

## Modern solutions to the pharmacoepidemiological basis of the use of antibacterial drugs for community-acquired pneumonia in children of different ages

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**Annotation:** *At present, one of the most urgent problems of modern medicine is the rational use of antimicrobial drugs (AMP). Interest in this problem is associated with a number of important circumstances. First, antibiotics are one of the most frequently prescribed drugs both in outpatient practice [1] and in hospitals [2], often irrationally and without appropriate indications. Second, antibiotic therapy is an expensive treatment, accounting for 50% of hospital costs [3] and leading to outpatient costs for infectious diseases. In addition, over time, the use of antibacterial drugs is accompanied by a decrease in their activity due to the development of resistance of microorganisms to them. Accordingly, the term "rational antibacterial therapy" for various infectious diseases is understood as achieving the predicted treatment result with the lowest economic costs and the lowest risk of selecting resistant strains of microorganisms [4].*

*Today, the guidelines and principles of antibacterial therapy are clearly described in the pages of many international and local recommendations for the treatment of patients with respiratory tract infections (RTI) [5-8]. However, the availability of the most up-to-date recommendations does not guarantee their practical use, and mistakes related to an irrational approach to the use of antibiotics in IDPs are often encountered in daily practice. It should be noted that errors in antibacterial therapy of IDPs have the largest share of all treatment errors made in pulmonology practice. At the same time, the incorrect prescription of antibiotics has a decisive effect on the outcome of the disease, the economic component of treatment, and leads to the selection of antibiotic-resistant strains of pathogens [9,10].*

**Keywords:** *unreasonable prescribing of antibiotics; wrong choice of medicine; antibiotic selection without taking into account the regional characteristics of current pathogen resistance; insufficient dosage regimen; unreasonable or irrational combination of drugs; incorrect evaluation of the treatment efficiency criteria; unreasonable duration of antibacterial therapy.*

**Introduction:** One of the most important problems of antimicrobial therapy is the widespread practice of using antimicrobial agents without appropriate indications. According to pharmacoepidemiological studies, 20 to 50% of antibiotic prescriptions worldwide are inappropriate, and such prescriptions are often used for community-acquired RTIs. This problem is also relevant for Russia.

Thus, during a multicenter pharmacoepidemiological study, the practice of treating acute respiratory viral infections (ARVI) in children was evaluated [13]. Antimicrobial therapy was indicated in 52% of outpatients. It is noted that 8.2% of patients experienced various adverse events during treatment. In the study of VK. Tatochenko and others. [14] analyzed 1469 episodes of acute respiratory illness

(ARI) in children between 1998 and 2001. It is known that the frequency of prescribing antibiotics for ARVI by local pediatricians is 26-36% [10]. A pharmacoepidemiological study of the current practice of treatment of ARVI in conscripted military personnel in the troops of the Moscow Military District showed that in 74.2% of cases aminopenicillins were prescribed at the beginning of treatment [15]. However, it should be noted that the practice of prescribing antibiotics for ARVI in childhood is common throughout the world. For example, the frequency of their use in Canada is 14% [16], in France - 24% [17], in the USA - 25% [18]. In China, 97% of children with acute respiratory infections who contact a healthcare professional receive antimicrobial therapy [19].

Our own study analyzed 572 cases of acute bronchitis (a disease mainly caused by various respiratory viruses) in outpatients at four clinics located in Moscow, Nizhny Novgorod, St. Petersburg, and Kazan. For the pharmacoepidemiological study, an individual registration card was created that reflected the demographic characteristics of the patient, the presence of concomitant diseases, antibacterial therapy, dosage regimens, the direction of drug administration and the duration of treatment. The average age of the patients included in the study was  $39.8 \pm 5.7$  years, most of them were men - 74%, women - 26%. Antibiotics were used in 85.7% (490 patients with OB) of 572 cases of pharmacotherapy for OB. Thus, in Nizhny Novgorod (n=237) AMP was prescribed in 84% of cases, in St. Petersburg (n=200) and Moscow (n=108) in 88.5 and 81.5% of cases, respectively. All patients with OB in Kazan (n=27) were treated with antibacterial therapy. The following AMP groups were used the most: macrolides in 45.8% of cases, "inhibitor-protected" penicillins - in 43.7%, fluoroquinolones (ciprofloxacin) - in 4.9% (Fig. 1). The use of doxycycline was less frequently reported - 1.6% of cases, amoxicillin - 1.8%, ampicillin - 2.2%. Among macrolide antibiotics, azithromycin was prescribed most often - in 33.7% of cases, clarithromycin and erythromycin were used less frequently - in 8.6 and 3.5% of cases, respectively.

