rar cu prezenţa de semne de denervare activă.*

INTRODUCTION

The ischemic neuropathy stands for the secondary damage of the peripheral nerves during the chronic obliterative arteriopathy. Although frequently encountered in the current clinical activity, the literature data regarding this form of neuropathy are scarce and scattered, which implies the need of thorough electrophysiological research in patients with chronic obliterative arteriopathy of the lower limbs.

The morphopathological aspect of the peripheral nerve, encountered in atherosclerotic peripheral vascular diseases, is quite difficult to set, the research data being extremely limited. Although the vascular architecture of the peripheral nerves provides a high degree of resistance, both the chronic as well as the acute ischemic diseases show a process of axonal degeneration of focal character, both of the myelined as well as of the non-myelined nervous fibers. Moreover, one could also encounter a demyelination process, secondary to axonal lesions or due to the damage caused to Schwann cells by ischemia. (3,5,13)

Clinically, the neuropathy associated with obliterative arteriopathy has been described through two forms: as a mononeuritis multiplex, where it is considered that the unequal and asymmetrical disposition of the nerves, the dispersion in time and space of the neurological symptoms and the electro-physiological alterations are connected rather to global ischemic phenomena, than a systemic disorder; as a polyneuropathy with mainly distal damage, more or less symmetrical, especially encountered in high arterial diseases (distal aorta, common iliac arteries, common femoral arteries). (1,3,4,6,11,19,20)

The encountered electrophysiological aspect is that of a monomelic neuropathy, multineuropathy or distal polyneuropathy with more or less symmetrical disposition. In the case of ischemic neuropathy, the electroneurographic findings are: the decrease of the CMAP (compound muscular action potential) amplitude, the moderate increase of distal latencies, the also moderate decrease of motor and sensorial conduction velocities (MCV and SCV) and the increase of the F wave latency. (2,9,10,12) From an electromyographic point of view, one notices anomalies in the sense of axonal loss (hence sharp positives and fibrillation potentials) in the intrinsic muscles of the leg and to a lesser extent in the anterior tibial, gastrocnemian and solar muscles, reduced recruitment (of neuropathic type) or lack of recruitment, as well as records of re-innervation (large motor unit potentials and / or polyphasic potentials), occurring several months after the lesion. (7,8,14,15)

PURPOSE OF THE STUDY

The objectives consisted of:

- assessing the degree of involvement of the peripheral nervous system and muscle fiber in ischemic pathology,

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comparing the functional/clinical aspects.
- establishing an electroneurographic (ENG) and a myographic (EMG) exploration grids in patients with ischemic pathology of the lower limbs.

MATERIAL AND METHOD

The study was performed on 47 patients with a diagnosis of chronic obliterative arteriopathy of the lower limbs, which addressed to the Clinical Recovery Hospital of Cluj-Napoca. A grid of biochemical tests (including ESR and determinations of glicemia, cholesterol, triglycerides, urea, hemoglobin, WBC and platelets) excluded those patients who had peripheral nervous system involvement with other etiology (non-ischemic). The diagnosis of obliterative arteriopathy was established clinically and through Doppler examinations of the lower limbs. The electrophysiological testing was performed with a Keypoint Portable type device, existent in the Laboratory of electrophysiology "Mircea Serban" of the Clinical Recovery Hospital. The electroneurographic exploration comprised: the stimulus intensity at the maximum amplitude of the action potential, CMAP latency and amplitude at both the proximal and distal stimulation, the motor conduction velocity on the common peroneal and tibial nerves, bilaterally. The electromyografic examination consisted of a detection study at rest and in muscle contraction in extensor digitorum brevis (innervated by the common peroneal nerve) and abductor hallucis (the tibial nerve area), bilaterally. The values obtained were compared with normal values for the parameters of existing record in the literature. Normal values for common peroneal nerve, stimulated distally on the ankle and proximally in popliteal fossa are considered more than 5 mV for potential amplitude and more than 42m/s for conduction velocity. For tibial nerve, stimulated in the same regions, normal values were more than 3 mV for potential amplitude and more then 41m/s for conduction velocity. (7,8,12,16,17) The statistical processing of data was performed using SPSS program.

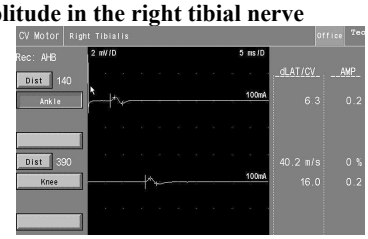
RESULTS AND DISCUSSION

The lot of 47 patients with chronic obliterative arteriopathy confirmed through arterial Doppler examination, without other associated pathologies that could cause neuropathy, consisted of 21,3% women and 78,7% men, in concordance with the existent epidemiological data, which show a higher incidence of this pathology in males. The average age was 63,6 years.

In neuropathy associated with chronic obliterative arteriopathy, electroneurographic aspects encountered are: the decrease of CMAP amplitude, the moderate increase of distal latencies, as well as the moderate decrease of the MCV. Motor conduction velocities are not significantly affected in some groups of patients (probably in early stages of the arterial disease), being predominantly axonal affected, or they may be slightly lower in other described groups of patients, the most likely explanation being the preferential loss of fast conduction, myelined axons, supported also by some histological studies (5,6,17,21,22).

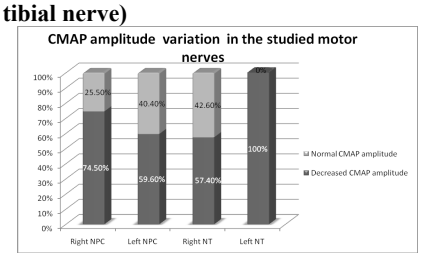
CMAP amplitude reflects the number of excitable nerve fibers in a semi-quantitative manner (as the number of fibers that respond to a maximal stimulus). When CMAP amplitude decreases, it specifically and sensibly suggests an axonal damage. (Fig. 1.) In the case of neuropathy associated with chronic obliterative arteriopathy, it is lower in case of pain at rest, than in that of intermittent claudication, there being a relationship between the degree of clinical impairment (pain intensity and character) and CMAP amplitude. (2,9,12). The reduction of CMAP amplitude in the symptomatic leg is the most prominent electrophysiological abnormality. The CMAP amplitude is a less sensitive parameter in the cases with moderate symptoms, due to its wide variation, even in normal subjects (16,18).

Figure no. 1. Patient M.I., female, 62 years old, diagnosed with ischemic neuropathy, presenting decreased MCV and CMAP amplitude in the right tibial nerve



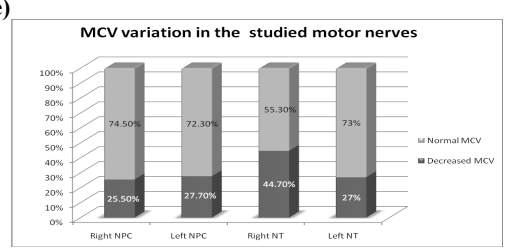
In our studied group of patients we found that there is an increased, irregular frequency of the CMAP decrease with percentages ranging between 59.6% and 100%, both in distal as well as proximal stimulation of the common peroneal and tibial nerves, bilaterally. This certifies axonal damage of the studied nerves and it is consistent with the previous data from literature. (Fig. 2.)

Figure no. 2. Changes in CMAP amplitude in the studied motor nerves (CMAP-compound muscle action potential, Right NPC – right common peroneal nerve, Left NPC – left common peroneal nerve, Right NT – right tibial nerve, Left NT – left tibial nerve)



On the other hand, the decrease of motor conduction velocity in the studied motor nerves occurs more rarely (ranging between 17% and 44.7%), suggesting that the process of demyelination is seen less frequently. (Fig. 3.)

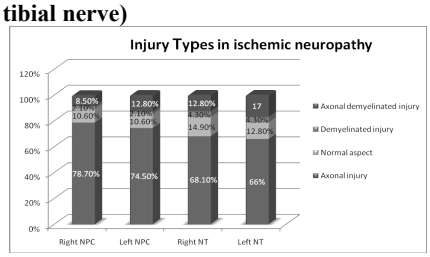
Figure no. 3. MCV variation in the studied motor nerves (VCM - motor conduction velocity, Right NPC – right common peroneal nerve, Left NPC – left common peroneal nerve, Right NT – right tibial nerve, Left NT – left tibial nerve)



In concordance with the CMAP amplitude decrease and/or the MCV decrease, correlated with the increase of distal latency, one classified the types of lesions encountered in the studied lot into 4 categories: axonal lesions (the most frequent, between 66% and 78,7%), axonal-demyelinating lesions (between 8,5% and 17%) and demyelinating lesions (between 2,1% and 4,3%). One notices the presence of a normal itinerary, with a variable frequency according to the studied nerve (between 10,6% and 14,9%). (Fig. 4.) The axonal lesion was defined based on the Ohr criteria, which consist in a severe decrease in amplitude of normal form and duration CMAP, the minimum increase of distal latencies (but by no more than 50% of the normal average values) and normal conduction velocities

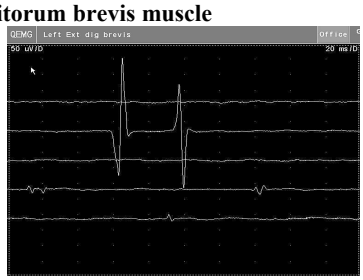
or decreased ones, but no more than 40% in the absence of conduction blocks or temporal dispersion. The demyelinating lesions were defined based on the decrease in motor conduction velocity, the increase of distal latency, and normal or slightly low CMAP amplitude.

Figure no. 4. Lesion types in the lot of studied patients (Right NPC- right common peroneal nerve, Left NPC – left common peroneal nerve, Right NT – right tibial nerve, Left NT – left tibial nerve)



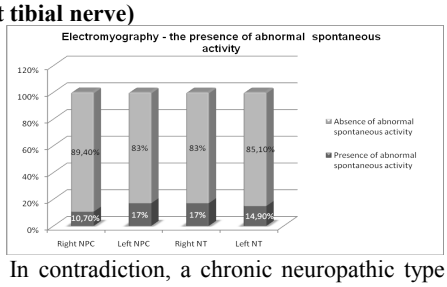
From an electromyographic (needle EMG) point of view, one notices severe anomalies in the muscles, within the lines of positive sharp waves (PSW) axonal loss and fibrillation potentials in the intrinsic leg muscles and, on a smaller scale, in the anterior tibial, gastrocnemian and solar muscles. If the ischemic lesion is severe, there can also be a decreased recruitment (of neuropathic type) or no recruitment at all. Evidence of the reinnervation can be seen months or years after the nerve was damaged, including motor unit action (MUAP) and/or polyphasic potentials.

Figure no. 5. Patient M. N, male, 56 years old, with chronic axonal polyneuropathy, presenting fasciculations in the left extensor digitorum brevis muscle



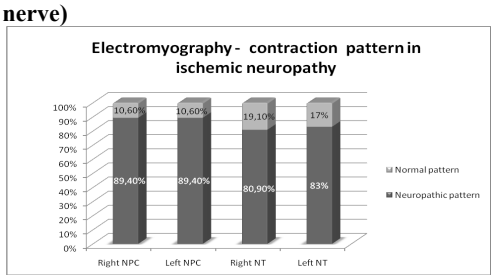
On the studied lot, we noticed during the electromyography (detection studies in extensor digitorum brevis muscle and the abductor halucis muscle), the presence of pathological activity at rest in a small number of patients (between 10, 7% and 17%).

Figure no. 6. Electromyographic aspects: the presence of pathological activity at rest in the studied muscles (Right NPC – right common peroneal nerve, Left NPC – left common peroneal nerve, Right NT – right tibial nerve, Left NT – left tibial nerve)



In contradiction, a chronic neuropathic type itinerary stood out, having a much higher frequency in comparison with the presence of anomalies at rest (between 80,9% and 89,4%). We noticed a reduced recruitment (of neuropathic type), as well as proofs of reinnervation, including large motor unit action potentials (MUAP) and/or polyphasic potentials.

Figure no. 7. Electromyographic aspects: itinerary types during contraction, in the studied muscles (Right NPC – right common peroneal nerve, Left NPC – left common peroneal nerve, Right NT – right tibial nerve, Left NT – left tibial nerve)



CONCLUZII

The patients diagnosed with chronic obliterative arteriopathy of the lower limbs present altogether damage of the peripheral nerves, which clinically manifests itself in two ways: as a polyneuropathy, with predominantly distal damage, more or less symmetrical or as a mononeuritis multiplex, with unequal and asymmetrical disposition of the affected nerves, which is more common encountered.

The electrophysiological picture consists mainly of the same aspects: monomelic neuropathy, multineuropathy or distal polyneuropathy with more or less symmetrical distribution. Electroneurographically, in the case of ischemic neuropathy one notices the CMAP (compound muscle action potential) amplitude decrease, distal latencies moderate increase, the also moderate decrease of motor and sensorial conduction velocities and the increase of the F wave latency. The damage on the motor nervous fibers, in the case of ischemic neuropathy, manifests itself through a decrease of CMAP amplitude, more frequently encountered than a decrease of the MCV. Both the motor potential amplitude as well as the decrease in motor velocity decrease differently on the studied nerves studied, which suggests the presence of multiplex mononeuropathies. The axonal lesions are much more frequently encountered than the demyelinating or axonal-demyelinating ones. A significant proportion of the studied nerves are normal, sustaining the predominantly inhomogeneous effect on the peripheral nerves in ischemic neuropathy. The most commonly encountered electromyographic aspect is the chronic neurogenic type itinerary, more rarely with the presence of active denervation signs.

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CLINICAL ASPECTS OF DIABETIC NEUROPATHY

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Keywords: *diabetic polyneuropathy; diabetic autonomic neuropathy; focal neuropathies; entrapment neuropathies; painful diabetic neuropathy*

Abstract: *Approximately 30–50% of all diabetic patients are affected by neuropathy and it is the commonest form of neuropathy in the developed world. Diabetic neuropathies are among most common long-term complications of diabetes. Diabetic neuropathy (DN) is defined as the presence of symptoms and/or signs of peripheral nerve dysfunction in people with diabetes mellitus after the exclusion of other causes. There is now little doubt that glycaemic control and duration of diabetes are major determinants of distal symmetrical neuropathy. Distal symmetric polyneuropathy, the most common form of diabetic neuropathy, usually involves small and large nerve fibers. Small-nerve fiber neuropathy often presents with pain and loss of intraepidermal nerve fibers, but without objective signs or electrophysiologic evidence of nerve damage. The greatest risk from small-fiber neuropathy is foot ulceration and subsequent gangrene and amputation. Large-nerve fiber neuropathy affects profund sensitivity. Some patients may be completely asymptomatic, and signs may be only discovered by a detailed neurologic examination.*

Cuvinte cheie: *polineuropatia diabetică, neuropatia diabetică autonomă, neuropatii focale, neuropatii de încarcerare, neuropatia diabetică dureroasă*

Rezumat: *Neuropatia diabetică afectează aproximativ 30–50% dintre pacienţii cu diabet zaharat şi este cea mai comună formă de neuropatie în ţările dezvoltate. Cea mai frecventă complicaţie a diabetului zaharat este neuropatia. Neuropatia diabetică este definită ca prezenţa semnelor şi/sau simptomelor de disfuncţie a sistemului nervos periferic la un pacient cu diabet zaharat după ce se exclud alte cauze. Nu este nicio îndoială că determinanţii majori ai neuropatiei simetrice distale sunt controlul glicemiei şi durata diabetului. Polineuropatia simetrică distală, cea mai frecventă formă de neuropatie diabetică, afectează atât fibrele cu calibru mare cât şi scăzut. Neuropatia de fibre cu diametru scăzut se prezintă cu durere şi pierderea fibrelor nervoase intraepidermice, însă fără semne obiective sau electrofiziologice de afectare a nervilor. Cel mai mare risc al neuropatiei de fibre cu diametru scăzut este ulceraţia piciorului care poate duce la gangrenă şi amputaţie. Neuropatia de fibre cu diametru crescut afectează în primul rând sensibilitatea profundă. Unii pacienţi pot fi complet asimptomatici dar pot să apară modificări la un examen neurologic detaliat.*

SCIENTIFICAL ARTICLE OF BIBLIOGRAPHIC SYNTHESIS

DNs are among the most frequent complications of diabetes mellitus. The frequency of neurological complication in diabetes mellitus has been variably estimated in published reports. About 15% of patients with diabetes have both symptoms and signs of neuropathy, but nearly 50% have nerve conduction abnormalities. DN is the most common form of neuropathy in developed countries and is responsible for 50% to 75% of nontraumatic amputations. Foot ulceration can lead to gangrene and ultimately to limb loss. DN also has a tremendous impact on patients' quality of life predominantly by causing weakness, ataxia, and incoordination predisposing to falls and fractures (1,3,8).

Classification of Diabetic Neuropathy after Low and Suarez (7)

Symmetrical neuropathies

- Distal sensory and sensori-motor neuropathy
- Large-fiber type of diabetic neuropathy
- Small-fiber type of diabetic neuropathy
- Distal small-fiber neuropathy
- "Insulin neuropathy"
- Chronic inflammatory demyelinating polyradiculoneuropathy

Asymmetrical neuropathies

- Mononeuropathy
- Mononeuropathy multiplex
- Radiculopathies
- Lumbar plexopathy or radiculoplexopathy
- Chronic inflammatory demyelinating polyradiculoneuropathy

A classification system by Thomas combines both anatomy and pathophysiology and is presented below with a few modifications: (10)

- Hyperglycemic neuropathy (acute)
- Generalized symmetric polyneuropathies
- Sensory
- Sensorimotor (chronic, symmetric)
- Autonomic
- Focal and multifocal neuropathies
- Cranial
- Proximal motor (amyotrophy)
- Thoracic or lumbar radiculopathies
- Focal limb (entrapment neuropathies)
- Superimposed chronic inflammatory demyelinating polyneuropathy

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Chronic Distal Symmetrical Neuropathy is probably the most common variety of diabetic neuropathy. Is an exclusion diagnosis. It can only be made after careful clinical investigation and after the exclusion of other causes, chronic inflammatory demyelinating polyneuropathy, vitamin B12 deficiency, monoclonal gammapathy, hypothyroidism, uremia. In type 1 diabetes mellitus, distal polyneuropathy becomes symptomatic after many years of chronic prolonged hyperglycemia. Conversely, in type 2, it may present after only a few years of known poor glycemic control. Patients with type 2 diabetes mellitus may sometimes already have neuropathy at the time of diagnosis (6,9).

Most frequently, DPN is a mixed sensorimotor neuropathy. Sensory symptoms are more prominent than motor symptoms and usually involve the lower limbs. When sensory symptoms reach the knees, hands develop similar symptoms, progressing proximally. Anterior aspect of the trunk and vertex of the head may be affected at a very late stage. Sensory symptoms include pain, paresthesiae, hyperesthesia, and allodynia wherein patients report pain with nonpainful stimuli such as touch, contact with bedclothes. Patients may experience negative symptoms such as hypo/analgesia, hypo/anestesia, reduction of thermal, vibration and pressure sensation, reduction of peripheral reflexes. Diabetic neuropathic pain is characteristically more severe at night, and often prevents sleep. A curious feature of the neuropathic foot is that both numbness and pain may occur, the so called “painful, painless” leg (1,9,13,14).

Muscle strength is usually normal during the early course of the disease, although mild weakness may be found in toe extensors. With progressive disease there is significant generalized muscular wasting, particularly in the small muscles of the hand and feet. Trophic changes in the form of deep ulcerations and neuropathic degeneration of the joints (Charcot joints) are seen in the most severe cases, due to sensory lost and repetitive injury (1,8,13)

The American Diabetes Association recommends that all patients with type 2 diabetes mellitus be screened for DN at diagnosis, and all patients with type 1 diabetes mellitus be screened 5 years after diagnosis. Screening should be repeated annually and must include sensory examination of the feet and ankle reflexes (6).

Small-fiber neuropathy is a distinct entity usually within the context of young type 1 patients. A prominent feature of this syndrome is neuropathic pain. Paraesthesae is also often experienced and allodinia may be present. The pinprick and temperature sensation are reduced in a “stocking” and “glove” distribution. There is relative sparing of vibration and position sense (because of relative sparing of the large diameter Aβ fibers). Muscle strength and reflexes are usually normal. Autonomic function tests are frequently abnormal and affected male patients usually have erectile dysfunction. Sural sensory conduction velocity may be normal, although the amplitude may be reduced. It is unclear, whether this syndrome is in fact distinct or it represents the early stages of distal symmetrical neuropathy (9,13).

Pure Diabetic autonomic neuropathy is rare. Some degree of autonomic involvement is present in most patients with diabetic polyneuropathy. Signs may include orthostatic hypotension, resting tachycardia, anhydrosis, pupillary and lacrimal dysfunction, nocturnal diarrhea, bladder disfunction, sexual impotence and necrobiosis lipoidica (polycyclic cutaneous atrophy in women) (1,8,11).

Acute Painful Neuropathy of Poor Glycemic Control may occur in the context of type 1 or type 2 diabetic subjects. There is no relationship to the presence of other chronic diabetic complications. There is often an associated severe weight loss. Ellenberg coined the description of this condition as “neuropathic cachexia”. Patients typically develop persistent burning pain associated with allodynia. The pain is most marked in the feet, but often affects the whole of the lower extremities. The pain is typically worse at night although persistent pain during day time is also common. These symptoms often lead to depression. There are usually no motor signs, although ankle jerks may be absent. Nerve conduction studies are also usually normal or mildly abnormal. Symptoms usually improve with prolonged glycemia control. Symptoms are often refractory to other pharmacologic treatment. Recovery may be incomplete and prolonged over many months (9,13).

In case of Acute Painful Neuropathy of Rapid Glycemic Control (“Insulin neuropathy”) the patient presents with burning pain, paraesthesiae, allodynia, often with a nocturnal exacerbation of symptoms; and depression may be a feature. There is no associated weight loss. Sensory loss is often mild or absent, and there are no motor signs. There is usually complete resolution of symptoms within 12 months. A recent study looking into the epineurial vessels of sural nerves in patients with acute painful neuropathy of rapid glycemic control demonstrated marked arterio/venous abnormality including the presence of proliferating new vessels, similar to those found in the retina (12).

Proximal Motor Neuropathy may occur in the cervical or lumbosacral distributions. Is referred to in the literature by various designations including diabetic amyotrophy, Bruns-Garland syndrome, and diabetic plexopathy. This condition often occurs in patients older than 50 years, in conjunction with weight loss and is associated with mildly elevated serum glucose levels. The patient presents with severe pain, which is felt deep in the thigh, but can sometimes extend lower than the knee and to the opposite side. The pain is usually continuous and often causes insomnia and depression. On examination there is profound wasting of the quadriceps with marked weakness. Hip flexors and hip abductors can also be affected. The knee jerk is usually reduced or absent. Sensory loss is unusual, and if present indicates a coexistent distal sensory neuropathy. Electrophysiological studies may demonstrate increased nerve latency and active denervation of affected muscles. (1,5,8,13).

Chronic Inflammatory Demyelinating Polyradiculopathy (CIDP) occurs more commonly among patients with diabetes. One should particularly be alerted when an unusually severe, rapid, and progressive polyneuropathy develops in a diabetic patient. Nerve conduction studies show features of demyelination. The presence of 3 of the following criteria for demyelination is required: partial motor nerve conduction block, reduced motor nerve conduction velocity, prolonged distal motor latencies, and prolonged F-wave latencies. CSF demonstrate increased protein and a normal or only slightly elevated cell count (11,13).

The most common cranial mononeuropathy is the third cranial nerve palsy. The patient presents with pain in the orbit, headache, followed by diplopia. There is typically ptosis and ophthalmoplegia. The pupil is usually spared. Recovery occurs usually over three months. Fourth, sixth and seven cranial nerve palsies (taste is not normally involved) have also been described in diabetic subjects. Most recover spontaneously in 3-6 months. Anterior ischemic optic neuropathy manifests as acute visual loss or visual field defects (usually inferior altitudinal). The optic disk appears pale and swollen. Flame-shaped hemorrhages may be present. Pupillary motility is disturbed in 10-20% of diabetics. Anisocoria and an anormally slow light response are the most common abnormalities (4,8,9,13).

Multiple nerves may be affected simultaneously and in different teritories (mononeuritis multiplex) (1,13).

Truncal radiculopathy is well recognized to occur in

diabetes. It is characterized by an acute onset pain in a dermatomal distribution over the thorax or the abdomen. The pain usually begins unilaterally; then may become bilateral There may be patchy sensory loss detected by pin prick and light touch examination. Single or multiple spinal roots are involved. Recovery is usually the rule within several months, although symptoms can sometimes persist for a few years (1,13)

Pressure Neuropathies (entrapment neuropathies). In the Rochester Diabetic Neuropathy Study, Dyck et al. (5), found electrophysiological evidence of median nerve lesions at the wrist in about 30% of diabetic subjects, although the typical symptoms of carpel tunnel syndrome occurred in less than 10%. Focal neuropathies in the extremities caused by entrapment or compression at common pressure points or by ischemia and subsequent infarction. Entrapment and compression tend to occur in the same nerves and at the same sites as in individuals without diabetes. Median nerve entrapment at the wrist (carpal tunnel syndrome) is more common in patients with diabetes and can be treated in the same manner as in patients without diabetes. Symptoms are often bilateral. The susceptibility to ulnar nerve entrapment at the elbow or common peroneal nerve entrapment at the fibular head is not definitely increased among patients with diabetes (4,9,13).

