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Pharmacoepidemiological Basis for the Use of Antibacterial Drugs for Community-Acquired Pneumonia in Children of Different Ages in a Modern Interpretation

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ABSTRACT

Objective: *This study addresses the urgent issue of rational antibiotic therapy for pneumonia, focusing on improving the effectiveness of treatment and minimizing negative consequences. Despite the availability of various antibacterial agents, pneumonia incidence and complications continue to rise.* ***Methods:*** *The study examines two main trends in antibiotic selection for pneumonia: 1) the use of selective drugs to ensure a rational and cost-effective approach, minimizing disruption to the patient's saprophytic flora, and reducing the risk of superinfection and immunosuppressive effects; 2) empirical prescription of broad-spectrum antibiotics.* ***Results:*** *Findings highlight the effectiveness of selective antibiotics in reducing adverse outcomes, while broad-spectrum antibiotics are commonly used in empirical treatments. However, overuse of broad-spectrum agents may lead to resistance and other complications.* ***Novelty:*** *The research emphasizes the importance of rational antibiotic selection, advocating for selective drugs over broad-spectrum antibiotics to reduce the risk of resistance, improve patient outcomes, and avoid unnecessary side effects. This approach proposes a more targeted and economical method of managing pneumonia, offering a potential solution to the rising incidence and worsening consequences.*

INTRODUCTION

Etiotropic therapy is the mainstay, but adequate antibiotic therapy is often difficult due to the difficulty of early pathogen identification [1], [2]. Antibacterial therapy for pneumonia should be early and adequate (the latter refers to the dose, method of administration and duration of use), and also adjusted during treatment depending on the clinical response of the pathogen and its sensitivity to the drug. The effectiveness of treatment depends, first of all, on the correct choice of antibacterial drug and its compliance with the etiology of the disease. Currently, the doctor has in his arsenal a huge number of different antibacterial drugs, which are very effective for various etiologies of pneumonia [3], [4].

The presumed etiological variant of pneumonia is the most important indication for choosing the initial antibiotic. Diagnosis of the etiological factor is only indicative and is based on such data as the epidemiological situation, the nature of the background pathology, and the features of the clinical and radiological picture [5]. It should be assumed that the majority of non-pneumococcal pneumonia caused by opportunistic microorganisms is characterized by the features of the clinical course of the disease [6].

So, Friedlander pneumonia usually occurs in people who abuse alcohol for a long time; Pneumonia caused by Haemophilus influenzae - when pneumonia develops in

patients with chronic bronchitis and in a patient receiving treatment in a hospital, the likely causative agent is gram-negative flora, in particular Escherichia coli or Pseudomonas aeruginosa.

RESEARCH METHOD

The choice of treatment method is also influenced by the following characteristics of the macroorganism: age, history of allergies, liver and kidney function, and pregnancy. The severity of pneumonia is also one of the clinical indications for the initial selection of an antibacterial drug and its route of administration [7].

When prescribing antibacterial therapy, it is necessary to take into account the possible side effects of drugs and avoid prescribing drugs that cause undesirable effects and worsen the course of the main and concomitant diseases [8]. It is necessary to take into account hypersensitivity to previously used antibacterial agents. In particular, other beta-lactam antibiotics should be prescribed with extreme caution to patients with allergic reactions to penicillin due to the risk of cross-hypersensitivity. If the patient's history contains information about repeated courses of treatment of various diseases with penicillin preparations and other antibiotics, the likelihood of manifestation of beta-lactamase activity in representatives of the patient's endogenous microflora increases sharply [9].

When choosing an antibacterial drug in patients with pneumonia against the background of chronic renal failure, it is necessary to reduce the dose of the drug excreted by the kidneys in proportion to the glomerular filtration rate or give preference to an antibacterial drug that is metabolized in the liver (erythromycin, clindamycin, metronidazole, cefoperazone). Conversely, in case of liver pathology, signs of its functional insufficiency, the doses of drugs that are mainly metabolized in the liver should be reduced by 1/3-1/2 or give preference to antibacterial drugs that are excreted by the kidneys (aminoglycosides), fluoroquinolones, cephalosporins, except cefoperazone). If the patient has heart failure or obesity, the excretion of antibacterial drugs from the body is impaired, their concentration in the blood and the risk of side effects increase, which should be taken into account when choosing an antibacterial drug with long-term pharmacokinetics (cefoperazone, ceftazidime, roxithromycin, clarithromycin).