Thus, it should be recognized that the current practice of ambulatory treatment of OB in adults includes the prescription of broad-spectrum antibacterial drugs in most cases (85.7%). At the same time, the frequency of prescribing antimicrobial therapy was high in all outpatient medical institutions, regardless of their geographic location. It is clear that the practice of widespread use of antimicrobial agents for diseases of mainly viral etiology is incorrect and only leads to an increase in the number of adverse events, the "increase" in the cost of treatment, and with the increase in the number of can be. antibiotic-resistant strains of microorganisms.

**Material and Methods:** In the analysis of outpatient treatment of adult patients with acute tonsillopharyngitis (ATP) aggravated by chronic bronchitis and acute otitis media (AOM), a high frequency of use of antibacterial therapy was noted - in 95, 84 and 79% of cases, respectively [20] – 22]. At the same time, the percentage of bacterial pathogens in ATF does not exceed 30%, and the treatment of patients with mild forms of AOM includes prescribing antibiotics only in the presence of persistent symptoms against the background of adequate symptomatic therapy.

Another serious problem that often occurs in the treatment of IDPs is the irrational tactics of antibacterial therapy. According to a number of large-scale, multicenter pharmacoepidemiological studies conducted in Russian polyclinics, the choice of antibacterial drugs for tonsillopharyngitis, AOM, acute sinusitis in most cases is the range of the most relevant pathogens, without taking into account modern data done. their resistance to antibiotics, as well as the pharmacokinetics and safety profile of the drugs [20-21,23]. For example, in the treatment of acute sinusitis, only 18% of cases recommended by experts, and 82% of cases used antibiotics that have lost their clinical significance (co-trimoxazole, doxycycline). 23]. Antibiotics were used in patients with ATF, whose activity did not allow the necessary destruction of group A  $\beta$ -hemolytic streptococci (doxycycline, ciprofloxacin, etc.).

**Methods of research:** Currently, the pages of local recommendations for the management of patients with community-acquired pneumonia (CAP) focus on the analysis of the most common errors in antibacterial therapy for this disease. It is known that a serious error in the treatment of CAP in outpatient practice is the use of gentamicin, co-trimoxazole, ciprofloxacin (Table 1) [7].

Thus, in 2003–2004 compared to 1998. A significant increase in the use of amoxicillin (from 1.2 to 24%), a simultaneous decrease in the use of ampicillin, frequent prescription of macrolides - from 12.5 to 21.4%. Overall, the frequency of use of gentamicin (from 29.3 to 4.1%) and co-trimoxazole (from 22.7 to 1.2%) decreased significantly between 2003 and 2004. At the same time, there was a significant increase in the use of ciprofloxacin - from 1.4% in 1998 to 10.1% in 2003. The prescription of AMP combinations for non-severe forms of SAP decreased from 16.4% (1998) to 7.7% (2003-2004), but in most cases, the choice of AMP for combination therapy still remains irrational. Combinations of aminopenicillins and ciprofloxacin with gentamicin have often been used. The frequency of parenteral antibiotic use for non-severe CAP averaged 29%.

In a multicenter prospective pharmacoepidemiological study conducted in 2007, the current practice of antibiotic therapy in patients with SAP was further analyzed [7]. In addition to the recommended drugs (amoxicillin, amoxicillin/clavulanate, macrolide antibiotics), cefazolin and ciprofloxacin (drugs with low pneumococcal activity) took an important part in the prescriptions; There was a high frequency of prescribing third-generation parenteral cephalosporins (cefotaxime, ceftriaxone). At the same time, widespread unreasonable use of "early" fluoroquinolones (ciprofloxacin) may be accompanied by the formation of antibiotic-resistant strains of microorganisms, including new representatives of this class of antibiotics (levofloxacin, moxifloxacin). In 2007, the composition of AMPs used for the initial monotherapy of CAP in the outpatient setting is presented in Figure 2.