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SALIVARY PH AND THE TAMPON CAPACITY OF THE STIMULATED SALIVA IN DIABETICS CHILDREN VERSUS NON-DIABETICS CHILDREN

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Cuvinte cheie: *pH, capacitate tampon, diabet*

Rezumat: *Modificările parametrilor salivari pot creşte riscul de apariţie a cariilor la copii cu diabet zaharat. Scopul studiului este de a măsura pH-ul salivar şi capacitatea tampon a salivei la subiecţii diabetici în comparaţie cu subiecţii nediabetici. Au fost cuprinşi în studiu 143 de copii, 68 de copii diabetici şi 75 copii nediabetici cărora cu ajutorul benzilor de testare le-a fost determinat pH-ul şi capacitatea tampon a salivei. Rezultatele au arătat existenţa corelaţiilor statistice semnificative ($p<0.0001$) relevând o diferenţă între media pH-ului diabeticilor, fiind o salivă moderat acidă, spre o salivă acidă (6,3529) şi media pH-ului nediabeticilor fiind o salivă sănătoasă (7,4133). La diabetici capacitatea tampon este foarte scăzută (5,09) iar la nediabetici este ridicată (9,61), existând astfel şi în cazul capacităţii tampon o diferenţă semnificativă ($p<0.0001$). În concluzie atât pH-ul salivar cât şi capacitatea tampon a salivei sunt semnificativ mai scăzute la pacienţii diabetici decât la cei nediabetici.*

Keywords: *pH, buffer capacity, diabetes*

Abstract: *Changes in salivary parameters may increase the risk of cavities in children with diabetes. The aim of the study is to measure the salivary pH and buffer capacity of saliva in diabetic subjects compared with non-diabetic subjects. In the study were 143 children, 68 diabetic children and 75 non-diabetic children on which using the test strips it was determined the pH and buffer capacity of saliva. The results showed the existence of significant statistical correlations ($p <0.0001$) revealing a difference between the average pH of diabetes, being a moderately acidic saliva, to an acid saliva (6.3529) and average pH of non-diabetic being a healthy saliva (7.4133). Buffer capacity in diabetics is very low (5.09) and in non-diabetic is high (9.61), so the buffer capacity has a significant difference ($p <0.0001$) also. In conclusion the salivary pH and buffer capacity of saliva are significantly lower in diabetic patients than in non-diabetic.*

INTRODUCTION

Studies show that the number of cases of diabetes type I and II in children is increasing in many countries. In the literature are data showing proof of differences of salivary secretion and composition in patients with diabetes compared to non-diabetic subjects.

PURPOSE OF THE STUDY

Measurement of salivary pH and the establishment of the buffer capacity of stimulated saliva of the diabetic subjects compared with non-diabetic subjects.

MATERIAL AND METHOD

In the study were 143 children, 68 diabetic children and 75 non-diabetic children. The study group ranged in age from 5-18 years. Both groups were homogeneous in terms of age and sex.

1. Salivary pH: We instruct the patient to expectorate any pooled saliva into the collection cup.Take a pH test strip and place it into the sample of resting saliva for 10 seconds(fig.1).After the 10 seconds it is checked the colour of the strip. The colour obtained is compared with the testing chart. Thus saliva may be:

- between 5 and 5,8 higly acidic
- between 6 and 6,6 moderately acidic
- between 6,8 and 7,8 healthy

2. Buffer capacity of saliva: We instruct the pacient to chew the piece of wax to stimulate salivary flow, after that on a period of 5 minutes the pacient expectorates the collected saliva(fig.2).

Figure no. 1. Salivary pH testing

Loosen the foil pack protection of the buffer capacity test strip and put the strip on an absorbent tissue. Test strips are used immediately after the package was opened. Ussing a pipette, it is collected sufficient saliva from the collection cup(fig.3) and a drop of saliva is distributed on each of the three areas on the test strip(fig.4). Immediately turn the stripe 90˚ so that the napkin can absorb the excess saliva. This maneuver will prevent the excess saliva from swelling the test strip and thus do not affect the accuracy of the result. Test strips will begin to change color immediately after 2 minutes (fig. 5). The final result is calculated by giving to each of the final color the corresponding table points after the conversion table(fig. 6). Where a colour combination provides an unclear result it is used an intermediate scores.

Test pad colour at 2 minutes:

- green 4 points
- green/blue 3 points
- blue 2 points

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- red/ blue 1 point
- red 0 points

Collect the three figures obtained and interpreted the final results:

- a very low buffer capacity
- 6-9 a low buffer capacity
- 10-12 normal to high buffer capacity

Figure no. 2. Expectorating the saliva

Figure. no. 3. The collection of saliva

Figure no. 4. Saliva droplet distribution

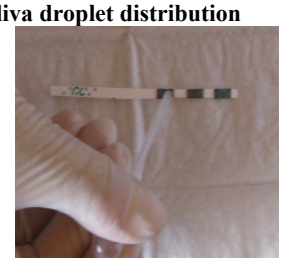
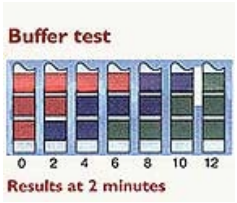


Figure no. 5. Test strips after 2 minutes

Figure no. 6. Conversion table



Data processing was obtained using statistical test T.

RESULTS

It is noted statistically significant correlations ($p < 0.0001$) revealing a difference between the average pH for diabetes and average pH for non-diabetes, meaning that people with diabetes have lower average pH, a moderately acidic saliva, to an acid saliva (6.3529) when the average of non-diabetic is more healthy(7.4133) (tabel no.1). Low salivary pH in patients with type 1 diabetes is a clear reduction of the saliva buffer capacity and an increased risk of dental caries. There are reports showing that diabetic patients have more acid saliva, while others reported no such difference. It is unclear whether the risk of caries may be greater in children patients with diabetes mellitus because of the damage to salivary factors, compared with non-diabetic children. In addition to conflicting reports, salivary parameters should be measured in children with diabetes, because most clinical trials have so far been conducted only on adults.

Table no. 1. Ph saliva in diabetic patients versus non-diabetic

Type	N	Mean	Std. Deviation
Ph diabetes			
non-diabetes	68	6.3529	.3458
	75	7.4133	.4428

Table no. 2. Buffer capacity of saliva in diabetics versus non-diabetic

Type	N	Media	Std. Deviation
Buffer capacity of saliva			
diabetes	68	5.09	1.59
non-diabetes	75	9.61	2.46

A high saliva buffer capacity can be observed in non-diabetic, mean buffer capacity of saliva being 9.61. This value is placed in the third category of normal to high buffer capacity. Buffer capacity of saliva in diabetics with an average of 5.09 is classified in the very low buffer capacity category. We have a significant difference indicated by $p < 0.0001$ between the average of the buffer capacity of saliva for diabetes and average of the buffer capacity of saliva for non-diabetes (table no. 2.).

Subjects with a low pH has also a lower buffer capacity existing a significant difference $p < 0.001$. It is known that an acid pH increases the risk of dental cavities.

DISCUTIONS

Lopez et al. observed small differences between sexes in both groups at the pH due to the differences in age and gender.

Some authors have found significant differences between diabetics and the non-diabetic patients regarding buffer capacity of stimulated saliva, as in this study, but there were authors that did not found differences. Average buffer capacity values found by Swanljung et al. in diabetic children was 5.1 and 7.4 in the non-diabetic(2).

Thorstensson et al. came at the conclusion after the study on diabetic vesus non-diabetic children, that there is no significantly differences between groups regarding the buffer capacity.

Differences between results may also be due to different methods for determining.

CONCLUSIONS

1. Buffer capacity of saliva in diabetics is significantly less and fits the category of very low saliva buffer capacity versus non-diabetic children who fit normal to high buffer capacity category.
2. Patients with diabetes had a significantly lower salivary pH compared with the non-diabetic patients pH. Average salivary pH was 6.35 for diabetic children representing an acid saliva while the non-diabetic have an alkaline saliva with an average of 7,41.

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OBESITY MANAGEMENT AS CARDIOVASCULAR RISC IN METABOLIC SYNDROME

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Keywords: *Obesity, Metabolic syndrome, Management*

Abstract: *Increased prevalence and aggressiveness of cardio-metabolic diseases justifies the growing interest worldwide in tracking and monitoring patients at risk of developing metabolic syndrome. Increased frequency of obesity and overweight with involvement and the succeeding metabolic status of weight gain more than 20% of ideal weight contributes to the diagnosis of metabolic syndrome. Obesity may be a consequence of metabolic disorders or repercussions of improper lifestyle but produces or is triggered by metabolic disorders and cardiovascular risk and represents a risk factor. The management of obesity as a risk factor associated with metabolic syndrome is the prerequisite of good medical diagnosis and treatment conduct.*

Cuvinte cheie: *obezitate, sindrom metabolic, management*

Rezumat: *Prevalenţa crescută şi agresivitatea afecţiunilor cardiometabolice justifică interesul crescând pe plan mondial în depistarea şi supravegherea pacienţilor cu risc de a dezvolta sindrum metabolic. Frecvenţa crescută a supragreutăţii şi obezităţii cu implcaţiile metabolice ce succed starea de creştere în greutate cu mai mult de 20% din greutatea ideală contribuie la diagnosticarea sindromului metabolic. Obezitatea poate fi consecinţa tulburărilor metabolice sau repercusiunea unui stil de viată necorespunzător dar care produce sau este declanşată de tulburări metabolice şi reprezintă un factor de risc cardiovascular. Managementul obezităţii ca factor de risc asociat sindromului metabolic reprezintă premisa unei bune conduite medicale de diagnosticare şi tratament al acestuia.*

SCIENTIFICAL ARTICLE OF BIBLIOGRAPHIC SYNTHESIS

The new millennium is facing, in medical terms, with complex metabolic disease highly aggressive with a population at high prevalence, with high morbidity and mortality, mainly cardiovascular and the impact on all areas of socio-economics.

Obesity is a multifactor consequence, characterized by an increase in body fat content from 15-20% to 20-30% in men and women, which leads to weight increase over 20% of ideal weight, in the same time affecting aesthetic, psychosocial and biological matter.

Obesity can be assessed using weight, waist, body and waist thigh circumference. An increase in body mass index greater than 27 kg/m2 and waist / hip higher than 0.9 in men and 0.8 in women increase cardiovascular risk (1).

In practice, obesity is the most common situation of insulin resistance and central obesity and abdominal called Android may be a clinical marker of metabolic syndrome.

Obesity is a nutritional-metabolic disorder characterized by weight loss (2). It is measured by body mass index (BMI), excluding the weight increase due to water retention or increased muscle mass:

Table no. 1. Obesity classification

Classification	IMC (kg/m2)
Normal range	18.5-24.9
Overweight	25.0-29.9
Obesity I	30.0-34.9
Obesity II	35.0-39.9
Obesity III	>40

The old methodology for assessing the degree of obesity (Broca's formula, Lorentz) and reporting to ideal weight, is not having the same predictive value as the newly adopted methodology, which is more important for cardiovascular risk assessment is the distribution of body fat.

Anthropometric assessment of obesity is achieved by:

- body mass index (BMI)
- abdominal index (IAF)
- waist measurement

Defining the degree of obesity will be made by using BMI and waist values indicate the distribution of body fat, presence of insulin resistance and cardiovascular risk.

Increased waist suggests increased cardiovascular risk, although BMI remains constant (1).

Table no. 2. RRS graduation based on classes and gender

SEX	Low risk (waist circumference)	Likely risk (waist circumference)	Certain risk (waist circumference)
Men	<=94 cm	95-101 cm	>=102 cm
Women	<=80 cm	81-87 cm	>=88 cm

Risk factors and causative of obesity, genetic and won (alcohol, smoking, sedentary lifestyle, hormonal) production by complex disturbances of behavior, food intake regulation and energy expenditure (3,4).

Contribute to the development of obesity and metabolic lipid disturbance, increased lipogenesis and reduced lipolysis.

Metabolic complications of obesity are complex:

- Carbohydrate metabolism

Insulin resistance in obesity is due to a combination of defects at the receptor and before receptor action of insulin.

Not all obese are insulin resistant, but only half of

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those with a BMI greater than 28kg/m2. Instead 40% of insulin resistance obese become diabetic after 40 years of development.

- Lipid metabolism

Obesity has a pronounced effect on VLDL metabolism. HyperTG is common and the degree of obesity correlated with TG level (5.6).

- Uric acid metabolism

There is a strong link between body weight and uric acid levels. in obesity.

- Cardiovascular complication

Almost invariably accompanies obesity hypertension. The frequency of hypertension among obesity is 50-90%. Cause and effect between the relationship of obesity and hypertension is proven to lower high blood pressure with weight loss (5).

Atherosclerosis, obesity appears to favor the development of ATS with approximately 10 years earlier due to an accumulation of vascular risk factors (dyslipidemia, sedentary lifestyle, hypertension).

Heart failure is favored by the extra effort required of the heart, hemodynamic changes induced pulmonary circulation and systemic circulation, fatty infiltration of the pericardium and myocardium.

Therapeutic targets in obesity management concerns: weight loss, new weight maintenance, prevention of obesity and lifestyle improvement is always having to review and control the complications of obesity associated conditions adapted to the risk class of patients (7).

Table no. 3. Adaptation of weight objectives to CVR risk classes

Risk Class	Weight Objective
Low	Weight maintenance 5% eventually fall
Medium	10% weight loss Maintenance of new weight Control of all risk factors and comorbidity presence
High	10-20% weight loss; BMI > 40kg/m2 Maintenance of new weight Control of all risk factors and comorbidity presence

Therapeutic Program:

- energy-restricted diet, reducing calorie intake is very important in view that each kilogram of fat is 7000 kcal. Featured were two types of diets:
  - deficient diet 500 kcal / day compared to the previous diet. It seeks to effect weight loss of 0.5 to 1 kg per week, 5 to 10 pounds in three months (approximately 5-10% of initial weight). This type of diet recommended in patients with overweight 1MC fall in group (BMI between 25 to 29.9 k/m2).
  - deficient diet 1000 kcal / day compared with previous feeding. It seeks to effect weight loss of 1-2 pounds per week, approximately 20% of initial weight. This type of diet has been recommended for patients rated as obese BMI group I / II (BMI between 33-37 kg/m2).

Regarding recommended diets were made following remarks:

- Meals should be split up throughout the day 5-6/zi number;
- Reduce consumption of unsaturated fats, sweets and salt concentrates on how possible.
- Exercise - the main modality of power consumption, is recommended both to prevent obesity, as well as its therapeutic method. Important in weight loss relationship is that low intensity to be less physical effort in weight loss, and will double in maintaining the new weight.
- Pharmacological therapy is associated with caloric regime, lipids, under the blood pressure control and heart rate in respect of any contraindications.

Optimizer also includes lifestyle and the recommendation to avoid alcohol and smoking cessation.

Ensure proper management of cardiovascular risk factors associated with metabolic syndrome requires effective communication and physician - patient aimed at optimizing the patient's lifestyle, therapeutic monitoring and ensuring psychological support.

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THE NOSOCOMIAL SEPSIS AT THE PATIENTS FROM THE INTENSIVE CARE UNIT

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Keywords: *sepsis nosocomialitate, antibiotic resistance*

Abstract: *The sepsis is a systemic inflammatory response resulting from the inability of the immune system to limit bacterial invasion after the onset of the infection. We conducted a study over a period of 4 years and 9 months in an intensive care unit of an emergency clinical county hospital to identify the frequency and aetiology of the nosocomial sepsis. The case definition for the selection of the patients was adapted according to the definition of the nosocomial septicaemia proven etiologically by laboratory testing of CDC Atlanta. The population at risk was composed of patients who had been hospitalized in ATI with the duration of at least 48 hours. We identified a total of 30 episodes of nosocomial sepsis cases with positive blood cultures, from a total of 3297 patients hospitalized in the range indicated, representing an incidence of 9.1‰. Of these, 23 cases were mono-etiologic and 7 – bi-etiologic (2 microbial species). We found that the isolated bacterial strains present in a significant percentage, resistance to antibacterial agents, which raises problems because of the treatment limitations and of the failures in the clinical course of cases.*

Cuvinte cheie: *sepsis, nosocomialitate, antibiorezistenţă*

Rezumat: *Sepsisul este răspunsul inflamator sistemic care rezultă din incapacitatea sistemului imunitar de a limita invazia bacteriană după debutul unei infecţii. Am efectuat un studiu pe o perioadă de 4 ani şi 9 luni într-o unitate de terapie intensivă a unui spital clinic judeţean de urgenţă pentru a identifica frecvenţa şi etiologia sepsisului nosocomial. Definiţia de caz pentru selectarea pacienţilor a fost adaptată după definiţia septicemiei nosocomiale dovedite etiologic prin examene de laborator a CDC Atlanta. Populaţia la risc a fost formată din pacienţi care au avut internare în ATI cu o durată de cel puţin 48 de ore. Am identificat un număr de 30 de episoade de sepsis nosocomial, cazuri cu hemoculturi pozitive, dintr-un total de 3297 de pacienţi internaţi în intervalul precizat, reprezentând o incidenţă de 9,1‰. Dintre acestea, 23 de cazuri au fost monoetiologice şi 7 – plurietiologice (2 specii microbiene). Am constatat că tulpinile bacteriene izolate prezintă într-un procent important rezistenţă la agenţii antibacterieni, ceea ce ridică probleme din cauza restricţiilor de tratament şi a eşecurilor în evoluţia clinică a cazurilor.*

INTRODUCTION

The nosocomial sepsis is an important cause of morbidity and mortality (1). Most episodes of nosocomial bacteraemia occur endemically, being secondary bacteraemia caused by wound infections, pneumonia or urinary infections; the primary bacteraemia often occur following the use of the intravascular devices, but in many cases the source remains unknown. The immune-compromised host is at risk of developing bacteraemia manifested endemically, but the epidemic ones occur at the immune-competent individuals being linked to specific therapeutic measures: the segregation of these patients in intensive care units where the risk is increased, the intravenous therapies, the invasive manoeuvres which involve the blood torrent.

PURPOSE OF THE STUDY

The identification of the incidence, aetiology and of the antibiotic susceptibility of the germs which cause the nosocomial septicaemia in intensive care units.

MATHERIAL AND METHOD

We realized a prospective study between January 2005 - September 2009 in the ATI section of the Emergency County Hospital Sibiu; there were taken to be studied the patients during the hospitalization period and who showed clinical signs of sepsis proven etiologically by blood cultures positive for the micro-organisms which were not the cause together with other infections of the patient, infections which were already present in the moment of the internment in ATI (to meet the criterion of disease); the pseudo-bacteraemia were excluded (transient bacteraemia or through the supra-infection of the samples collected or transported incorrectly). The data source was the patient case report forms, supplemented by the laboratory analysis. There were recorded germ / isolated germs from blood cultures and their antibiotic resistance. The collecting of the blood cultures was done in the moment of the maximum febrile/chill ascension, taking into account the protocol recommended by the medical microbiologist. Excel programme was used to meet the database and graphics processing. The following abbreviations have been used for the graphic representation of the antibiotic diagrams: P = penicillin, amp = ampicillin, amc = amoxicillin + clavulanic, Sat = amoxicillin + sulbactam, ox = oxacilina, ipm = imipenem, mem = meropenem, atm = aztreonam, tzp = piperacillin + tazobactam, prl = piperacillin, fox = cefoxitin, cec = cefaclor, event = ceftazidime, ctx = cefotaxime, cpo = cefpirom, fep = cefepime cro =

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cetftriaxon, g = gentamicin, ak = amikacin, str = streptomycin, cip = ciprofloxacin, lev = levofloxacin, mox = moxifloxacin, ofx = ofloxacin, nor = norfloxacin, e = erythromycin, da = clindamycin, lzd = linezolid, te = teicoplanin, va = vancomycin, te = tetracycline, dox = doxycycline, rd = rifampicin, c = chloramphenicol, sxt =**s**ulfamethoxazole trimethoprim.

RESULTS

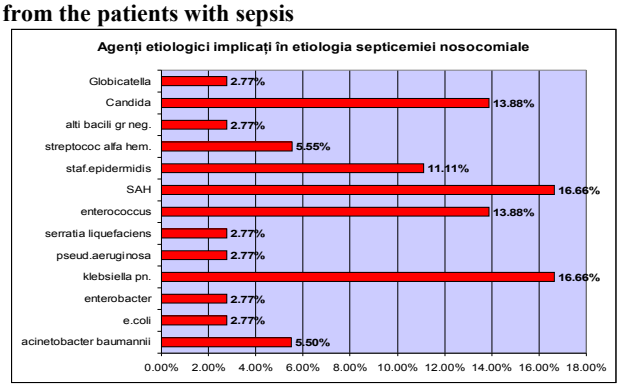
In the period under review a total of 3297 patients were admitted to the ATI, department of S.C.J.U.S., of which 30 patients were diagnosed with nosocomial sepsis (table 1) as defined by the case, the incidence of the illness being of 9.1%o; 23 cases were mono-etiologic, the remaining of 7 being bi-etiologic, (2 germs isolated in the blood cultures):

Table no. 1. The aetiology of the nosocomial sepsis

TOTAL SEPSIS			
30 cases			
MONO-ETIOLOGIC		BI-ETIOLOGIC(2 germs)	
23 cases		7 cases	
Bacterial	Fungicide	Twp bacterial species	Mixed (bacterial +fungicide)
19 cases	4 cases	6 cases	1 cases

13 gram-negative bacilli were isolated from blood cultures: 6 strains of Klebsiella pneumonia, 2 strains of Acinetobacter Baumann, 1 strain of Escherichia coli, 1 Enterobacter strain, 1 strain of Pseudomonas aeruginosa, 1 Serratia liquefaciens strain and 1 strain of unidentified Gram-negative bacilli. Also, 18 gram positive hull were isolated: 10 Staphylococcus (of which 6 haemolytic staphylococci aureu - SAH - and 4 staphylococci epidermidis), 5 Enterococcus, 1 Globicatella sanguine and 2 alpha haemolytic streptococci. Candida albicans was isolated in 5 blood cultures (in 4 as the sole etiologic agent of septicaemia and 1 case in combination with SAH) (Figure No. 1).

Figure no. 1. The proportion of the isolated etiologic agents from the patients with sepsis



The Resistance to Antibiotics of the Isolated Bacteria Strains from Blood Cultures

1. Strains of **staphylococcus** (Figure no. 2)

For the 10 strains of staphylococcus isolated from the blood culture, the antibiotics diagram was performed only in 7 cases (3 strains of white staphylococci were not tested). From the tested SAH strains, 100% of them showed resistance to oxacilina and cefoxitin, being classified as methicillin resistant strains (MRSA) (cefoxitin with a higher potential of sensitivity than oxacilina to detect meticilino-resistance). These strains showed concomitantly high resistance to amino-glycosides (over 70%), macro-lides (including clindamycin-phenotype MLSBI-over 50%), rifampicin and fluoro-quinolones. All MRSA strains were susceptible to vancomycin, teicoplanin and linezolid.

1. Strains of **enterococci** (figure no.3)

I found an increased resistance to aminoglycosides and fluoroquinolones at the strains of enterococci isolated from septicaemia. 100% of strains were susceptible to linezolid, vancomycin and teicoplanin.

Figure no. 2. The resistance to the antibiotics of the staphylococcus strains

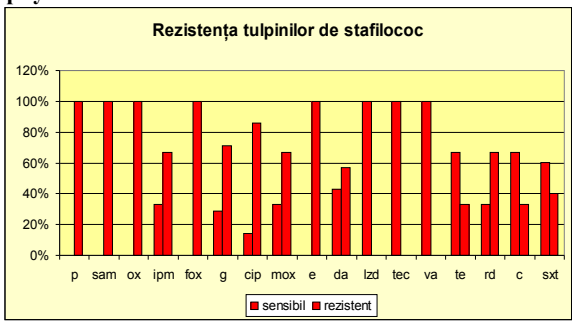
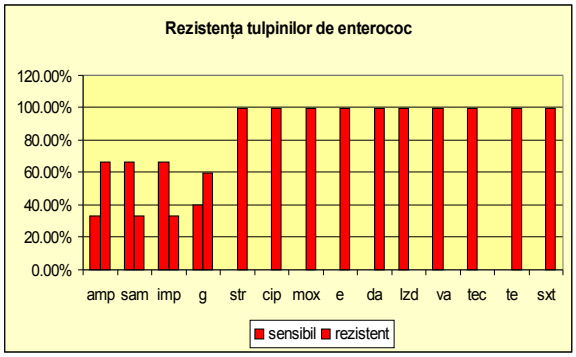


Figure no. 3. The resistance to the antibiotics of the enterococci strains



3. Strains of Acinetobacter **baumannii** (figure no.4)

The two strains of Acinetobacter isolated from blood cultures are extremely resistant to an impressive number of antibiotics: combinations of clavulanat or of sulbactam, the combination of tazobactam with piperacillin, cephalosporin of Ist, IInd, IIIrd and IVth generation, fluoro-quinolones, amino-noglicozide, chloramphenicol. Both strains were sensitive to colistin, but this antibiotic (even if it has an excellent in vitro activity) should be administered in large therapeutic doses, puts problems of toxicity and pharmacokinetics and its use by first intention in septicaemia is questionable.

4. Strain of E**. coli**

E. coli strains isolated from blood cultures was resistant to combinations containing beta lactamase inhibitors (clavulanic and sulbactam) in combination with piperacillin tazobactam to all cephalosporins and aztreonam, being a strain which produces extended spectrum beta lactamases (ESBLs +), what affects its sensivity to a wide range of classes of antibiotics. The strain was sensitive to carbapeneme to ciprofloxacin, colistin and chloramphenicol. From the amimoglicozide, it was resistant to gentamicin, but sensitive to amikacin.

5. Strains of **Klebsiella pneumoniae** (figure no.5)

Over 80% of strains of Klebsiella isolated from blood cultures were strains which secrete beta lactamases with a large spectrum. This explains the high level of resistance to penicillins (including combinations with clavulanic) and all classes of cephalosporins. The sensitivity of the tested strains was 100% for colistin and chloramphenicol.

