Abstract: Objective: The pursuance of the evolution of 115 patients with chronic active hepatitis with HVC, in treatment with Peginterferon α2A, 180 µg / week and Ribavirină in dose adapted to the weight, with the aim of establishing the frecuency of apparition of the thyroid dysfunction in the context of the specific treatment. Concomitantly, it has been pursued the establishing of correlations between age, sex, degree of activity of the disease, the possible moment of the infection and the apparition of the clinical and paraclinical thyroid modifications. Methods: The prospective clinical study was realised on a lot of 115 patients with chronic active hepatitis with HVC, aged between 18 – 65 years. The patients were taken from the clinic and ambulatory of the Clinical Emergency Hospital of Sibiu, during 2005 – 2010. The criteria of inclusion and exclusion were the ones imposed by the CNAS protocol: age between 18 – 65 years, the increased level of the transaminases normal or increased, detectable viremy, hepatic biopsy function. Results: I have remarked since the beggining the increased incidence (statistically meaningful) before the beggining of the therapy with antithyroid antibodies in the studied lote in comparison with the population without viral hepatic pathology. Thus, 11 patients presented at the beggining of the treatment antithyroid antibodies, representing 9.6 %. Among them, 8 were females and 3 were males. Ulterior, during treatment, the number of patients that had antithyroid antibodies increased progressively, being of 18 patients at 3 months, respectively 21 patients at the end of the treatment. It has been observed that the majority of the patients that developed chronic autoimmune thyroiditis at the end of the treatment had antithyroid antibodies in the first three months. Also, it has been observed a predominance of the cases at the females (14 among 18). The last determination of the antithyroid antibodies was effectuated at the end of the therapy. The monitorisation after treatment is currently developing, so we can not appreciate the extension during the time of the chronic autoimmune thyroiditis. Concomitantly, the evaluation of the TSH, T3 and T4 at the beggining of the treatment evidenced the existence of a number of 2 patients with hypothyroidism and the absence of hyperthyroidism. Both patients with hypothyroidism were females. During treatment the number of patients with hypothyroidism increased, as in the end of the therapy the cases were 9, among them 6 women and 3 men. Again, it has been remarked the prevalence of the females. The majority of the cases had medium and simple hypothyroidism. There was a case, a female aged 48 years, a patient that presented antithyroid antibodies at the beggining of the treatment, also a simple hypothyroidism, whose evolution under the treatment with Peginterferon α2A was to mixedem coma, the patient neccessitating specialty treatment in an intensive therapy unit. Conclusions: The thyroidian events manifested on the whole had an incidence of 9.5% in our study (thyroditis, hyp – and hyperthyroidism), situating our study at least in percentage in the limits of the studies developed at an European level.

Keywords: Interferon α2A; thyroid gland; viral chronic hepatitis HVC

Cuvinte cheie: Interferon α2A; glândula tiroidă; hepatită cronică virală HVC

De asemenea, s-a observat o predominanță a cazurilor la sexul feminin (14 din 18). Ultima determinare a anticorpilor antitiroidei s-a efectuat la sfârșitul terapiei. Monitorizarea post tratament este în curs de desfășurare, neputându-se aprecia încă extensiva în timp a tiroidei cronice autoimune. Totodată, evaluarea TSH, T3 și T4 la inițierea tratamentului a evidențiat existența unui număr de 2 pacienți cu hipotiroidism și absența hipertiroïdismului. Ambii pacienți cu hipotiroidism au fost de sex feminin. În cursul tratamentului, numărul de pacienți cu hipotiroidism a crescut, pentru că la finalul terapiei s-a contabilizat un număr de 9 cazuri, din care 6 femei și 3 bărbați. Din nou s-a remarcat prevalența sexului feminin. Majoritatea cazurilor au fost de hipotiroidism ușor și mediu. A existat un caz de sex feminin, în vârstă de 48 ani, pacientă cu anticorpi antitiroidei prezenți la debutul tratamentului, de asemenea cu hipotiroidism ușor, a cărei evoluție sub tratamentul cu Peginterferon α2A a fost înspre comă mixematoasă, pacientă necesitând tratament de specialitate în unitatea de terapie intensivă. Concluzii: Evenimentele tiroidiene s-au manifestat per ansamblu cu o incidență de 9,5% în cazul studiului nostru (tiroïde, hipo – și hipertiroïdism), studiindu-ne astfel procentual între limitele studiilor derulate la nivel european.

