# DIFFERENCES IN PRESCRIBING ANTIBIOTICS BETWEEN SURGICAL AND NON-SURGICAL SPECIALISTS

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***Abstract:*** *Introduction: One of the biggest medical problems for clinicians is to establish antibiotic treatment. Irrational prescribing and abuse is an explanation of failures in the treatment of infectious diseases. This fact has led to the emergence of antibiotic resistance, which can seriously threaten public health. The purpose of our study was to identify antibiotic prescribing practices of doctors of various specializations, as well as to identify knowledge and attitudes related to microbial resistance. Materials and Methods: The study was based on a questionnaire which was distributed to doctors of different medical and surgical specialties in state hospitals. Results: The questionnaire was filled out by 110 physicians (response rate 84.6%). 73.6% of physicians found that too many prescriptions of antibiotics are issued needlessly. Most antibiotics used by doctors were cephalosporins, followed by aminopenicillins. Some of the factors involved in bacterial resistance include self-medication, prescribing inappropriate antibiotics, and increased and prolonged hospitalization. The problem of antibiotic resistance is a major one (89.1%). Conclusions: This study identified medical concepts related to antibiotics and bacterial resistance. Limitation of bacterial resistance to antibiotics is necessary and can be accomplished by reducing the prescription of antibiotics, and by informing doctors (treatment protocols, conferences) to establish an effective antibiotic treatment.*

## INTRODUCTION

Antibiotics have been used to treat infectious diseases since 1940, which has resulted in considerable lifesaving. However, their indiscriminate use (which is estimated at 50% of total antibiotic use) increases the cost of health care, causes a lot of side effects and drug interactions, and promotes bacterial resistance, making previously valuable drugs ineffective.(1)

Both World Health Organization (WHO) as well as other bodies, such as the European Centre for Disease Prevention and Control (ECDC), or the Centre for Disease Prevention and Control (CDC) have developed programmes and strategies related to the rational use of antibiotics and to microbial resistance. WHO started an international campaign of microbial resistance in May 2015, with the aim to raise awareness and understanding of antimicrobial resistance, reduction of infections, i.e. optimizing the use of antibiotics.(2)

The situation of microbial resistance in Europe displays large variation depending on bacteria, antibiotics, and geographic region. In general, lower rates of resistance are reported by northern countries, and higher percentages by southern and eastern Europe.

Antibiotic resistance is a serious threat to public health in Europe leading to increased healthcare costs, prolonged hospitalization, treatment failures, and deaths. In cases of invasive bacterial infections, prompt treatment with effective antibiotics is particularly important and is one of the single most effective interventions to reduce the risk of death.(3)

The first report in Romania issued in 2012 investigated three components of a public health field: consumption of antibiotics, microbial resistance, and nosocomial infections. The most visible manifestation of microbial resistance to antibiotics is the care of patients with nosocomial infections which involves frequent use of backup antibiotics. Romania, due to high consumption of antibiotics in 2012, was among the top three European Union countries along with Greece and Cyprus. Consumption of antibiotics in our country would be in the top 5 for each type of consumption except for the consumption of macrolides which places us at the middle of the rank. Thus, consumption of penicillin would take 1st place, consumption of quinolones 3rd, and cephalosporins 5th which translates into an excessive and high risk prescribing of a range of selection of antibiotic resistance.(4)

Due to the increasing resistance of the body to antibiotic treatments, the multiple side effects they cause and the fact that nationally, there are few studies that address this issue, the problem of antibiotics and microbial resistance is very topical. Thus, the importance of this study is obvious, because in small quantities and lengthy intake, antibiotics can have negative effects on both the environment and on humans.

## PURPOSE

The aim of this study was to identify the doctors' knowledge and attitudes regarding antimicrobial resistance, in case they had encountered such situations, to assess how often they prescribed antibiotics, and current practices in prescribing antibiotics.

## MATERIALS AND METHODS

This cross-sectional study was conducted in state hospitals in Tîrgu-Mureș between January – March 2016. The study targeted both surgical and non-surgical specialists. Group size was 130 doctors.

*Inclusion criteria:*

- physicians working in state hospitals;
- physicians who have agreed to participate;
- physicians who prescribe antibiotics frequently;

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*Exclusion criteria:*

- physicians who did not agree to participate;
- physicians who never or infrequently prescribe antibiotics (e.g. radiologists, diabetologists, laboratory physicians, etc.).

