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Basic Principles of Rational Antibacterial Therapy in the Treatment of Urinary Tract Infections in Children

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Annotation: The purpose of the article: to describe the principles of rational antibacterial treatment of respiratory infections in real practice.

Basic rules. The constant increase in the resistance of infectious disease pathogens and the sharp decrease in the number of new antibiotics make rational antibiotic therapy one of the urgent problems of modern medicine. Based on the analysis of current federal recommendations for the treatment of respiratory tract infectious diseases and the analysis of specific clinical examples, the article reviews the principles of antibacterial therapy for respiratory tract infections.

Conclusion. The main principles of successful antimicrobial therapy are accurate diagnosis, selection of the initial antibiotic taking into account the causative agent involved in the development of the disease, the level of resistance in the country and region, as well as individual risk factors for infection with resistant pathogens; adherence to the exact dosage of the drug; correct assessment of the effectiveness and duration of antimicrobial therapy.

Keywords: respiratory tract infections, antibacterial therapy, resistance, rational use of antibiotics.

Introduction: Modern therapy of respiratory tract infections is unthinkable without antibacterial drugs. However, despite the fact that doctors have a huge number of drugs active against almost all pathogenic microorganisms in their arsenal, the choice of an antimicrobial drug in a particular clinical situation often raises many questions for the doctor. This is explained in most cases by the

inability to decipher the etiological process of the infectious process, changing ideas about the etiology of infectious and inflammatory diseases of the respiratory tract, and the growth of resistance of microorganisms. In some cases, the choice of an antibiotic is complicated by the fact that practicing doctors do not have sufficient knowledge of the pharmacokinetics, antimicrobial activity spectra, and toxicity of modern antibacterial drugs. According to some international studies, more than 60% of antibiotic prescriptions are unjustified or irrational [1-3].

Below we discuss principles that will help the physician make a quick decision when choosing effective antibacterial therapy.

A serious problem in the treatment of upper and lower respiratory tract infections is the unreasonably frequent prescription of antimicrobial drugs without appropriate indications, primarily for viral infections. The prevalence of respiratory tract infections is steadily increasing every year, which causes patients to seek help from doctors of various specialties more often. According to domestic and foreign sources, an adult patient experiences an episode of the so-called cold 2-3 times a year [4, 5].

The development of diseases is facilitated by stress, reduced immunity and an unfavorable epidemiological situation, especially in the cold season, as well as chronic background pathology. Most acute diseases are viral, easily tolerated by the patient and successfully resolved with adequate therapy [6].

Research methods and materials: Errors can occur due to misinterpretation of symptoms (the doctor mistakes ARVI for a bacterial infection) and the desire to prevent bacterial complications of a viral infection. Antibiotics do not prevent bacterial superinfection; moreover, they contribute to the selection of more aggressive pathogens and the development of undesirable side effects. Irresponsible use of antibacterial therapy has serious consequences [7].

If the bacterial etiology of the disease is highly probable, the second step is to select a drug that is active against the potential causative agent of the infectious disease. In most cases, antimicrobial therapy is prescribed empirically, that is, the pathogen and its sensitivity to antibiotics have not been determined.

The spectrum of antimicrobial activity of the drug should cover the majority of possible bacterial pathogens of infection at a given localization. In the case of bacterial infections of the respiratory tract, the drug should be active against the most common pathogens (Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis, Streptococcus pyogenes).

Pneumococcus (S. pneumoniae) is the most common bacterial cause of respiratory tract infections. Diseases caused by pneumococci are one of the most serious health problems worldwide. To date, more than 90 different serotypes (immunological variants) of pneumococci have been identified. All of them are potentially pathogenic, and about twenty of them cause severe infections. According to statistics, up to 70% of all pneumonias, about 25% of otitis media, 5-15% of purulent meningitis, and about 3% of endocarditis are caused by pneumococcus [8-10].

Haemophilus influenzae has long been considered the causative agent of influenza, as infection with this pathogen often occurs as a nonspecific nasopharyngitis or acute respiratory viral infection, which gave rise to the name of the microorganism. However, H. influenzae can also cause serious diseases (pneumonia, exacerbation of COPD, sinusitis, meningitis, sepsis) [11].

M. catarrhalis is involved in the development of respiratory infections, especially in children. The pathogen often coexists with Haemophilus influenzae and pneumococcus. It is the second most common cause of bacterial exacerbations of COPD [12].

