ANTIMICROBIAL RESISTANCE OF NOSOCOMIAL STRAINS OF *S. AUREUS* ISOLATED FROM PATIENTS WITH SKIN AND SOFT TISSUE INFECTIONS IN RUSSIA

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Introduction and Purpose

Staphylococcus aureus is one of the leading causes of nosocomial wound infections. Thus, according to the data from National Nosocomial Infections Surveillance System (NNIS, USA) this pathogen is responsible for 19% of postoperative wound infections. At the same time the resistance rates of *S. aureus* to commonly used antimicrobials has increased recently and its rate varies significantly among different regions and countries. One of the main problems is increased prevalence of methicillin-resistant strains, which are resistant not only to all beta-lactams, but also to other classes of antibiotics including macrolides, lincosamides, aminoglycosides, tetracyclines, chloramphenicol, fluoroquinolones.

Success of antimicrobial therapy depends on appropriateness of the choice of antibiotics that should be based on the known susceptibility of causative pathogen. But on the other hand in the majority of cases clinicians have to start therapy empirically and local susceptibility data plays the key role in the choice of antimicrobials.

The main objective of this study was to determine *in vitro* activity of antimicrobials against *S. aureus* isolated from hospitalised patients with wound infections in different regions of Russia.

Methods

A total of 624 *S. aureus* strains isolated from patients with nosocomial wound infections were studied. Patients were hospitalized in 17 hospitals in different parts of Russia - 4 in Central region, 2 in North-West region, 3 in South region, 2 in Volga region, 3 in Ural region, 3 in Siberia. Susceptibility testing was performed by agar dilution method according to NCCLS recommendations. Double series dilutions in Muller-Hinton agar (Beckton Dickenson, USA) of the following antimicrobials were used: chloramphenicol (Fluka, Germany), ciprofloxacin (Sigma, Germany), clindamycin (Sigma, Germany), erythromycin (Sigma, Germany), fusidic acid (Leo Pharmaceutical, Denmark), gentamicin (Sigma, Germany), levofloxacin (Aventis Pharma, France), lincomycin (Sigma, Germany), linezolid (Pharmacia, USA), moxifloxacin (Bayer, Germany), mupirocin (GlaxoSmithKline, United Kingdom), oxacillin (Sigma, Germany), quinupristin/dalfopristin (Aventis Pharma, France), rifampicin (Fluka, Germany), teicoplanin (Sigma, Germany), tetracycline (Sigma, Germany), trimethoprim/sulfamethoxazole (Sigma, Germany), vancomycin (Eli Lilly, USA).

Susceptibility testing results were interpreted in accordance with NCCLS recommendations with the exception of fusidic acid, mupirocin, moxifloxacin and lincomycin. Recommendations of Antibiotic Committee of French Microbiological Society (Comite de l'Antibiogramme de la Societe Francaise de Microbiologie) were used for fusidic acid. Results of susceptibility testing to mupirocin were interpreted according to manufacture's recommendations. There where no available interpretation criteria for moxifloxacin and lincomycin.

S. aureus ATCC 29213 was used as a control strain for susceptibility testing.

Results and Discussion

Majority of strains (45%) were isolated from patients hospitalized in general surgical units, 25% of patients were hospitalized in burn units, 14.9% - in traumatology/orthopedic units, 8% - in ICUs, 4.5% - in neonatal units, 2.6% - in general medical units (figure).

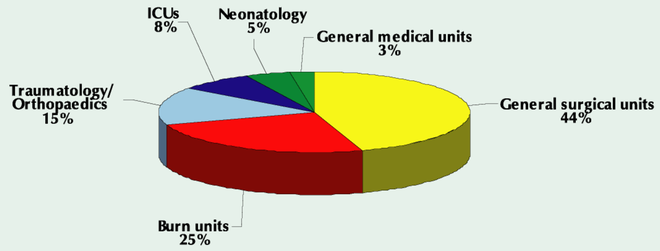

Figure. Units from which tested strains were isolated

Among all tested antimicrobials the most potent were glycopeptides (vancomycin and teicoplanin), linezolid and fusidic acid with all strains susceptible to these agents. MIC_{50}, MIC_{90}, MIC ranges and MIC distributions are shown in the tables 1 and 2.

Low resistance rates to the following agents were found:

mupirocin - only 2 (0.3%) strains from one hospital in Novosibirsk with low level of resistance (MIC=16 mg/L) were detected;

trimethoprim/sulfamethoxazole - 7 (1.1%) strains were resistant;

quinupristin/dalfopristin - 12 (1.9%) non-susceptible strains, 2 of them were resistant and 10 - intermediately resistant;

rifampicin - 47 (7.5%) strains were non-susceptible, from which 23 were resistant and 24 intermediately resistant.