The study included physicians with specialties such as internal medicine, pediatrics, infectious diseases, gastroenterology. Surgical specialty physicians included: general surgery, urology, otolaryngology, gynecology.

*Data collection*

Data were collected using a questionnaire which contained 33 questions. The reliability of the questionnaire was tested in a pilot study on 10 physicians. Subsequently, minor modifications were made in drafting the final questions. The questionnaire consisted of three parts: social and demographic, medical use of antibiotics in the practice of the surveyed physicians, perceptions about bacterial resistance to antibiotics. The demographic part collected information related to gender, level (resident, specialist, senior) and experience in the profession. The second part included questions related to antibiotics: the ones used most frequently, the number of antibiotics prescribed the previous week, factors that influence prescribing antibiotics. The third part investigated the perception of the physicians regarding microbial resistance, namely: what factors they think are involved, whether they encountered antibiotic-resistant infections, and how they think this problem might be stopped or limited. The questionnaire included both single answer questions, as well as multiple choice questions, and tables where doctors were asked to give a score from 1 to 3 (least important, important, very important) regarding factors contributing to resistance. Questionnaires were distributed during the report call in each department. After receiving explanatory information, the physicians were asked to provide oral consent for participation.

*Statistical analysis*

Microsoft Office Excel software was used to centralize the data. Data were analysed using SPSS (Statistical Package for Social Sciences). Chi square test was used to identify differences in knowledge, attitudes, and practices among surgical and non-surgical specialists. P-value $\leq 0.05$ was considered statistically significant.

## RESULTS

Of the 130 questionnaires distributed to physicians, 110 (84.6% response rate) were eligible for statistical processing. Of these, 60 (54.5%) were surgical specialists and the remaining 50 (45.5%) were non-surgical specialists. The majority of the surveyed physicians (60.0%) had a 6-to-10-year experience in the field, 15.5% 1-5 year, 10.0% between 10-20 years, and 14.5% had an experience of over 20 years. The attitude of doctors on prescribing or using antibiotics, as well as antibiotic resistant bacteria are shown in table no. 1. The most often prescribed classes of antibiotics were: cephalosporins with a percentage of 66.6%/ 80.0 % aminopenicillins 30.0%/ 22.0%, fluoroquinolones 18.0%/ 20.0%, natural penicillins 11.6%/ 22.0%. Carbapenems and carboxipenicillins were less frequently used. The use of additional drugs that reduce the risk of side effects was often encountered 78.3%/ 62.0 (surgical/ non-surgical specialists). About 22.7% of the surveyed physicians always use these drugs, and 6.4% of them never use them because they consider them unnecessary.

**Table no 1. Differences between surgical and non-surgical specialist regarding the prescription of antibiotics, their use, and the perceptions of the specialists related to bacterial resistance to antibiotics**

| Questions | Surgical 60 (54.5%) | Non-surgical 50 (45.5%) | P value |
|---|---|---|---|
| Male, nr (%) | 35 (58.3) | 10 (20.0) | **0.0001** |
| *Do you think that too many antibiotics are prescribed without need?* no (%) | | | |
| Yes, | 43 (71.7) | 38 (78.0) | 0.44 |
| *What do you think are the most common errors occurring in the prescription of antibiotics?* no (%) | | | |
| Treatment period is not mentioned | 10 (16.6) | 13 (26.0) | 0.61 |
| Insufficient treatment period is mentioned | 22 (36.6) | 21 (42.0) | |
| Antibiotic dosing is not respected | 25 (41.6) | 23 (46.0) | |
| Prescribing an amount of drug that cannot be released by the pharmacy | 4 (6.6) | 3 (6.0) | |
| *What do you think are the reasons why patients turn to self-medication with antibiotics?* no (%) | | | |
| Lack of time to see a doctor | 16 (26.6) | 22 (44.0) | **0.004** |
| Lack of trust in doctors | 3 (5.0) | 10 (20.0) | |
| Lack of money for medical services | 13 (21.6) | 5 (10.0) | |
| Underestimation of the condition | 20 (33.3) | 14 (28.0) | |
| Overestimation of knowledge in medication | 40 (66.6) | 30 (60.0) | |
| *What factors do you think influence you in prescribing antibiotics?* no (%) | | | |
| Professional experience | 21 (35.0) | 13 (24.0) | 0.42 |
| Clinical guidelines | 32 (53.3) | 31 (60.0) | |
| Treatment protocols | 36 (60.0) | 32 (53.3) | |
| Recommendation of the microbiologist | 23 (31.6) | 18 (36.0) | |
| Advice from colleagues | 3 (5.0) | 4 (8.0) | |
| Cost of antibiotics | 8 (13.3) | 1 (2.0) | |
| *What do you think are the risk factors for infections with antibiotic-resistant bacteria?* no (%) | | | |
| Prolonged hospitalization | 29 (48.3) | 28 (56.0) | 0.40 |
| The increased resistance in the community and the hospital | 26 (43.3) | 20 (40.0) | |
| Self-medication | 44 (73.3) | 44 (88.0) | |
| Outpatient intravenous therapy | 3 (3.3) | 1 (2.0) | |
| *How do you think antibiotic resistance can be limited?* no (%) | | | |
| Reducing the use of antibiotics | 44 (70.0) | 41 (80.0) | 0.23 |
| Restricting antibiotics | 25 (41.6) | 27 (54.0) | |
| Hygienic precautions to prevent transmission of resistant strains between persons | 33 (55.0) | 30 (60.0) | |
| Reducing the use of antibiotics in livestock | 10 (16.6) | 8 (16.0) | |
| Manufacturing new vaccines | 8 (13.3) | 6 (12.0) | |
| *In your opinion, who should provide the most information about the resistance of bacteria to antibiotics?* no (%) | | | |
| Ministry of Health | 20 (33.3) | 20 (40.0) | 0.38 |
| General practitioner | 40 (65.0) | 40 (80.0) | |
| Specialist | 29 (25.0) | 34 (68.0) | |
| Pharmacist | 8 (13.3) | 15 (30.0) | |