6. Strain of **Serratia liquefaciens**

It was a strain with high sensitivity, being the only resistance to colistin.

7. Strain of **Pseudomonas aeruginosa**

The strain was sensitive to common anti-piocianic antibiotics (piperacillin, ticarcilină, ticarcilină with clavulanic), cephalosporins and fluoro-quinolones

Figure no. 4. The resistance to the antibiotics of the acinetobacter strains

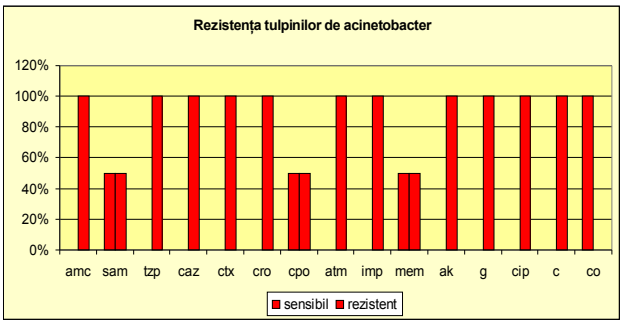
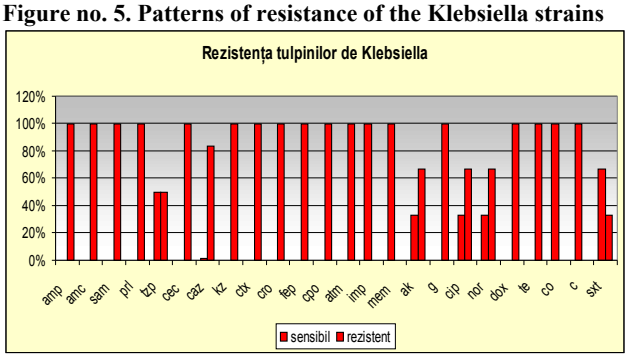


Figure no. 5. Patterns of resistance of the Klebsiella strains



DISCUSSIONS

Although the blood cultures provide an important number of information for the diagnosis of sepsis, there are some problems which should be avoided, one of them being the contamination of the samples collected. The contamination can occur from the moment of the collection, one of the common mistakes being related to the collecting of the central catheter or peripheral vein catheter mounted. Therefore, one of the first steps in this study was to formulate a protocol for proper blood cultures, the blood cultures collected incorrectly were not taken into study, even if they were positive.

Besides this aspect, the diagnosis of sepsis may be significantly delayed because of the time passing between the issue of clinical suspicion and the results of blood cultures; that is the reason for which it is necessary an empirical antibiotic therapy administered until a precise identification of aetiology. The more therapy is started later, the more difficult the patient's healing becomes (2) and therefore it seemed to be important to identify the most frequently involved germs in the aetiology of the septicaemia in Section ATI and their sensitivity to antibiotics.

In this study we found that during the studied period, the septicaemias were produced by more than 10 bacterial species, both gram positive and gram-negative and by the fungus (Candida), part of the infections having dual or mixed bacterial aetiology (bacterial and fungal).

The species of the Staphylococcus type were isolated with the biggest frequency from the blood cultures (over 27% of cases); all the strains of the staphylococcus aureu (involved in over 16% of septicaemias) were meticilino- resistant strains. These strains showed high resistance towards the aminoglycosides, macrolides (including clindamycin - phenotype MLSBI), rifampicin and fluoroquinolones. On the second place in frequency was located the septicaemia caused by Klebsiella pneumoniae (over 16%), over 80% of the strains isolated from the blood cultures were ESBLs +, resistant to all classes of cephalosporins. Klebsielelor resistance to aminoglycosides is also very high (only 2 of 6 isolates were sensitive to amikacin), fluoroquinolones and tetracyclines. Enterococci and Candida occupied the third place in frequency in the aetiology of septicaemia (each about 14%). Acinetobacter baumannii was isolated in 5.5% of cases; the frequency is not high, but the strains have been particularly resistant in an impressive number to the antibiotics. The strains of Acinetobacter can easily produce septicaemia in the immune-compromised bodies, and the resistance in an inert environment of the hospital is very high, which is why it puts serious problems related to the easy spread among patients.

E. coli strain isolated from blood cultures was a resistant strain, ESBL +, which affects its sensitivity to penicillins and cephalosporins. The only “wild” strain, with almost full sensitivity to the tested antibiotics were those of Serratia liquefaciens and piocianic bacillus which caused one case each of sepsis.

The resistance to the antibacterial agents involved in the aetiology of the septicaemia is a matter of current, well documented and growing importance, due to the restrictions of the treatment and the failures in the clinical course of cases (2, 3).

CONCLUSIONS

1. The incidence of nosocomial sepsis documented by positive blood cultures in the period studied was 9.1 cases per 1000 hospitalizations.
2. The most common etiologic agent involved was Staphylococcus (over 27% of cases); 100% of strains of staphylococcus aureu were methicillin resistant (MRSA).
3. On the second placed, was septicaemia caused by Klebsiella pneumonia (over 16%), over 80% from the strains isolated from the blood cultures secrete extended beta lactamases with a large spectrum.
4. Only two cases of sepsis were caused by “wild” strains, with almost full sensitivity to tested antibiotics: Serratia liquefaciens and bacillus piocianic; the rest of the septicaemias were caused by resistant "hospital" germs.
5. The situation of multiple resistances of the germs to septicaemia is alarming and requires close supervision to isolate and control of the existing strains, with the respect of the guidelines and antibiotic therapy to reduce new variants resistant to antibiotics.

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THE EFFECTS OF THE INHALATORY CORTICO THERAPY ON THE SOMATOTROPE AXES IN ASTHMATIC CHILDREN GROUPE OF AGE (0-18 YEARS) UNDER TREATMENT WITH INHALATORY CORTICOTHERAPY, PROSPECTIVE STUDY WITH CONTROL LOT

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Keywords: *asthmatic children, inhalatory corticosteroids treatment,growth hormone,serum alkaline phosphatas*

Abstract: *This prospective study, assessing the growth of 106 asthmatic children age group 0-18 years old, in treatment with low and medium doses of different types of inhaled corticosteroids with different treatment durations, compared with a control group of 107 children without asthma and/or corticosteroids treatment, showed no statistically significant differences between average height, weight scores, in the study group but a statistically significant decrease in pulsatile secretion of growth hormone (GH), and a significant increase in serum alkaline phosphatase values, compared with control group (p <0.05).*

Cuvinte cheie: *copii astm la copii, terapie cu corticosteroizi inhalatorii, hormoni de crestere, fosfataza alcalina serica*

Rezumat: *Studiul prospectiv de evaluare a creşterii unui lot de 106 copii astmatici cu vârste cuprinse între 0-18ani aflaţi în tratament cu corticosteroizi inhalatori diferiţi în doze mici şi medii, cu durate de tratament diferite, comparativ cu un grup de control 107 copii fără astm bronşic şi/sau corticoterapie arată că deşi nu există diferenţe semnificative statistic între mediile taliei, scorurile greutăţii, în lotul studiu există o scădere semnificativă statistic a secreţiei pulsatile a hormonului de creştere (GH), şi o creştere semnificativă a valorilor fosfatazelor alcaline serice, comparativ cu lotul martor (p<0,05).*

INTRODUCTION

Corticosteroids have an important role in reducing inflammation in days or weeks and improving lung function in patients with asthma, and decreasing bronchial reactivity in a few months. They also significantly inhibit each component of the GH axis hormones: reducing GH's pulsatile release, lowering the expression of growth hormones, lowering IGF-1 bioactivity, inhibiting the activity of osteoblasts, suppressing collagen synthesis, adrenal androgen production, intestinal absorption of calcium, and promoting bone resorption and increasing urinary calcium excretion (1,2, 3,4,6,7)

In asthmatic children receiving inhaled corticosteroid treatment, an important problem is represented by the potential effects of inhaled corticosteroids on linear growth. (1,2,3,25)

PURPOSE OF THE STUDY

The data mentioned in various randomized control group studies, published in various medical databases and prestigious journals in the world for almost 30 years and so far(25) show linear growth impairment at high doses of inhaled corticosteroids and a minimum effect on linear growth using both small and medium doses (1,3,6,7,9,10,12,15,19,20,23). Reductions were observed of aproximately 1 cm in the first year of treatment in children but the final height was reached (1). According to the recommandations of Expert Panel Report 3 2007 (1, 25) growth in asthmatic children with inhaled corticotherapy must be monitored , and should be monitored by knemometry , with stadiometers and as much as possible by the same person in each visit.

The study was conducted on asthmatic patients being in treatment with inhaled corticosteroids in various doses (small and medium) and at different durations of treatment when the samples were harvested, using as control group patients with various intercurrent respiratory problems but without asthma and/or corticosteroids orally, inhaled, or parenterally. The major objective was to evaluate growth in both groups by measuring anthropometric parameters (height-T, weight-G, body mass index-BMI) and the biological parameters such as growth hormone GH dosage (two determinations), IGF-1 secretion (1determination) and serum levels of phosphatase alacaline - FAS.

MATHERIAL AND METHOD

The prospective study was conducted on a group of 213 patients. The study group, 106 asthmatics aged between 0-18 years, was divided in three major age groups 0-5 years, 5-13 years, 13.6-19 years, a sex ratio M:F of approximately 1:1, and at the moment of colecting the blood samples they were treated at low and medium doses of inhaled corticosteroids , with different durations of treatment up to that time (less than 3 months, 3-6 months, 6-12 months, more than 12 months). The control group - 107 patients without asthma without corticosteroids, were also divided into three major age groups 0-5 years, 5-13 years, 13.6 years-19 years, with a sex ratio M:F of approximately 1 1.

The criteria for inclusion : both the study group and the control group entered the study only if there were normal levels for T3, T4, TSH, SGOT, SGPT, PT, glucose, ureea(bun), creatinine, Ca, Mg, normal urine exams, normal-sized parents, proper nutrition status, normal diet for each patient (3,12, 18)

Study exclusion criteria were represented by abnormal levels (increased or decreased values of the parameters mentioned above), a medical history of low birth weight or smaller family heights, metabolic diseases, genetic diseases, chronic inflammatory diseases, positive heterophile antibody (18)

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Method In both groups, for each case were measured the followings: GH (two successive determinations at a 120.min interval, the first measurement in 09.00 am, in a state of rest), IGF-1 (a single determination), T3, T4, TSH, SGOT, SGPT, PT, glucose, ureea, creatinine, Ca, Mg, FAS, urine exams . Blood samples were also collected for performing blood counts. The heights (T) were measured with the same stadiometer and that same infant stadiometer and for weight (G) using the same scale. For hormonal dosage (GH, IGF-1, T3, T4, TSH) an chemiluminescence immunoassay was used for detection .

The statistical methods used (27,28) were based on studies of the distribution in the first phase for each parameter (both anthropometric variables and biological ones) in order to establish if there is a normal distribution, uniform, poisson or exponential) with the Kolmogorov-Smirnov testing for a sample. If the value of this test "asymp. Sig (2-tailed)" was less than 0.05 ($p < 0.05$) it was statistically significant and the test had 95% of confidence . For this situation we have rejected the null hypothesis (normal distribution) and we have accepted the alternative hypothesis (different from the normal distribution). For variables with normal distribution, T test was applied to test whether the media of the two groups were equal and the test is statistically significant if there is a statistically significant difference between the averages of two groups($p < 0.05$). For variables with uneven distribution with the test Mann-Whitney U we have verified if the study group ranks are much higher ranks or lower than the ranks of the control group, without testing the differences between the means of the test (the test is statistically significant if $p < 0.05$). It was considered useful to assess in both the study and the control group the GH1, GH2 respectively with normal or low values (<1ng/ml or > 1/ng/ml), IGF-1 (low range or below the median), FAS (normal or elevated) using a binomial test for which the null hypothesis that refers to the two categories have equal chances of occurence for each group . A p value < 0.05 express the tendancy of occurring in a particular group

RESULTS

1. In the category of GH1 less than 1 ng/ml, the number of patients in the study group did not differ statistically significant with the number of patients in the control group ($p > 0.05$). Regarding the category of GH1 more than 1ng/ml in the study group also, there was no statistically significant difference with the number of patients in the control group ($p > 0.05$)
2. In the category of GH2 less than 1 ng/ml, the number of patients in the study group was statistically bigger than the number of patients in the control group ($p < 0.05$). Regarding the category of GH2 more than 1ng/ml in the study group there was also a statistically significant difference (a lower number) than the number of patients in the control group ($p < 0.05$) see table 1
3. In the category of low IGF-1, the number of patients in the study group was significantly lower than the number of patients in the control group ($p < 0.05$) and in the category of IGF-1 in range but below the median, the number of patients in the study group did not differ significantly from the number of patients in the control group ($p > 0.05$)
4. In the category with normal ALP , the number of patients in the study group is significantly lower than the number of patients in the control group ($p < 0.05$) and in the category with ALP increased, the number of patients in the study group was significantly higher than the number patients in the control group ($p < 0.05$)
5. The variable height had a normal distribution ($p > 0.05$). T test for independent samples revealed that the average height of the control group was not significantly different from the average height of the study group ($p > 0.05$) (see Table 3)
6. The variable weight had a normal distribution. Mann-Whitney U test for independent samples revealed that scores for weight in the control group scores were not significantly different than the scores for weight in the study group ($p > 0.05$)

DISCUSSIONS AND CONCLUSIONS

1. Small and medium-dose corticosteroids having minimal effects as many authors concluded (1) still have the potential to reduce even at low or medium doses, in the asthmatic patients compared to the control group, the pulsed secretion of growth hormone but regarding anthropometric measurements there is no statistically significant difference between the height averages in study group compared to the control group or for the scores of weights in the control group compared to the study group .
2. It is difficult to assess if the IGF-1 secretion is impared because the number of patients with IGF-1 below the median but in normal range) in study group, did not differ significantly from the control group and the numbers with low levels of IGF-1 for both groups were not statistically significant

Table no. 1. Categories GH1,GH2: (< 1 means low levels, >1 normal levels), Asy sig- p represents statistical significance, SG-study group, CG-control group)

Parameters	GH1<1			GH1>1			GH2<1			GH2 >1		
	LS	LM	Asy sig-p	LS	LM	Asy sig-p	LS	LM	Asy sig-p	LS	LM	Asy sig-p
No .pacients / p	68	57	,371	38	49	,284	74	27	,000	31	75	,000

Table no. 2. Categories : IGF-1 low or in range but below the median value , ALP – normal or elevated

Parameters	IGF-1 low			IGF-1 in range below the median			ALP normal			ALP increased		
	LS	LM	p	LS	LM	p	LS	LM	p	LS	LM	P
Nr .pacienți/ p	4	14	,031	35	44	,368	37	91	,000	69	19	,000

Table no. 3. Test T (Height)

Parameter	Group	Number of patients	Media	Standard deviation	t	p value
Height	Study	106	130,12	21,24	**1,430**	**,154**
Height	Control	107	125,95	21,33		

Table no. 4. Mann- Whitney U test for independent samples

Parameter	Lot	N	Mean Rank	Sum of ranks	Mann-Whitney U	Z	P value
Weight	Study	106	106,31	11268,50	5597,500	**-,163**	**, 870**
Weight	Control	107	107,38	11522,50			

In conditions which may rule out other causes of growth of alkaline phosphatase values and normal values for calcium and magnesium, serum alkaline phosphatases may be considered useful markers for monitoring the speed of growth and the effects of corticosteroid on growth and bone metabolism. (15,16,17,18,21,22,23,24)

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CARIES PREVALENCE OF PERMANENT FIRST MOLARS IN A SAMPLE OF 1 TO 4TH GRADERS FROM THE CITY OF SIBIU

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Keywords: *dental caries, schoolchildren, the 6 year molar*

Abstract: *The aim of this study is to assess caries prevalence in a group of 1st to 4th grade schoolchildren, especially analyzing the prevalence of decay of the first permanent molars. Also, based on the clinical observations, we tried to establish the treatment needs of these teeth (the amount of fillings, root canal treatments or extractions needed). The study sample consists of 574 students from grades 1 to 4. The caries prevalence of the 6-year molars was 44%. 3.5% of the individuals had all four first permanent molars affected by decay. The caries prevalence in lower first permanent molars was higher than in upper ones (46.5% vs. 36%). 34.5% of upper and 43% of lower first permanent molars needed fillings. 1% of upper and 2% of lower first permanent molars had to be extracted.*

Cuvinte cheie: *carie dentară, elevi, molarul de 6 ani.*

Rezumat: *Studiul de faţă are ca obiectiv surprinderea incidenţei cariei dentare la nivelul unui lot de elevi din clasele I-IV, punându-se accent pe afectarea prin carie a primilor molari permanenţi. De asemenea, pe baza observaţiilor clinice, am încercat şi stabilirea necesităţilor de tratament pentru aceşti dinţi (numărul obturaţiilor, tratamentelor endodontice sau extracţiilor necesare). Lotul de studiu este compus din 574 de elevi ai claselor I-IV. Incidenţa cariei molarului de 6 ani este de 44%. 3,5% dintre subiecţi aveau toţi cei 4 molari de 6 ani afectaţi de carie. Molarii de 6 ani inferiori sunt afectaţi de carie în proporţie mai mare decât cei superiori (46,5% faţă de 36%). 34,5% dintre molarii de 6 ani superiori şi 43% dintre cei inferiori necesitau efectuarea de obturaţii. 1% dintre molarii de 6 ani superiori şi 2% dintre cei inferiori au indicaţie de extracţie.*

INTRODUCTION

Around the age of 6, the first permanent molar perforates the oral mucosa and progresses towards the occlusal plane, eventually meeting its antagonist. As the 6-year molars occlude, a rise in vertical occlusal dimension occurs. Thus, the dento-maxillary system receives an element of increased masticatory efficiency, which determines a change in the forces that are transmitted to the bony framework and influences its further development (2).

PURPOSE OF THE STUDY

The aim of this study is to assess caries prevalence in a group of 1st to 4th grade schoolchildren, especially analyzing the prevalence of decay of the first permanent molars. Also, based on the clinical observations, we tried to establish the treatment needs of these teeth (the amount of fillings, root canal treatments or extractions needed).

MATERIAL AND METHOD

The type of the study is cross-sectional, the clinical examination has been carried out in two different schools from the city of Sibiu, Romania. These were chosen because they were equipped with dental offices, thus providing optimal conditions for the clinical examination.

The study sample consists of 574 students from grades 1 to 4. From these, 282 (49%) were boys and 292 (51%) were girls. 159 subjects (28%) were 1st graders, 145 (25%) were 2nd graders, 143 (25%) were 3rd graders and 127 (22%) were 4th graders.

The students were aged 6 to 11, distribution among age groups was as follows: 5 pupils were 6 years old, 114 were 7 years old, 146 were 8 years old, 120 were 9 years old, 131 were 10 years old and 58 were 11 years old.

The mean age of the 1st grade students was 7 years and 3 months, for the 2nd graders it was 8 years and 3 months, for the 3rd graders 9 years and 6 months and for the 4th graders, 10 years and 6 months.

The examination was carried out according to the WHO recommendations, by direct and indirect inspection using a dental mirror and by palpation with a dental probe; the findings were registered in patient charts and statistically processed using the software SPSS v.16 for Windows.

RESULTS

Of the 574 examined individuals, 253 (44%) had at least one decayed permanent first molar.

The distribution by age groups of the number of cases with decayed first permanent molars is displayed in table 1 and the distribution by grades is shown in table 2.

As shown, of the 159 1st graders, 18 (11%) have one decayed first permanent molar, 21 (13%) have two decayed molars, 3 (2%) have three decayed molars and 2 (1%) have all four 6-year molars affected by caries.

Of the 145 2nd graders, 18 (12%) have one decayed molar, 16 (11%) have two decayed molars, 18 have three decayed molars and 4 (2.5%) have all four molars decayed.

Of the 143 3rd graders, 41 (44%) have one molar that is affected by caries, 24 (17%) have two decayed molars, 10 (7%) have three decayed molars and 5 students (3.5%) have all fours first permanent molars affected by decay.

In 4th grade, 26 of the 127 students (20%) have one molar affected by decay, 19 (15%) have two affected molars, 18

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(14%) have three decayed molars and 10 (8%) have all 4 molars affected by caries.

Table no. 1. Number of cases with decayed 1st permanent molars and number of decayed molars by age

Nº. of decayed M1 / age	0	1	2	3	4	Total
6	4	0	1	0	0	1
7	81	13	16	2	2	33
8	101	18	14	9	4	45
9	59	28	17	15	1	61
10	52	29	25	14	11	79
11	24	15	7	9	3	34
Total	321	103	80	49	21	253

Table no. 2. Number of cases with decayed 1st permanent molars and number of decayed molars by grade

Nº. of decayed M1 / grade	0	1	2	3	4	Total
1	115	18	21	3	2	159
2	89	18	16	18	4	145
3	63	41	24	10	5	143
4	54	26	19	18	10	127
Total	321	103	80	49	21	574

The increased caries-susceptibility of the first permanent molar is due to its posteruptive occlusal morphology and its defective mineralization characteristics. Also, the first permanent molar erupts into an oral cavity with increased septicity, due to carious lesions of the temporary teeth, which limit their remineralization potential. This molar is vulnerable throughout its development, all its surfaces being prone to the carious attack due to the local conditions that increase that risk. The most common localization of the carious lesions is the occlusal surface, followed by the mesial and distal surfaces and finally the buccal and oral surfaces (6).

The number of individuals with caries-free first permanent molars decreases with age (from 115 in 1st grade, to 89 in 2nd grade, to 63 in 3rd grade and finally to 54 in 4th grade). At the same time, a slight increase of the number of cases with all four decayed molars is observed.

After one year of their eruption (at age 7), 33 (29%) of the individuals in this age group had decayed first permanent molars. Two individuals had three decayed molars and another two had all four molars affected by caries.

After two years of the eruption (at age 8) 31% of the students in this age group had decayed first permanent molars. 9 individuals (6%) had three decayed molars and in 4 cases (2.7%), all four molars were decayed.

At age 9 (after three years of the eruption of the first permanent molars), 51% of the individuals in this age group had decayed molars. 12.5% of the individuals in this age group had three decayed molars.

At age 10, the prevalence of first permanent molar caries was 60%. 14 subjects (10.7%) had three affected molars and 11 (8.4%) had all four molars affected by caries.

58% of the 11-year-olds had decayed molars. 9 students (15.5%) of this age had three decayed molars and 5% had all four permanent first molars affected.

Although right after their eruption the 6-year molars are unaffected by caries, after one year they already start to decay.

One of the reasons for this alarming situation is that dental visits for preventive dental treatment and regular checkups are relatively rare; often, an "evaluation" of the child's dental status is performed by a parent, which lacks the proper training and does not realize that the tooth that erupts distally of the temporary molars is a permanent one; thus they consider it to be a temporary tooth which they do not consider necessary of treating as it will be replaced. That is why, in many situations in which a patient sees a dentist and a carious lesion of the 6-year molar is detected, it has already reached the stage of complicated caries; in this case, complicated treatment or sometimes even the extraction of the tooth is necessary, thus leading to the loss of a major element of stability of the dental system and its functions.

Based on the clinical findings, treatment needs for the first permanent molars of the studied sample have been established.

Table 3 summarizes the treatment needs of the first permanent molars of 1st graders.

Table no. 3. Treatment needs of 6-year molars of 1st graders

Tooth / Treatment	1.6	2.6	3.6	4.6
Fillings	19	21	17	17
Endodontic treatment	0	0	2	1
Extractions	0	0	0	1

The lower first permanent molars required 34 fillings (17 on the left as well as on the right ones).

The tooth 3.6 require root canal treatment in two cases, and the tooth 4.6 in one case. These presented deep carious lesions, which penetrated into the pulpar chamber.

One case required the extraction of the tooth 4.6 which had extensive decay.

The prevalence of dental decay was 25% in the upper and 23% in the lower first permanent molars.

The treatment needs for the 6-year molars of 2nd graders are shown in table 4.

As in 1st graders, 25% of upper molars were decayed, but the prevalence of caries in lower molars was considerably higher (46%).

Table no. 4. Treatment needs of 6-year molars of 2nd graders

Tooth / Treatment	1.6	2.6	3.6	4.6
Fillings	14	22	28	35
Endodontic treatment	0	0	1	1
Extractions	0	0	0	1

Except for the upper right permanent first molar, the other molars required more fillings than those of 1st graders, according to the longer period of time that has passed from their eruption and their exposure to cariogenic factors.

The treatment needs of permanent first molars of the 3rd graders are shown in table 5.

45 upper permanent first molars required fillings, 4 required root canal treatment and another 4 had to be extracted.

79 lower molars needed fillings, 3 needed endodontic treatment and 3 needed extractions.

31% of the upper permanent first molars were affected by dental caries whilst more than half of the lower molars were

decayed (55%).

Table no. 5. Treatment needs of 6-year molars of 3rd graders

Tooth / Treatment	1.6	2.6	3.6	4.6
Fillings	21	24	28	51
Endodontic treatment	3	1	1	2
Extractions	1	3	1	2

An increase of caries prevalence was noticed as well as an increase of the number of complications that required endodontic treatment or even removal of the tooth. Thus, 2.8% of upper molars and 2% of lower molars needed to be extracted. At age 9, this percentage is cause for serious concern.

The treatment needs of 6-year molars of 4th graders are summarized in table 6.

Table no. 6. Treatment needs of 6-year molars of 4th graders

Tooth / Treatment	1.6	2.6	3.6	4.6
Fillings	37	40	32	38
Endodontic treatment	0	0	2	2
Extractions	1	0	4	2

77 upper and 70 lower first permanent molars needed fillings.