When choosing an antibacterial drug, the patient's age should be taken into account [10]. Treatment of the elderly and the elderly is associated with serious difficulties. The main principle of drug therapy in geriatrics should be to use only the necessary drugs, the most effective with minimal side effects. At the same time, in addition to drug therapy for pneumonia, people over 60 often have to take drugs to treat concomitant diseases [11]. The need for combination therapy is determined by the frequent exacerbations of the underlying disease [12]. Of course, mandatory polytherapy can lead to an increase in the frequency of side effects. However, it is often impossible to combat polypharmacy by canceling antiarrhythmic, coronary-active and some other drugs. Multidisciplinary

treatment of pneumonia should be considered a feature of old age [4]. Broad-spectrum antibiotics are more commonly used for people over 60 years of age. This is justified by the polyetiology of pneumonia in this population and the prevalence of associations of gram-positive and gram-negative microorganisms.

The antibiotic to be taken should be characterized by optimal pharmacokinetic parameters: achieving high tissue concentrations, including at the site of inflammation, the maximum possible intervals between doses of the drug and the minimum need for monitoring [13], [14]. In particular, in the treatment of patients with pneumonia, such a pharmacokinetic parameter as the ability to penetrate into sputum is important. In patients with pneumonia, preference should be given to drugs that create high and stable concentrations in sputum. In particular, among aminopenicillins, the concentration of amoxicillin in sputum is twice as high as the concentration of ampicillin when taking the same doses of drugs. In addition, the concentration of amoxicillin in sputum remains at a therapeutic level for a long time [15], [16]. Aminoglycosides do not penetrate sputum well enough, which is one of the reasons for their inadvisability in this pathology.

It is very difficult to predict the clinical efficacy of an antibacterial drug in a particular patient, since there are many factors that affect the possible outcome of antibiotic therapy [10]. These factors can be divided into three groups: macroorganism factors - the human immunological system and its interaction with the pathogen; pharmacodynamic factors of the interaction between the antibacterial drug and the microorganism in the macroorganism: bactericidal effect, activity at subinhibitory concentrations, post-antibiotic effect, pharmacokinetic factors [17], [18], [19], [20].

The adequacy of antibiotic therapy determines the time to recovery, the risk of complications, and the outcome of treatment [1]. The correctly selected antibiotic at the onset of the disease and the timely correction of antibacterial therapy over time provide high efficiency and, most importantly, significantly reduce the cost of treatment. In the treatment of severe pneumonia of local origin, it is necessary to prescribe a broad-spectrum antibiotic that is active against beta-lactamase-producing staphylococci and streptococci, as well as gram-positive microorganisms E. coli, Klebsiella, Enterobacter, H. influenzae, etc. The initial prescription of very potent antibiotics and / or their combinations does not provide advantages, but at the same time increases the risk of selecting problematic microorganisms [21], [22], [23].

RESULTS AND DISCUSSION

The initial effect of the prescribed antibiotic can be assessed no later than 48 hours, since during the first day the growth and reproduction of sensitive microorganisms are suppressed, and then, in response to a decrease in intoxication, the first positive signs appear in the clinical state, temperature reaction and laboratory parameters. If on the third day of treatment it is concluded that the therapy is adequate, the course of treatment is continued until the clinical, radiological and laboratory signs of inflammation normalize. The absence of positive dynamics 72 hours after the start of antibiotic therapy

indicates the need to adjust the treatment regimen. After selecting an antibacterial drug for empirical therapy, it is necessary to determine the optimal route of administration of the drug, the adequate dose of the drug, adequate monitoring during treatment, and the optimal duration of therapy.

