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Pharmacoepidemiological Rationale for the Use of Antibacterial Drugs for the Treatment of Community-Acquired Pneumonia in Children of Different Ages

Kodirova Shahlo Salokhitdinovna
Samarkand State Medical University Faculty of Pediatrics, assistant

Abstract: Community-acquired pneumonia (CAP) is a common clinical problem faced by physicians worldwide. EP is an indicator of the consumption of antibacterial drugs (AP), since this disease constitutes the majority of antibiotic prescriptions for therapeutic patients in the hospital. Hospital spending on medicines (MD) is on average 20% of their budget, more than half of which is AP spending.

Key words: Moraxella, Haemophilus influenzae, Streptococcus pneumoniae.

Modern recommendations for the diagnosis and treatment of CAP determine the treatment tactics and the rational choice of antibacterial therapy (AT). In our country, at the beginning of 2003, the first edition of the consensus of national recommendations for the management of adult patients with SAP, prepared by experts of the Russian Respiratory Society, the Interregional Association of Clinical Microbiology and Antimicrobial Chemotherapy (IACMAC), was published. and the Alliance of Clinical Chemotherapists and Microbiologists requested a 3-year review [1]. However, the availability of the most up-to-date recommendations and standards does not guarantee their daily use, and the rational prescription of drugs remains an urgent problem of local health [2].

The etiology of CAP is directly related to the normal microflora of the "non-sterile" parts of the upper respiratory tract (oral cavity, nose, oropharynx and nasopharynx). Of the many types of microorganisms that colonize the upper respiratory tract, only a few can cause an inflammatory reaction by penetrating the respiratory parts of the lungs, even with a minimal violation of protective mechanisms. Typical bacterial pathogens of SAP:

- Streptococcus pneumoniae - gram-positive cocci, the most common cause of pneumonia in all age groups (30% or more of all cases);
- Haemophilus influenzae - gram-positive bacilli responsible for the development of pneumonia in 5-18% of adults, often in smokers and patients with chronic obstructive bronchitis;
- Moraxella (Branhamella) catarrhalis - Gram-negative coccobacilli, an insignificant cause of pneumonia (in 1-2% of patients), usually of etiological significance in patients accompanied by chronic obstructive bronchitis.

Other frequently identified etiological agents of CAP differ from the microorganisms listed above with slightly different pathogenicity and biological characteristics. Asymptomatic colonization of the upper respiratory tract by these microorganisms is unlikely.

Since the 1940s, the term "atypical pneumonia" has been used to refer to interstitial or segmental lung disease that is milder than typical pneumococcal lobar pneumonia. Later, pneumonia with an unusual clinical appearance, which can occur in a muted form or with a clear intoxication syndrome, began to be considered atypical. In some cases, atypical pneumonia is also understood as viral pneumonia in the countries of Indochina, but in clinical practice, pneumonia caused mainly by

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microorganisms of intracellular localization: mycoplasma, chlamydia and legionella is of great importance.

The main methods of infection by microorganisms in SAP caused by atypical pathogens are aspiration of the contents of the oropharynx and inhalation of microbial aerosol in Legionella pneumonia. Under normal conditions, a number of microorganisms, such as S. pneumoniae, can colonize the oropharynx, but the lower respiratory tract remains sterile. Microaspiration of oropharyngeal secretions is a physiological phenomenon observed in 70% of healthy people, mainly during sleep. At the same time, the coordinated work of mucociliary cleaning, lactoferrin, lysozyme, interferon, and the bactericidal effect of class A secretory immunoglobulin found in bronchial secretions prevent the adhesion and colonization of microorganisms and the subsequent development of CAP.

Let's look at some biological features of atypical CAP triggers.

Mycoplasma pneumoniae is a microorganism without an outer membrane, which determines its natural resistance to β-lactam antibiotics; it is characterized by close contact with the membrane of eukaryotic cells (membranotropic pathogen), intracellular localization is possible.

Chlamydia pneumoniae is a microorganism that is only an intracellular parasite, similar in structure to gram-positive bacteria; causes pneumonia, usually not severe, in 2-8% of cases. Information is collected on the frequent isolation of this microorganism together with other "lung" pathogens.

Microorganisms of the genus Legionella are gram-negative bacilli that are obligate pathogens. Legionella spp. (primarily Legionella pneumophila) is a rare causative agent of CAP (2-10%), but Legionella pneumonia ranks second (after pneumococcal) in terms of the death rate of the disease.