The issue of antibiotic resistance is considered a major problem both by doctors in surgical specialties (52.0%) and by other physicians (48.0%). In about 59.1% respondents believe that this issue is a national problem, while 43.6% consider it a matter of practice. The difference between the specialties is not statistically significant (p = 0.22). vThe main sources of information about antibiotic resistance are books, journals, and specialized brochures at a rate of 70.0% for surgical specialties and 62.0% for the other physicians. Conferences (45.0% and 38.0%), colleagues - doctors and healthcare professionals (36.6% and 44.0%) are also sources of information. The Internet is not a primary source of information (30.0% and 26.0%).The interviewed doctors were also asked to give a score from 1 to 3 (least important, important, very important) to factors involved in bacterial resistance to antibiotics (table no. 2).

**Table no. 2. Scoring of the factors involved in microbial resistance**

| Variables | Score | Surgical 60 (54.5%) | Non-surgical | P value |
|---|---|---|---|---|
| Increase in prescribing antibiotics | least important | 6 (3.6) | 3 (1.5) | 0.33 |
| | important | 24 (14.4) | 10 (5.0) | |
| | very important | 30 (18.0) | 37 (18.5) | |
| Prescribing broad-spectrum antibiotics | least important | 18 (10.8) | 5 (2.5) | **0.005** |
| | important | 28 (16.8) | 21 (10.5) | |
| | very important | 14 (8.4) | 24 (12.0) | |
| Needless antibiotic prescriptions | least important | 4 (2.4) | 0 (0.0) | 0.14 |
| | important | 11 (6.6) | 7 (3.5) | |
| | very important | 45 (27.0) | 43 (21.5) | |
| Empirical therapy | least important | 16 (9.6) | 15 (7.5) | 0.93 |
| | important | 23 (13.8) | 19 (9.5) | |
| | very important | 21 (12.6) | 16 (8.0) | |
| Mutations and evolution of bacteria | least important | 4 (2.4) | 5 (2.5) | 0.87 |
| | important | 23 (13.8) | 19 (9.5) | |
| | very important | 33 (19.8) | 26 (13.0) | |
| Misdiagnosis | least important | 14 (8.4) | 7 (3.5) | 0.18 |
| | important | 29 (17.4) | 21 (10.5) | |
| | very important | 17 (10.2) | 22 (11.0) | |
| Self-medication | least important | 3 (1.8) | 0 (0.0) | 0.33 |
| | important | 13 (7.8) | 20 (10.0) | |
| | very important | 44 (26.4) | 30 (15.0) | |
| The influence of pharmaceutical companies | least important | 22 (13.2) | 21 (10.5) | 0.86 |
| | important | 27 (16.2) | 21 (10.5) | |
| | very important | 11 (6.6) | 8 (4.0) | |
| Lack of restricting antibiotic use | least important | 15 (9.0) | 15 (7.5) | 0.82 |
| | important | 29 (17.4) | 24 (12.0) | |
| | very important | 16 (9.6) | 11 (5.5) | |
| Poor hygiene | least important | 25 (15.0) | 18 (9.0) | 0.21 |
| | important | 22 (13.2) | 26 (13.0) | |
| | very important | 13 (7.8) | 6 (3.0) | |
| The use of antibiotics in livestock | least important | 27 (16.2) | 24 (12.0) | 0.70 |
| | important | 28 (16.8) | 20 (10.0) | |
| | very important | 5 (3.0) | 6 (3) | |