One upper and 6 lower molars had to be extracted and 4 lower molars required root canal treatment.

61.4% of the upper and 63% of the lower molars were decayed.

Although in 4th grade the number of decayed upper and lower molars was approximately the same, the lower molars presented a higher rate of complications, with 4.7% of them having to be extracted.

The ratio between the number of decayed 6-year molars to the number of 4th grade students was 1,25, which means that, in average, every 4th grade pupil had at least one first permanent molar that was decayed or presented complications of dental caries.

At 4 years after their eruption, caries prevalence of these teeth is at an alarming level.

For the entire studied sample, the prevalence of dental decay of upper 6-year molars was 36% and that of lower molars was 46.5%.

CONCLUSIONS

- The caries prevalence of the 6-year molars was 44%.
- The caries prevalence of the first permanent molar was 27.7% in 1st graders, 38.6% in 2nd graders, 56% in 3rd graders and 57.5% in 4th graders.
- 3.5% (21) of the individuals had all four first permanent molars affected by decay.
- The 6-year molars start to decay after just one year of their eruption.
- The caries prevalence in lower first permanent molars was higher than in upper ones (46.5% vs. 36%).
- 34.5% of upper and 43% of lower first permanent molars needed fillings.
- 1% of upper and 2% of lower first permanent molars had to be extracted.

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CARIES PREVALENCE IN A SAMPLE OF 1ST TO 4TH GRADERS FROM THE CITY OF SIBIU

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Keywords: *dental caries, schoolchildren, DMFT index*

Abstract: *The study's aim is to evaluate the dental status of schoolchildren from grades 1 to 4, for both the temporary and the permanent dentition. The article at hand addresses the prevalence of dental decay in the permanent dentition. The study sample included 574 schoolchildren from grades 1 to 4 from two different schools from the city of Sibiu, Romania. The sample is representative for the population of 1st to 4th graders; sex and grade distribution of the sample is homogenous. The examination was carried out by direct and indirect inspection using a dental mirror and palpatory, using a dental probe. The clinical findings were registered in patient charts and were then statistically analyzed using the software SPSS v.16. In order to evaluate the caries experience of the subjects, the DMFT index was used. The caries incidence of the permanent dentition for the entire studied sample was 67.2%. The mean value of the DMFT index for the entire sample was 1.71. The value of the DMFT index is mainly given by the component that indicates the number of decayed teeth.*

Cuvinte cheie: *carie dentară, elevi, indice DMFT*

Rezumat: *Studiul îşi propune să evalueze statusul oro-dentar al elevilor de clasele I-IV, atât pentru dentaţia temporară cât şi pentru cea permanentă. Articolul de faţă tratează problema afectării prin carie dentară a dentaţiei permanente la acest grup populaţional. Lotul studiat a fost compus din 574 de elevi ai claselor I-IV din municipiul Sibiu. Lotul de elevi este reprezentativ pentru segmentul populaţional respectiv şi este omogen din punct de vedere al distribuţiei pe sexe şi pe clase. Examinarea s-a făcut prin inspecţie directă şi indirectă cu ajutorul oglinzii stomatologice şi prin palpare cu sonda stomatologică, conform recomandărilor Organizaţiei Mondiale a Sănătăţii (OMS), observaţiile fiind înregistrate în fişe speciale şi prelucrate statistic cu programul SPSS versiunea 16. Pentru a evidenţia experienţa carioasă a subiecţilor s-au utilizat indicele DMF-T. La nivelul dentaţiei permanente, incidenţa cariei dentare pe întreg eşantionul este de 67,2%. Valoarea medie a indicelui DMFT este de 1,71. Valoarea DMFT este dată mai cu seamă de componentele care indică numărul dinţilor/suprafeţelor dentare afectate de carie.*

INTRODUCTION

Although dental caries prevalence has significantly decreased in Western countries, due to well-established and implemented preventive programs, it still constitutes one of the widest-spread diseases worldwide, and it is considered a public health issue, especially in developing countries.

The problem of dental decay represents one of the priorities on the World Health Organization's agenda (WHO); the organization recommends and supports the carrying out of national surveys on a regular basis, regarding caries prevalence, and also proposes preventive measures that should be implemented at community level.

The WHO objective for the year 2000, regarding caries prevalence in the permanent dentition of children states that, at the age of 12, the value of the DMFT index should not be greater than 3, and for the year 2020, the value maximum value of should drop to 1,5.

PURPOSE OF THE STUDY

The study's aim is to evaluate the dental status of schoolchildren from grades 1 to 4, for both the temporary and the permanent dentition. The article at hand addresses the prevalence of dental decay in the permanent dentition.

MATERIAL AND METHOD

This is a cross-sectional study that was carried out in 2009 on a sample of 574 schoolchildren from grades 1 to 4 from two different schools from the city of Sibiu, Romania. The schools were chosen as they were equipped with a dental office, offering optimal conditions for the clinical examination. The sample is representative for the population of 1st to 4th graders; sex and grade distribution of the sample was homogenous.

282 subjects (49%) were boys and 292 (51%) were girls.

159 pupils (28%) were from 1st grade, 145 (25%) were from 2nd grade, 143 (25%) were from 3rd grade and 127 (22%) were from 4th grade.

5 pupils were 6 years old, 114 were 7 years old, 146 were 8 years old, 120 were 9 years old, 131 were 10 years old and 58 were 11 years old.

Clinical methods: The examination was carried out according to WHO recommendations, by direct and indirect inspection using a dental mirror and palpatory, using a dental probe. The clinical findings were registered in patient charts and were then statistically analyzed using the software SPSS v.16 for Windows.

In order to evaluate the caries experience of the subjects, the DMFT index was used. The initials stand for the words decayed, missing, filled teeth. The index refers to the number of teeth that show active carious lesions, of those that were extracted due to caries complications and those that are filled.

Statistical methods: The *correlation* between two variables reflects the degree to which the variables are related. The most common measure of correlation is the Pearson Product

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Moment Correlation (called Pearson's correlation for short). When measured in a population the Pearson Product Moment correlation is designated by the Greek letter rho (ρ). When computed in a sample, it is designated by the letter "r". Pearson's correlation reflects the degree of linear relationship between two variables. It ranges from +1 to -1. A correlation coefficient of +1 means that there is a perfect positive linear relationship between the variables. If the coefficient has negative values, the variables are in an inverse relationship to each other. The closer the value of the coefficient to 1 (or -1), the stronger the dependence of the variables to each other; if the coefficient is 0, there is no relationship between the variables.

Statistical significance is a mathematical tool used to determine whether the outcome of an experiment is the result of a relationship between specific factors or due to chance. In other words, the statistical significance of a result represents the probability that the relationship between variables within a sample is due to chance, and that, at population level, no such relationship exists.

The level of statistical significance is designated by the letter p.

In the present study, the statistical significance level was set at p=0,05.

RESULTS

The mean age for the 1st graders was 7 years and 3 months, for the 2nd graders, 8 years and 3 months, for the 3rd graders it was 9 years and 6 months and for the 4th graders, 10 years and 6 months.

The DMFT index' values ranged, in the present study from 0 to 10 (as shown in table 1).

Table 2 shows the number of cases with a specific value of the DMFT.

Table no. 1. Number of cases with a certain value of DMFT

DMFT	Number of cases	Percent
0	188	32,8
1	99	17,2
2	109	19,0
3	85	14,8
4	71	12,4
5	15	2,6
6	3	0,5
7	1	0,2
8	1	0,2
10	2	0,3
Total	574	100

The evolution of the index' mean values by age and by grade is shown in figure 1 and 2 respectively.

The components of the DMFT index (namely the number of decayed, missing or filled teeth) were designated D_T, M_T and F_T.

The evolution of the D_T and F_T components by age is shown in fig. 3 and the evolution by grade, in fig. 4.

The mean DMFT value for the whole sample was 1,71; in the first grade, its mean value was 1,08, in the 2nd grade its mean value was 1,43, in 3rd graders its mean value was 2,68 and in 4th graders it was 1,75 (fig. 2).

Table 1 shows that only 33% of the subjects had all permanent teeth caries-free (DMFT=0), 51% of them had DMFT values between 1 and 3 (17% with DMFT=1, 19% with DMFT=2 and 15% with DMFT=3) and the remaining 16% had DMFT values ranging from 4 to 10.

Table 2 shows that in 1st grade 80 individuals (50,3%) had permanent teeth that were not affected by caries, whereas in 2nd grade 51 pupils (35,2%), in 3rd grade 19 students (13,3%) and in 4th grade 38 individuals (30%) had caries-free permanent teeth.

Table nr. 2. Absolute values of DMFT by grade

DMFT \ grade	1	2	3	4	Total
0	80	51	19	38	188
1	32	29	11	27	99
2	22	29	37	21	109
3	10	23	31	21	85
4	10	13	32	16	71
5	5	0	8	2	15
6	0	0	2	1	3
7	0	0	1	0	1
8	0	0	1	0	1
10	0	0	1	1	2
Total	159	145	143	127	574

Figure no. 1. Evolution of mean DMFT values by age

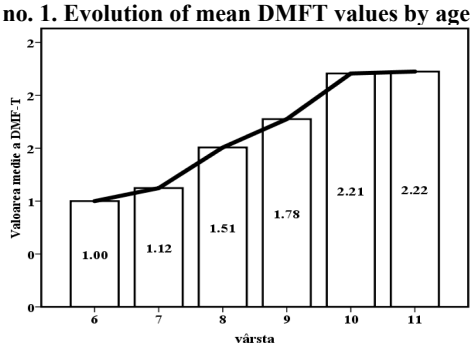


Figure no. 2. Evolution of mean DMFT values by grade

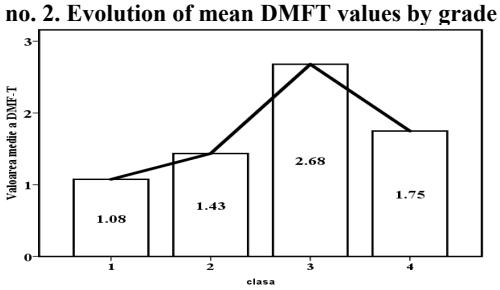
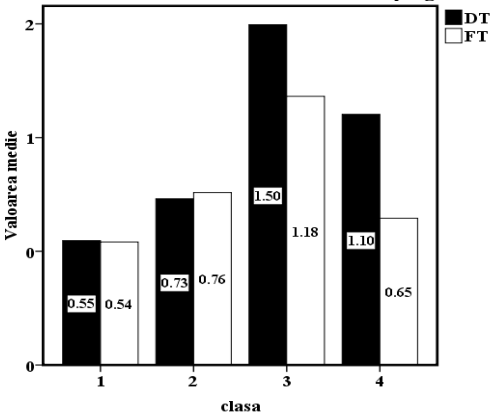


Figure no. 3. Evolution of D_T and F_T values by age



The DMFT indexes increased with age (fig.1), as shown from the correlation of the index' values with age (table 3).

Figure no. 4. Evolution of D_T and F_T values by grade

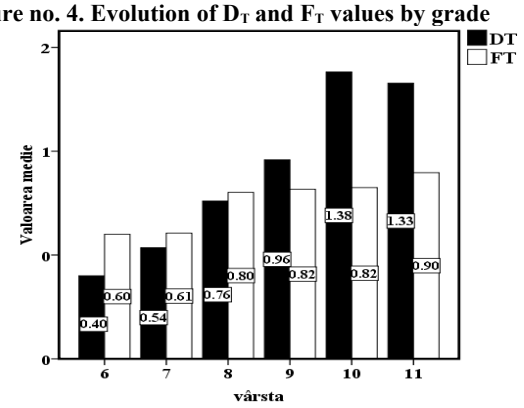


Table no. 3. Correlation of the DMFT index' and its components with age

		D_T	F_T	DMFT
age	r	0,238	0,067	0,244
	p	0,000	0,110	0,000
	N	574	574	574

The Pearson correlation coefficient had a positive value, which indicates a linear realtion between the index' values and age.

The D_T component also increased with age (r=0.238), as the newly erupted permanent teeth are gradually affected by caries.

The F_T component increases with age, but its increase is less marked then the D-component's (r=0,067), due to the fact that the treatment of the carious lesions is not given the proper importance. The correlation of the values of the F-component with age was not statistically significant (p=0,110).

We aimed to analyze which of the components contributes most to the value of the DMFT index.

M_T being 0, the value of DMFT is given only by D_T and F_T.

Table 4 shows that, for the correlation of DMFT and D_T, the correlation coefficient was 0,670 and for the correlation with F_T it is 0,640, which means that the value of DMFT depends equally on the D_T and the F_T components.

Fig. 4 shows that in grades 1 and 2, the number of caries-affected teeth was aprroximately equal to that of filled teeth, whereas in third grade, the number of the former was 1.3 times higher than of the latter and in 4th grade, it was almost twice as high.

Table no. 3. Correlation of the values of the DMFT index with its components

		D_T	F_T
DMFT	p	0,670	0,640
	t	0,000	0,000
	N	574	574

Table no. 3. The difference between mean DMFT values of boys and girls

Index	sex	Number of cases	Mean value	Standard deviation	p	Mean difference
DMFT	boys	282	1,80	1,728	0,212	0,171
	girls	292	1,63	1,553		

Thus, if all decayed teeth could be filled, in the first two grades, twice as many teeth would have to be filled, in third grade 2.3 times more teeth and in fourth grade 2.7 times more teeth would have to be filled in order to counter the D-component and to maximize the F-component's contribution to the index' value.

When comparing the DMFT index' values of boys and girls, we found that in boys the values were higher, but the differencies were not statistically significant (p=0.212) (table 5).

CONCLUSIONS

- The caries incidence of the permanent dentition for the entire studied sample was 67.2%.

  By grade, the situation was as the following:
  - in 1st graders 49.7%;
  - in 2nd graders 64.8%;
  - in 3rd graders 86.7%;
  - in 4th graders 70%.

  In developed countries, the caries prevalence of the permanent dentition at age 12 is between 30 and 40%; thus, the percentage found in 4th graders in the present study is considerably high.

  In the other grades, the prevalence of dental caries was also at a high level, indicating an early onset of the disease in the permanent dentition.
- The mean value of the DMFT index for the entire sample was 1.71, and its values by grade were:
  - 1.08 in 1st grade;
  - 1.43 in 2nd grade;
  - 2.68 in 3rd grade;
  - 1.75 in 4th grade.

  In 4th grade, which includes children whose age is closest to that of the WHO recommendations for the year 2000 (12 years), the DMFT value was below the one recoomended by the WHO (below 3).

The value is still high compared to the one of developed countries, where DMFT values of 1.1-1.2 (the U.S.A., Italy) or even below 1 (Denmark, Germany, Switzerland etc.) were reported.

- The value of the DMFT index is mainly given by the component that indicates the number of decayed teeth.
- The differencies between the DMFT values of boys and girls were not statistically significant, which indicates that the disease affects both sexes approximately at the same extent.

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THE INCIDENCE OF PERIAPICALE PAIN AFTER ROOT CANAL FILLINGS OF VITAL TEETH

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Keywords: *Endomethasone, AH26Plus, endodontic treatment, postoperative pain*

Abstract: *The purpose of this study was to compare the effect of two root canal filling material, Endomethasone and AH_{26}Plus in the incidence of painful reactions immediately after completion of Endodontic treatment. Materials and methods. The study was conducted on a sample of 55 patients with various types of pulpitis, which I made Endodontic treatment and root fillings in one session using alternative Endomethasone and AH_{26}Plus. Postoperative, each patient specified intensity of pain within 7 days after the seal, under a scheme designed by us. Results. Postoperative pain occurred more often in cases obstructed with AH_{26}Plus (56.6%) than with Endomethasone (43.4%). Conclusions. Whatever the material, the pain giving up in the first 5 days, both materials being clinically acceptable.*

Cuvinte cheie: *Endomethasone, AH26Plus, tratamentul endodontic, durerea postoperatorie*

Rezumat: *Scopul acestui studiu a fost de a compara efectul a două materiale de obturaţie radiculară, Endomethasone şi AH_{26}Plus, în ceea ce priveşte incidenţa reacţiilor dureroase imediat după finalizarea tratamentului endodontic. Material şi metodă. Studiul a fost realizat pe un lot de 55 pacienţi cu diferite forme de pulpită, la care am efectuat tratamentul endodontic şi obturaţia radiculară într-o singură şedinţă folosind alternativ Endomethasone şi AH_{26}Plus. Postoperator, fiecare pacient a precizat intensitatea durerii în primele 7 zile după obturare, conform unei scheme concepute de noi. Rezultate. Durerea postoperatorie a apărut mai des la cazurile obturate cu AH_{26}Plus (56,6%) faţă de cele obturate cu Endomethasone(43,4%). Concluzii. Indiferent de materialul folosit, durerea a cedat după primele 5 zile ambele materiale fiind acceptabile din punct de vedere clinic.*

INTRODUCTION

Materials used for root fillings are protected within the dentine into root canal and occlusal by the long lasting coronary fillings. At the apical foramen they are in direct contact with periapical connective tissue, which can sometimes lead to the emergence of inflammatory reactions of different intensities (7).

Ideally, root canal filling material should provide a safe, permanent sealing of endodontic space from microorganisms or their products coming from the mouth or gingival ditch.

Must have no irritant effect on the periapical tissue and does not dissolve under the action of tissue fluid. It would also be radiopaque to be easily identifiable on the radiography, the only examination which allows evaluating the quality of root restorations (5).

In the years have proposed many pasta fillings, but to date no one has been identified to meet the conditions of ideal material.

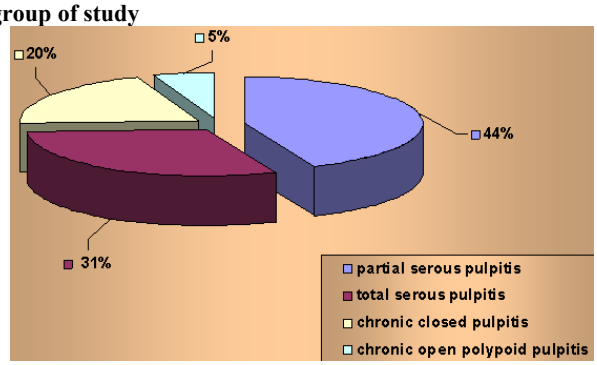
PURPOSE OF THE STUDY

The purpose of this study is to assess the incidence of postoperative pain after root canal fillings of vital teeth, with various pulp inflammations, after using the 2 pastes: Endomethasone and AH_{26}Plus.

MATERIAL AND METHOD

The study was conducted on a sample of 55 patients, 23 men and 32 women aged 16-53 years, who were presented to the Department of Odontology - Parodontology for treatment of various forms of pulp inflammation. Thus, we recorded 24 cases of partial serous pulpitis (43.6%), 17 cases of total serous pulpitis (30.9%), 11 cases of chronic closed pulpitis (20%) and 3 cases of chronic open polypoid pulpitis (5 , 5%) (Fig. 1). Each patient was treated for a single tooth to facilitate the record of intensity and duration of painful phenomena as the form in Table I.

Figure no 1. Repartition of inflammatory afection in the group of study



At the initial presentation was noted the tooth, diagnosis and filling material used. Each patient received the form and must record information about postoperative pain for 7 days after completion of treatment.

For biomechanical treat was used step-back technique for preparation of root canals, we used 2.5% sodium hypochlorite and hydrogen peroxide to wash, dry paper cones for root canals and cones of gutta-percha with root canal filling paste (AH_{26}Plus or Endomethasone used interchangeably). As a provisional crown filling we chose zinc eugenol because of antibacterial properties and good marginal closure they offer.

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We give particular attention to the maintenance of root canal length in order not to have exceeded the apex with paste filling or main gutta-percha cone.

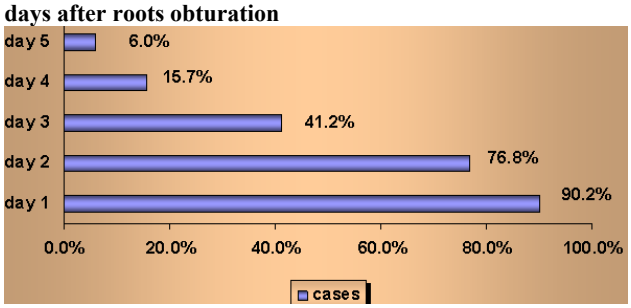
Table no. 1. Individual Form for follow up of daily symptoms after root obturation

Day postoperative / Intensity of pain	1	2	3	4	5	6	7
X							
XX							
XXX							
XXXX							

RESULTS

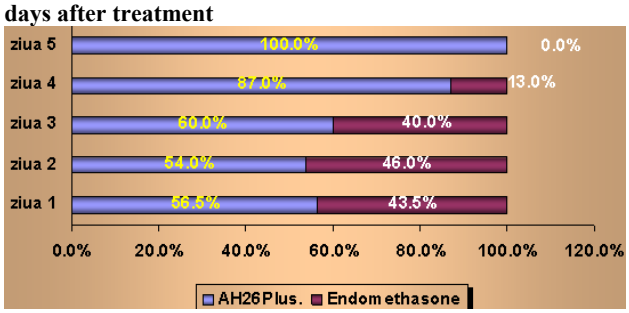
Of the 55 patients who entered the study, a total of 51 (92.7%) returned the forms after the interval of 7 days after completion of treatment. The final evaluation was performed on 49 teeth, 2 were over obturated. Of these 46 have been pain within 24 hours (90.2%), 39 in the first 48 hours (76.8%), 21 in the first 3 days (41 , 2%), 8 after 4 days (15.7%) and 3 after 5 days (6%) (Fig. 2).

Figure no. 2. The Incidence of postoperative pain in the first days after roots obturation



After this period has been recorded no pain in either case.

Figure no 3. Percent values of cases with pain in the first days after treatment



Regarding paste fillings used within each time (days) we recorded the following results:

- Day 1 of the 46 cases with postoperative pain, 26 occurred after filling with AH_{26}Plus (56.5%) and 20 cases (43.4%) after Endomethasone.
- On Day 2, we recorded 21 cases of pain (54%) after AH_{26}Plus and 18 (46%) after Endomethasone,
- The 3rd day after 12 cases AH_{26}Plus s (60%) and 9 cases (5%) after Endomethasone,
- On Day 4 of 7 cases (87%) after AH_{26}Plus and 1 Endomethasone (13%)
- On 5th 3 cases, 100% after AH_{26}Plus (Fig. 3).

DISCUSSIONS

In the literature is widely accepted that it is good to obstruct the root canals immediately after biomechanical preparation. This entails two advantages: it reduces the risk of microbial contamination and provides a significant time savings. (2)

This can be prevented by subjective and objective factors:

- The first type is the long duration of pulpectomies, which may be interrupted by the doctor or patient.
- The 2nd part is hemorrhage or hyperemia in periapicales region that appears periapical at sectional beam from vascular-nervous, which is why you should leave a period of several days before filling root canals, during which the phenomena inflammatory disappear.

We chose the step-back technique for preparation of root canals because it ensures the maintenance of a small diameter of the apical root canal, the pulp protect against overrun with fillings or gutta-percha cone main (2).

In addition, the apical region form is moderately divergent to a coronary, which tends to keep the materials used in root inside root canal fillings. (3, 8).

Paste AH_{26}Plus is classified as plastic resin. They are generally tough, being more difficult to des obstruction for Endodontic treatment failure. Freshly prepared paste is relatively strong and sticky, is easily inserted into root canal. Physical properties of material are good, ensuring a tight closure of the root canal and its solubility in the tissue liquid is reduced (6, 7).

It is known that during the outlet reaction paste AH_{26}Plus released small quantities of formaldehyde which can cause a severe inflammatory reaction in contact with tissue (4, 6). Moreover, once polymerization is complete, the material is well tolerated and the initially observed inflammation disappears in 10-14 days.

Endomethasone is a root filling material containing dexamethasone, was chosen precisely to reduce the incidence of inflammatory nature painful phenomena that may occur after completion of Endodontics treatment.

Alaçam (1) conducted a clinical study comparing postoperative pain occurred after use of 4 paste for fillings the root including Endomethasone, AH_{26}Plus without finding a significant difference statistically between them in terms of postoperative discomfort.

As expected, in our study the largest number of patients recorded the presence of pain after root canal fillings were grouped within 48 hours and was described as moderate or low intensity pain.

The absence of severe pain and loss phenomena in the first 6 days of pain regardless of paste filling restorations make us to consider both materials as biologically acceptable.

CONCLUSIONS

1. Old controversy in Endodontics, choosing a root filling paste remains the subject of numerous clinical and experimental studies.
2. Although the incidence of painful phenomena in this study differ depending on the filling material used, both pastes can be considered biologically acceptable because the changes are minor to moderate and disappear during the first 6 days after completion of treatment.
3. Data from the literature related to this issue are contradictory, so that we can not exclude either the use of clinical material, part confirmed previous experimental study conducted by us.

