

COMPARISON OF ANTIMICROBIAL RESISTANCE OF *S. PNEUMONIAE* IN RUSSIA IN 1999-2000 AND 2001-2002 (PeHASus-I PROJECT)

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Abstract

The purpose of this study was to compare antimicrobial resistance of clinical strains of *S. pneumoniae* isolated in different Russian regions.

Identification of 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), erythromycin (ERY), azithromycin (AZI), clarithromycin (CLA), midecamycin (MID), clindamycin (CLI), levofloxacin (LEV), tetracycline (TET), co-trimoxazole (SXT), chloramphenicol (CHL) and vancomycin (VAN) was determined by broth microdilution. Breakpoints were those of NCCLS (2002) except for MID (≤ 1 ; 2-4; > 4 mg/L) for susceptible, intermediate resistant and resistant isolates, respectively.

A total of 210 and 581 pneumococci, respectively were isolated in 15 Russian centers in 10 cities in 1999-2000 and 25 centers in 21 cities in 2001-2002. The susceptibility testing results are presented in the Table.

Table. Percentage on intermediate resistant and resistant isolates of *S. pneumoniae*

Antimicrobial	MIC breakpoints			I/R%, 1999-2000	I/R%, 2001-2002	p
	S	I	R			
PEN	≤ 0.06	0.12-1	≥ 2	7.0/2.0	8.3/1.9	ND
AMO	≤ 2	4	≥ 8	0/0.5	0	ND
AMC	≤ 2	4	≥ 8	0/0.5	0	ND
CTX	$\leq 0.5^*/1$	1/2	$\geq 2^*/4$	1/1*	0.2/0*	ND
CFP	$\leq 0.5^*/1$	1/2	$\geq 2^*/4$	0.5/1.5*	0.2/0*	ND
ERY	≤ 0.25	0.5	≥ 1	0/6.0	0.2/8.8	ND
AZI	≤ 0.5	1	≥ 2	0.5/5.5	0.5/8.3	ND
CLA	≤ 0.25	0.5	≥ 1	0.5/5.5	0.5/8.1	ND
MID	≤ 1	2	> 4	4.0/2.0	0.5/4.0	ND
CLI	≤ 0.25	0.5	≥ 1	0/2.0	0.2/3.3	ND
LEV	≤ 2	4	≥ 8	0	0	ND
TET	≤ 2	4	≥ 8	2.0/25.0	2.4/25.1	ND
SXT	≤ 0.5	1-2	≥ 4	26.0/7.0	26.5/5.0	ND
CHL	≤ 4	-	≥ 8	0/5.0	0/8.6	ND
VAN	≤ 1	-	-	0	0	ND

* - for non-invasive isolates

In general, there were no statistically significant differences in non-susceptibility rates found between 1999-2000 and 2001-2002. All β -lactams and macrolides retained high *in vitro* activity against *S. pneumoniae*. High resistance to TET and SXT compromises their usage for the empirical therapy of pneumococcal infections. LEV and VAN demonstrated excellent *in vitro* activity against both penicillin- and macrolide-resistant strains.

Introduction

Streptococcus pneumoniae is a leading cause of community-acquired respiratory tract infections. Currently community-acquired respiratory tract infections are significant medical problem as the prevalence of pneumococcal resistance to β -lactams, macrolides and fluoroquinolones is increasing globally. 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.

Study Objective

To compare the antimicrobial resistance of clinical strains of *S. pneumoniae* isolated in adults and children in 1999-2000 and 2001-2002 in different regions of Russia.

Materials and Methods

This study was conducted in 15 centers in 1999-2000 (Kazan, Krasnodar, Moscow, Nizhniy Novgorod, Novosibirsk, Saint Petersburg, Smolensk, Tomsk, Ryazan, Stavropol, Tyumen, Ufa, Yakutsk, Yaroslavl) (Fig.1) and in 25 centers in 2001-2002 (Chelyabinsk, Irkutsk, Kazan, Kovrov, Krasnodar, Moscow, Nizhniy Novgorod, Novokuznetsk, Novosibirsk, Roslavl, Ryazan, Saint Petersburg, Smolensk, Stavropol, Tomsk, Tyumen, Ufa, Yakutsk, Yaroslavl, Yartsevo, Yekaterinburg) in Russia (Fig. 2).

Fig. 1. Distribution of centers participated in the study in 1999-2000



Identification of strains was done on the basis of colony morphology, Gram stain, 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. 2. Distribution of centers participated in the study in 2001-2002



Results

The total of 210 (1999-2000) non-duplicate clinical strains of *S. pneumoniae*, isolated from patients of 1 month to 78 years of age and 581 strains (2001-2002), isolated from patients of 1 month to 87 years of age were included in this study. Clinical specimens from which *S. pneumoniae* have been isolated are presented in Fig. 3-4. In 1999-2000 the majority of strains were isolated from sputum (62%), CSF (9.5%), sinus aspirate (8.7%), middle ear fluid (6.7%) and BAL (6.2%). In 2001-2002 – from sputum (61%), sinus aspirate (18%), BAL (6%), middle ear (4%) and CSF (3%).

