CURRENT STATE OF ANTIMICROBIAL RESISTANCE OF *S. PNEUMONIAE* IN RUSSIA: RESULTS OF PROSPECTIVE MULTICENTER STUDY (PeHASus-I, PHASE «B»)

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Abstract

Purpose: To determine the antimicrobial resistance of clinical strains *S. pneumoniae* isolated in adults and children.

Methods: This study was conducted in 20 cities (Chelyabinsk, Ekaterinburg, Irkutsk, Yakutsk, Yaroslavl, Kazan, Kovrov, Krasnodar, Moscow, N. Novgorod, Novosibirsk, Novokuznetsk, Saint Petersburg, Smolensk, Stavropol, Tyumen, Tomsk, Ryazan, Ufa, Voronezh) in different regions of Russia in 2001-2002. Identification of the strains was done on the basis of colony morphology, Gram stain, optochin susceptibility and bile solubility tests. Susceptibility to penicillin G (PEN), amoxicillin (AMO), amoxicillin/clavulanate (AMC), cefotaxime (CTX), cefepime (CFP), imipenem (IMP), erythromycin (ERY), azithromycin (AZI), clarithromycin (CLA), midecamycin (MID), clindamycin (CLI), telithromycin (TEL), levofloxacin (LEV), moxifloxacin (MOX), tetracycline (TET), co-trimoxazole (SXT), chloramphenicol (CHL), vancomycin (VAN) was determined by broth microdilution. Breakpoints were those of NCCLS (2002) except for TEL (⩽ 0.5; 1-2, ⩾ 4 mg/L) and MID (⩽ 1; 2-4, > 4 mg/L) for susceptible, intermediate resistant and resistant isolates, respectively.

Results: The total of 581 non-duplicate clinical strains of *S. pneumoniae* were included in this study. The susceptibility testing results are presented in the Table 1.

Conclusions: All β-lactams retained high activity against *S. pneumoniae*. High resistance to TET and SXT compromises their usage for the empirical therapy of pneumococcal infections. LEV, MOX, TEL and VAN demonstrated excellent *in vitro* activity against both penicillin- and macrolide-resistant strains.

Table 1. Non-susceptibility rates, MIC_{90s} and MIC ranges of isolated S. pneumoniae

Antimicrobial	MIC breakpoints			I/R%	MIC_{90}, mg/L	MIC range, mg/L
	S	I	R			
PEN	⩽0.06	0.12-1	⩾2	8.3/1.9	0.125	0.008-2
AMO	⩽2	4	⩾8	0	0.06	0.03-2
AMC	⩽2	4	⩾8	0	0.06	0.03-2
CTX	⩽0.5*/1	1/2	⩾2*/4	0.2/0*	0.03	0.008-1
CFP	⩽0.5*/1	1/2	⩾2*/4	0.2/0*	0.125	0.008-2
IMP	⩽0.12	0.25-0.5	⩾1	2.6/0.3	0.06	0.008-2
ERY	⩽0.25	0.5	⩾1	0.2/8.8	0.06	0.016-128
AZI	⩽0.5	1	⩾2	0.5/8.3	0.125	0.03-128
CLA	⩽0.25	0.5	⩾1	0.5/8.1	0.06	0.016-128
MID	⩽1	2	⩾4	0.5/4.0	0.5	0.05-128
CLI	⩽0.25	0.5	⩾1	0.2/3.3	0.03	0.016-128
TEL	⩽0.5	1-2	⩾4	0	0.03	0.004-0.25
LEV	⩽2	4	⩾8	0	1	0.25-2
MOX	⩽1	2	⩾4	0	0.125	0.015-0.5
TET	⩽2	4	⩾8	2.4/25.1	16	0.25-64
SXT	⩽0.5	1-2	⩾4	26.5/5.0	2	0.06-16
CHL	⩽4	–	⩾8	0/8.6	4	0.5-16
VAN	⩽1	–	–	0	0.5	0.06-1

* – for non-invasive isolates

Introduction

S. pneumoniae is one of the most common bacterial pathogens in children and adults causing community-acquired respiratory tract infections (e.g. acute otitis media, sinusitis, pneumonia, meningitis etc.) which are among the most frequent reasons for seeking of medical advice. Currently the prevalence of antibiotic resistance is increasing globally. For the time being, β-lactams, macrolides and fluoroquinolones are recommended as drugs of choice for the variety of pneumococcal infections. Situation with resistance is not uniform and there are substantial differences in patterns of resistance do exist between countries and regions. Thus, regional and local data on resistance are of extreme importance.