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TEMPORARY PROSTHESIS AS PART OF FIXED IMPLANT DENTURE SUPERSTRUCTURE RESTORATIONS

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Keywords: *mobile and fixed temporary restoration, over-implant restoration, late-loading implants, immediate-loading implants*

Cuvinte cheie: *restaurare provizorie mobilă şi fixă, restaurări supraimplantare, implante cu încărcare tardivă, implante cu încărcare imediată*

Abstract: *The article describes the temporary prostheses employed during the osseointegration of the late-loading two-step implants. Benefits and weaknesses are briefly described for each type. Owing to the said weaknesses, for two patients immediate –loading implants were applied. The therapy plan was influenced by the patients' preferences, for urgent restoration of the frontal edentatias and the intolerance to the discomfort caused by the mobile prosthesis for a period of three or four months. The patients preferred temporary yet fixed dentures.*

Rezumat: *Articolul prezintă protezele provizorii folosite în perioada de osteointegrare a implantelor în doi timpi cu încărcare tardivă. Pentru fiecare tip sunt descrise succint avantajele şi dezavantajele. Datorită unor dezavantaje. Pentru doi pacienţi, s-a recurs la introducerea implantelor cu încărcare imediată. Planul de tratament a fost influenţat de preferinţele pacienţelor, pentru restaurarea urgentă a edentaţiei frontale şi de imposibilitatea suportării disconfortului determinat de prezenţa protezei mobile pentru o perioadă de 3-4 luni de zile. Pacienţii erau adepţii restaurărilor provizorii dar fixe.*

SCIENTIFICAL ARTICLE OF BIBLIOGRAPHIC SYNTHESIS

Owing to the success achieved in the past decades, oral implantology has come to high development, during which many types of osseous implants have been imagined and employed.

At present, oral implantology is considered a breakthrough in dental prosthetics, since il allowed the restoration of the dental crown and the dental arch without affecting the teeth adjacent to the edental space.

The Kennedy class I and class II (terminal, E.Costa) edentulous situations now can enjoy the benefits of fixed prostheses in every aspect.

The prosthetic fixed implant denture superstructures on late-loading implants required and were conditioned on using both mobile and fixed temporary dentures durin osseointegration (3-4 months). Thus, as a result of the clinical observations tens of articles have been published in the specialized journals with regard to temporary dentures.

The purpose of such articles was to describe the two categories of prostheses, that is the traditional partial acrylic mobile prostheses and the modern fixed prostheses that are cemented either to the adjacent teeth of the edentulous space or to the new types of transition implants.

Each prosthesis category has been analyzed following the clinical observations acquired in long periods of time with application to a large number of patients.

The conclusions spell out the following:

The traditional partial acrylic mobile prosthesis have been used for the following **benefits:**

- the flow process (the clinical and the laboratory phases) is very simple;
- low cost resulting from the low value of the consumables and the flow process;
- insertion and desinsertion from the field are easy to do, which helps keeping an hygienic condition;
- allow for a correction to the mucosal and the occlusal surfaces;
- when a tooth serial extraction is needed, teeth can be added with much easiness.

The **weaknesses** are limiting the indications, since they may cause the occurrence of some physio-pathological reactions in the form of:

- psycho-nervous and oral-lingual discomfort that is more severe during phonation;
- the occlusal pressures are carried to the structures of the non-physiological prosthetic field;
- the compression applied to the peri-implantary surgical site, if hard, is not favourable to the healing of the mucous-periosteal tissues; the compression mught become a harmful factor qwing to the perturbation caused at the capillary level, which results in delayed wound healing.

The shortcoming of the oral and general discomfort has generated limit clinical situations, in that the patients refused to use the mobile prosthesis and showed the tendency to quit the over denture restorative treatment for reduced edentulous spaces (1-2) in the frontal area.

Since the temporary restoration was very necessary, they came up with the fixed prostheses, which are attached by use of the following techniques:

- bonding to the adjacent teeth;
- the transition implants.

Prostheses bonded the adjacent teeth

The features of such fixed prostheses are hereby evaluated in terms of benefits and weaknesses:

The **benefits** are given by:

- the comfort ensured both by fixity in the oral cavity and by small sizes equal to those of the natural teeth; the patient

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shows neither phonation perturbations nor any interest in possibly moving the prosthesis out of the prosthetic field, as the companions notices.

The weaknesses are given by:

- reductive preparation of the adjacent teeth in the areas of contact with the antagonist teeth, in order to create the clearance necessary for the adhesive resin layer;
- the preparation of the adjacent teeth is in contradiction to the implant benefits, which claim to prepare the teeth for the prosthetic restorations in the class III and IV Kennedy edentias;
- fixity does not mean strength, the prosthetic work might get mobile, particularly if the edentoulus space resulted from the extraction of two or three teeth;
- it is time –consuming and requires particular manual skill at the surgery for preparing and bonding the prosthesis;
- the dental technique laboratory needs to perform a particular prosthetic work;
- the recommendation is conditional on the teeth volume and shape and on the occlusal relations with the antagonist teeth.

Such weaknesses are limiting the recommendations for bonded prostheses so that they end up being viewed as exceptional alternative solution.

Temporary dentures attached to transitions implants

Owing to the weaknesses limiting their use, the mucous-periosteal anchor mobile dentures and the fixed ones cemented to the adjacent teeth have been decisive factors that led to using the transition implants in order to cement the fixed implant denture superstructures.

The transition implants display the following features:

- reduced dimensions, they can be inserted into small bone tissue;
- loading can be achieves immediately, which could be favorable to the formation of the bone tissue;
- favourable to the healing process of the peri-implantary surgical site;
- the dentures applied have sizes and shapes similar to those of the natural teeth.

Weaknesses:

- present if the occlusal pressures are big;
- excessive loading could cause fractures to happen;
- requires further intervention which increases the effort and the attention.

The temporary dentures are necessary, being recommended for the osseointegration of the two-step implants.

However, the temporary dentures cannot deal with all clinical cases, since the clinica; practice has come across very different clinical cases in terms of:

- the conformation distribution of the endentulous space, being known the perturbations of the different functions of the dental-maxillary apparatus, that is, for the frontal area, the physiognomy and the phonation and, for the side areas, the mastication; the edentulous space in the frontal area is a prosthesis emergency for a number of patients; the interest in restoring the integrity of the dental arch increases according to age, profession, gender, concrn for the look of the lower face part during phonation.
- The size of the edentulous space, particularly for the frontal area which, the larger it is, the more intense are the perturbations it produces, which renders even more urgent the restoration;
- The psycho-nervous behavior of each patient during everyday's activities may suffer significant changes of lower to higher degree, in terms of relationships they have with their companions in the healing period following the implantation surgery; the mobile dentures present in the frontal area of the oral cavity might induce discomfort, hence the refusal to use prosthesis; a subjective clinical examination should identify and define the patient's attitude and psycho-nervous behavior before determining a therapy plan; in the patients of relatively young ages requesting over-implant frontal denture repulsion can be noticed as to the mobile dentures, therefore the doctor should take a prudent stance on it.

The therapy plan provides two additional alternatives consisting in:

- fixed dentures with classic bridge affecting the adjacent teeth, which was denied;
- fixed dentures with over-implant bridge, where immediate-loading implants must be used.
- the request for the restoration of the dental arch integrity in a very short time, that is in two or three procedures;
- time (2005-2006), the patients displayed very similar responses and accepted the risk of potentially unfavourable results.

The patients were informed about the running of the risk of potential failure of the immediate-loading implants.

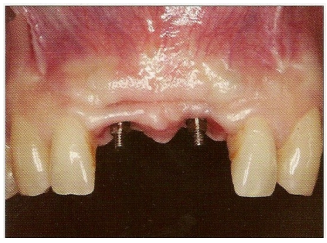
We proceeded to informing them about the content of the therapy sheet and the request to sign it. The patients showed a highly optimistic mindset and confidence in the success of the therapy, as proven by the words "we should try".

In the relation to the fixed and mobile dentures, here are two clinical cases conducted between 2004-2005, with the diagnosis Kennedy IV class edentatia caused by losing the two maxillary central incisors. The cases are hereby described as the patients refused the two-step implantation with temporary prosthesis.

Case n.1

The patient V.I. of age 39 requested the dental arch integrity to be restored in the maxillary frontal area corresponding to the two central incisors, which were restored by means of acrylic crowns attached to a prefeb post inserted into the root canal and cemented.

Figure no. 1. The frontal maxillary area – the free extremities of the two prefab posts are visible; the acrylic crowns were attached to them



According to the anamnesis, the procedure was chosen since it was an urgent request for immediate restoration of the dental arch integrity. The patient decided to have that type of restoration five years ago. The acrylic crowns did not fit properly to the dental crown horizontal surfaces, which caused an infiltration process to occur with the consequence of root tissue damage.

The urgent therapy consisted in the following operations:

- emergency extraction of the irretrievable roots;
- immediate mobile temporary denture for three days, which was not tolerated;
- insertion of two immediate-loading implants;

The therapy plan was influenced by the patient's request, who had some knowledge about implantation and disagreed to the use of two-step implants.

Figure no. 2. Immediate temporary denture in which the vestibular flange was cut out, since the upper lip could not tolerate it

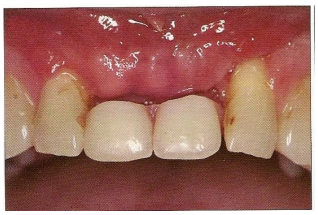
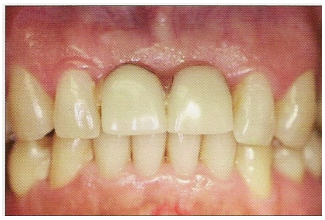


Figure no. 3. Esthetic crowns attached to the two implant crowns stumps



The crowns were fitted to the mouth so as to allow the free movement of mandible, without taking any pressure. The patient was advised not to use the frontal area.

The therapy solution was chosen upon the request of the patient, who desired temporary anf fixed prosthetic works.

Case 2

The patient D.O. of age 27 came with the request for an examination of the two maxillary central incisors, which showed mobility and violent pain.

Objective clinical examination

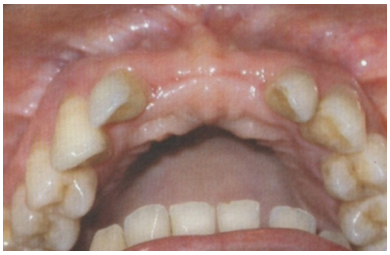
The crowns of the maxillary central incisors were covered with acrylic crowns axially and transversally unfitted to the cervical area, where they created chronic inflammation with deep periodontal pockets. The infection process has caused very painful sensations.

Therapy

The therapy plan was made known to the pacient, since it consisted in the following operations:

- extraction of the central incisor;
- mobile temporary denture, which was tolerated very baddy for 27 days;
- insertion of two immediate-loading implants on which the acrylic crowns were attached;
- the patient requested not to use the mobile dentures longer than 30-35 days, for the following considerations:
  - very badly psycho-nervous discomfort;
  - perturbed pronunciation of certain words;
  - lack of patience to wait for the osseointegration of the implants.

Figure no. 4. Alveolar crest healed after extraction of the maxillary central incisor



The patient has been subject to regular examinations for two years, the implants showed no mobility and the crowns proved cervical and occlusal fittingness.

Figure no. 5. Screw implants in the fixed prosthesis stage

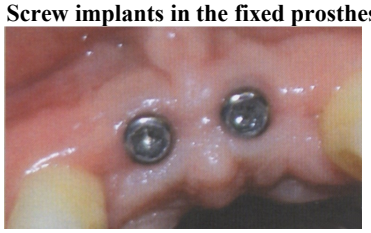
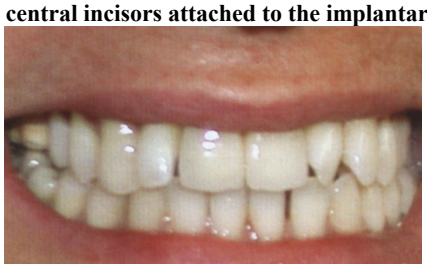


Figure no. 6. Fully ceramic covering crowns for the maxillary central incisors attached to the implantary stumps



In conclusion, the patients were subject to regular examinations in order to monitor the evolution of the prosthetic restoration, in clinical and radiography terms, and to find out any tendency of implant mobility.

Five or six years have passed since the over-implant therapy was conducted and no changes were noticed in morpho-clinical and radiography terms.

CONCLUSIONS

The implant denture superstructures restorations abutted late-loading implants are appreciated for highly favourable results, since it allows for the osseointegration process to take place, however they cannot deal with absolutely all the clinical cases, particularly in the frontal edentitias. The patients concerned, owing to biological considerations and social and professional conditions, requested immediate prosthetic restorations, therefore immediate-loading implants were used.

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UNIDENTAL THE ANTERIOR MAXILLARY IMPLANT

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Keywords: *Unidental implant, implanto-prosthetic reconstruction*

Abstract: *Single implant plateau connection must be provided with antirotational design. With greater is hexagonal internal or external space dimention with the more resistant the distribution of forces when mounting of the blunt. The risk of screw loosening or loss is lower. Modern conexions have conical outlet and internal antirorational system with bigger sides.*

Cuvinte cheie: *implant unidentar, restaurări implanto-protetice*

Rezumat: *Platoul şi conexiunea implantului unic trebuie să fie prevăzut cu un design antirotaţional. Cu cât este mai mare dimensiunea spaţiului hexagonal intern sau extern cu atât este mai rezistentă la repartiţia forţelor în momentul montării bontului. Riscul slăbirii sau pierderii şurubului este mai mic. Conexiunile moderne au priză conică şi sistem antirotaţional intern cu laturile cât mai mari.*

Implant positioning in relation to the ridge

Implant position is made in relation with the bone, not with the free edge of the teeth neighbors gums.

Some authors consider that the implant must be lowered to 4 mm below the free gingival margin adjacent teeth to develop a profile according to the crown with a flat shape, to maintain health and to support the adjacent tissues adjacent natural teeth. In the same time resorption is prevented by lowering the hard and soft tissues of the zone of single implant site *(Fig. 1)*.

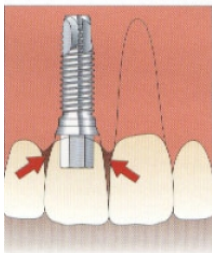
In conception of the authors such placement provides emerging profile of the crown about 4-5 mm on the vestibular wall which approaches width of a natural tooth. Will disappear as "black spots", wide spaces between implant crown and adjacent teeth, this technique provides successful aesthetic restorations. Periimplantar bag depth of 4 mm provides sufficient scaling porcelain necessary to achieve contour and color of a natural-looking crowns. However, several questions arise regarding health ditch around the implant.

After the first year of prosthetic loading is a significant loss of periimplantar bone rated between 0.8 and 1 mm, especially when the insertion was immediately postextractional.

Sometimes this general resorption adds a bone loss of at least 0.5 mm below the connection blunt / implant that can extend beyond edge of crest, depending on the degree of adaptation of implant design on bone quality and density.

The existence of a ditch in the vestibular of 4-5 mm, or more, creates difficulties in using cleaning and maintenance tools and plaque flora and have many opportunities to develop and produce inflammatory phenomena. In situations where periimplantary bag has 4 mm vestibular in interproximal areas of implant crown, interdental papilla corresponding areas are exposed to probing areas deeper than 4-5 mm to higher risk of bacterial retention. A thick and compact cortical withstand high occlusal stress. When the implant is lowered under cortical index bone, trabecular bone weaker which surrounds implant package has a lower ability to sustain occlusal loads. Another negative effect is biomechanically elongation crown and decreasing root resistance. Term will occur periimplantar resorption and decreased bone, periimplantar groove deepening and deficiencies in daily care. Finally clinical crown lengthening occurs which decreases in width at the package because as the crown narrows approaching the implant body diameter (3.75 to 4.2 mm).

Figure no. 1. Periimplantary papilla appearance after the first year after insertion after an improper positioning of the implant in relation to the alveolar bone. (M. Engelman)



Aesthetic consequences are disastrous, occurs papilla retraction with black triangular spaces instead of buds and space food outlet.

Depth of the periimplantary gingival space must be maintained long-term from 3 up to 4 mm depth which may make cleaning and maintenance of superstructures on implants.

In a trench more than 4 mm anaerobic bacteria that produce periimplantitis have chances to develop. Lean the connective tissue surrounding the implant has only fibers arranged parallel to implant. Therefore, the mechanism of attachment is less adherent when compared with the tooth, where fibers are arranged perpendicularly forming a circle ligament around him. In peridentar sounding gum bag, dental probe stops in epitelio-conjunctiva junction circular is almost at the bone. Dental probe from the periimplantary bag penetrates almost all soft tissue depth and the doctor can not effectively assess the actual depth of the groove junction epitelio-attachment attachment.

Numerous studies on the effect of accumulation of plaque around the tooth and implant showed that the apical extension of bacterial infiltration was more pronounced around

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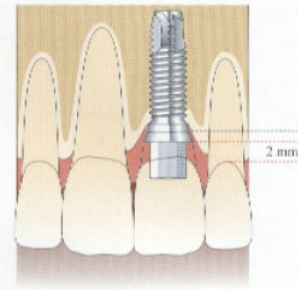
the implant. Explanation is given by the availability of titanium to receive plaque proteins and weak defense of connective soft tissue around the implant. At unidentar implant anaerobic bacteria that grow in areas close to the implant may affect the adjacent natural teeth.

Figure no. 2. Implant platform off the external cortex of the bone when the the ideal place of catalytic unidentar is placed from 1-2 mm apical from conjunctival insertion zone adjacent teeth gum (M. Engelman).



It was demonstrated that long-term reduction of gingival may relate with periimplantary groove depth which will produce a long-term poor aesthetics. *(Fig. 2).*But not all trenches around teeth more than 4 mm with anaerobic bacteria will lead to loss of cortical bone. Immune system and strict hygiene prevents pathological bone resorption and tooth stability.

However success in implantology and periodontology not depends entirely on the patient's immune system or the nature of its bacterial flora. Therefore, few things are needed:

- groove depth monitoring;
- reinforcing oral hygiene;
- periodic inspection of the restoration;
- periimplantar radiology of bone;
- application of periodontal procedures to limit the groove depth.

Only implant survival is not the only criterion in contemporary dental practice. Crown appearance, color and shade crown pottery and especially the presence of cervical region ideal spaces, a normal gingival contour and gingival papilla design are equally important aesthetic criteria. Health of the soft tissues around the implant within the professional responsibility of the physician and patient obligation after awareness and instruction.

After the above mentioned we recommend that the implant is not placed under the bone index. Modern implants have cervical zone evazive and often wound and drains and less depper recommended for compact bone and harder as cortical. That is why the implant platform will stop at the external cortex of the bone when the ideal unidental catalytic is placed from 1 to 2 mm apical to the gingival conjunctival insertion zone adjacent teeth. This ensures at least 3 mm of soft tissue emergence vestibular implant crown.*(Fig. 3, fig. 4, fig. 5, fig. 6, fig.7, fig. 8, fig. 9).*

Figure no. 3. Measuring length edentulous space

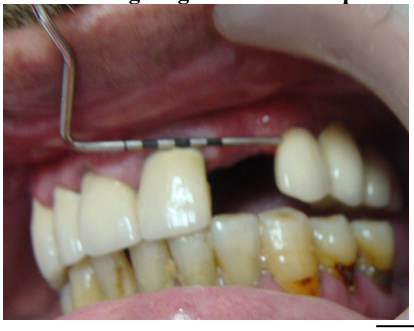
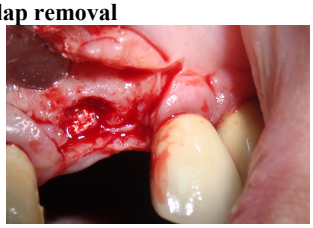
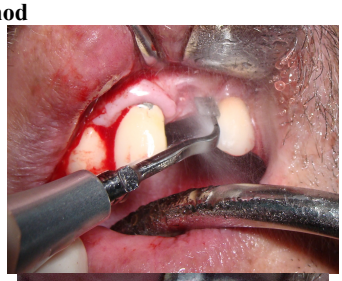


Figura nr. 4. Flap removal



Figures no. 5 and 6. Ridg splitting on piezosurgery and classical method



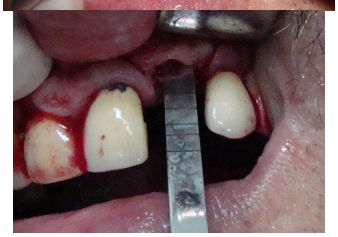
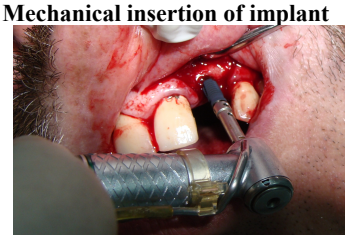


Figure no. 7. Drilling of alveolar bone

Figure no. 8. Mechanical insertion of implant

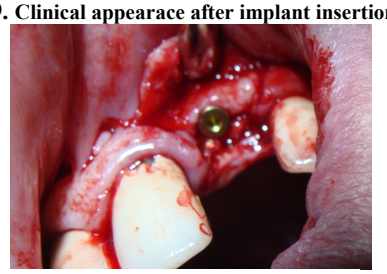


This is an ideal and desirable situation. In most cases requires the application of augmentation material that is put on the vestibular and distal implant to increase soft tissue contour frome the vestibular zone. Additive periimplantar graft has some advantages:

- attached vestibular lining thickness increases;
- facilitate surgical shaping of the interdental papilla;
- improves facial contour ridge and vestibular slope;
- prevents observation of color transparency implant titanium gray body with vestibular mucosa.

At bone augmentation techniques are added fixed soft tissue grafting surgical techniques. A connective tissue graft can be used to achieve an additional thickness of the vestibular soft tissue and papilla. A bone augmented and structured well which is added conjunctival graft provides stability and desired height of the interdental papilla. After unique implant insertion radiological control is recommended with an examination of the implant to recomply position and relationship with adjacent teeth.

Figure no. 9. Clinical appearace after implant insertion



Provisional prosthesis made above, is recontoured to prevent the contact with soft tissue which covers the implant. Acrylic provisional prosthesis is worn to suturing removal (10-14 days) is then replaced with a bridge from a resin adhesive. Recommend to wait two weeks to fix because the acid content deck adhesive gel may migrate in gingival wound and healing is compromised. In addition, the wires are easily removed when the deck is still positioned adhesive. Unidental acrylic prosthesis is stored for reuse when adhesive bridge will fracture during uncementation.

Unidental implant discovery

The second surgical meeting begins with clinical and radiological examination. On a retroalveolar radiography is examined carefully interface crest bone / implant to ensure the absence of bone loss before blunt indeed be added to the implant body.

If you suspect a bone loss biger than 2 mm periimplantary tissue must be examined directly. Horizontal defect correction cervical includes local autogenous graft and covered with barrier membrane and reconstruction by suturing the soft tissue.

If the fault is down less than 2 mm autogenous bone implant can be added and discovery of the implant continues because the registry integration is between the side walls of bone and implant.

Shaping soft tissue design

Exposure of the implant platform should be made having regard to the final architecture of soft tissue.

Some architectural criteria are valid and enforceable in different stages of treatment:

- periimplantar groove depth;
- interdental papilla;
- appropriate height and facial contours;
- attached gingiva;
- soft tissue thickness;
- gingival margin location

Soft tissue shaping is done in three stages

1. Phase I operation - addition of granular autogenous graft alloplastic (xenogeneic)
2. Stage II surgery - free of connective tissue grafts; plastic gum
3. Step Prosthetics
   - application stump healing and contour
   - outline provisional with temporary work
   - anatomical blunt
   - final restoration with ceramic-metal restoration or ceramic on zirconium dioxide structures.

Plasty gum shortens the gum tissue on the ridge to produce cervical ridge contour of the crown, the interdental papilla and vestibular contour.

After discovering the implant with the scalpel is created a palatal flap and inserted a healing profile of 2 mm thick. If there is bone defect can add granular xenogeneic or alloplastic graft around the lid and flap is sutured over the healing cap. After three weeks is discovered the implant by gingivoplasty shaping, with the scalpel, the contour of the interdental papilla. An interdental papilla can be created in an edentulous region near two adjacent teeth by a protocol. Carved excess tissue papilla initially creates a desired contour of soft tissue. However there is a disadvantage in addition to interdental papillae placement near the unidental implant.

Epitelio-conjunctiva interproximal insertion of a natural tooth extends to the incised edge followed by interproximal alveolar bone placing it above the vestibular and palate walls. At a polling peridental ditch is equal everywhere, even if the bone has a different shape: higher interproximal and lower oral and vestibular sides. Interproximal bone around the implant is not subjected to such a shape. As a result interdental papillae which occur natural and are raised to fill the interproximal areas between adjacent teeth corresponds to deeper at sounding than other areas of the implant crown.

Interproximal region can be treated as an interproximal area of a three-unit bridges. Interdental papillae rarely develops near a bridge, instead interproximal contact is extended towards the gum and neck region of the deck is slightly overcontoured by etching model. By assimilation is done at unidental when the contact areas of one tooth crown is extended in particular proximally to the gums and cervical region of the crown is slightly overcontoured in width, similar to a bridge. This concept makes small compromises in the aesthetic zone interproximal papilla not near as high as between teeth implant crown like natural teeth and crown width of the package is 0.5 mm larger. We obtain a lower groove depth around the implant and so much improved daily hygiene. This protocol is applicable also in superior frontal areas but the position of the upper lip during the smile does not show gums spaces around the teeth. Once soft tissues are recontour with a bistoury apply a healing blunt. Its size and shape mimics the final crown contour neck and extends over and around the gums to 1-2 mm.

Acrylic provisional prosthesis is modified to accommodate cape healing and still carry 4 to 6 weeks longer to mature and full of gum epithelization. Are patients who require temporary prosthesis to wear a prosthesis without mobilization. In this case will turn out a provisional fixed prosthesis which is carried by a protocol:

- fitting provisional abutment (abutment pickup) by raising moderate (10 NCM);
- prepare blunt with turbine mills;
- blunt is imprinted and a crown is manufactured in the laboratory or is made a immediate crown by the doctor;
- crown remains is cemented provisionally without occlusal contact.

Profile and edges provisional crown are modeled and completed by direct intraoral observation. If using composite resin material may be added intraoral to create desired vestibular profile, similar to the desired final restoration.

Before cementation crown stump pressure is put on gradually extending soft tissue. Gum tissue is allowed four weeks to heal in that position.

