ANALYSIS OF CONSUMPTION OF MACROLIDES IN UKRAINE

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Resume: The structure of the pharmaceutical market of antibiotics of the macrolide group in Ukraine was analysed. The analysis of consumption on the basis of outpatient consumption of the drugs during 4 years in Ukraine was conducted using the ATC/DDD methodology, which is of particular interest to society in terms of health, social and economic consequences of irrational use and allows for long-term research at different levels of consumption of the drugs. In course of study, the indicator DDDs/1000 inhabitants/day, which gives an idea of the proportion of people receiving a certain type of treatment, was calculated. The analysis revealed that the most consumed drug in the course of study is azithromycin. At the end of the study period in 2013, the indicators of consumption increased by 27% compared with 2010. The second place in terms of consumption in DDDs/1000/day is occupied by preparations based on clarithromycin. Preparations on the basis of erythromycin were used in slightly different dynamics: consumption decreases with time, and by 2013 this led to a decrease of 20% compared with 2010. The same trend is observed in the consumption of spiramycin and midecamycin. These preparations are natural macrolide antibiotics. There is a positive trend in consumption of macrolides: increase in total consumption by 30% in 2013 compared to 2010. This trend is observed in other countries.

Резюме: Проанализирована структура фармацевтического рынка антибиотиков группы макролидов на основании амбулаторного потребления препаратов в течение четырех лет по всей территории Украины с помощью ATC/DDD-методологии, которая представляет особый интерес для общества с точки зрения медицинских, социальных и экономических последствий их нерационального применения и позволяет проводить длительные исследования на разных уровнях потребления препаратов. При проведении исследования был рассчитан показатель DDDs / 1000 жителей / день, который дает представление о доле населения, получающая определенный вид лечения. Проведенный анализ позволил установить, что наиболее употребительным препаратом за весь период исследования является азитромицин. На конец исследуемого периода в 2013 году показатели его потребления выросли на 27% по сравнению с 2010 годом. На втором месте по объемам потребления в DDDs /1000 жителей/ день находятся препараты на основе кларитромицина. Препараты на основе эритромицина использовались в несколько иной динамике: потребление со временем снижается, и к 2013 году это приводит к снижению на 20% по сравнению с 2010 годом. Такая же тенденция наблюдается и в потреблении спирамицина и мидекамицин. Указанные препараты относятся к природным макролидным антибиотикам. Отмечается положительная тенденция потребления макролидов: увеличение общего объема потребления на 30% в 2013 году по отношению к 2010. Эта тенденция наблюдается и в других странах.

Introduction. As a result of antibiotic-resistant infections, about 25 thousand people die in the European Union each year. Man. According to the WHO, the losses associated with multidrug-resistant bacterial infections in Europe account for more than $ 1.5 billion. The WHO indicates that this serious danger is not only forecast for the future, as it is already evident now in every region of the world and can affect anyone, regardless

of age and geography of residence. In the absence of rapid and concerted action of many parties concerned, our world is entering an era when antibiotics lose their effectiveness, and common infections and minor injuries joined by a secondary infection that could be treated for decades, can now again be incurable and lead to death.

One way out of this situation is tight control over the rational prescription of antimicrobials of all groups. This should be done systematically and in all countries.

The widespread use of antimicrobial therapy, often irrational, contributes to the incidence of adverse reactions, the growth of bacterial resistance, an increase in the frequency and duration of hospitalization. All this contribute to increase in the cost of treatment and require strategic control of antimicrobials prescription, i.e. the consumption of antimicrobials in different countries in DDDs/1000 inhabitants/day.

One group of drugs that each year are increasingly being used in the clinic is macrolide antibiotics. Now macrolides occupy a leading position in the treatment of infectious diseases due to a number of advantages: a high antibacterial activity of macrolides against intracellular pathogens such as chlamydia, mycoplasma and legionella; efficacy in infectious respiratory diseases; they show mucoregulatory action, moderate steroid-like effect as well as anti-inflammatory and immunoregulatory influence.

Objective of the study: to analyze the outpatient consumption of antibiotics of macrolide group during 2010-2013 in Ukraine using the ATC/DDD methodology.

Results of the study. At the moment, in the pharmaceutical market of Ukraine there are 7 INN of macrolides, on the basis of which 185 drugs under the TN taking into account the different dosage forms and manufacturers are presented. The share of drugs of domestic production is 25% (48 drugs).

Macrolide antibiotics have various pharmaceutical forms, that promotes ease of use: from the tablets with various doses to suspensions and syrups, which can be administered to infants. The most widely used drugs in the range of macrolide group are tablet and capsule forms, amounting to 78% (144 drugs). Drugs in the form of granules for oral suspension comprised 17% and 9 drugs (5%) in the form of suspensions for the preparation of injection solutions.