## DISCUSSIONS

Resistance to antibiotics has become a global concern and this underlines the need for physicians to be aware of it and of the factors that lead to its development. Any treatment with antibiotics is a compromise between the beneficial action and its potentially harmful action, the only solution is the rational use of antibiotics in order to benefit from their effect. Rational use of antibiotics depends on understanding their mechanism of action, spectrum of activity, pharmacokinetics, pharmacodynamics, toxicity and interactions; bacterial resistance and the underlying mechanisms; strategies used by physicians to limit resistance.

Although the phenomenon of antibiotic resistance can be accelerated and amplified by several factors, the most important cause is misuse of antimicrobials.(5) Both the amount of antibiotics and the way they are used contribute to the development of resistance. Other current mistakes in antibiotic use are: the choice of an ineffective antibiotic, inadequate or excessive doses, inefficient periods, and prescribing antibiotics for viral infections.(6) The European Centre for Disease Prevention and Control issued a warning in 2015 that bacteria in humans, in foods and animal products continue to show resistance to the commonly used antimicrobials.(7)

Antibiotics are used in animals for therapy, prophylaxis and growth promotion. For example, Salmonella, Campylobacter, and some strains of Escherichia coli are zoonotic bacteria whose resistance is clearly linked to the use of antibiotics in animal feed. Resistance to ciprofloxacin – an extremely important antibiotic to treat infections in people – is very high in the case of Campylobacter bacteria, which consequently reduces the options for effective treatment of serious food poisoning.(8,9)

Our study identified a rate of 26.4% of the doctors surveyed who used aminopenicillins compared to 16.4% of those who used natural penicillins. This is beneficial because penicillins coupled with β-lactamase inhibitors have a broad spectrum of action but without any addition to aminopenicillins in streptococcal infections, pneumonia, or enterococcal infections that are among the main community infections.

Many studies have been performed to ascertain the effectiveness of additional drugs that reduce the risk of side effects.(10) Such studies indicate that their use in suitable amounts confer a health benefit to the host body. Of the 110 respondents, 70.9% sometimes prescribe these drugs and 22.7% always use them.

The main factors that both surgical and non-surgical specialists take into account when prescribing antibiotics are the treatment protocols and clinical guidelines. Apart from conferences, these are among the main sources of information regarding the prescription of antibiotics and bacterial resistance to antibiotics. Thus, conferences and guides which contain precise indications on criteria relating to the choice of antibiotics, the duration and the optimal dose, route of administration, as well as combinations of antibiotics may help to improve therapy in infections resistant to antibiotics as well as their limited use.

In the view of the surveyed doctors, the microbiologist plays an important role in the rational use of antibiotics. Thus, the presence of a greater number of microbiologists and the development of this area could provide important information about identifying potential health risks to the community or monitoring the development of strains which are potentially virulent or resistant to antibiotics.

Although 89.1% of our respondents consider that bacteria resistance to antibiotics is a major problem, only 59.0% consider it a national issue. We noted very little difference between the two specializations as regards the factors involved

in microbial resistance. Almost all physicians agree that widespread and inadequate use of antibiotics is the causes of this problem. The use of antibiotics in livestock is not considered an important factor by respondents.

In scoring from 1 to 3 (least important, important, very important) regarding the importance of good hygiene practices as a factor in the emergence of microbial resistance, 13 surgeons stated that it was very important (score 3) as opposed to 6 non-surgical specialists. However, both surgical and non-surgical specialists think that bacterial antibiotic resistance could be achieved by increasing hygiene measures to prevent transmission of resistant strains between persons.