Unidental prosthetic implant abutment

Required unidental implant blunt should be equipped with an ideal antirotational system and discussions about conexions are still ongoing. For unidental implant prosthetic abutment with internal hexagon and taper connection and angulation of 5-10° is most used. These require at least two pieces:blunt with hexagonal design and screw of the blunt that connects blunt with the implant body. Abutments may be titanium gold or zirconium, but screws will always be from titanium. There are abutments of two body parts that come directly from the implant, anatomical abutments and bio-aesthetic, gold abutments.

For each category are provided different angulation, heights and different thicknesses. For special circumstances exist abutments manufactured in laboratory. Calcined implant

abutments are mounted in analog implant after imprinting prosthetics field and transfering in the laboratory. Here is poured gold, steel or titanium a blunt with desired design and after specific situation. Unidental abutments still have several characteristics:

- requires minimal preparation if the implant is not in the ideal position;
- abutment in implant placement to be done without interference from hard or soft tissue;
- use it to build abutments thicker crown abutments with cervical wider;
- profile crown: bigger abutments are used to induce a gingival outline that can be the first requirement for achieving aesthetics;
- straight and angulated unidental abutments are prepared only for aggregation by cementing

Disposing cause problems with removal screw crown. If you want to be reused is recommend creating an access hole from the oral until you identify the screw and remove the crown. Disposing causes the screw would be:

- mismatch components;
- insufficient raising;
- excessive raising;
- excessive occlusal loading;
- inadequate screw design

To ensure that the abutment is fully seated on the implant body (maximum tolerance of 60 microns) and fully charged piece socket and is locked antirotational recommend radiologic examination.

CONCLUSION

A crown not aggregated by screwing is not closing the interface and the edge blunt-crown. In this space the bacteria will colonize and in occlusion these gaps may act as a endotoxin pump even encouraging their proliferation in the periimplantar ditch, totally undesirable situation.

A crown cemented closes gaps between crown and stump. There is still a free space at the platform interface and the implant abutment. At the horizontal platforms space allows bacteria to grow within the implant body to escape from this level. This connection is placed in the bone or under the bone and can cause trouble. Conical connections reduce this risk.

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AESTHETIC RECONSTRUCTIONS IN THE PREVIOUS JAW

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Keywords: *Zirconium Dioxide, aesthetical reconstructions, unidental implant*

Abstract: *For a practicioner with experience , the restoration with one or two individual crowns is relatively simple from clinical and technical point of view,but if a single cronw has to be rebuilt in areas with major aesthetic concern, the prosthetic restoration becomes a challenge for any team of professionals. A major challenge for such a team si the unidental restoration , with or without implants , of a single incisor from the frontal maxilar area , especially the central superior incisors. These teeth have ahighly aesthetic part since they are in direct connection with the shape and the aspect of the face. This connection is widely described in papers reffering to the principles of aesthetic integration , of aesthetical approach in the frontal fixed prosthesis or aesthetical analysis and systematical approach of the prosthetic treatment in the aesthetical rehabilitations through fixed prosthesis as emphasised in Rufenacht and Goldstein's works presented in the bibliography.*

Cuvinte cheie: *dioxid de zirconiu, reconstrucţii estetice, implant unidentar*

Rezumat: *Pentru un protetician cu experienţă, restaurarea cu una sau două coroane individuale este relativ simplă din punct de vedere clinic şi tehnic, dar dacă trebuie reconstituită o singură coroană în zone cu interes estetic major, restaurarea protetică devine o provocare pentru orice echipă de profesionişti. O provocare majoră pentru o astfel de echipă este restaurarea unidentară, cu sau fără implante, a unui dinte incisiv din zona frontală maxilară, în special a incisivilor centrali superiori. Acestor dinţi le revine un rol estetic foarte mare deoarece se află în relaţie directă cu forma şi aspectul feţei. Această relaţie este descrisă pe larg în tratate cu referire la principiile de integrare estetică, de abordare estetică în protezările fixe anterioare, sau de analize estetice şi abordare sistematică a tratamentului protetic în reabilitările estetice prin protezare fixă, aşa cum reiese din lucrările lui Rufenacht şi Goldstein, prezentate în bibliografie.*

INTRODUCTION

In the evaluation of the dental shape of the central incisors we can use different parameters which are closely related to the individual anatomical aspects of each patient: the shape and aspect of the face , the analysis of the existing casts or photos from the youthof the patient with the natural teeth. Finally, the decision is taken together with the patient after we establish the expectations and his possible personal demandings. We should not forget that, through the increasingly modern methods of mass media spreading, the patient is more curious and informed, consequently more demanding. All these requirements must be weight and if achievable, they will be analysed by the medical team then discussed with the patient.

CLINICAL CASES

In all the situations of prosthetical reconstruction of the frontal maxillary group, the main aim is to obtain a natural aesthetic of the white or soft tissue in the context of the occlusal-articular functioning. There are situations when a central incisor sufferes aesthetically from colour alterings, due to endodontic treatments or to the restorative failures unadapted to the prosthetical principles: acrylic crowns, metal- aclylic crowns, metal ceramic crowns older than 10 years or incorrectly adapted in the cervical area, or failures in the veneering of the vestibulary face of the frontals. *(Fig. 1)*

In these cases a butt joint margin preparation of the natural teeth is imposed or a correct subgingival preparation of the frontals already unaesthetically covered. (Fig. 2).The preparation around the neck of the abutment and the attitude towards the free gum and interdental papilae is very improtant in the achievment of anatural passage from the red gum to the white face or our crown.(Fig. 3)

Figure no. 1. Unaesthetic appearance of the upper front group(Archive Dr. V. Nicolae)

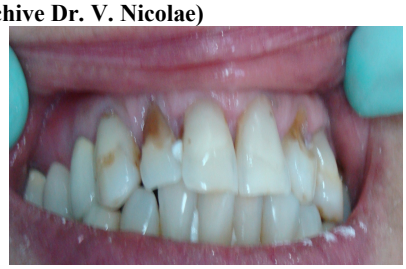

Figure no. 2. Prosthetic abutments prepared with threshold (Archive Dr. V. Nicolae)

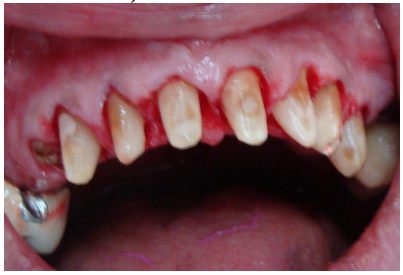

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Figure no. 3. Ceramic crown on zirconium oxide structure 1.1, with remarkable aesthetics. (Archive Dr. V. Nicolae)

The restorer dentist and the dental technician and responsible for that white/red crossover from the shaped gum to the prosthetic crown which will cover the abutment.

The crowns, 8 years old, have caused stasis and a purple aspect of the gingical tissues and in the pasage from the red gum to the white face of the crown, the metal border was visible, which upsets the aesthetic perception of the patient and creates a visible handicap: his smile.

The crowns with composite veneerings do not last long , they get wasted in time, thus the borders of the metal crowns will be uncovered.

Meanwhile, the composite veneerings suffer from pigmentation through the aging of the material; in time, microporosities appear on the surface of the composite which retain the food pigments.

The presence of the metal borders in the cervix is more visible in the case of the patient with gingival smile when the level of the upper lip goes beyond the free edge of the cervix.

After the removal of the old prosthetic work, the conical prepared abutments are visible with the massive distruction of the crown, a completely unprofessional preparation.

In such situations, we are forced to reconstruct the abutments after Xray examination. Through the direct composite restoration and appliance of the root pins armed with glass fiber , the abutments have gained the desired prosthetic shape.

The abutments require a strong preparation with well calibrated borders around the cervix (1,5 mm) which out of aesthetic considerations have been done slighly subgingival.

The reconstruction of the two crowns has been done on a ceramic without a metallic component, but not through the pressing technology as known in the integral ceramic system , but through the CAD/CAM technology, based on the layer application of the ceramics of fluor apatitis on caps prepared through pressing techniques.

In the impression, the limits of the preparation must be marked with precision, thus all the data will be correctly tranferred to the dental technique laboratory *(Fig.4).* In the laboratory the provisional restoration is immediately created and it will be tranferred to the patient.

After the wax model of the cap, it is fixed and pressed in an oven from a ceramic type „1PS max CEM" constantly checking the precision of the marginal closing up.

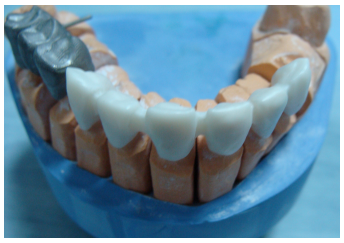
Then the veneering and lamination of the dentinary, enamel and incisal structures follows with mmax CERAM until the modelling of the final shape.

After the final burning the shape and superficial structure have been optimised and the gloss after which it has been polished. For the acokplishment of the patient's demandings he is invited to take part in the final steps of the work. After the isolation of the prosthetic field with a rubber dam, the abutments are cleaned, skimmed and conditioned with acid then covered with adhesive. The polimerization in the adhesive cements is done with the photopolimerisable lamp. The crownd should not be bonded in the same time and the margin is closely checked for the removal of any cement remainings.

Figure no. 3. The polieter impression with the limits of the preparation precisely marked

The reconstruction of the superior centrals with zirconium structures computer made CAD/CAM. The precision and the productivity of these materials, as well as the technology, have evolved in the past years and they can satisfy even the highest aesthetical and functional demands of the patients. Almost every producer of the CAD/CAM systems (Lava, Cercon, etc), uses a certai type of zirconium for the preparation of the framework. For every type of framework there is a matching ceramics, which means that the structures must be covered with a certain ceramics. (Fig, 5, fig. 6, fig. 7, fig. 8)

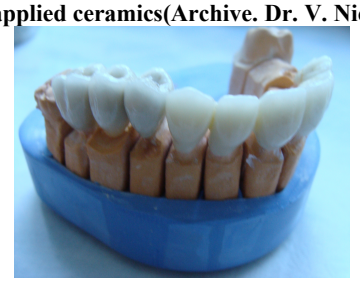
Figure no. 5. Structures of zirconium and metal (Cr-CO) obtained by CAD-CAM technology. (Archive Dr. V. Nicolae).



The reconstruction of a frontal central incisor after its loss due to an endodontic failure finalised with the longitudinal fracture of the root. In this case there are problems connected to the bone loss and the asimmetries.

Even if the prosthetic restoration corresponds to the current technological demandings (high tech implants, optimal surgical techniques, zirconium abutments, ceramic crowns on zirconium), when we have bone loss and assimetry in the gingival border by comparisson to the natural tooth, an acceptable functionnal intergration is created but the aesthetic result is not satisfactory.

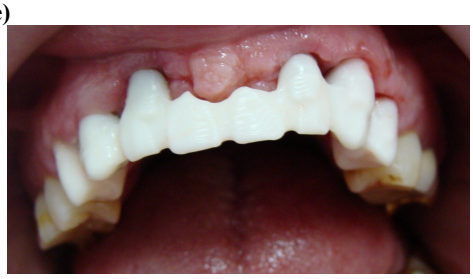
Figure no. 6. Different aspect of the brightness of two framework applied ceramics(Archive. Dr. V. Nicolae)



Here, when we talk about aesthetisc, we reffer to the passage between the red gum and the white tooth, the emergence level of the crown on the implant comparing to the cervical width of the similar natural tooth, to the black points and the papila level, the vestibulary excavation next to the implant. *(Fig. 9, 10, 11, 12).*

Figures no. 7 and 8. Upper front work group recovery through ceramic structure zirconium.(Archive Dr. V. Nicolae)

Figure no. 9. Sample structure of zirconium. (Archive Dr. V. Nicolae)



Figures no. 10 and 11. The final aspect of the work on the structure of yirconia ceramic. (Archive Dr. V. Nicolae)

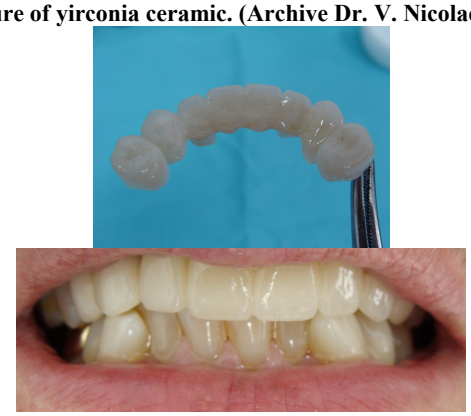
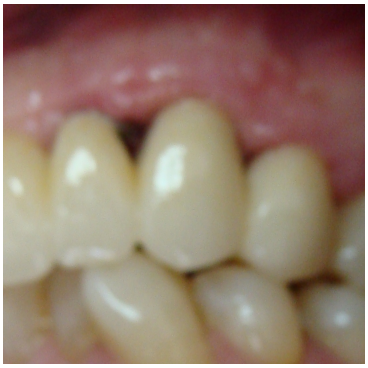


Figure no. 12. Failure in the passage from the red aesthetics to the white one



CONCLUSIONS

Without doubt, more and more prosthetic cases, with or without implant solutionings become increasingly complex from the aesthetical, functionality and quality point of view, for the team consisting of the prosthetician, dental technician, implantologist, hygienist.

To obtain a remarkable result regarding the functionnal and the aesthetic, an imperative requirement is the team work where all the experience of the participants is manifested and put into practice.

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FORMING THE DENTAL CAP OR THIMBLE IN FIXED PROSTHETICS

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Keywords: *dental cap, thimble, immersion technique*

Abstract: *The use of modern technology (immersion bath, special immersion waxes) in the immersion technique of the prepared tooth obtaining the crown model, permits the creation of the dental cap model or the thimble, which is exactly adapted at the preparation sides with a minimum of effort.*

Cuvinte cheie: *capa, degetarul, tehnica de imersie*

Rezumat: *Utilizarea tehnologiei moderne (baie de imersie, ceruri speciale de imersie) în tehnica de imersie a bontului pentru obținerea machetei coroanei de înveliș, permite formarea machetei capei sau a degetarului exact adaptată la nivelul fețelor preparației (bontului) cu minim de efort.*

INTRODUCTION

The wax inprint represents the exact copy of the final piece of work, being a reproduction of all the tissue details removed by filing the pillar tooth and the teeth which are replaced by the dental bridge.

The method of obtaining the wax inprints in a indirect mode is done by modelling on the models, obtained after the impress, most frequently with special waxes for the wax inprint (1).

The deformation of the wax inprints is dependent on the temperature, time and storage conditions of the wax inprints (2). The dental cap or thimble is made from a uniform wax layer (0,5 mm), and it is made so that we can realize a framework of the models agregational elements (retentionists) which assure the necesarry rigidity so it may not deform and ease the modelling of the axial and occlusal sides details of the finished crown (1).

The immersion bath (the bath were the wax is heat up) is an electric device, that attains in a controled way the melting and maintaining of the special waxes at the recommended temperature given by the producer's prospectus (3).

The wax inprint of the microprothesis, aggregational elements can be made diversifiedthrought a various of methods, depending on the clinical situation, the equipment of the dental laboratory, the training and professionalism of the dental technician (4).

PURPOSE OF THE STUDY

We wanted to show the many problems that occur considering the equipment, technique and measurements imposed for obtaining the dental cap or the thimble throughtout the immersion technique of the prepared tooth into an recipient of liquid wax.

MATERIAL AND METHOD

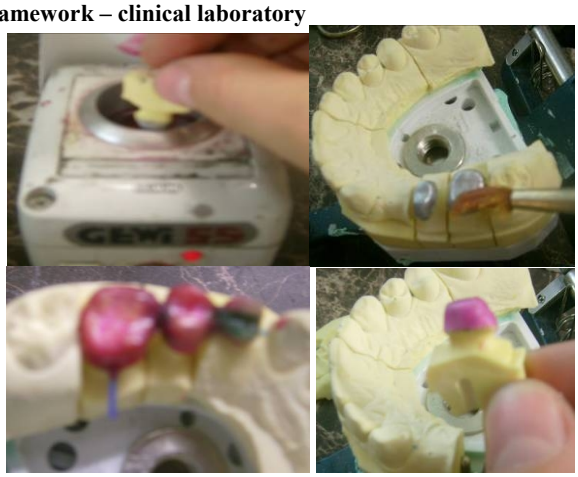
We took into our study a lot of 77 pacients, which had partial edentations and coronary affections that were fixed with fixed unitary and/or multiple prosthetics. We elaborated case files in which we noted the time needed for the restoration, the technology used to obtain the models metal frame (the waxes we used, the technique of the model's obtainement, the devices we used, the necessary time for the making of the model, preparation concerning the cast, etc.)

Forming the cap retentors on the pillar teeth, through the immersion procedure in wax, like this: the isolation of the prepared tooth with isolating material, applied with a paintbrush in a uniform, thin layer; the rapid immersion of the prepared tooth in the immersion bath; the slower immersion of the tooth favours the contraction of the wax, with the formation of the contractional lines, which slacken the capes resistance; succesive immersion until we obtain a uniform layer of 0,5 mm thickness; the control of the capes margins and the adaptation with a blunt instrument, a little heated (so it may not deform the cape); at this point the cape of wax (degetarul) is ready for the modelling of the anatomical details of the axial and oclussal sides through the addition-technique or additive technique (1,5).

RESULTS AND DISCUSSIONS

Pacient M.R. 24 y.o. with a right unidental maxilary edentation given by the absence of 1.4, has been restored prothetically through a fizionomical metal ceramics bridge, aggregated on a 1.5.,1.6., where the formation the thimble of the metallic framework on the pillar teeth has been realized throught the immersion of the prepared tooth in the bath (Fig.1,2).

Figure no. 1. Obtaining the wax inprint of the metallic framework – clinical laboratory



Pacient N.A., with a right lateral maxillary edentation, by the absence of 1.4., and 1.6., we made a dental metalo-ceramical fizionomical bridge, aggregated on 1.3.;1.5.;1.7;, the

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creation of the thimble on the pillar teeth has been made through the immersion technique of the prepared tooth into the bath (Fig.3.)

Figure no. 2. The finished metalo-ceramical piece

Figure no. 3. Creating the caps with the immersion technique

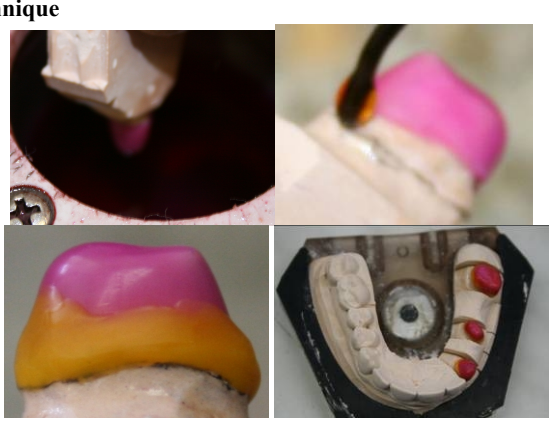
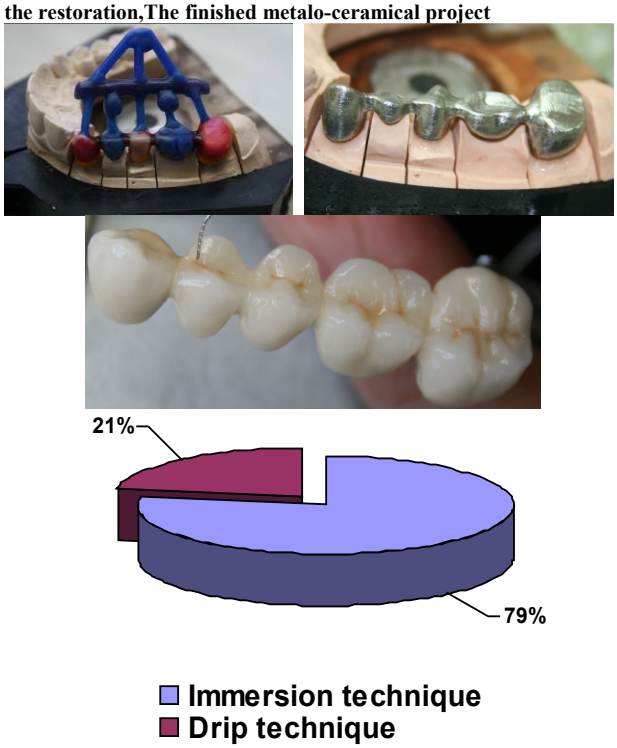


Fig.4. Model with metallic components, The metallic framework of the restoration,The finished metalo-ceramical project



CONCLUSIONS

1. The wax bath maintains constant temperature of the wax, which permits the rapid application of the wax on the prepared tooth.
2. The immersion technique of the prepared tooth into the bath, assures the confection in time of the high precision capes exactly adaptated to the prepared tooth.
3. In the addition technique with wax in succesive layers exists the risk of including air bubbles or extending the not uniformity of the wax layer, so that certain area of the prepared tooth remain uncovered.
4. The obtained cap through immersion represents a framework of the coronary wax inprint with total thickness and assures the rigidity needed so that it may not difform, easing the modelling of the details axial and ocllusal side of the finished crown.
5. The immersion technique needs models with a mobile prepared tooth, the equipment therefore must be pretty good, but if offers in exchange high precision at a minimum effort.

Dental Tehnician: Popescu Maria Madalina, Simion Oana-Dental Tehnical College, Sibiu

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THE ROLE OF ENDOGENOUS FACTORS IN DEVELOPMENT AND GROWTH

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Keywords: *body development, growth, height, body mass*

Abstract: *A height lower by 2 SD to the one considered normal defines a retard in growth. It should be acknowledged even since childhood when it could undergo treatment; otherwise this might lead to a short stature in adulthood. The internal factors of the human body that have implications regarding children's embryonic, foetal and postnatal development shall be examined. Genetic factors control the pace of individual growth. The genetic disorders of the metabolism of some aminoacids determine serious development disorders, especially at the level of the nervous system. The influences of the secretion tonus of various endocrine glands will be examined some having a stimulatory, other an inhibitive role for the final height of the individual.*

Cuvinte cheie: *dezvoltarea organismului, creşterea, înălţimea, greutatea corporală*

Rezumat: *O talie inferioară cu 2 DS celei considerate normale defineşte retardul creşterii. El trebuie recunoscut în copilărie, când este accesibil unui tratament; altfel, poate conduce la o talie mică la adult. Sunt examinaţi factorii interni ai organismului uman care au implicaţii privind dezvoltarea embrionară, fetală şi postnatală a copiilor. Factorii genetici controlează ritmul creşterii individuale. Tulburările genetice ale metabolismului unor aminoacizi determină tulburări grave ale dezvoltării, mai ales la nivelul sistemului nervos. Sunt examinate infuenţele tonusului secretor al diverselor glande endocrine, unele cu rol stimulator, altele cu rol inhibitor, asupra taliei definitive a individului.*

SCIENTIFICAL ARTICLE OF BIBLIOGRAPHIC SYNTHESIS

The child's growth is normal if the height-weight parameters evaluate parallel with the reference curves ranging between +2 and –2 standard deviation or between 3° and 97° percentile. Consequently, it is considered that children whose height is lower by 2 SD have a retard in growth.

It is very important to acknowledge growth retardation during childhood, because this might lead to a short stature in adulthood. The growth retard may be the expression of a pathological process, of which the child's vital or functional prognosis may depend on. Disregarding some type of retard, means not finding out an accessible potential situation leading to a treatment, this would allow the amelioration or the normalisation of the height (1).

The stages of growth: between 0-2 years, nutrition has an essential role, between 2-12 years the growth hormone is of primary importance; between 12-18 years, the sexual steroids and the growth hormones have the main effect.

The internal factors of the maternal body are important for the children's embryonic, foetal, postnatal development: the malformations of the uterus, the pressure caused by uterine tumours or by the shape of a narrow pelvis, defects of the placenta, the presence of diabetes, hypothyroidism, severe pulmonary and cardiovascular diseases, severe anaemia, the disorders of the placenta, the insulin administration, sexual and suprarenal hormones may trigger development disorders (2). The pregnant woman's nutrition disorders, its exposure to X-rays, the intake of some teratogenic drugs during pregnancy (thalidomide, vitamin A overdose), abortive ones (aminopterins, quinine, sulphamides, some antibiotics), some viral infections (rubella, herpes viruses, flu, neural viruses) streptococcus, staphylococcus infections, toxoplasmosis, malaria, the pregnant woman's syphilis may affect the intrauterine development of the baby. During the pregnancy complicated by asthma bronchitis, there is a sexually specific effect for the immune maternal body, with side effects on the placental function and on the growth of the foetuses of feminine gender. The use of steroids taken by inhalations by women suffering from asthma bronchitis was beneficial for the growth of foetuses of feminine gender due to the control of their maternal systemic inflammation (3). The children of younger mothers, babies from first pregnancies, the babies of mothers with a lower height have lower height and weight at birth as compared to those of older, multiparous mothers or those with a better physical development. In over 90 % of the cases, the children with a retard in growth will normalise their height in the first 2 years after birth. The treatment with somatotropine hormone (0.4mg/kg/day dosed in 7 weekly injections) must be followed for 3 years and may be interrupted, or extended depending on its results on the height (4). In a multicentric study in which somatotropine hormone was given in a 66 micrograms/ kg/ day dose at children with a low height at birth as compared to gestational age, their height significantly increased after 3 years (from -3.0 SD to -1.3 SD). At the control group (untreated) the growth in height was very little (from -3.2 SD to -2.9 SD) (5, 6, 7).

Genetic factors

Girls have an advance as regards skeletal maturation during growth; their ossification of growth cartilage ends 2 years earlier than boys'. Genetic factors control the pace of individual growth. There is pathology of development which is genetically transmitted to offspring: pituitary dwarfism, pituitary gigantism and hereditary dwarfism. Also the basic characteristics of the

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morphology of the various human races are transmitted.

