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ANTIBIOTIC RESISTANCE IN ROMANIA -AN ECONOMIC AND MEDICAL CHALLENGE -

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Abstract

The use of antibiotics, without regard to the importance of first obtaining a prescription, is one of the current challenges, both in health and economic terms. At the global level, resistance to different classes of antibiotics is developing at an alarming rate, and the effects over time are worrying. Romania is one of the European countries facing this problem at the macro level, with the latest statistical data exposing this alarming situation. The lack of basic knowledge of the population regarding the purchase of medication and the habit of administering treatment without the clinician's advice make this situation difficult to improve.

This article discusses the importance of adequate education in antibiotic use, proposing concrete measures to improve the current situation. This study is based on results obtained by the author in previous research on antibiotic resistance in children diagnosed with unitary tract infection in the Brașov area. Thus, the need to apply the proposed solutions is based on the reality found in hospitals.

Keywords: *urinary tract infections, UTI, antibiotic use, antibiotics, resistance to antibiotics.*

JEL: *I12.*

Introduction

According to the U.S. Centre for Disease Control and Prevention, antibiotic (AB) resistance causes approximately 2 million infections in the USA and 23,000 deaths resulting in a direct cost of \$ 20 billion, and an extra cost of \$ 35 billion in productivity decline. Figures for Europe show that 25,000 deaths per year have this cause, with a total cost of 1.5 billion Euros, including treatment and costs associated with the lack of productivity at work. In the CDDEP report for 2015, Romania is not ranked as a country investing in campaigns for optimal use of antibiotics. However, statistics place it on the penultimate spot on the consumption of this type of medication (CDDEP, 2015). The main two European countries that allocate considerable budget expenses for these

campaigns are France (\$ 22,500,000 in 2002-2004) and Spain (€ 11,500,000 in 2006-2007).

In view of these considerations, we considered necessary to carry out an analysis on the measures that can be taken at a national level in order to improve the situation in regards to the consumption of antibiotics. Based on the literature and the conclusions of the author's study at the Children's Hospital in Braşov, a series of guidelines could be drawn up by local authorities in each county to educate and raise awareness of the importance of observing medication guidelines.

Stage of Knowledge

Infection is defined by the Merriam Webster online medical dictionary (2015) as the sum of manifestations produced by the settling of an infectious agent in a susceptible host organism. The hospital environment is well suited for infectious agents, and antibiotic resistant strains have the evolutionary advantage. According to WHO, out of all infections, those acquired during hospitalization which were not present before entering such an environment are called nosocomial infections (Ducel et al., 2002).

Some of the most common infections in pediatric practice are urinary tract infections (UTI), and they are caused almost entirely by bacteria coming from the digestive tract - there are also adenoviruses that can cause UTI, although this type of infection is rarely encountered in practice (Kliegman, 2011). UTIs acquired in the community are caused by *Escherichia coli* in 70% to 90% of cases - the uropathogen strains are capable of causing UTI, also. Cases of recurrent urinary tract infections in several family members indicate the presence of genetically transmitted defects by affecting the proteins that confer urinary epithelia innate resistance to bacterial colonization. According to the European Guidelines for Pediatric Urology, the diagnosis of urinary tract infections is based on the patient's history, clinical signs and symptoms, examination, urine samples followed by urine analysis and cultures. Further blood tests and additional investigations such as ultrasonography (Jadresic, 2014) may also be necessary.

In parallel with the antibiotic treatment, bacterial cells develop mechanisms to combat AB over time. To sum up microbial resistance, it can be defined as the insensitivity of a pathogenic microorganism to a chemotherapeutic agent (medication/drug). Resistance may be natural - genetically determined and characteristic to species outside the spectrum of action of an antibiotic and it is the result of genetic changes and selection processes induced by antibiotic therapy (Tullus, 2011). Major factors that promote the emergence of resistance to antibiotic therapy are natural evolution, incorrect therapeutic practices and to a lesser extent the excessive use of antibiotics in the food industry - implemented in order to increase productivity.

Recent studies have shown the presence of numerous multi-resistant bacteria in slaughtered animals. A study in Germany showed the presence of *E. coli* ESBL (Extended Spectrum Beta Lactamase) multi-resistant strains in the intestines of 90% of the

slaughtered animals but in very low concentrations (0.07%), living alongside with antibiotic-sensitive strains (Fulga, 2006).

In the study Chaves BD et al., conducted in Costa Rica, samples from slaughtered animals in 3 slaughterhouses - 2 of which were destined for export to destinations including Europe, were analysed. The results showed increased prevalence of *E. coli* strains producing Shiga-like toxin in all slaughterhouses (a highly virulent strain), with a higher incidence in the warm season (Reich et al., 2016).