Oral administration of drugs has a number of undeniable advantages over parenteral administration, in particular, it is safer, simpler and cheaper. Parenteral administration of antibacterial agents is indicated in the following cases: for severe or generalized infections, when it is necessary to quickly achieve maximum and stable levels of drugs in the blood and tissues; when oral administration of drugs is difficult or impossible (patients are unconscious, have impaired behavior, central nervous system damage, memory or intellectual impairment); for diseases or conditions that lead to impaired absorption of drugs in the gastrointestinal tract (severe gastroenteritis, resected stomach or part of the small intestine); when there is no dosage form of the selected drug intended for oral administration. In practice, the possibility of switching to oral administration of antibiotics occurs on average 3-5 days after the start of parenteral treatment. Preference should be given to drugs with different forms of administration (parenteral, oral) using a "stepped" therapy scheme.

In most cases, preference should be given to monotherapy, the advantages of which are a sufficient degree of interaction of antibacterial drugs, a decrease in the risk of developing undesirable interactions with other drugs, simplification of the work of medical personnel and a reduction in the cost of treatment.

According to the European Guidelines for the Clinical Evaluation of Antiinfectives, it is recommended that immunocompetent patients with pneumonia continue treatment for 3-5 days after achieving stable temperature normalization. The duration of antibiotic therapy with this approach is usually 7-10 days. The following point should be considered important: after the initial effect is achieved, it is not recommended to change antibiotics within the prescribed duration of treatment. The duration of antibacterial therapy for complicated community-acquired pneumonia is determined individually. The main criterion for stopping antibiotic therapy is persistent apyresis (3-4 days in a row).

The persistence of individual clinical, laboratory and/or radiological signs of the disease is not an absolute indication for continuing or changing antibacterial therapy. In most cases, their disappearance occurs spontaneously or under the influence of symptomatic therapy. If within 48-72 hours after the start of treatment, there is a continuation or progression of the clinical manifestations of the disease, the appearance of new focal infiltrative changes in the lungs, the selected antibacterial therapy regimen is considered ineffective. replaced by an alternative (taking into account the in vitro determination of the sensitivity of the isolated culture of the pathogen to antibiotics).

A. Patients under 60 years of age with mild pneumonia

Patients aged 60 years and older and/or with comorbidities (diabetes, chronic renal failure, congestive heart failure, chronic liver disease, mental illness, alcoholism, etc.); patients with clinically severe pneumonia, regardless of age.

In patients in the first group, a clear clinical effect can be achieved by oral administration of antibacterial drugs. As the means of choice, aminopenicillins (amoxicillin is preferable to ampicillin in pharmacokinetic parameters) and macrolides are recommended. To date, no differences in the effectiveness of individual representatives of these groups, as well as macrolide antibiotics, have been identified. Doxycycline is recommended as an alternative.

In the second group of patients, a clear clinical effect can be achieved by treatment with oral antibiotics. In elderly patients or people with concomitant diseases, due to the increased likelihood of the etiological role of gram-negative microorganisms (including those with some mechanisms of resistance development), "protected" aminopenicillins (ampicillin / sulbactam, amoxicillin / clavulanate) or cephalosporins are recommended. The second type is recommended as the agent of choice (cefuroxime axetil). Given the possibility of chlamydial or legionella infection in this group of patients, combination therapy with macrolide antibiotics seems justified.

The drugs of choice for severe community-acquired pneumonia are macrolides (erythromycin, spiramycin) for parenteral administration in combination with third-generation cephalosporins without antipseudomonal activity (cefotaxime or ceftriaxone, preferably used at maximum doses). The above combination covers almost the entire spectrum of potential etiological agents of severe community-acquired pneumonia - both "typical" and "atypical".

B. Chest X-ray of patients with pneumonia

In Russia, severe community-acquired pneumonia is often treated with a combination of β-lactams and aminoglycosides, which is not considered sufficiently proven. Aminoglycoside antibiotics are inactive against pneumococci and atypical pathogens, have low activity against staphylococci. When arguing for the use of such a combination, they usually refer to the possibility of expanding the spectrum of action of the combination, demonstrating synergy, and overcoming possible resistance. There are objections to each of these arguments. If gram-negative aerobic microorganisms are sensitive to third-generation cephalosporins, the addition of aminoglycosides does not increase the clinical effect. The idea of a high frequency of synergism between β-lactams and aminoglycosides is somewhat exaggerated

Resistance of gram-negative aerobic microorganisms to third-generation cephalosporins is now almost always associated with resistance to gentamicin and tobramycin (at least in Moscow). Thus, it is unrealistic to exclude possible resistance when using such combinations. An additional argument against the widespread use of aminoglycosides is that their use should be accompanied by monitoring of renal function and hearing. Thus, it is clear that there is no strong evidence in favor of the widespread

use of aminoglycosides for the empirical treatment of severe community-acquired pneumonia, which, of course, does not preclude their use according to indications.