The frequency of mycoplasma pneumonia increases during epidemic epidemics, which are repeated every 4-5 years, and in the autumn-winter period, pneumonia can make up an average of 20% of the total number. This pathogen is more likely to cause disease in young people. The clinical presentation usually includes fever, pharyngitis, myalgia, asthenia, and extrapulmonary complications. The disease can heal on its own within 1-2 weeks, but often lasts 4-6 weeks. and is accompanied by all its characteristic manifestations, including cough with mucous sputum. Cultural diagnosis of mycoplasma infection is difficult. The diagnosis can be confirmed by detecting a 4-fold seroconversion of mycoplasma-specific IgM antibodies using the Elisa test.

Pneumonia caused by chlamydia became known relatively recently. Cl. pneumoniae causes infection in at least 10% of young patients. The clinical presentation of this infection includes pharyngitis and laryngitis, in addition to the specific manifestations of bronchitis and pneumonia. Common symptoms are hoarseness, low-grade fever, and a persistent cough that is often dry and sputum is usually non-mucous and purulent. In patients with bronchial asthma, chlamydia infection often leads to exacerbation of asthma attacks. Bronchial inflammation caused by chlamydia usually occurs in young patients and is rarely observed in old age. The diagnosis can be confirmed by seroconversion data, the Elisa test is the most modern. Currently, polymerase chain reaction (PCR) is used to diagnose mycoplasma and chlamydia infections.

Pneumonia caused by L. pneumophila is not a common cause of SAP, but is usually characterized by a severe course, development of a systemic inflammatory response, and extrapulmonary symptoms. Rifampicin, often used in combination with macrolides, has the highest natural activity against Legionella. Atypical CAP

clinical and radiological signs Large multicenter studies based on the principles of evidence-based medicine have reliably shown that in many cases it is not possible to speak sufficiently based on the analysis of the clinical and radiological appearance of the disease. Level of confidence in the probable etiology of CAP. In particular, the division of CAP into typical (for example, pneumococcal) and atypical (mycoplasma or chlamydia) is not of particular clinical importance, since it does not affect the choice of the initial antibiotic for empiric therapy. At the same time, some

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features of atypical CAP were noted: the formation of destroyed spaces in the lungs that are not typical for pneumococcal, mycoplasma and chlamydial pneumonia, on the contrary, staphylococcal infection, aerobic gram-negative enterobacteria and anaerobes shows; reticulonodular infiltration in the basal parts of the lungs is characteristic of mycoplasma pneumonia (in 20% of cases, mycoplasma pneumonia may be accompanied by focal confluent infiltration in the projection of several segments or even lobes). Laboratory diagnosis of atypical CAP

Serological diagnosis of infections caused by M. pneumoniae, C. pneumoniae, and Legionella spp. is not included in mandatory research methods, taking into account the need for repeated sampling of blood serum during the acute period of the disease and in the recovery period. a few weeks from the onset of the disease), the epidemiological level of the diagnosis, not the clinical one. Recently, the enzyme-linked immunosorbent test has become widespread - with the detection of a specific soluble antigen of L. pneumophila (serotype 1) in urine, but in our country the use of these rapid diagnostic methods is used only in certain clinics. centers.

Currently, the PCR method is promising, it is used to diagnose pathogens such as Cl. pneumoniae and M. pneumoniae. However, the role of the PCR method in diagnosis has not yet been determined and it cannot be recommended for widespread clinical practice.

In foreign medical practice, there is the following algorithm for laboratory diagnosis of SAP caused by atypical pathogens: when the patient is hospitalized, a blood serum sample for serological examination should be taken and kept frozen. In the case of severe CAP, the ineffectiveness of β-lactam antibiotics, the presence of epidemiological risk factors, as well as in other cases where an accurate etiological diagnosis is necessary, a repeated serum sample is taken after 7-10 days and at the same time "atypical" (legionella, mycoplasma, chlamydia, etc.) were tested to determine the increase in antibody titers. For the same indications and if available, additional diagnostic methods are used, including detection of Legionella antigen in urine, PCR (according to the recommendations of the British Thoracic Society).