INTRODUCTION

In our study we have pursued the evolution of 115 patients with chronic active hepatitis with HVC, in treatment with Peginterferon α2A, 180 µg / week and Ribavirină in a dose adapted to the weight. The study was performed in the context of the specific treatment.

1. Appreciating the incidence of the thyroidal pathology in patients with chronic active hepatitis with HVC in treatment with Peginterferon α2A 180 µg / week and Ribavirină in dose adapted to the weight.

2. The clinical epidemiological analysis of the studied population (the distribution of the patients on age groups, sex groups, study of the risk factors and way of life).

3. The evaluation of the correlations between the thyroidal pathology appeared during therapy and paraclinical parameters (the level of hepatitis cytolysis, of viremia).

4. The evaluation of the severity of the thyroidal pathology appeared under the influence of the therapy with Peginterferon α2A 180 µg and the impact on the last one.

5. The appreciation of the incidence of the dysthyroid pathology in patients with active chronic hepatitis with HVC before the beginning of the therapy with Peginterferon α2A 180 µg.

6. Determining the interval of apparition of the thyroidal dysfunctions from the beginning of the therapy with Peginterferon α2A 180 µg.

THE AIM OF THE STUDY

The pursuance of the evolution of 115 patients with chronic active hepatitis with HVC, in treatment with Peginterferon α2A, 180 µg / week and Ribavirină in dose adapted to the weight, with the aim of establishing the frequency of apparition of the thyroid dysfunctions in the context of the specific treatment. Concomitantly, it has been pursued the establishing of correlations between age, sex, degree of activity of the disease, the possible moment of the infection and the apparition of the thyroid modifications clinical and paraclinical.

MATERIAL AND METHOD

During the period 1 January 2005 - 1 January 2010 we have pursued the evolution of 115 patients with chronic active hepatitis with HVC, in treatment with Peginterferon α2A, 180 µg / week and Ribavirină in a dose adapted to weight, with the aim of establishing the frequency of apparition of the thyroid dysfunctions in the context of the specific treatment. At once, it has been pursued the establishing of correlations between age, sex, the degree of activity of the disease, the possible infecting moment and the apparition of the thyroid clinical and paraclinical modifications.

The patients have been pursued at the beginning of the treatment, when the values of the transaminases were determined, hemoleucogram, coagulogram and the level of the TSH, T3, and T4. Also it has been documented the presence or absence of the antithyroid antibodies. The test of evidentiating in serum of the anti HVC antibodies was ELISA, the IInd generation or III-a (Murex anti-HVC – III version, Menolisa(R) anti HVC PLUS, ORTHO (R) HVC 3.0 ELISA).

The biopsy hepatic punction determined the degree of fibrosis. It has been noted the beginning of the symptomatology, the moment of diagnosis, the way of finding out of the viral infection, the epidemiological investigation with the establishing of the possible moment of infection.

For every patient it has been effectuated a short case presentation for evidentiating the diagnosis particularities, evolution and treatment. Every three months the level of the transaminases, antithyroid antibodies, TSH, T3, T4 were determined.

The viremy was effectuated at 3 months from the beginning of the treatment. The diagnosis of thyroiditis was established on clinical data, laboratory investigations, respectively of the presence of the antibodies thyroid antiperoxidasa.

The diagnosis of hypothyroidism respectively of hyperthyroidism, was established through clinical data correlations with the hormonal dosations (T3, T4, TSH).

The total number of the patients included in the study was 115, among witch 62 women (53,9 %) 53 men (46,1 %).

The age limits were comprised between 18 and 65 years, existing 3 age categories, respectively 18 – 35 years, 36 – 51 years and 51 – 65 years.

Most of the patients (43) were situated in the age group 51 - 65 years, the equivalent was of 37,4 %. Those age limits were imposed by the actual treatment criteria of the national commission of treatment of the chronic active hepatitis.