For instance the Turner syndrome is accompanied by growth retardation existing even since birth in 1 of 2 cases, which progressively aggravates, over the years, it becomes more accentuated at puberty, due to the absence of the pubertal growth rate in such a way that the final height in the absence of any treatment and despite late growth is on average 142+/-5cm (8). The treatment of height retardation is today mainly performed with somatotropine hormone in a 0.35mg/ kg/ week doses assigned in 7 injections. The treatment of the absence of puberty entails the administration of estrogens for its triggering followed by estroprogestative (9).

The genetic malformation syndrome is accompanied by a precocious retard in height, a mental retard and a dimorphic syndrome of the face and limbs. It has a wide aetiology: the Rubinstein, Taybi Prader Willi, Cornelia de Lange syndromes (10).

The constitutional bone disease of the skeleton is diagnosed with the aid of radiography which shows epiphyseal, metaphyseal, vertebral malformations (10, 21). There are: achondroplasia, skeletal dysplasia, pychodysostosis (1).

Metabolic factors

The genetic disorders of the metabolism of some aminoacids trigger serious development disorders, especially at the level of the nervous system (phenylketonuria with phenylketonuric mental retardation) but also at the level of the plasmatic protein synthesis, of the carbon hydrates and the plasmatic lipids metabolism; there can be enzymatic deficits in the synthesis of the thyroid hormones of suprarenal steroids, hemoglobin synthesis disorders (hemoglobinopathies and thalassemia) metal, sulphur and potassium metabolism disorders (2). It is necessary the early identification of these disorders and the immediate start of therapy to prevent serious symptoms of genetically determined growth pathology.

Endocrine factors

The final waist of the individual may be influenced more or less by the secretor tonus of various endocrine glands, some with stimulatory some with an inhibitory role.

The pituitary growth hormone (STH) stimulates linear growth through its predominantly condrogenetic and less osteogenetic role. The STH stimulation of the growth cartilage is made with the aid of some sulfactation factors (somatomedines). STH has a tissular construction protein synthesis and morphogenetic role action stimulating the DNA and RNA synthesis. A somatomedine named insulin-like growth factor I (IGF -1) entitled somatomedine A or C, was purified out of human plasma and it was proved that it reacted with specific cellular receptors. A similar substance – IGF-II was also purified out of human plasma, but it is less dependent on STH and less active on the cartilage. The levels of IGF-1 reflect the levels of STH: they are high in acromegaly and low in pituitary dwarfism. IGF has a stimulatory effect on the synthesis of collagen by osteoblasts and has a less specific effect on the proliferation of bone cells. It has also been demonstrated that STH has direct effects on the cartilage.

Idiopathic short stature is particular to patients with a height more than 2 SD below average, normal or slowed growth pace, normal weight according to their age, the absence of any specific obvious chronic physical or psychological disorder. Children have usually short stature at birth and insufficient growth during the first 2 or 3 years of life, afterwards the growth rate becomes normal. Global bone age is equal to height age during the first years, and then during puberty it is accelerated to reach actual age. Puberty commonly takes place at a normal age, and despite pubertal growth, the final adult height remains short as compared to their parents. Endocrine tests are normal. Some patients with idiopathic short stature might have anomalies of the STH-TGF-I accompanied by a certain degree of STH insensitivity. The levels of IGF-I of these children may be below the value average of normal children (14, 15, 16).

Evocative clinical symptoms of STH deficiency are excess weight around the trunk area, small limbs, round forehead, doll-like face, the presence of a micropenis and bouts of hypoglycemia; these are inconstant ant frequently growth failure appears sparsely.

The growth curve indicates a slowdown, leading to a modification of the growth chart. The deficiency diagnosis is made based on the deficit or lack of the STH secretion after stimulation. STH deficit is considered when the level after stimulation is lower than 10 ng/ml. The observance of a STH deficit leads to the examination of another pituitary deficit or a possible lesion to the hypothalamus-pituitary area through CT scan or magnetic resonance imaging (10, 17).

It is allowed that about 1 out of 100 children may be thought of having idiopathic short stature, but not all are candidates are advised to follow STH therapy. U.S Food and Drug Administration endorsed in July 2003 the use of somatrotropine for the treatment of idiopathic short stature. STH treatment should not be administered only to get a higher stature; it has been observed that height is associated with success (men with average height earn more than the short or the taller ones). STH therapy is efficient only after the ossification of growth cartilages. If the treatment starts from the age of 5, it will probably last 5 to 8 years. The treatment consists in administering growth synthesis hormones in a 0.25/mg/kg/day, dose divided in 7 weekly injections. It must be followed until the end of the growth period and of puberty. If there are other pituitary disorders, they will be treated in a parallel way (10, 17).

Insulin is a hormone with a protein synthesis and cellular multiplication role, stimulating growth. Newborn of diabetic mothers are overweight at birth and have the height superior to the normal average and children suffering from Type 2 diabetes have at the onset of the disease a height superior to the normal one and an excess of insulin levels.

Thyroid hormones stimulate the growth and maturation of the growth cartilage and of the muscle cells; their action in bone maturation is predominantly osteogenetic. They act synergic with STH on somatic growth. Children with congenital myxedema have a slower growth rate. At the age of 20, they reach 1 meter height retardation, thus the disharmonious thyroid dwarfism is produced. The dosage of thyroid hormones (the T3 and T4 parts) allows the confirmation of thyroid insufficiency disorder diagnosis. TSH evaluation allows the distinction between primary hyperthyroidism (elevated TSH) and secondary ones (low or normal TSH). The treatment is of hormone replacement and it is made with Levothyroxine 6-8 microg/kg at birth then 100 microg/sm (1).

Androgen hormones have a protein synthesis effect; they stimulate the STH production and act directly on growth cartilages. In moderate doses, they stimulate both linear growth and bone maturation, through condrogenetic and osteogenetic action. Estrogen hormones stimulate somatic growth, having a synergic action with that of STH. They favour osteogenesis and they have a calcipexic action, of calcium fixation at the level of the bone.

Glucocorticoid hormones have an inhibitory effect on somatic growth, favouring protein catabolism; they have an antagonist competitive action with STH at the level of growth cartilage. The Cushing syndrome is exceptional at children. It associates growth retardation, a defect in the repartition of adipose tissue predominantly on the face and trunk area, hirsutism, muscular atrophy, seborea and acne (18). The diagnosis is based on the evaluation of free urinary cortisol. At

children who undergo the administration of glucocorticoids (iatrogenic hypercortisolism) a slower growth rate was observed, leading to cortisol determined dwarfism (1).

The thymus, until its involution which appears at the onset of puberty, has an activating stimulatory effect on growth by increasing STH action and though its intervention in the glucid and calcium metabolism (12).

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OZONE THERAPY IN MEDICINE

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Keywords: *ozone, ozone therapy, intense electric fields, antimicrobian*

Abstract: *Since its introduction in 1840, ozone therapy is providing to be a new therapeutic modality with great benefits for patients. The potent antimicrobial power of ozone, along with its capacity to stimulate the immune response, makes it a therapeutic agent in a lot of medical pathologies. The biological processes from the living organisms and pathogens agents can be stimulated or inhibited, according to requirements by using the electrostatic fields, of corona discharging or different concentrations of ozone. The nature, intensity and shape of the field, exposure times and ozone concentration represent as many influence modes on the biological processes. While in some medical domains ozon therapy proved its efficiency, in others the results are in validation process.*

Cuvinte cheie: *ozon, ozonoterapie, câmpuri electrice intense, antimicrobian*

Rezumat: *De la introducerea ei in anul 1840, ozonoterapia s-a dovedit a fi o terapie alternativă in medicină, cu beneficii importante pentru pacienti. Potentialul antimicrobian al ozonului, impreună cu capacitatea de stimulare a sistemului circulator si de modulare a raspunsului imun, au dus la utilizarea ozonului intr-o multime de afecţiuni. Anumite procese biologice ale organismelor vii şi ale agenţilor patogeni pot fi stimulate sau inhibate, in funcţie de necesităţi, utilizând câmpuri electrice, descărcări corona şi concentraţii diferite ale ozonului. Natura, intensitatea si forma câmpului, timpul de expunere şi concentraţia oxigenului pot influenţa in diverse moduri procesele biologice. In timp ce in unele domenii medicale ozonoterapia şi-a dovedit eficienţa, in altele aceasta urmează sa fie validată.*

SCIENTIFICAL ARTICLE OF BIBLIOGRAPHIC SYNTHESIS

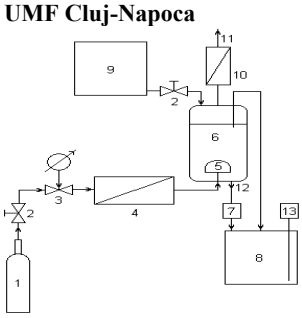
Although ozone was mentioned by Homer, only during the 19th and 20th century it was discovered the method of its generation and its chemical property. Ozone is a chemical compound made of three oxygen atoms (O3- tri-atomic oxygen), a form having a higher energy state compared to the normal atmospheric oxygen (1). There have been very few studies performed regarding the potential of ozone in medicine; the domain being controversial and is one of those that still pioneered in an international level. Therapy with ozone, i. e. the treatment of patients with a mixture of ozone and oxygen, was utilized from a long time ago as an auxiliary method to the conventional treatment, especially in those cases where the traditional treatment did not provide satisfactory results. Ozone is considered to be one of the strongest oxidizing agents, having antiseptic, especially antibacterial property which makes it very effective in combating microbial infections (2).

Obtaining ozone and its mode of action:

Principal modality of obtaining ozone for medical applications is the method of unloading the corona. Advantages of this method are its technical facility, production of ozone in an increased concentration and the possibility of adjusting concentration of ozone in different solutions (1).

In the last few years, strong oxidizing character of ozone was utilized complementarily along with other benefits offered by ultraviolet radiation, hydrogen peroxide, chlorines, strong electric fields etc., which had conferred enlargement of the area of applicability of ozone in preservation of some mediums as well as food products, in the process of obtaining medicine in stomatology, in the treatment of diseases refractory to medicinal treatments etc. Generally the strong antimicrobial property along with the phenomenon of local stimulation of leucocytes offered by ozone is utilized in medicine.

Figure no. 1. Plant for the ozonation of watery solution – UMF Cluj-Napoca



1 – tub (tank or rezervoir) of oxygen; 2 – valve ; 3 – regulator of pressure; 4 – controllable generator of ozone; 5 – porous diffusor of ozone; 6 – column for the diffusion of ozone in the watery solution (reactor with bubbles); 7 – measures rezidual of ozone in the watery solution; 8 – collecting vessel for the ozonated watery solution; 9 – vessel for watery solution to be ozonated; 10 – destroyer of rezidual ozone; 11 – evacuation route for gas; 12 – evacuation route for the ozonated solution,(samples); 13 – measuers the pH or other physio-chemical parametres of the watery solution.

Ozone represents a highly unstable form of oxygen, having a half life of less than an hour in the normal working conditions. Decomposition of ozone into oxygen can be controlled partially by association of liquid, "vector", whose composition, watery or viscous, can influence the speed of conversion of these two forms of oxygen.

As the process of solubilization of ozone in the watery solution more importantly in the process of its decomposition and recombination can result in a huge number of free radicals; so the behavior of ozone respectively the behavior of free radicals in the watery solution can be considered as approximately identical phenomenon (4).

Processing of the watery solution should be done with ozone resulting from oxygen or through application of strong electric fields to the watery solution in the presence of oxygen

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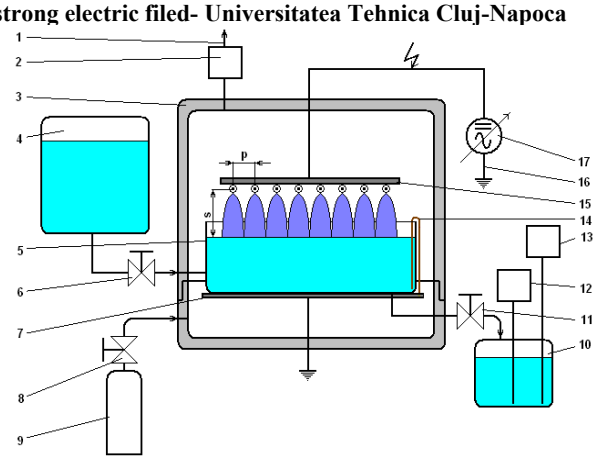
and in complete absence of air, as it can result in ammonium dioxide which is harmful and can compromise totally the beneficiary effects of ozone (3,4).

Remnants of ozone or amount of free radicals found in the watery solution treated in the ozonizer or those found in the unit of processing electric field depends upon a lot of factors out of which the most important are: temperature of the watery solution (at a temperature above 50° C, the speed of decomposition and recombination of ozone increases highly), pH of the watery solution, type and the grade of the impurity in the watery solution, pressure of the solution, material of the stocking recipient and medium with which the watery solution comes into contact (4).

Figure no. 2. Plant for direct processing of watery solution in strong electric filed- Universitatea Tehnica Cluj-Napoca



1- evacuation route for gas; 2 – destroyer of rezidual ozone (optional); 3 – unit for direct processing; 4 – vessel for the watery solution to be processedt; 5 – petri dish for direct processing, with the liquid kept in a stationary state; 6 – valve for the alimentation Petri dish; 7 – electrode connected to earth, plate type; 8 – vavle to regulate the pressure; 9 - tub (tanc or reservoir) of oxygen; 10 – collecting vessel for the processed watery solution; 11 - valve (tap) for the collection of watery solution; 12 – measures the rezidual ozone in the watery solution; 13 - measuers the pH or other physio-chemical parametres of the processed watery solution; 14 – piece that connects the watery solution to earth; 15 – active electrode, corona, of high tension; 16 – bridge between the belt and socket of earthing; 17 – regulator of high tension.

The antimicrobial effect of ozone is due to both its direct action as well as its capacity to form very active peroxides with unsaturated fatty acids which has a destructive effect upon the microorganism. In small dozes ozone has a locally destructive action upon the cell membrane but in large doses it blocks some specific enzymatic systems and cellular receptors leading towards the death of the pathogenic microorganism. Bactericidal effect of ozone is twice that of chlorine and is equally effective in those cases resistant to antibiotherapy without inducing any resistance of its own. Equally good results were reported also against viruses, funguses and protozoa's (5).

The initial mechanism through which ozone acts upon microorganisms is by the oxidation of their cell membranes, the process where glycoprotein's, glycolipids and different amino acids of the cell membrane gets affected resulting in the intrusion of the ozone molecule inside the cell and in turn resulting in blocking the enzymatic system of the cell finally leading to death (6).

Other than its direct action upon microbial agents, ozone also has an immunomodulating action which is conferred by stimulating not only the cellular mechanism (T lymphocytes, Monocytes) but also the humoral mechanism (synthesis of cytokines, interferons and of tumoral necrosis factors) (7). Hence upon administration of an well judged concentration of ozone, it plays an important therapeutic role in different kind of infections through the generation of free radicals of oxygen (O2, OH, H2O, NO, HOCL), radicals that are produced also inside granulocytes and macrophages during the time of an infectious process (8).

The effect of ozone upon microorganisms is proportional to the concentration of ozone and the time of its exposure upon them. Studies performed had showed that ozone is equally effective upon gram positive as well as gram negative bacteria, only later needing a higher concentration of ozone for neutralization than the gram positive ones. Upon the anaerobes and micro-aerophils, ozone has a dramatic toxic effect mainly because of the energetic metabolism specific to these bacteria's which uses organic compounds as a final receptor of oxygen and also because of the fact that they does not possess protective enzymes against toxicity of oxygen (9).

The oxidation property of ozone was used in combating facial infections mainly those encountered in dental surgeries (10). In a study upon 83 patients undergoing surgical intervention for a complete prosthetic replacement of hips, Dr. Bioloszenski (11) did not find any septic complication in those patients who have received intraoperative prophylaxis of ozone therapy. In the same time there have not been reported adverse or negative effects of ozone upon the patients or on medical staffs. Chen H. in 2007 (12), had demonstrated the anti-apoptotic and anti-inflammatory potential of ozone in an experimental study performed on rats suffering from acute renal ischemia, and again Parkhishenko IuA in 2003 had obtained a more rapid amelioration of hepatic insufficiency and more rapid efficient detoxification of the organism in case of an icteric patient who had received par-eneteral ozone therapy (13). The antimicrobial effect of ozone was shown in the cases of necrotizing fascitis (14), maxillary osteonecrosis (15), prostatic surgeries (16), super infected wounds and ulcers refractory to treatment (17) where besides having an accelerated healing through continuous irrigation of ozone there was also obtained a reduction of pain, mental stress and hence a final reduction of overall cost of the treatment. Ozone therapy was also applied under the form of extracorporeal oxygenation and ozonation of blood. Di Paolo N in 2005 had performed a study upon 82 patients and demonstrated the stress controlling therapeutic property of ozone where the patients had suffered from different kinds of immune dysfunctions as well as some degenerative processes (18). Ozone therapy also had proved its efficacy in case of those patients suffering from degenerative muscular diseases, ischemic diseases, infections and refractory wounds where the conventional therapy had found to be failed (19). Oxidizing property and the antimicrobial property of ozone was proved also in the cases of peritonitis, by Ozmen V et al. who had used intraperitoneal irrigation of ozonated saline solution in the cases of mice and obtained a reduction in the rates of mortality and reduction in the rates of postperitonitic residual abscesses (20). Hence was obtained a reduction of mortality rate from 62.07% to 37.23% (21) in those mice suffering from acute severe peritonitis; an overall fall of 1.7 times in the rate of mortality and 1.8 times fall in the rate of infectious complications (22). In the patients who had developed sepsis or septic shock, use of ozone therapy as an adjuvant treatment had led to a reduction of mortality rate from 39.2% to 25.6% (23). Ozone can have an important therapeutic role in different types of infections as it generates free oxygen radicals (O2, OH, H2O2, NO, HOCL) similar to those produced by granulocytes and macrophages during the process of an infection (24). Ozone is extremely active and does not induce any resistance as they are highly efficient also against anaerobic bacteria's as well as bacteria's resistant to antibiotics.

In Romania, recent studies performed by University of Medicine and Pharmacy Cluj Napoca, had proposed the combined utilization of ozone and strong electric fields to treat different

biologic mediums, as it led to the inhibition of noxious processes and at the same time bio-stimulation of useful processes of the respective treated medium (3,4).

As far as the mode of administration of ozone is concerned, according to the result desired ozone can be administered systemically, locally or in a combined way. Where there is an antimicrobial effect of ozone is desired, ozone is administered in a large concentration targeted directly at the foci of infection. In case of infections inside the abdominal cavity (infected pancreatitis, peritonitis of different causes) the optimal way of administration is intraperitoneally where one has to ensure a constant flux of ozonated solution in such a way that a constant concentration of ozone similar to that of minimal concentration having bactericidal effect is obtained in the respective zone of interest. The process can be obtained through a system of drainage tube that offers a continuous lavage.

Capacity of ozone (a strong oxidizing agent) to induce an increase in the level of cellular antioxidant enzymes thereby reducing oxidative stress forms the base of utilization of this form of oxygen in different diseases. The study on the effect of ozone upon acute pancreatitis with necrosis of the pancreas and peripancreatic tissues is still in an experimental level in University of Medicine and Pharmacy Cluj Napoca. Acute pancreatitis represents one of those pathological entities where the oxidative modifications caused by the access of free radicals remains the main mechanism of pathogenesis. In the same way, another point of interest is the enzymatic autodigestion of the gland itself. Some of the studies have showed that ozonated saline solution containing smaller doses of ozone produces a positive effect upon the proteolytic system and on the other hand larger doses induces a decrease in activity of plasmatic alpha 1 antitrypsin and of plasmatic alpha 2 macroglobulin levels (25).

CONCLUSIONS

In this was, in contrast to the dogma which says that "ozone is always toxic", recently it had been shown that at certain concentrations ozone can have properties like disinfectants, immuno-modulators, inducer of antioxidant enzymes, can contribute to stimulation of the metabolism, induction of the synthesis of endothelial nitric oxide and can also activate the stem cells with beneficial effects in neo-vascularization and tissue healing. Ozone therapy is a promising domain for the non-conventional medicine, proving its efficacy in certain pathologies and through studies and researches is on its way to prove its efficacy in the rest of the pathologies in the near future.

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THE PURPOSE OF HOME VISITING THE PATIENT IN THE EDUCATION OF THE DOCTOR AND PROPER INDIVIDUALIZING OF THE TREATMENT

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Keywords: *patient, diagnosis, therapy, heredity, prognosis*

Abstract: *In this paper, the authors make references relevant to the important role of doctor to patients' homes, which method contributes to the professionalism and knowledge of clinical and precise delineation of the diagnosis, therapy and bio-psychosocial classification of the patient. In this regard it concluded that the visits and conversations with family members must clear the atmosphere, reduce or eliminate the tense-family conflicts and mobilize the therapeutic process and overcome unavoidable, helping to rebalance the "homeostasis" of the family.*

Cuvinte cheie: *bolnav, diagnostic, terapie, ereditate, prognostic*

Rezumat: *În prezenta lucrare autorii fac referiri pertinente la importanţa rolului medicului la domiciliul bolnavului, metodă prin care se contribuie atât la profesionalismul clinic cât şi la cunoaşterea şi delimitarea mai precisă a diagnosticului, terapiei şi încadrarea bio-psiho-socială a pacientului. În acest sens ei concluzionează că vizitele şi convorbirile cu membrii familiei bolnavului trebuie să limpezească atmosfera, să diminueze sau să înlăture stările tensional –conflictuale şi să mobilizeze membrii familiei în procesul terapeutic şi în depăşirea unor situaţii inevitabile, contribuind la reechilibrarea "homeostaziei " familiale.*

SCIENTIFICAL ARTICLE OF BIBLIOGRAPHIC SYNTHESIS

The main objectives of the visit to address, confine not only to the knowing of the in-family relations, the role of the patient in these relationships, socio-economic conditions and it's deficiencies but also to the transverse and longitudinal analysis of patient's personal development and the accurate and comprehensive family involvement in the therapeutic process.

Knowing the in-family relationship not only allows to discover how they influence personality development during the formative years and adulthood but rather that these influences are transmitted from one generation to another, justifying the concept of "social heredity", which enlarges and reduces the effects of biological heredity on personality development. The argument of this assertion, is that adopted children from an early age eventually behave in a manner so similar to the adoptive parents, that sometimes we are surprised that among them there is no direct genetic link.

Therefore visiting the family of the patient by the doctor has a special significance in comparison with the examination at the doctor's office or territorial polyclinic. In their family may be more objective about the suffering of those who require medical aid, or assistance with reviewing patients - can detect elements of lesser or greater sanogenic or pathogenic importance, with which they could find the best measures of therapeutic individualization.

Currently, beginning from the premises of creating new bases of modern preventive and curative health care, these visits must regain value, the important place in the healthcare of the population expanding to both the patient and family's and place of work.

During home visits, the physicians must apprize with tact and spirit of observation the dominant in-family relationships, psychosocial status of individual members in particular and the patient, the family's goals and joint actions, the behavior and pre-aid in difficult situations.

Seldom, in a paradoxal way, the improvement or healing of the patient is accompanied by the emergence of somatic-emotional disorders at other family members, as the family tries to maintain homeostasis, would require one or more sick. The functioning of a unite family can not be inferred only from the study of individual members. Provided each member of the family's behavior is different from outside the family, which explains why some family members of anxious, depressed, psiho-pathogenic patients, as individuals function normally in society, while the family - all working as a pathological form or reverse.

To illustrate this assertion, we quote the case of a child with mitral stenosis who was carefully groomed by his family and spared of any effort, so addicted to his own family. Under these conditions, the family functioned in a harmonious balance, the parents and his brothers felt useful, until he was operated successfully. Him not being disable anymore, the family members had to change the system to adapt. If the family is flexible, its members will be able, after a while to accept the qualitative change occurred and to help children build confidence in himself, being aware that they have less need and adapting it to new situation. If the in-family relationships are rigid due to fear facing this new situation, family members are inset above to restore balance and treat the child as an invalid, a situation in which the child can accept this status, requiring parents to treat him as such, satisfying thus their need for dependency.

As you can see the patient adapts to his own health conditions and still retain the status of disabled and dependent, relies heavily on dynamical family communication interactions that may favor or disfavor the bio-psycho-social rehabilitation.

If mentally ill, home visits must monitor the removal

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of apato-aboulic phenomenology or the contrary, the concerns of hiper-acknowledging of the disease, also boosting initiative directed towards activities and concerns that detach him of the parological phenomenology. To achieve this goal, in addition to the initiation, it is also needed the training of doctors and nurses from the "Family Practitioners" in psychiatric assistance. Moreover, piho-pathological phenomena may manifest both within and outside her family and to avoid misinterpretation of the disease must not forget that, sometimes, the patient expresses his own pathology patronized and enganced in more or less defective family interactions. Interactions and mutual dependence between family members are the so called "family homeostasis."

Under normal conditions most famous roles of the family are those of father, mother, daughter, sister, brother, etc., but in abnormal situations we meet other roles such as "parent" black sheep, or family treasure, there are "one guilty "seen as" responsible "for all the family troubles and sufferings, like if it's disease, if not consumed alcohol in excess, whether it would be too harsh and aggressive, too soft, too fragile, if not be heard, if they learned whether or not it would be "X" or "Y" etc. "I would have no problem in the family."

Other in-family aspects are linked to the so-called "family myth", made up by increasing the extremes of positive traits accepted without criticism, distorting the reality as "Dad never gets tired from anything," his mother is never angry, she never complains, "our baby is the smartest and will succeed in all", etc.. this "myth "may lead to the establishment of rules and rigid in-family conducts, even pathogenic because those people are working to identify themselves with their myth, and when they lose the possibility to continue the myth of the family emotional imbalances occur.