Treatment of atypical CAP

Despite the wide introduction of standards of outpatient treatment of SAP in our country, a very high percentage of hospitalization of patients remains - 50% of patients who are sick at home are admitted to inpatient treatment. This is almost double the global figure. Such a negative situation can occur due to the following reasons:

- availability and availability of a large number of non-prescription drugs in the pharmacy network, patients can take them as an alternative to antibiotics;
- stereotypes established among local therapists for the treatment of pneumonia and compliance with modern recommendations [3].

The analysis of empirical antibacterial therapy for CAP on the example of a multidisciplinary medical institution in Moscow showed that the financial costs of patients whose AT met modern recommendations were much lower than the costs of patients whose treatment did not meet modern standards and recommendations. [4]. Penicillin, amoxicillin, cefazolin, gentamicin and lincomycin are unreasonably often prescribed by many local doctors. It was found that in the treatment of SAP, gentamicin was prescribed in 40% of cases, cefazolin at a daily dose of 2.0 g/day in 30%, amoxicillin in 16%, and a combination of amoxicillin and cefazolin. only in 14% of cases. In addition, monotherapy with "traditional" APs was prescribed in 86% of cases (Figure 1).

The practice of widespread use of aminoglycosides (gentamicin, etc.) in the treatment of CAP, which is widespread in some regions of the Russian Federation, should be considered incorrect, because they are not active against pneumococcal and atypical pathogens [5]. From the point of view of the practitioner, the sensitivity of microorganisms and their resistance to the performed AT are of more interest. If a group or species of bacteria are not sensitive to AP, we talk about what is called natural resistance (occurs before the onset of AT in a certain patient), all other cases of resistance

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development are called acquired resistance. Secondary resistance develops directly in a certain course of AT (resistance of respiratory pathogens to macrolides). It is the problem of resistance that calls for limiting the unreasonable widespread use of AP, developing standards and algorithms for implementing AP [6].

Currently, the variety of forms of release of modern drugs allows the doctor and the patient to have the opportunity to choose the most convenient drugs from a practical point of view. Among antibacterial drugs, macrolides are in wide demand in the retail and hospital sectors of the pharmaceutical market [7,8]. Ease of use, broad spectrum of antibacterial activity, bactericidal effect, clinical effectiveness, possibility of use in many infectious diseases, relatively favorable safety profile and pharmacoeconomic component of the treatment process, due to its availability in the pharmacy sector for the end user. (RX drug group), drugs of this category are included in the top 10 sales of Russia.

One of the brightest representatives of this group of drugs is azithromycin. Different manufacturers produce it under their own trade names. A total of 22 trade names of this drug are registered in Russia. In such a situation, the selection of a specific drug can be made on the basis of the Health and Longevity Code developed by the Association of Medical Societies for Quality (ASMOK) and approved by the Ministry of Health and Social Development of the Russian Federation. Federation. The leaflet lists all azithromycin drugs approved for use in our country [9].

In this regard, when choosing a particular drug, it should be taken into account that the price of azithromycin in the modern pharmaceutical market is very diverse: from expensive original drugs to cheaper generics, some of which are also of good quality [10]. This ensures the availability of drugs of this group for all segments of the population. In recent years, the emergence of many generic drugs of azithromycin has led to a decrease in the course of treatment and the widespread use of this drug in outpatient practice. However, when prescribing treatment for a patient, the doctor pays attention not only to the price of the drug, but also to the personal experience of its use. One of the popular antibiotics in Russia is Azitral® produced by the pharmaceutical company Shreya Life Sciences Pvt. Ltd." (India).

Azithromycin preparations are available on the market in different dosage forms, including 250 and 500 mg capsules. This is due to the wide antibacterial spectrum and the low level of resistance of pathogens to it (for example, in Russia, in contrast to the countries of Western Europe, the USA and Southeast Asia, a favorable situation remains with the sensitivity of pneumococci to macrolides. , and today they almost the only group of antibiotics to which intracellular infectious agents are highly sensitive). Therefore, due to its pharmacokinetics (high lung deposition) and good tolerance, azithromycin is the drug of choice for the treatment of "atypical" (mycoplasma, legionella, chlamydia) pneumonia, which accounts for more than 30% of cases. All cases of CAP.

Thus, in most cases of SAP caused by atypical pathogens, treatment is chosen empirically based on the patient's risk factors and clinical and epidemiological assumptions about which pathogens are likely to cause the disease [11]. Since the 1990s, azithromycin has been one of the leading antibiotics for use in various infectious diseases, including CAP.

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