When dealing with infections, prophylaxis (or the prevention of infections) is indicated primarily for patients with previous episodes, but proper hygiene practices and measures taken to educate the caregivers are beneficial for the entire population. Prophylaxis in UTI can be accomplished with simple means such as cranberry juice or probiotics, with favourable results in patients predisposed to recurrent infections (ex. patients with diseases of the urinary tract due to obstruction). Although initially it was thought that cranberry juice works by lowering urinary pH, further studies have shown that protective action is due to inhibition of adhesion of bacteria to urinary epithelia (Chavez et al., 2015).

The antibiotic treatment in most cases of acute and symptomatic UTIs is effective before receiving antibiotic analysis results, meaning empirical treatment with antibiotics is a must, targeting the bacteria most likely to trigger the infection. The most common antibiotics used in empirical treatment of UTIs are third-generation Cephalosporins and the association of Ampicillin with Gentamicin (Kontiokari, 2005). In most cases, the short duration of AB treatment is enough to hinder the emergence of resistance.

Infection with *E. coli* is a particularly important issue, debated in recent years in different contexts. *E. coli* infections are characterized by severity, especially in young children, due to the immaturity of the urinary system. Possible sources of contamination with *E. coli* bacteria are multiple: drinking water, food, poor hygiene, cross-contamination when preparing food and often one cannot identify when the infection was contacted. It may be wrong food preparation practices (ex. the meat was not cooked at a temperature of at least 70 °C), the use of contaminated food products (ex. raw milk), the purchase of food from unauthorized places that do not comply with state regulations, improper storage, poor hygiene (ex. inadequate hand washing or not washing hands after changing diapers) or by ignoring good hygiene rules in the kitchen - ex. improper cleaning of cooking utensils after contact with raw food (Garbam & Florescu, 2015).

Children are particularly vulnerable to the spread of infections with bacteria of digestive origin, such as *E. coli* to other systems – as the urinary system - because they are in the process of acquiring basic knowledge of sanitation standards, with younger children being the most susceptible (Bouissou et al., 2008).

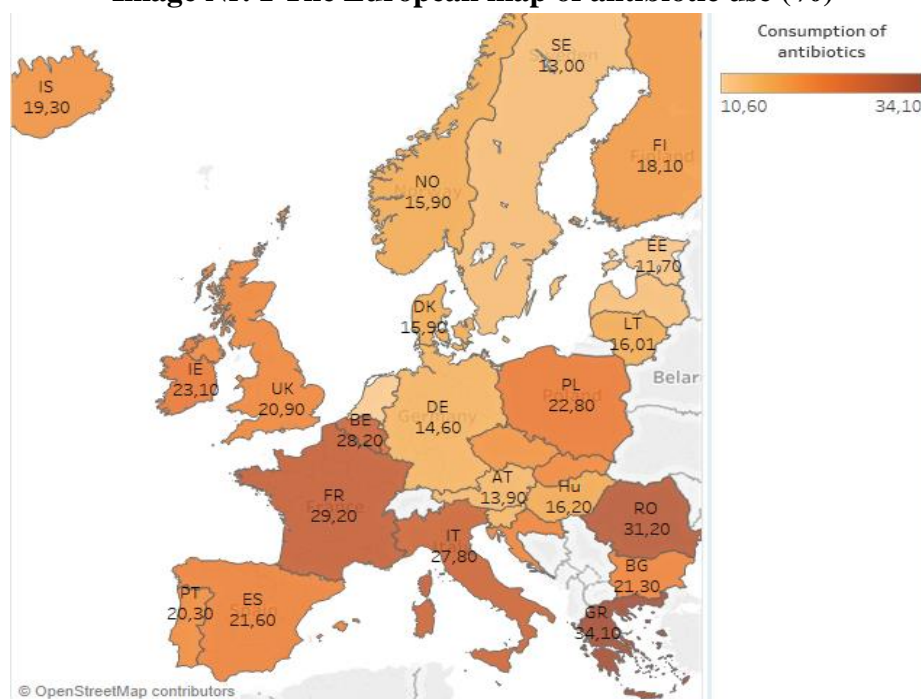
In light of these aspects, we considered it appropriate to conduct a study on this topic. This article aims to outline the rates of antibiotic resistance at the national level and it presents the main measures that can be taken in the near future in order to make progress on the issue.

Methodology

Romania is a country with some of the lowest resistance rates in the European Union. However, according to data provided by the European Center for Disease Prevention and Control, it ranks second at antibiotic consumption, with a percentage of 31.2%, being surpassed by Greece with 34.1% (Fig. 1), which places our country in a worrying situation and raises an alarm signal about health practices.

This ranking is known by the competent authorities, with programs being launched at the national level. The National Program for the Supervision and Control of Nosocomial Infections and The Monitoring of the Use of Antibiotics and Antibiotic Resistance was started in 2015 by the Ministry of Health. Also, a national information program called "No to the random use of antibiotics" was launched to inform patients about the dangers of developing resistance to these drugs. It includes information about who can prescribe AB treatment and under what conditions (www.ms.ro).