In what regards the TGP value, most of the patients, respectively 59,1 % presented normal values, 33,9 % values between 2-5 x the normal value and 7% value of 5 x the normal value.

The viremy was of < 100.000 copies / ml at 64 patients and of > 100.000 copies / ml at 51 from the patients, respectively 55,7 % and 44,3 %.

61 from the patients, the equivalent was 53 % presented normal values of the triglycerides while in 54 patients, the equivalent was 47 % the registered values were over the normal values.

The majority of patients (49,6 %) presented first degree fibrosis, followed by 36,5 % with second degree fibrosis, 9,6 % presented third degree while in 5 patients, the equivalent of a 4,3 % fibrosis was absent.

The antithyroid antibodies were present at the beginning of the treatment at 11 patients, the equivalent was 9,6 %, while the majority of patients, respectively in a number of 104 patients, the equivalent was 90,4 %, they were absent.
At the determination of the antithyroid antibodies effectuated at 3 months, those were present in a number of 18 patients, the equivalent was 15.7 % and absent in a number of 97 patients, the equivalent was 84.3 %. After the treatment, the antithyroid antibodies were absent at the majority of patients, respectively 94, the equivalent was 81.7 % and present in only 21 patients, the equivalent was 18.3 %.

At the beginning of the treatment, only 2 patients, the equivalent of 1.7 % manifested hypothyroidism, the rest of 113 patients, respectively 98.3 % hadn't a hypofunction of the thyroid. After treatment, the number of patients with hypothyroidism increased from 2 to 9, meaning a percentage growth of 6.1 %; the percentage of patients without hypothyroidism decreased implicitly from 98.3 % to 92.2 %.

At the beginning of the treatment no patient presented a thyroid hyper function. After the treatment, hyperthyroidism was present in 2 among the 115 patients, the equivalent was 1.7 %.

### RESULTS

1. Among the 115 cases of chronic active hepatitis with HVC included in the study, 21 cases presented antithyroid antibodies (ATPO) positive at the end of the therapy, the equivalent of 18.3 %.
2. The majority of the cases forementioned presented ATPO positive in the first 3 months of therapy (18 cases from 21 cases positivated at the end of the therapy).
3. From the 115 cases of chronic active hepatitis with HVC, 9 cases presented hypothyroidism, the equivalent of 7.7 % and 2 cases of hyperthyroidism at the end of the therapy, the equivalent of 1.7 %.
4. There weren't noted any statistical differences in what regards the association between the thyroidian dysfunction and the fibrosis degree.
5. The dose reductions of the Peginterferon α2A that were used during the therapy, in the context of the iatrogenic hematological modifications, at the patients with positive antithyroid antibodies, didn't determine their dissappearance.
6. The thyroid dysfunctions are more frequent in the context of the therapy with Peginterferon α2A, 180 µg in weekly administration versus Interferon α2A, 9 MUI x 3 / week.
7. The incidence of the chronic autoimmune thyroiditis is bigger in the patients with active chronic hepatitis with HVC in contrast with the healthy population, raising the problem of implication of the hepatitis virus C in the etiology of the autoimmune thyroiditis.
8. The females seem to be more affected by the chronic autoimmune thyroiditis, with predominance in the age group of 36-50 years.
9. As a conclusion to the results obtained from this study, the recomandation is of monitoring ATPO, TSH, T3, T4 in the patients with chronic active hepatitis with HVC at the beggining of the therapy, periodically, preferably at 3 months.
10. Concomitantly it is useful the documentation of the anti HCV antibodies at the patients diagnosed with chronic autoimmune thyroiditis.
11. It is neccessary the monitorization of the patients after treatment, minimum 6 months, for the prevention of the aggravation of the thyroidian dysfunction.
12. RVS is not correlated with the existence of the ATPO antibodies at the begginning of the therapy at the patients with chronic active hepatitis with HVC.

### CONCLUSIONS
The thyroidian events manifested on the whole had an incidence of 9.5% in our study (tiroiditis, hypo – and hyperthyroidism), situating our study at least in percentage in the limits of the studies developed at an European level.

### BIBLIOGRAPHY