Fig. 3. Distribution of clinical specimens in 1999-2000

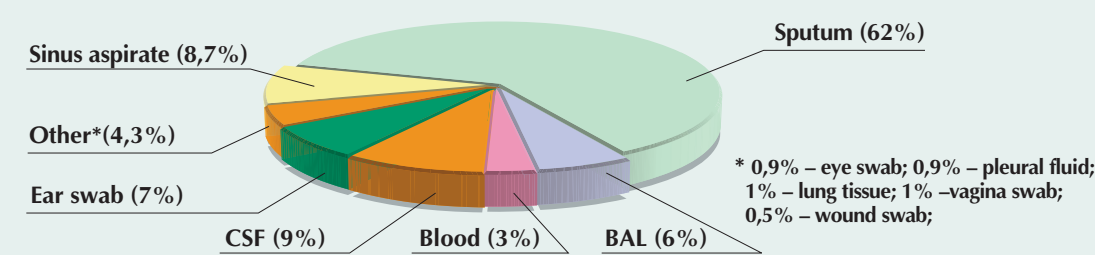
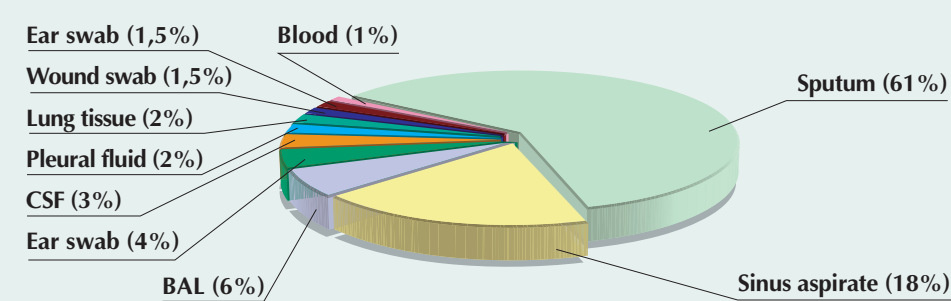
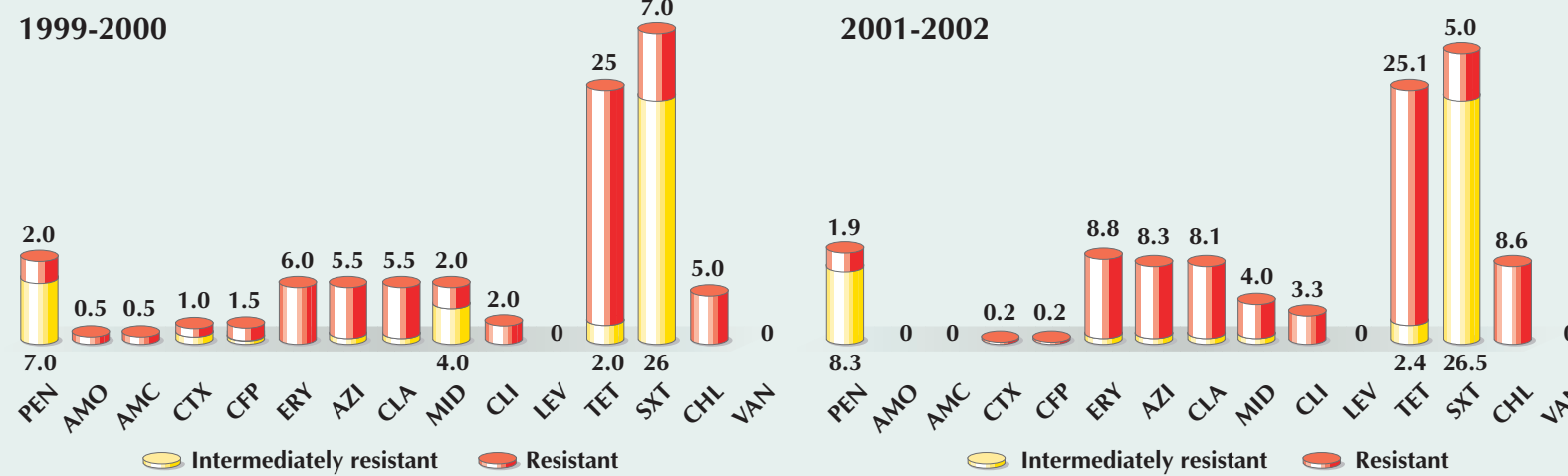


Fig. 4. Distribution of clinical specimens in 2001-2002



The percentages of non-susceptible (intermediately resistant plus resistant) to tested antimicrobials isolates are presented in Fig. 5.

Fig. 5. Resistance of *S. pneumoniae* in Russia (%)



The majority of erythromycin-resistant *S. pneumoniae* in 1999-2000 and in 2001-2002 retained susceptibility to 16-membered macrolides (midecamycin) and clindamycin (M-phenotype) – 77% (10 of 13) and 61.5% (32 of 52), respectively.

Conclusions

- The rates of pneumococcal resistance between 1999-2000 and 2001-2002 in Russia have no significant differences.
- β -lactams (amoxicillin, amoxicillin/clavulanate, cefotaxime) possessed high activity against tested *S. pneumoniae*. These antimicrobials still might be considered as drugs of choice for empirical treatment of pneumococcal infections.
- Macrolide resistance in pneumococci did not exceed 9% to 14- and 15-membered compounds. Clindamycin retained activity against majority of erythromycin-non-susceptible strains.
- High rates ($> 25\%$) of non-susceptibility to TET and SXT significantly compromises their usage for the empirical therapy of infections caused by *S. pneumoniae*.
- LEV and VAN were active against all strains independently on their resistance to other classes of antimicrobials.