Maintaining human and family relationships is based on communication, transmission of messages through verbal language with which to communicate the significance they know. At the same time, communication acts on the condition of individuals (pragmatic aspect) and thus the non-verbal communication and the meta-communication plays an equally important role as the transmission of verbal messages. In fact, the first axiom of the communication theory is that "any behavior is communication and therefore it is impossible not to communicate."

Mostly, the patient's home and household give us conclusive evidence of the disease. Arranging your home can be a sign of lack of heat, for psychological tension or existential difficulties, the doctor easily recognizing if the patient is alone or surrounded by loving carers. Along twith the patient's home visit, it is exposed an intimate part of his life, revealing himself easily, as in his home is tempted to honest communication. Family members are less retained than in the offices of the clinic or hospital, often not having the outburst that they desire. Within the family, even in the presence of the doctor, the communication and behavior patterns do not change. Careful observation may uncover deep divergences, critical or other substrates, we can approach the core issues quickly, thus leading to a new therapeutic-diagnosis vision.

The link between medicine and the world the patients live in is maintained by both doctor visits at home and the carer visits to hospitalized patients. Doctors who make periodic visits to patient's homes are very well informed about the nature and extent of their health problems. Knowing the patient's family situation requires a delicate insight into family homeostasis, requiring an ethical-moral stance and fairness from the doctor. In general, family homeostasis are based on the balance of the relationships and the communications between family members, among whom the is established a mutual dependency .

Home visits should not only contribute to clarification, comforting and loosening the atmosphere within the family, but also to alleviate family fears and worries, which effectively lead to a therapeutic process to stimulate the patient to regain self-confidence in his own forces and his capacity to reclaim his previous role in the family and previous position at work.

It should not be overlooked the fact that you can not always delete events and risk factors of life and nor the chronic or fatal development of the disease . In these cases physicians should intervene in order to a more effective rehabilitation of the patient or remodeling existential conditions of functional-dynamical and balanced family homeostasis .

Home visits have both a ellementary human act and a maximum evidence of professional dedication by the doctor, confering to the patient faith in healing and the feeling that he is not alone in facing the disease.

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LEGISLATIVE ASPECTS OF SOCIAL ASSISTANCE IN ROMANIA

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Keywords: *social protection, measures, rights*

Abstract: The article contains general considerations and concepts regarding the social protection. The social politic objectives are aproached to assure the effective exertion of the rights and the levels of the social assistance.The aptness of the system of social assistence at the requests of developing a democratic regime imposes the redefinition of the social assistance concept.In conclusion, the social protection actions aim more domains in which there are necessary collective efforts such as: health, education and training, culture, rest and recreation conditions, socio-political medium, in a word the social living conditions.

Cuvinte cheie: *protecție socială, România, măsuri, drepturi*

Rezumat: *Articolul cuprinde considerații generale şi concepte privind protecția socială. Sunt abordate obiectivele politicilor sociale pentru a asigura exercitarea efectivă a drepturilor precum şi nivelele asistenței sociale. Adecvarea sistemului de asistență socială la cerințele dezvoltării unui regim democratic impune redefinirea conceptului asistenței sociale. În concluzie, acțiunile de protecție socială vizează mai multe domenii în care sunt necesare eforturi colective, respectiv: sănătatea, instruirea şi educația, cultura, condițiile de odihnă şi recreere, mediul social-politic, într-un cuvânt, condițiile sociale de trai.*

SCIENTIFICAL ARTICLE OF BIBLIOGRAPHIC SYNTHESIS

In a democracy, social protection is a fundamental element of state policy due to the fact that implementation is done for preventing, restricting or eliminating the consequences of events considered "social risks" to the living standards of the population.

With roots in antiquity, which included protective elements in Roman law, the appearance of the first significant forms of social assistance were observed in the 13th and 14th centuries, when monasteries were built around places of social assistance for the poor, the elderly and the sick.

The first forms of social protection appeared in the early 19th century and were related to social security measures. These social protection elements were added at this time to the social assistance elements and both were named referred to "social security". This term was first used in U.S. when the government created institutions with the adoption of the Social Security Act of 1935, which included rules on risk prevention for old age, death, disability and unemployment.

The concept of social protection was first introduced in the United States by John Kenneth Galbraith and set policy to protect disadvantaged populations through measures aimed at aligning these categories to a decent living. He believed that the most urgent measure is "to provide rights to those who can not find a job to have a guaranteed income or alternative.

As part of international law, International Labour Organization adopted in 1952 (Convention. 102) the term "social security including social security as complementary elements and social assistance.

Currently, social protection activities cover several areas where collective efforts are needed, namely: health; training and education; culture; conditions for rest and recreation; social and political environment, in a word, the social conditions of living.

Need, content and role of Welfare and Social Security

Social protection is designed to ensure a basic standard of living for all people, regardless of the means available to them. There are several categories of persons requiring social protection: the unemployed; the disabled; children and youths; and any additional situations requiring social protection (in case of death, incapacity for work, occupational disease).

Specific conditions and different situations that need to be covered are as modalities of social protection are different. Such programs are differentiated based on assumptions for social security, to cover personal needs due to temporary or permanent loss of work capacity or where worker protection at work - environment, working conditions - needs to be transferred to production costs and whose satisfaction is included in the product.

Social welfare reform objectives include the material claimed in the state be such that it can be substantiated and ensure the achievement of restoring or maintaining equilibrium between public and private, between protection and self, between needs and resources, between development present human generation and future generations.

Diversity and amount of the benefits and social services are subject to the state economy, the financial resources of that time, and the need to build the administrative framework for implementation, especially as regards staff training and computerization activities.

Social protection programs, administered by the state, are funded on the principle of division, compensation, intergenerational resources from contributions, and taxes based

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on the principle of collective responsibility.

Romania has adopted the objective of social policies that ensure effective exercise of rights and the following principles:

- any person should be able to earn a living by work freely chosen;
- all workers are entitled to fair working conditions;
- all employees have the right to safe and healthy working;
- all workers are entitled to an equitable remuneration that ensures them and their families a level of life satisfaction;
- all workers and employers have the right to associate freely under national or international association for economic and social interests;
- all workers and employers have the right to bargain collectively;
- children and adolescents have the right to social protection against physical and moral hazards to which they are exposed;
- workers in case of maternity, and other business, if necessary, are entitled to special protection at work;
- everyone has the right to appropriate professional guidance to help them choose a profession according to his personal skills and their interests;
- everyone has the right to appropriate training;
- everyone has the right to benefit from any measures which would allow them to enjoy the highest attainable standard of health they can achieve;
- all workers and family members are entitled to social security entitlement;
- any person without adequate resources has the right to social and medical assistance;
- everyone is entitled to receive social welfare services;
- any person is entitled to invalid and social training, regardless of its origin and nature of disability;
- the family, as the fundamental unit of society, is entitled to social protection, legal and economic nature of ensuring full development;
- mothers and children, regardless of marriage and the family situation, are entitled to adequate social and economic protection;
- citizens of either Contracting Party shall be entitled to exercise on the territory of another Party any gainful occupation on an equal footing with nationals of the latter, subject to limitations based on or through economic or social reasons;
- migrant workers of one Contracting Party and their families are entitled to protection and assistance within any other Contracting Party.

The structure of social protection in Romania is complicated due to the mixture of different schemes addressing the same social risk, financial and organizational arrangements, sometimes inappropriate, of institutional tasks and responsibilities which overlap and are unclear.

Romanian social protection schemes operate on the principle of social insurance, non-contributory schemes financed from the state budget, social assistance schemes and schemes based on funding from state budget subsidies for free goods and services or at low cost for certain categories of people.

Social welfare covers several areas where collective efforts are needed, namely: health; training and education; culture; conditions for rest and recreation; social and political environment, in a word, the social conditions of living. To these are added, the material conditions of living (housing and living environment, employment and working conditions, income and consumption), family life, and respect for social order and law.

In Romania, since December 1989, the transition from planned economy to market economy has required a reconsideration of social protection.

The Constitution enshrines the use and concept of social protection. Thus the state is obliged to ensure economic development and social protection of nature to ensure citizens a decent living.

Citizens are entitled to pensions, paid maternity leave, health care in health centers, unemployment benefits, disability pensions, survivors' pensions and other forms of social assistance provided by law.

Currently, social assistance is defined differently than usual. Dimitrie Gusti said that she "left the track of mere sentimentality, generous and good intentions to walk in an orderly social and ethical action and duly justified, with the sole purpose of serving company books and not by theory but by finding the truth in the midst of the difficult social conflicts of life."

Failure of reforms initiated during the transition period led to a deep crisis in all spheres of social life. Consequently, much worsened living standards of the population are growing poverty, unemployment, proliferating social ills, revived crime, frequent cases of family abandonment, child delinquents, vagrancy, decreased birth rates and increased mortality. In these circumstances, Romanian society must establish a system of social protection to ensure support and protection of persons and groups that have no material resources, social and moral, and are no longer able to obtain the necessary means in their efforts for a decent life.

A major component of social protection, social assistance is a way of implementing operational support programs across multiple and specialized social services for those temporarily in need.

Social assistance is based on a system of values, principles and moral standards requiring a professional code of ethics. The whole social scientific technique, as refined as it is, is devoid of real efficiency and does not always match the themes of the lessons of Christian charity, so called charity.

The social assistance component is a non-contributory social protection system and represents all the institutions and measures that the State, public authorities of local government and civil society and ensures the prevention, restriction or removal of temporary or permanent effects of situations that can generate the social marginalization or exclusion of individuals.

The main objective of social assistance is to protect persons who, because of economic reasons, physical, psychological or social deficiences, are unable to provide social needs or to develop their own capabilities and skills for active participation in society.

Adequacy of social support system development requirements of a democratic regime must define the concept of social assistance, as identification of objectives, mission and related institutional measures. It is a health benefit but carried out with state money and other institutions, and is addressed to those in poverty. Social insurance contributions are made by those who work, being by nature a preventive measure, to ensure citizens a certain measure of independence. The social assistance system is based on the following principle: the state budget funds or private funds (obtained from individuals or the community) are designed to support people in difficulty depending on their needs. Therefore, in this case, the benefit is based on the needs of the principle of solidarity and not dependent on any previous personal contribution, as with social security.

Social assistance deals with issues at different levels:

- individual level - economic assistance, psychological, moral for those who need such as the unemployed, those addicted to drugs or alcohol, the problems of integration at work, victims of abuse of any kind;

- interpersonal and group level - family therapy, the couple, groups of marginalized people;
- community level - ethnic conflict resolution, individual and collective energies to mobilize the necessary resources to restore their normal integration.

Through the combination of methods, intervention, action strategies, programs and special measures, social assistance provides direct support, effective for those individuals and groups who, for some reason, can not provide themselves, as this legislation does, income, economic resources and sufficient supplies, health care, pension social, physical or moral needs, or are in relation to their needs.

Legislative issues regarding social assistance in Romania

A public pension system and other social insurance work rights are provided, in Romania, in accordance with Law no. 19 of March 17, 2000, updated in 2010.

Under the general provisions of this law:

"Article 1. Right to social security is guaranteed by the state and must be exercised in accordance with this law, the public pension system and other social insurance rights, 'the public system.

Article 2. The public system is organized and operates with the basic principles:

a) the principle of unity, whereby the state organizes and guarantees the public system based on the same rules of law;
b) the principle of equality, providing all participants in the public system, taxpayers and beneficiaries, non-discriminatory treatment in respect of rights and obligations under the law;
c) principle of social solidarity, participants in the public system that assumes reciprocal obligations and enjoy rights to prevent, restrict or remove social risks under the law;
d) the principle of compulsory, that individuals and legal entities by law are required to participate in the public system, social security benefits is correlated with exercise obligations;
e) the principle of contribution, under which social security funds are based on contributions from individuals and legal persons participating in the public system, social security benefits are due under the social security contributions paid;
f) the principle of distribution, made on which funds are redistributed to the public system payment obligations under the law;
g) the principle of autonomy, based on independent management of the public system, according to law. "

Under this law it was established the National House of Pensions and Other Social Insurance Rights, which is subordinated to her county retirement homes in each city, county, according to Art. 3 (1) and (2) of this Act.

According to "Art 4. - (1) In the public system are provided in this law, individuals, hereafter insured, (2) The insured may be Romanian citizens, foreign citizens or stateless persons, who, under the law, domicile or residence in Romania (3) The insured are obliged to pay social security contributions and are entitled to social security benefits under this law. "

Chapter IV of this law deals with pensions, as well as types of social insurance.

According to Art. 40. "The public system of pensions shall be granted the following categories:

a) old-age pension,
b) early retirement,
c) partial early retirement
d) invalidity pension;
e) survivor's benefit."

Social assistance is the main mechanism by which society intervenes to prevent, limit or eliminate the adverse effects of events occurring on people or vulnerable groups without their will or are little affected by them.

The main objective of social protection is the reduction or even elimination of the consequences of environmental risks and living standards of some segments of the population.

In substantiation and promotion of social policy are considered the following principles:

- human dignity;
- elimination of all forms of discrimination in all social protection policy;
- promotion of social partnership as a means of control and efficiency of all measures and social policy;
- flexibility, social protection measures that adapt to the real needs of groups and individuals;
- guidance and policy objectives and measures of social protection towards capacity, mobilization and participation of all social forces to boost growth, labour is the primary source of wealth and individual freedom, the most stable source of health economy;
- gradual decentralization of social protection and with it the engagement in social welfare activities of traders, local government units, the government institution and NGOs, charitable societies and individuals, through contributions, financial and social implications of their in an adequate legal framework.

According to Art. 53, paragraph (1) of Section 4, of Chapter IV of the Law 19/2000, updated in 2010: "There are entitled to disability pension policyholders who have lost all or at least half of the work capacity because:

a) accidents, according to law;
b) ocupational diseases and tuberculosis;
c) common diseases and accidents unrelated to work. "

Because this class represents the highest risk population in impaired quality of life, it requires attention from the authorities and decision-makers.

Businesses and institutions are obliged to provide employees the necessary conditions for the smooth conduct of business and must take measures to protect labor and to remove and prevent the causes that may lead to reduction or loss of their jobs.

Invalidity pension is granted to employees who have lost all or at least half of the work capacity of the following causes: accidents; occupational diseases; and, common diseases and injuries unrelated to work.

In relation to loss of work capacity, there are 3 degrees of disability:

- I grade disability is when an individual has completely lost the ability to work and needs constant supervision and care from another person;
- II grade disability is when an individual has completely or mostly lost their work capacity, the disabled person serves himself, having no need care from another person;
- III grade disability when losing at least half of the work capacity and the disabled can provide the same work, but with a reduced schedule or other work easier.

Recruitment of persons of the III degree of disability is made by an expert medical commission, taking into account the following basic criteria: the nature, seriousness, circumstances and course of the disease, the possibility of recovery of work capacity, evidence which might lead to worsening business continuation.

Disability pensioners must undergo medical checks, according to the disease at intervals of 6-12 months, until they reach the standard retirement age. After each check, the Social Security expert issues a new decision, which shall, as appropriate, maintain the same degree of disability, recommend

employment in another degree of disability, or terminate disability retirement due to regaining the ability to work.

There are not subjects to medical review of disability retirees who:

- have an irreversible disability that affects work capacity;
- have reached the age required by law to obtain a pension for work and retirement;
- are younger than five years up to the standard retirement age and have achieved complete contribution.

For I and II grade disability, pension is determined in relation to seniority, the percentage of tariff wage and other labor income on pension establishment, on a differentiated salary cuts and labor groups. Pension employed persons, whose seniority is less than 5 years and have lost all or most work capacity due to an accident, illness or other diseases contracted while being employed, are determined in fixed amounts differentiated on the degree of disability.

At the standard age for work necessary to obtain pension for work and for old age, invalidity pension recipient can choose the most advantageous of retirement.

The state has an obligation to provide protection against deterioration of quality of life, and this support forms a set of measures designed to work specifically on preserving not only scaled quantitative indicators, but also qualitative quality of life.

This protection is especially required during the transition period, when the danger of deteriorating living standards push the whole population, but particularly the disadvantaged population groups, by the existence of some degree of disability.

This requires the efforts and support from the decident state and forums in meeting the desire by adding those factors to supplement their dignified and civilized living.

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7. Ordonanța de urgență a Guvernului nr. 108 din 18 septembrie 2008 pentru modificarea unor acte normative din domeniul social, publicată în Monitorul Oficial al României, Partea I, nr. 661 din 22 septembrie 2008 – prin care se modifică calculul indemnizației pentru însoțitorii persoanelor cu un anumit grad de invaliditate.

CERAGRAFT: BONE GROWTH STIMULATING BIO-MATERIAL

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Keywords: *alloplatic materials, osteoinduction, osteogenesis, apposition, opacity*

Cuvinte cheie: *materiale aloplastice, osteoinducţie, osteogeneză, apoziţie, opacitate*

Abstract: *Alloplastic biomaterials, in this case, Ceragraft, by their features and properties have proved to have osteogenetic effect. These materials introduced into bone loss following traumatism or maxillary cysts are not imunogenic, citotoxicity tests being negative. Bone results were radiologically relevant 12 weeks after application.*

Rezumat: *Biomaterialele aloplastice, în cazul nostru, Ceragraftul, prin calităţile şi proprietăţile lor s-au dovedit a avea un efect osteogenetic. Aceste materiale introduse în pierderi osoase în urma unor traumatisme sau chiste maxilare, nu sunt imunogenice, testele de citotoxicitate – negative. Rezultatele osoase au fost relevante radiologic la 12 săptămâni după aplicare.*

INTRODUCTION

Materials used for bone growth are introduced into areas of bone loss, caused by pathology, infection or trauma. Substituents may act upon the bone through three types of mechanism: osteoconduction, osteoinduction and osteogenesis.

Osteoconduction determines bone growth by apposition to and on a preexisting bone.

Biocompatible osteoinductive materials give no toxic reactions, are entirely synthetic in nature and may be classified into ceramics, composites and polymers.

Of alloplastic materials, bioactive ceramics, including hydroxyapatite and trycalcic phosphate are the most numerous and are used for bone growth.

These materials are of two kinds: resorbable and non-resorbable.

Hydroxyapatite

Inorganic components of bone make up approximately 50% of bone frame mass. Calcium and phosphorus are the most common components, followed by bicarbonates, magnesium, sodium, potassium, etc. Research has proven that phosphorus and calcium can form together hydroxyapatite crystals. Visual images have been taken of 40x25x3 nm hydroxyapatite crystals, disposed along collagen fibres, surrounding amorphous matter. The association of hydroxyapatite and collagen fibres gives the bone tissue resistance and hardness. Thus, hydroxyapatite has been used on a large scale as a good bone replacement material.

The material is osteophilic and nonresorbable. It is recommended to be used in bone preparation for maxillary cysts where tissue interface is more probable on bone. It needs to be emphasised that all hydroxyapatite based products are reabsorbed in case of decreased pH (infection).

In bone composition, collagen together with the calcium-phosphorus combination forms a structure almost identical to that of hydroxyapatite.

In Romania, hydroxyapatite obtains under the form of powder or granules of between 0.2-1.4 mm, under the tradename Ceragraft.

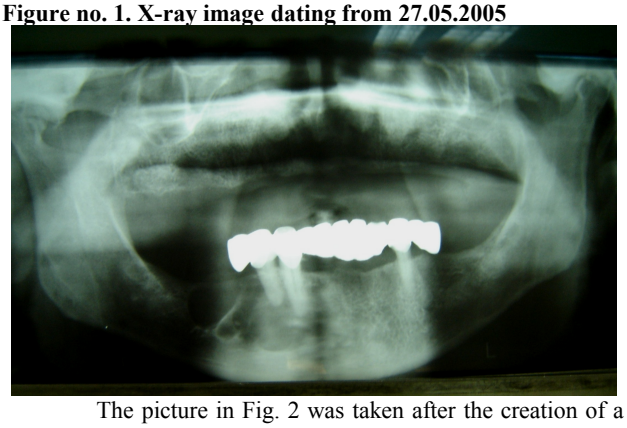
The main characteristics of these biomaterials are:

- easily soluble
- resorbable as the bone regenerates, the rest is maintained intact
- determines bone regeneration and not reparation
- in animal testing, newly formed bone attains the density and structure of pre-existing bone in 12 weeks
- not immunogenic
- biocompatibility is proved by the absence of cytotoxicity and hemocompatibility
- its use as bone replacement represents an alternative to autografts

CLINICAL CASE

27.05.2005 – Pacient aged 80, without major health problems presents with tumefaction, extensible at intraoral palpation, extending between 4.3 and 4.6. Vitality tests for teeth 4.4 and 4.3 are negative, sensitivity of lower alveolar is not affected. Orthopantomography provides the image of a possible ameloblastoma (Fig. 1).

Figure no. 1. X-ray image dating from 27.05.2005



The picture in Fig. 2 was taken after the creation of a mucoperiosal flap; macroscopically the presence of a bone-cyst affecting the bone is detected, after removal of the diseased tissue as well as of the surrounding membrane.

The diagnosis of radicular cyst affecting the bone was confirmed by the result of histopathology. (Fig. 5) Post-

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operative clinical evolution was good and X-ray images taken 8 weeks after the operation (Fig. 4) and 5 years later (Fig. 6) confirmed the presence of bone regeneration process.

Figure no. 2. Intraoperatory image

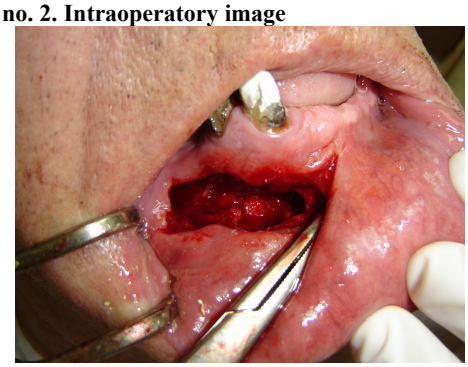


Figure no. 3. Suture of the mucoperiost after cystectomy

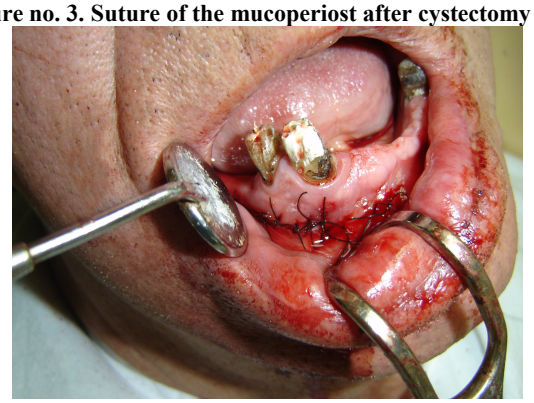


Figure no. 4. Radioopacity showing development and bone apposition (4.4, 4.3) (X-ray image dating from 08.08.2005)

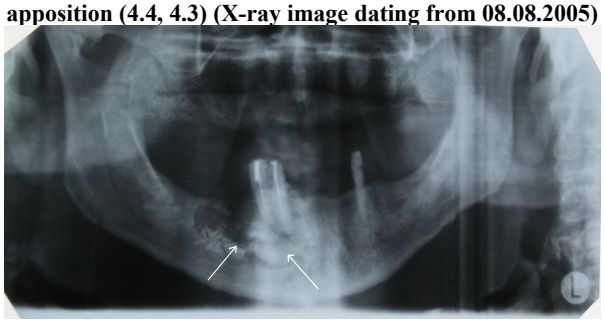


Figure no. 5. Odontogenic cyst with surroundig moderate lymphocytic inflammatory infiltrate visible

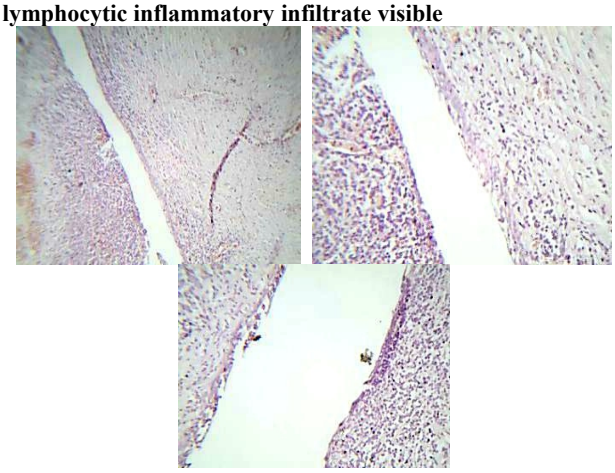
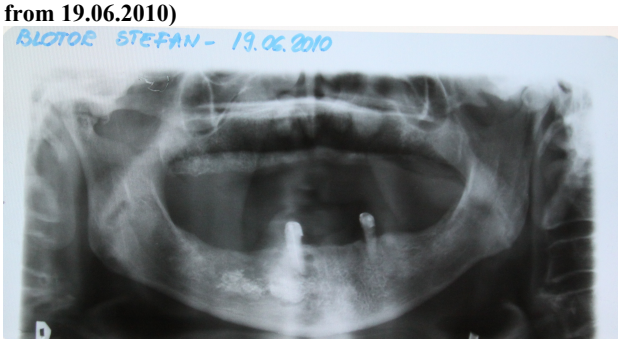


Figure no. 6. Zone of regeneration with bone apposition extending over the whole area of the former cystic cavity, radiopaque images and absence of 4.4 (X-ray image dating from 19.06.2010)



CONCLUSIONS

Applying Cerograft in bone loss caused by a cystic formation has proved over time the bone regenerative, not reparative qualities of the bio-material; thus they offer a good alternative to autograft.

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