Group A β-hemolytic streptococci (pyogenic streptococci, S. pyogenes) cause many diseases, including tonsillitis, pharyngitis, scarlet fever, erysipelas, peritonsillar abscess, cervical phlegmon, sepsis, otitis media, meningitis, streptoderma, glomerulonephritis [3.3.3].

Conclusions: The main limitation of the effectiveness of antimicrobial drugs is the ability of

microorganisms to develop resistance to their effects. This natural process is accelerated many times by the unreasonable and excessive use of antibiotics as a means of prevention and self-treatment. The threat of the emergence and spread of antibacterial resistance was recognized by the scientific community almost immediately after the appearance of the first antibiotics, but for many years the problem was solved by the development and introduction of new drugs that overcome resistance [14]. According to some forecasts, the losses associated with antibiotic resistance will amount to about 100 trillion US dollars by 2050. Even more terrible is the loss of up to 10 million human lives per year [15].

A significant problem in our country with pathogens of community-acquired respiratory tract infections over the past 10 years has been a steady trend towards an increase in the proportion of pneumococcal strains resistant to β-lactams and macrolides. Thus, the sensitivity of pneumococci to penicillin has decreased in recent years to 96.3%, and to ceftriaxone to 91.9%. According to data obtained using the open online platform for analyzing antibiotic resistance data (AMRmap), in Russia, the resistance of pneumococci (as the main bacterial pathogen of respiratory tract infections) to modern macrolides in community-acquired infections already exceeds 30% [16].

The main mechanism of resistance in H. influenzae is associated with the production of β-lactamases that hydrolyze aminopenicillins. One recent study showed that the rate of resistance to aminopenicillins among clinical strains of H. influenzae in the Russian Federation is 19% [17].

Currently, the majority of clinical isolates of M. catarrhalis produce β-lactamases that are inhibited by clavulanic acid [18].

The microbial landscape of community-acquired infections may contain individual resistant strains of microorganisms. Therefore, when choosing a particular antibiotic, it is necessary to know in advance the risk of the presence of resistant pathogens. The methodology for such forecasting consists in stratifying patients according to risk factors. The main indicators of stratification are the use of antibiotics in the last 3 months and the presence of concomitant pathology. This approach allows you to initially make a choice in favor of drugs that are able to overcome possible mechanisms of resistance of pathogens [19].

The initial assessment of the effectiveness of therapy should be carried out 48-72 hours after the start of treatment. It is recommended to contact the patient by telephone one day after the start of therapy. The criteria for effectiveness during these periods are a decrease in temperature, a decrease in signs of intoxication and other manifestations (for example, shortness of breath). If the patient has a high temperature and intoxication or symptoms persist, the treatment should be considered ineffective. In this case, it is necessary to reconsider the tactics of antibacterial therapy and reconsider the advisability of hospitalization of the patient [20].

To date, the optimal duration of treatment for patients with respiratory infections remains a matter of debate. For example, in the case of mild community-acquired pneumonia, the main criterion for stopping antibacterial therapy is the persistent normalization of body temperature for 48-72 hours with positive dynamics of other symptoms and the absence of signs of clinical instability. The duration of treatment with this approach usually does not exceed 7 days.

Experts consider the criteria for the adequacy of antibacterial therapy to be a persistent decrease in body temperature to $\leq$ 37.2 °C, the absence of signs of intoxication, respiratory failure (respiratory rate (RR) less than 20 / min) and purulent sputum; positive dynamics of peripheral blood indices (leukocyte count in the blood < 10 × 10 9 / l, neutrophils < 80%, young forms < 6%), as well as the absence of negative dynamics on the X-ray [20].

The persistence of individual clinical, laboratory or radiological signs of pneumonia is not an absolute indication for continuing or changing antibacterial therapy. In most cases, they resolve spontaneously or under the influence of symptomatic therapy. Prolonged subfebrile temperature is not a sign of bacterial infection.

Radiographic signs of pneumonia resolve more slowly than clinical signs, so a follow-up chest radiograph cannot be used as a guide to the duration of antibiotic therapy. However, if clinical, laboratory, and radiographic signs persist for a long time, differential diagnosis with diseases such as lung cancer, tuberculosis, congestive heart failure, etc. should be considered [21].