The analysis of the outpatient consumption of the study drugs during 4 years was conducted below using the ATC/DDD methodology with the calculation of the index of DDD/1000 inhabitants/day. The results are shown in Table 1.

Table 1. Indicators of consumption of macrolide antibiotics

INN	DDDs/1000 inhabitants/day			
	2010	**2011**	**2012**	**2013**
Erythromycin	0.055	0.042	0.043	0.037
Spiramycin	0.118	0.109	0.103	0.091
Midecamycin	0.086	0.053	0.057	0.051
Roxithromycin	0.033	0.027	0.022	0.018
Josamycin	0.014	0.017	0.019	0.022
Clarithromycin	0.307	0.319	0.322	0.343
Azithromycin	0.559	0.679	0.793	0.963

Total	1.172	1.246	1.360	1.525

The most widely used drug for the entire study period is azithromycin. Its indicators for four years are 0.559 in 2010, 0.679 in 2011, 0.793 in 2012 and 0.963 in DDDs /1000/day in 2013. At the end of the study period in 2013, indicators of its consumption increased by 27% compared with 2010. Azithromycin is a broad-spectrum bacteriostatic antibacterial. This is the first representative of a group of semisynthetic 15-membered macrolide antibiotics which has been used in clinical practice since 1991 and is one of the most commonly prescribed drugs in many countries of the world, including Ukraine, as evidenced by our study. Currently, azithromycin is approved by the FDA for use in adults and children older than 6 months for the treatment of infections caused by pathogens susceptible to it.

The second place in terms of consumption in DDDs/1000/day is occupied by preparations based on clarithromycin. These indicators have also positive dynamics: 0.307 in 2010; 0.319 in 2011; 0.322 in 2012 and 0.343 DDDs/1000/day in 2013. Clarithromycin shows in vitro and in vivo activity against many gram-positive and gram-negative bacteria, the most active in comparison with other macrolides in affecting Helicobacter pylory, it is more active in comparison with other antibacterial agents and directly affects the intracellular forms of the pathogen, so it is widely used in gastroenterology. Unlike other macrolides, clarithromycin is highly active against atypical mycobacteria (M. avium, M. leprae) and exceeds the antimicrobial activity of azithromycin in vitro by 4 times, which is of value in the treatment of opportunistic infections in immunodeficiency patients. These pharmacological properties of clarithromycin ensure its high consumption.

Preparations on the basis of erythromycin were used in slightly different dynamics: consumption decreases with time, and by 2013 this led to a decrease of 20% compared with 2010.

The same trend is observed in the consumption of spiramycin and midecamycin. These preparations are natural macrolide antibiotics. Erythromycin is the first macrolide antibiotic, it was obtained in 1952 and is still widely used in clinical practice. However, its applicability is limited due to the high frequency of relatively light, but unpleasant side effects: low bioavailability, inconvenience of administration 4 times a day, low activity against Haemophilus influenzae.

The study found that in 2010 the total macrolides consumed amounted to 1.172 DDDs /1000/day, in 2011 – 1.246, in 2012 – 1.360 and in 2013 – 1.525 DDDs /1000/day. There is a positive trend in consumption of macrolides: increase in total consumption by 30% in 2013 compared to 2010. This trend is observed in other countries.

In recent decades, macrolide usage worldwide has increased significantly. The increase in the use of antimicrobials of this class in 14 European countries from 1997 to 2003 averaged to 30-60% (S. Coenen et al., 2006).

Widespread use of macrolides caused significant increase of resistance to them. The frequency of the formation of resistant strains of the main pathogens varies widely in different countries around the world. For example, in the Asian countries it is 60%,

reaching in some regions 89% (J.H. Song et al., 2004). In the U.S., the prevalence of resistant strains ranges from 30 to 50% (D. Farrell et al., 2007). In Europe, this figure does not exceed 36% (EARSS, 2007); in Russia it is registered at the level of 6-10% (R.S. Kozlov and co-authors, 2006). Some authors believe that the tendency to increase the number of microorganisms resistant to antimicrobials action acquires the features of a hidden pandemic of macrolide-resistant S. pneumoniae (KP Klugman et. al., 2005). In particular, in the U.S. an increase in the use of macrolides by 60% over 4 years (1995 and 1999) led to an increase in the prevalence of resistant S. pneumoniae by more than 2 times.

Unfortunately, information about resistance to macrolide antibiotics in Ukraine is virtually absent. In this regard, we must rely solely on indices and experience of other countries, and monitor the rational consumption of macrolide antibiotics to prevent the development of microbial resistance to this group of drugs.

Conclusions. The analysis of outpatient consumption of antimicrobials of the macrolide group showed that during the study period the consumption of new drugs such as azithromycin and josamycin increases and the consumption of early drugs of the macrolide group, that is erythromycin and spiramycin, decreases. In the future, we plan to conduct a comparative analysis of the consumption of drugs of the macrolide group in monetary terms and in terms of consumption with the level of respiratory diseases.

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