## Regional specifics of microbial landscape in outpatients with lower respiratory tract infections

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**BACKGROUND:** The last years have witnessed progressive growth of antimicrobial resistance (AMR) both in hospital-acquired and community-acquired respiratory infections. Regional guidelines (2006) presented standard approaches to pharmacotherapy and provided an important contribution to improvement of antimicrobial therapy at healthcare facilities of both the City of Stavropol and the Stavropol Region. At the same time, recent years have witnessed substantial changes in sensitivity to antimicrobials; besides, newer antibiotics have become available now. This substantiates the need for update of the regional guidelines [1].

**OBJECTIVE:** To determine the issues related to standardization of antibiotic therapy of lower respiratory tract (LRT) infections at an outpatient setting; to assess regional changes (2007–2012) in the spectrum of pathogens causing LRT diseases in patients of the regional healthcare facilities in view of their age and the diagnosis as compared with the years of 2003–2006.

**METHODS:** In 2007–2012, we examined sputum microbiology of patients with LRT infections at the bacteriological laboratory of the Centre for Clinical Pharmacology and Pharmacotherapy (Stavropol, Russia), following the methodology guidelines [2]. The comparison was carried out with the results of the microbiological examination of 7051 sputum samples (held in 2003–2006). Statistical analysis was carried out using arithmetic means, standard errors, and Student's t test involving a software package STATISTICA 6.0.

**RESULTS:** In the outpatient practice, half of the patients with LRT infections were identified to have *Str. Pneumoniae*. The sputum of every fifth examined patient allowed isolating *Enterobacteriaceae* family members such as *Klebsiella spp.* (*Klebsiella pneumoniae* in most cases), *Serratia spp.*, *E. coli, and Enterobacter spp.* It is essential to note that almost a quarter of the patients were found to have *M. pneumoniae*. *C. Pneumoniae* was detected quite often as well (19%). *Str. pneumoniae*, *M. pneumoniae*, and *C. pneumoniae* were found in virtually 80% of all the cases of community-acquired pneumonia in adults. *H. influenzae* and *M. pneumoniae* were 2-3 times more often isolated from the sputum of patients with chronic obstructive pulmonary disease (COPD) and chronic non-obstructive bronchitis.

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Along with an increase in the patients' age, regardless of the diagnosis, the proportion of pneumococci, *Haemophilus influenzae* and various members of the *Enterobacteriaceae* family went up, while the share of mycoplasmas went down. However, even in patients over 60 years of age *M. pneumoniae* accounted for a significant share in the overall spectrum of pathogens, which indicates the need for microbiological monitoring, especially as far as COPD is concerned.

In contrast to the previous years, only 35% of the patients (previously 60%) underwent bacteriological examination (p<0.05) while receiving antibiotic therapy. Significant prevalence of mycoplasmas in the structure of the isolated microorganisms was found in patients who had been previously treated with  $\beta$ -lactam antibiotics.

Associations of pathogens were detected in 14% of cases, which is half the rate found 2-3 years ago. The associations were found to reveal more frequent presence of *H. influenzae* in patients with acute exacerbation of chronic non-obstructive bronchitis, and *Enterobacteriaceae* – in patients with COPD and pneumonia. The recent years have shown that, combined with other microorganisms, there can be detected pneumococci (p<0.05), *H. influenzae*, as well *M. pneumoniae*, while there have been fewer cases of enterococci and enterobacteria; as for non-filterable bacteria, they have been never detected again (p<0.05).

Strains of *H. influenzae* maintained high sensitivity to aminopenicillins, including the protected ones. The antibiotic resistance possessed by *Str. pneumoniae* to aminopenicillins doubled (12.4% strains vs. 6.4% 3 years ago, p<0.05). The resistance to Co-trimoxazole and Ofloxacin was 27.9% and to macrolides it was 17.9%. Various representatives of the *Enterobacteriaceae* family maintained high sensitivity to aminopenicillins, second and third generation cephalosporins, fluoroquinolones.

Of the 20 *M. pneumoniae* strains that were tested, 8 (40%) displayed resistance to one or more antimicrobials. The highest numbers of cases with resistance were detected to Ciprofloxacin (25%) and Erythromycin (20%). 10% strains of mycoplasma showed resistance to Doxycycline and Ofloxacin, while only 5% of mycoplasmas were identified as having non-sensitivity to Clarithromycin and Azithromycin.

**CONCLUSIONS:** The results of the research carried out in the recent years in comparison with the data of the previous years, call for reviewing of the standard approaches to the choice of antimicrobial agents in respiratory tract infections. In order to improve the standard of care, the choice of medicines should be based on a number of factors, namely the age, the severity of the respective pathological condition, previous antimicrobial use, and the level of care.

Keywords: Antimicrobial resistance, respiratory tract infections, antimicrobial agents

**Conflict of interest statement:** The Center For Clinical Pharmacology And Pharmacotherapy (Stavropol, Russia) has offered free access to the data obtained through the microbiological examination of sputum samples in cases of respiratory tract infections.

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