CLINICAL PHARMACOLOGICAL APPROACH TO THE USE OF ANTIBACTERIAL DRUGS WITH DIFFERENT CHEMICAL STRUCTURES

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Article history:		Abstract:	
Received: June 26th 2024 **Accepted:** July 20th 2024		Cephalosporins are β-lactams, which are the basis of modern chemotherapy, as they occupy a leading or important place in the treatment of most infectious diseases. In terms of the number of drugs used in the clinic, this is the most numerous group among all antibacterial agents.	

INTRODUCTION

Antibacterial agents are one of the most widely used groups of drugs (DR) applied in various fields of clinical medicine. Drugs for the treatment of infectious diseases occupy the second place in the world in terms of sales [3]. Among them, a significant share is accounted for by antibiotics. The leading pharmacotherapeutic classes in terms of sales include cephalosporins, penicillins and quinolones. Currently, a large number of antibacterial agents enter the Uzbekistan market, therefore, marketing research of the antibiotic market is relevant and promising.

MATERIALS AND METHODS

An important section of marketing research has become the analysis of the pharmaceutical market, in particular the analysis of the range of cephalosporin antibacterial drugs, using the method of content analysis. Cephalosporins, like penicillins, carbapenems and monobactams, are β-lactams, which are the basis of modern chemotherapy, as they occupy a leading or important place in the treatment of most infectious diseases. In terms of the number of drugs used in the clinic, this is the most numerous group among all antibacterial agents. Their diversity is explained by the desire to obtain new compounds with a wider spectrum of antibacterial activity, improved pharmacokinetic characteristics and resistance to constantly emerging new mechanisms of microorganism resistance [1].

RESULTS AND DISCUSSION

Currently, cephalosporins occupy a leading place in the treatment of various infections in hospitals; in most cases, they are preferred in the schemes of initial empirical therapy for infections of various localizations [5]. At the same time, the limiting factor in the use of cephalosporins is the development of resistance in microorganisms as a result of their production of β-lactamases. This problem has become especially relevant in recent years due to the widespread use of cephalosporins, sometimes unjustified and often uncontrolled. Due to their high efficiency and low toxicity, cephalosporins occupy one of the first places in terms of frequency of clinical use among all classes of antibiotics [4]. There are four generations of cephalosporins (Table 1), with the first three represented by drugs for parenteral and oral use.

Table 1. Classification of antibacterial drugs of the cephalosporin group [4]

1st generation	2nd generation	3rd generation	4th generation
Parenteral			
cefazolin	cefuroxime	cefotaxime	cefepime
		ceftriaxone	
		ceftazidime	
		cefoperazone	
		cefoperazone/sulbactam	
Oral			
cephalexin	cefuroxime axetil	cefixime	
cefadroxil	cefaclor	ceftibuten	

In the structure of the range of antibacterial drugs of the cephalosporin series, the distribution by generations in relative terms can be presented as follows (taking into account the INN): 1st generation - 22.7% (cefazolin); 2nd generation - 7.5% (cefuroxime); 3rd generation - 65.9% (ceftriaxone, cefotaxime, ceftazidime); 4th generation - 3.9% (cefepime).
The share of drugs for parenteral use is 88.6%, among them the leading forms of release are powder for intravenous and intramuscular administration (55.6%),

powder for injections (24.3%). Oral dosage forms (11.4% of the total number of dosage forms) are represented by capsules - 42.8%, film-coated tablets - 22.8% and granules for suspension - 20.0%.

Antibacterial drugs of the cephalosporin series are produced in 17 countries, the leaders among which are Russia (42.8% of all registered drugs of this group), India (25.6%), Italy (6.5%), China (5.2%). Among Russian manufacturers, the share in the market is occupied by: Abolmed LLC (21.83%), Sintez AKO OJSC (20.42%), Krasfarma OJSC (11.27%). Among foreign companies, the following can be distinguished: Orchid Chemicals&Pharmaceuticals Ltd (India), Lupin Ltd (India), Nectar Lifesciences Ltd (India), GlaxoSmithKline S. p. A. (Italy), Bristol-Myers Squibb S. r. L. (Italy).

Although success of the translation of β-lactam-ring-containing β-lactamase inhibitors and various diazabicyclooctane derivatives to clinical application provides more treatment options for serious infections caused by β-lactam antibiotic-resistant bacteria, neither is effective against class B metallo-β-lactamases (MBLs). These enzymes are extremely important because they can hydrolyze all clinically useful β-lactam antibiotics, including carbapenems (except for monobactams). Nevertheless, monobactams are degradable by Ser-BLs, which are frequently found in pathogens along with MBLs.

β-Lactams comprise an important antibiotic class in the current antibiotic arsenal, and combination therapy using β-lactam antibiotics with β-lactamase inhibitors represents a validated strategy to overcome β-lactamase resistance in bacteria, which has extended the life of β-lactam antibiotics. Although many promising β-lactamase inhibitors have been discovered, resistance to these new inhibitors and their combinations has already been detected in both the laboratory and clinical settings, which may be attributed to the specific protein targets of these inhibitors. Therefore, continuous exploration of new β-lactamase inhibitors is needed, which should be accompanied by strict controls on the use of these new inhibitors to avoid, as much as possible, the emergence of resistance to these drugs. Despite fruitful progress in the discovery of β-lactamase inhibitors, the most significant challenge lies in the development of new class B MBL inhibitors, which are not in clinical use at present. Although several MBL inhibitors such as RPX7009 have entered clinical trials, it is still too early to judge their clinical promise. Thus, additional efforts to discover novel MBL inhibitors are needed.

Divalent cationic ions cross-link LPS molecules by forming ionic bridges with negatively charged phosphate groups in lipid A and are essential for the outer membrane integrity of Gram-negative bacteria. Various molecules can compromise the physical integrity of the outer membrane of Gram-negative bacteria by removal of or competition with divalent ions, therefore breaking the cross-linked structure between divalent cationic ions and LPS molecules. Examples of these molecules include charge-containing small-molecular-weight drugs, cationic antimicrobial peptides, chelating agents, and cationic polymers.

CONCLUSION

Thus, a necessary condition for conducting marketing research is a deep knowledge of drugs as a product, its main pharmacotherapeutic properties, indications for use, release forms and other commodity characteristics. As a result of the content analysis, the structure of the range of antibacterial agents registered in Uzbekistan was revealed. Cephalosporins occupy a leading position not only among all antibacterial agents, but also among β-lactam antibiotics. Cephalosporin antibacterial drugs are mainly represented by drugs for parenteral administration (powder for intravenous and intramuscular administration, powder for injections). The share of oral dosage forms of cephalosporin drugs is very small and is limited to the dosage forms of drugs of the first three generations (coated tablets, capsules). The main manufacturers of these drugs registered in Uzbekistan are Russia, India and Italy. The data obtained as a result of content analysis are the basis for conducting comprehensive marketing research.

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