Purpose

To determine the antimicrobial resistance of clinical strains *S. pneumoniae* isolated in adults and children in different regions of Russia.

Methods

This study was conducted in 20 cities (Chelyabinsk, Ekaterinburg, Irkutsk, Yakutsk, Yaroslavl, Kazan, Kovrov, Krasnodar, Moscow, N. Novgorod, Novosibirsk, Novokuznetsk, Saint Petersburg, Smolensk, Stavropol, Tyumen, Tomsk, Ryazan, Ufa, Voronezh) in Russia (Fig. 1). Identification of the strains was done on the basis of colony morphology, Gram strain, optochin susceptibility and bile solubility tests. Susceptibility testing was performed using cation-adjusted Mueller-Hinton broth (BBL, USA) with 2-5% lysed horse blood. Microtiter plates were incubated for 24 h at 35°C at ambient air. *S. pneumoniae* ATCC 49619 was used for quality control. Interpretation of results was done according to NCCLS guidelines (2002).

Fig. 1. Distribution of centers participated in the study

Results

A total of 581 non-duplicate clinical strains of *S. pneumoniae* isolated from patients of 1 month to 87 years were included in this study. Clinical specimens from which *S. pneumoniae* have been isolated are presented in Fig. 2. The majority of strains were isolated from respiratory specimens (89%) and 4% – from sterile sources.

The percentages of non-susceptible (intermediately resistant plus resistant) to tested antimicrobials isolates are presented in Fig. 3. The MIC distribution of PEN, ERY, CLI, MID, TET and SXT are presented on Fig. 4-9.

The majority 61.5% (32 of 52) of erythromycin-resistant *S. pneumoniae* retained susceptibility to 16-membered macrolides (midecamycin) and clindamycin, indicating M-phenotype of resistance (Fig. 10).

Fig. 2. Distribution of clinical specimens

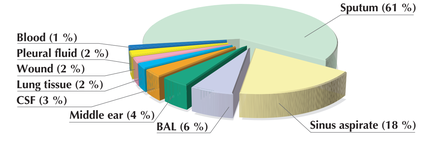


Fig. 3. Non-susceptibility rates (%) of S. pneumoniae in Russia

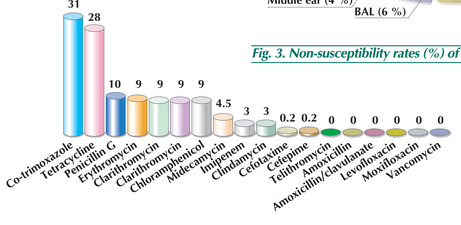


Fig. 4. MIC_S distribution of penicillin G

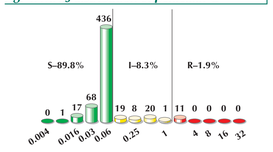


Fig. 5. MIC_S distribution of erythromycin

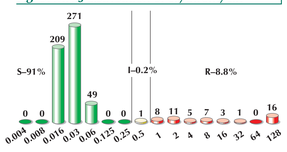


Fig. 6. MIC_S distribution of midecamycin

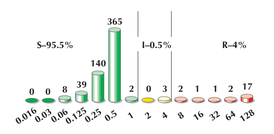


Fig. 7. MIC_S distribution of clindamycin

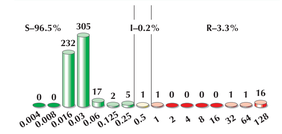


Fig. 8. MIC_S distribution of co-trimoxazole

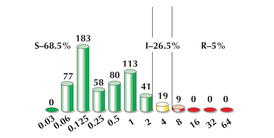


Fig. 9. MIC_S distribution of tetracycline

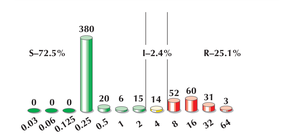
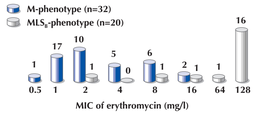


Fig. 10. Phenotypes of macrolide-resistant S. pneumoniae



Conclusions

All β-lactams and macrolides retained high activity against *S. pneumoniae*. These antimicrobials still might be considered as drugs of choice for empirical treatment of pneumococcal infections.

Majority (61.5%) of erythromycin-resistant strains possessed M-phenotype of resistance.

High (>25%) non-susceptibility to TET and SXT significantly compromises possibility of their usage for the empirical therapy of infections caused by *S. pneumoniae*.

There was no resistance detected to LEV, MOX, TEL and VAN.