According to the surveyed doctors, the influence of pharmaceutical companies is not a factor involved in the development of microbial resistance. This is consistent with a study that includes the opinion of some residents of internal medicine linked to gifts offered by pharmaceutical companies. The conclusion of this study was that doctors are delighted with these gifts, but their decision of prescribing antibiotics is not influenced.(11)

Of the 60 surgeons surveyed, 35% believe that the combination of *Klebsiella pneumoniae* - carbapenems is the most frequently encountered, and 26.6% consider the combination between *Pseudomonas aeruginosa* - carbapenems as being frequent. In comparison, the non-surgical specialization respondents consider that the most common combinations are *Klebsiella pneumoniae* - fluoroquinolones (34%), and *Pseudomonas aeruginosa* - carbapenems (32%). According to the *Annual report of the European Antimicrobial Resistance Surveillance*, *Klebsiella pneumonia* has a 50% resistance to fluoroquinolones, 25%-50% to carbapenems in Romania.(3) According to the same report, *Pseudomonas aeruginosa* has a resistance of over 50% to macrolides, and 25%-50% resistance of *Streptococcus pneumoniae* to macrolides. Thus, the non-surgical specialists interviewed have more information about these associations. However, the differences were not statistically significant ($p = 0.14$).

Both groups of respondents have the same views about the ways of limiting microbial resistance. They believe that reducing the consumption of antibiotics and their restriction may curb this problem. On the other hand, the production of new vaccines is not an effective method.

Even if, usually, a well-chosen monotherapy is sufficient in only certain cases, such as severe infections, mixed bacterial infections or in immunocompromised persons the combination of antibiotics is required, 65% of the respondents combine two or more antibiotics, of which 52.4% are surgeons, and 47.6% are non-surgical specialists. The differences are statistically insignificant ($p = 0.83$). In such cases, it is necessary to know how to take advantage of the beneficial effect and avoid associations that produce antagonism.

Our study shows that the Ministry of Health should be one of the sources of information on bacterial resistance to antibiotics from the perspective of the physicians surveyed.

Following the worldwide increase in antibiotic consumption and resistance of bacteria to antibiotics, a number of programs and strategies have been developed. These strategies include further education, guidelines and policies on the use of antibiotics in hospitals, promoting cautious use of antibiotics in several areas, restrictive measures and consultations from doctors, microbiologists and pharmacists, aimed at better practice of prescribing antibiotics and reducing the resistance to them.

The World Health Organization considered antibiotic resistance a "global threat" for the first time in 1995. In 2010, the WHO report on disease transmissibility was entitled "Overcoming Antimicrobial Resistance", and in 2011 WHO announced the year of the battle against antibiotic resistance under the slogan "If we do not take action today - we will not have the means to treat patients tomorrow".(12,13,14)

The European Centre for Disease Prevention and Control along with health authorities in the European Union launched the celebration of the European day of awareness about the use of antibiotics in 2008. This day is celebrated annually on 18th November.(15) Romania joined the programme in 2010.

There are many types of microbial agents under development in response to the emergence of microbial resistance, but the need for new antibiotics still does not cover the increased prevalence of infections caused by antibiotic resistant microorganisms.(16)

The Infectious Diseases Society of America (IDSA) reports that since 2010 only one new antibiotic has been approved, while the Report of the European Regional regarding the action plan on the issue of antibiotic resistance (EUR/RC61/14) states that only two classes of new antibiotics (oxazolidines and cyclic lipopeptides) have appeared on the market in the last thirty years, both used against positive microorganisms. No new medication against negative microorganisms such as E. coli and Klebsiella pneumoniae has entered the market.(17,18)

Rapid development of resistance of microorganisms to antibiotics is one of the main factors for which the industry has abandoned the research and development of new antibiotics. In addition, we have to include the fact that investments cannot be recouped quickly, due to the increased regulations and strict price controls imposed by many governments.(19)

## CONCLUSIONS

Our data show that too many antibiotics are prescribed without a clinical reason. Overestimation of medical knowledge is one of the reasons why physicians believe that patients resort to self-medication with antibiotics. Also, increased and inadequate prescribing of antibiotics is among the main factors in microbial resistance. Limiting antibiotic resistance can be achieved by reducing the use of antibiotics and restricting them, as well as increasing hygiene measures. Doctors give information to patients related to microbial resistance, and believe that the patient plays an important role in this matter.

We believe that this study may contribute to a better knowledge and understanding of the risks and possible developments in the field of microbial resistance in Romania. The information obtained could be used in developing programmes of good practice of antibiotic therapy to reduce risks to the patients of the Romanian medical system.

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