In our country, intramuscular administration of penicillin has been used for many years in the empirical treatment of pneumonia, but a change in the spectrum of pathogens, including a high percentage of Haemophilus influenzae, mycoplasma and other bacteria that are not sensitive to penicillin, has forced us to reconsider the tactics of antibacterial therapy. The emergence of penicillin-resistant strains of pneumococcus, as well as the need to administer penicillin every 3-4 hours, requires a change in the first-line drug for the treatment of ambulatory pneumonia [24], [25].

Since the 1990s, national recommendations for the treatment of pneumonia have been developed and widely disseminated in many countries of Western Europe and North America, which are designed, on the one hand, to provide highly effective medical care, and, on the other hand, to minimize the cost of treatment [26], [27], [28].

Currently, the need to introduce pharmacoeconomic approaches into everyday medical practice has become obvious for domestic medicine. Numerous pharmacoeconomic studies have proven that the cost of treating a patient is not determined by the price of the antibiotic. To a large extent, it depends on the recovery time and the costs of treating complications.

Pharmacoepidemiological studies provide information on the use of antibacterial drugs for various diseases throughout Russia and in individual regions. Pharmacoeconomics allows you to find new approaches to the most rational use of funds. The hospital should have a local passport of antibiotic resistance and a formula of antibacterial drugs developed on its basis, taking into account pharmacoeconomic indicators [8]. It is recommended to more actively use oral antibiotics and introduce stepwise therapy. Another advantage of antibacterial therapy formulas is the ability to plan and timely replenish the drug supply in the pharmacy, avoid stressful situations associated with the lack of a particular antibiotic for the treatment of a particular patient, as well as sharply reduce the list of drugs. what the hospital needs [29].

The importance of introducing a rationally structured list of antibiotics into clinical practice is associated with an unjustified high frequency of their prescription. The basis for compiling the formula is the nosological structure of patients, the microbial landscape of infectious agents, the nature and degree of their resistance to antibiotics, the results of evidence-based studies on the comparative assessment of the effectiveness of antimicrobial drugs, pharmacoeconomic analysis, as well as the real possibilities of the budget, Compulsory Health Insurance funds (CHI) and the patients themselves [30].

Among infectious diseases, bronchopulmonary diseases occupy a leading position in terms of the total volume of prescribed drugs and the financial costs of their purchase, with more than 30% of antibiotics used to treat lower respiratory tract diseases. When prescribing drugs, the cost of treatment should also be taken into account, and preference should be given to economically feasible antibiotic regimens.

CONCLUSION

Fundamental Finding : The study emphasizes the complexity of selecting appropriate antibiotic therapy for pneumonia due to challenges in early pathogen identification. Effective treatment requires a precise choice of antibacterial drugs tailored to the pathogen's sensitivity, taking into account factors such as patient age, comorbidities, and drug side effects. The importance of early and adequate antibiotic administration is highlighted, with variations in treatment strategies based on the severity of pneumonia and the patient's medical history. **Implication :** The findings suggest that healthcare providers must adopt a personalized approach to pneumonia treatment, considering factors such as drug pharmacokinetics, the patient's age, and comorbidities. Emphasis on stepwise therapy and rational antibiotic use can optimize outcomes, reduce complications, and minimize unnecessary drug use, which aligns with current global healthcare trends towards personalized medicine and pharmacoeconomics. **Limitation :** The research does not account for all possible patient factors, such as rare comorbid conditions or genetic variability that might affect antibiotic efficacy. Additionally, the reliance on available evidence might limit the applicability of the findings in regions with differing antibiotic resistance patterns. **Future Research :** Future studies should explore alternative treatment regimens and further investigate the role of pharmacogenomics in tailoring antibiotic therapy. Research could also focus on the long-term effectiveness of stepwise therapy and its impact on antibiotic resistance, particularly in diverse patient populations across different regions.

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