Image Nr. 1 The European map of antibiotic use (%)



Source: made by the author, based on <http://ecdc.europa.eu/en/eaad/antibiotics-news/Documents/antimicrobial-consumption-ESAC-Net-summary-2015.pdf> in the Public Tableau program.

However, these measures are not fully effective. The message does not appear everywhere it is needed and it is not accessible to vulnerable groups. Some parents do not have an average education level to understand the information they receive, and some of them live with a high degree of illiteracy, so they can not read the posters. Although promoted in the online environment on the Ministry of Health website, these campaigns are hard to access the target audiences who are mostly interested in using social platforms.

This analysis is based on the results obtained by the author in a retrospective quantitative study at the Braşov Hospital for Children. The topic includes the development of antibiotic resistance in children with UTI, based on data taken from patients during the time period 2010-2014. The items used in the research focused on the structure and description of the target group (sex, age, background, allergy to medication, number of days of hospitalization, diagnosis, comorbidities, personal history, antibiotics administered prior to admission) along with aspects related to the UTI diagnosis and antibiotic resistance (urinary analysis positive for E. coli and antibiotic resistance analysis, urinary sediment analysis, leukocyte count, inflammatory markers, urea, creatinine, uric acid, Astrup blood gas analysis). The information was obtained from the archives at the Braşov Hospital for Children and the hospital's Microbiology Laboratory, with a total of 349 subjects.

The results showed that the resistance to the AB currently used in the treatment of UTI in children was higher to that found in literature and recent studies. The average duration of admission was 6 days, with most patients receiving antibiotic treatment. Most patients received Ceftriaxone, a third generation Cephalosporin, and it was also the preferred antibiotic for continuing the treatment.

Comments

Taking into account the present context and the significant economic importance of antibiotic resistance for the Romanian population, we have conceived a number of steps aimed at improving the situation at the national level. Since UTI cases can be diminished through information and appropriate health education, the author's suggestions in this regard are as follows:

- To create an informative poster with the measures families must take in order to avoid contamination. The information must be accurate, clear, written with easy to navigate and large fonts and presented in a simplified form. The text should alternate with suggestive images, given that the degree of illiteracy in rural areas is high. The language must be simple, easy to understand for those who lack education, also. The color palette must take into account marketing principles and reader's concerns (ex. Color-blind)
- To provide counseling tailored to the mother's knowledge and intellectual level starting in the maternity ward. Thus, once she is home with the infant, she will know what to do in order to avoid infection.
- To implement informative campaigns in schools and kindergartens during health education class and distribute leaflets and informative posters in places such as toilets, classrooms, cafeterias.
- To start campaigns on media channels targeting economic agents. This way, they will raise awareness and be reminded of their responsibility to comply with the rules imposed by the authorities.
- To use social platforms and youtube channels as information vectors.

- Free counseling service offered by the authorities to economic agents, public catering establishments and healthcare establishments to ease compliance with the rules and avoid possible contamination. Representatives of these units will be able to address the authorities on their own initiative in order to receive the necessary information and support without being pressured by sanctions at this stage.

Regarding the adverse effects of the use of AB without prescription, it is also necessary to adequately educate adults to get them to abandon the practice of procuring ABs without written recommendation from the doctor. Increasing antibiotic resistance at an early age narrows the treatment regimen considerably, with severe consequences for patients.

Awareness of the negative effects of antibiotic resistance in the adult population is necessary because it models the behavior of children. This means the information must reach all groups, since living in the urban environment does not guarantee proper practice. One aspect that should be taken into account is that antibiotic treatment is easier for families living in towns, as there are more pharmacies.

Providing accurate and meaningful information to the targeted population may be done by many means, but the role of healthcare professionals is the most important. The counseling they can provide for avoiding infection and for minimizing antibiotic resistance is very important and necessary.

Conclusions

The use of antibiotics is widespread and often it is done without the doctor's recommendation. This practice leads to alarming rates of antibiotic resistance, and children are at risk more than adults due to the immaturity of their immune system. Romania ranks high at antibiotic resistance, and few measures are implemented for lowering the AB resistance rate. Braşov, one of Romania's main tourist attractions, is a good example for AB resistance.

Infections in children are an important topic because children are highly susceptible to infections and hard to treat. UTIs in children are of concern because often the main causes of infection are improper practices or hygiene. Based on data from a study conducted at Braşov's Hospital for Children by the author, the resistance rates are higher than those found in literature. However, the present practice methods when treating UTIs (broad-spectrum AB therapy) ensure proper infection eradication and excellent results. This, coupled with lower rates of infection would be sufficient measures to work towards lowering AB resistance in the near future, for the majority of cases.

In order to lower resistance, the most important practice is to prevent infection. We propose a series of easy to implement information campaigns meant to teach all parents the basic sanitation principles, starting before they even leave the maternity ward. This can be accomplished through flyers and posters and on social media networks. This

information needs to be accessible to the entire population, based on their level of education.

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