The largest number of antimicrobial drugs is prescribed by primary care physicians, primarily for the treatment of acute respiratory infections. Therefore, the determining components, including antibiotic resistance, are the restriction of antibiotic use in outpatient practice and the rationalization of their use. This is facilitated by both the training of primary care physicians in the basics of the rational use of antibiotics, and strict adherence by physicians to recommendations for the selection of antibiotics, the state of antibiotic resistance in the country and region, the concomitant pathology, the patient's risk of developing an infection that causes antibiotic resistance, and the determination of an adequate dose of the antibiotic.

Thus, the Russian Respiratory Society is a professional organization designed to develop clinical guidelines for pneumonia, COPD and bronchial asthma, which are received by the community. The National Medical Association of Otorhinolaryngologists is approved by the Ministry of Health of Russia as a developer of clinical guidelines for ENT diseases. Information on current clinical recommendations is available on the official website of the Ministry of Health of the Russian Federation [22].

Discussion: The recent revision of the recommendations marks a shift in the paradigm of antibacterial therapy for lower respiratory tract and ENT infections adopted by the community. Thus, macrolides have lost their position as first-line drugs in most cases. They may be recommended if the patient is intolerant to beta-lactam antibiotics or if an infection caused by atypical pathogens is suspected.

Resistance of bacterial pathogens to unprotected aminopenicillins is steadily increasing worldwide. Currently, these drugs have lost their relevance in the treatment of many infections, the etiological structure of which is dominated by bacteria with a high level of secondary resistance, primarily due to the production of β-lactamases. This is explained by the fact that aminopenicillins, like natural penicillins, are hydrolyzed by all known β-lactamases. Unprotected aminopenicillins can be considered as drugs for initial therapy only in patients without risk factors for infection with drug-resistant pathogens. Some third-generation oral cephalosporins (cefixime, ceftibuten) are not included in clinical guidelines for the treatment of pneumonia in adults and children. WHO does not recommend the use of these antibiotics in the treatment of respiratory infections. This is due to the low activity of these drugs against the main causative agent of respiratory tract infections - pneumococcus. According to the conclusion of the European Committee for Antimicrobial Susceptibility Testing, all pneumococcal strains can be considered resistant to cefixime, therefore, it is not recommended to determine the susceptibility of pneumococci to cefixime. Amoxicillin / clavulanate occupies an important place in the recommendations for the treatment of respiratory tract infections. This drug has been successfully used in clinical practice for almost 40 years. During this time, it has reliably proven its high efficacy and safety for children and adults.

The drug has a high stable activity against the main bacterial pathogens of respiratory tract and ENT infections: S. pneumoniae, S. aureus, H. influenzae, M. catarrhalis, anaerobes (Table 1). Amoxicillin/clavulanate is the drug of choice in patients with risk factors for infection with drug-resistant pathogens and/or a high probability of involvement of β-lactamase-producing pathogens [23-29].

Conclusion: We present two clinical examples that demonstrate the role of amoxicillin/clavulanate in the treatment of respiratory tract infections.1

Patient T., 59 years old, consulted a general practitioner with complaints of a rise in body temperature to 37.8 °C, cough with yellow sputum, and weakness.

From the anamnesis it is known that 4 days ago he was acutely ill and had a temperature of 37.5 ° C. I took antipyretic drugs myself, but the temperature did not decrease. After 2 days, pain appeared in the left side of the chest with coughing and deep breathing.

The patient does not smoke and does not abuse alcohol. There are no occupational hazards. The history of allergies is not severe. History: hypertension and type 2 diabetes (regularly taking glibenclamide). On examination: the condition is moderately severe, body temperature is 37.5°C. Respiratory rate - 20/min. On percussion, there is a slight dullness of percussion sound in the lower parts of the left lung. Breathing is vesicular, slightly weakened in the lower parts of the left side, crepitations are also heard there. Saturation - 96%.

Heart sounds are muffled and rhythmic. Heart rate - 78 beats/min, blood pressure - 130/80 mm Hg. Art.

Clinical blood test: leukocytes - 10.7 × 10 9 /l, segmented neutrophils - 70%, banded neutrophils - 4%, ESR - 28 mm/h.

Blood biochemistry: glucose - 4.5 mmol/l, CRP - 115 mg/l, total protein - 76 mg/l, creatinine - 81 μmol/l.

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