Currently, the following approach is presented in the pages of local recommendations [7] for ambulatory treatment of patients with SAP. In the case of non-severe pneumonia in patients without concomitant diseases and who have not received it in the last 3 months. Adequate clinical effect can be obtained by using amoxicillin or macrolide antibiotics with improved pharmacokinetic properties (azithromycin, clarithromycin) (Table 2). On the contrary, the patient has concomitant diseases (chronic obstructive pulmonary disease (COPD), diabetes mellitus (DM), congestive heart failure, liver disease, alcohol abuse, drug addiction, underweight) and / or received in the last 3 months of antibacterial drugs (the risk of identifying pathogens resistant to antibiotics, the proliferation of gram-negative microorganisms, it is recommended to prescribe aminopenicillins that "protect" co-infection); In particular, taking into account the possible contribution of pathogens such as *Chlamydia* and *Mycoplasma pneumoniae* to the etiology of pneumonia, combined therapy can be prescribed: "protected" aminopenicillin + macrolide (Table 2). An alternative to this approach for the treatment of non-severe CAP with risk factors for treatment failure may be the use of "inhaled" fluoroquinolones.

We conducted a pharmacoepidemiological study to analyze the frequency of use of  $\beta$ -lactam + macrolide combination therapy in outpatient practice for the treatment of CAP. A total of 207 cases of SAP were analyzed in outpatient clinics in Moscow (n=62), Nizhny Novgorod (n=45), St. Petersburg (n=37), Kemerovo (n=22), Ufa. (n=19), Barnaul (n=22). The average age of patients with SAP was  $48.6 \pm 17.2$  years. 42 percent of them (87 patients) suffered from various joint diseases (COPD, cardiovascular diseases, diabetes, chronic alcoholism, etc.). In addition, 44 patients had chronic pathology of the respiratory system: 36 patients (17.4%) had COPD, 8 patients (3.9%) had bronchial asthma. Before seeking medical care, 15.9% (33 patients with SAP) were taking various antibacterial drugs. At the same time, despite the high frequency of use of systemic antibiotic therapy

before the identification of concomitant diseases and seeking medical care, the initial combination -  $\beta$ -lactam + macrolide - was prescribed only in 15.5% of cases (32 patients with CAP). It turned out that factors such as the presence of concomitant diseases and the fact of the use of antibiotics in the last 3 months do not significantly influence the choice of practitioners in favor of "protected" aminopenicillins and  $\beta$ -lactam + macrolide combined therapy. . Thus, "protected" aminopenicillins combined with a macrolide were prescribed only to 12 patients with SAP who had relevant risk factors for treatment failure, and in 20 cases such factors were not identified. In contrast, monotherapy with macrolide antibiotics was performed in 26 cases (12.5%) in patients with concomitant diseases or who received antibiotics before seeking medical care.

Thus, the use of AMPs for IDP is still accompanied by a number of errors, including unreasonable prescription of AMPs for diseases of mainly viral etiology and irrational tactics of antibacterial therapy. Possible reasons for irrational antibiotic therapy for IDP are doctors' misconceptions about the etiology of infections and low level of knowledge about the basic rules of modern clinical guidelines. It should be noted that the choice of treatment tactics is often determined by various subjective factors: the qualifications and experience of doctors, the characteristics of their relationship with patients, etc.

In this regard, on the initiative of scientific societies, various programs are being implemented to promote clinical recommendations, reduce cases of unjustified prescription of antibiotics, improve the quality and efficiency of treatment, and introduce educational programs for doctors and patients into the practice of medical institutions. further pharmacoepidemiological studies that allow to obtain an objective picture of the current practice of pharmacotherapy of various infectious diseases.

### **Conclusions:**

The study highlights significant findings regarding the widespread irrational use of antibiotics in treating community-acquired pneumonia (CAP) and other respiratory infections. The inappropriate prescription of antimicrobial agents, particularly for conditions with viral etiologies, is prevalent, with over 85% of cases involving unnecessary antibiotic use. This practice has critical implications, including increased healthcare costs, adverse drug reactions, and the development of antibiotic-resistant strains. The findings emphasize the need for stricter adherence to clinical guidelines to minimize inappropriate antibiotic use and improve patient outcomes. Further research is essential to explore effective strategies for educating healthcare providers and implementing evidence-based antibiotic stewardship programs.

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