Activity of fluoroquinolones varied among compounds.

Among all tested strains 8.3% of isolates were non-susceptible to levofloxacin compared to 12.5% of strains non-susceptible to ciprofloxacin. Levofloxacin had lower MIC_{50} and MIC_{90} (0.25 and 0.5 mg/L, respectively) than ciprofloxacin (0.5 and 4.0 mg/L, respectively). Moxifloxacin was the most active fluoroquinolone with MIC_{50}=0.06 mg/L, MIC_{90}=0.125 mg/L.

High resistance rates were detected to the following antimicrobials:

lincosamydes - among all tested strains 29% were non-susceptible (28.8% - resistant, 0.2% - intermediately resistant) to clindamycin. Lincomycin with MIC_{50}=2 mg/L and MIC_{90}=256 mg/L was noticeable less active than clindamycin. In addition among staphylococci susceptible to clindamycin 21 strains had MIC for lincomycin equal or higher than 64 mg/L;

gentamicin - 32.9% of strains were resistant;

tetracycline - resistance was detected in 37.7% of strains;

erythromycin - 41.2% of strains were non-susceptible including 40.1% of resistant strains and 1.1% intermediate resistant.

chloramphenicol - 47% of tested staphylococci were non-susceptible (46.5%-resistant, 0.5% - intermediately resistant).

Table 1. Results of susceptibility testing

	I+R, %	MIC_{50}/MIC_{90}, mg/L	MIC ranges, mg/L
Vancomycin	0	1/1	0.5-4
Linezolid	0	2/2	1-4
Fusidic acid	0	0.125/0.125	0.03-2
Mupirocin	0.3	0.25/0.25	0.125-16
Trim./Sulfa.	1.1	0.125/0.5	0.06-64
Quinu./Dalfo.	1.9	0.5/1	0.125-16
Rifampicin	7.5	0.03/0.03	<0.03-128
Levofloxacin	8.3	0.25/0.5	0.06-16
Ciprofloxacin	12.5	0.5/4	0.125-64
Clindamycin	29	0.125/256	0.06->256
Gentamicin	32.9	0.5/256	0.125->256
Oxacillin	35.9	0.5/128	0.125->256
Tetracycline	37.7	0.5/64	0.125-256
Erythromycin	41.2	0.5/256	0.125->256
Chloramphenicol	47	8/128	0.5-256
Lincomycin	NA	2/256	0.25->256
Moxifloxacin	NA	0.06/0.125	<0.015-4

Table 2. MICs distribution (%) of antibiotics tested

Antibiotic	MIC, mg/L														
	≤0.015	0.03	0.06	0.125	0.25	0.5	1	2	4	8	16	32	64	128	≥256
Oxacillin				0.8	16.5	39.4	5.8	1.6	1.4	0.8	1.8	10.4	9.9	5.3	6.3
Vancomycin						7.1	86.8	6.1	0.2						
Teicoplanin						7.7	65.9	25.8	0.6						
Linezolid							7.7	90.2	2.1						
Fusidic acid		2.9	21.3	66.5	7.9	0.3	0.5	0.6							
Cotrimoxazole			49.0	31.9	8.6	5.1	2.1	2.2	0.3	0.3	0.3		0.2		
Erythromycin				1.6	14.2	43	0.9	0.2							40.1
Clindamycin			1.3	62.5	5.1	2.1	0.2								28.8
Lincomycin*					0.2	0.3	30.9	36.4	0.5			0.2	1.4	0.6	29.5
Gentamicin				0.2	4.2	58.3	4.2		0.3			0.5	0.5	17.2	14.6
Mupirocin				44.6	50.5	3.0	1.4	0.2			0.3				
Rifampicin		90.4				0.5	1.6	3.9	0.3		0.5	1.0	1.0	0.8	
Tetracycline				1.6	24.6	34.0	1.9		0.2		0.2	3.8	24.4	8.2	1.1
Chloramphenicol						0.2		0.2	21.3	31.4	0.5	0.5	27.4	18.3	0.2
Quinupristin/dalfopristin				0.8	19.7	52.7	24.8	1.6	0.2		0.2				
Ciprofloxacin				0.3	11.5	70.5	5.1	2.4	1.9	0.2	1.8	2.4	3.9		
Levofloxacin			0.2	22.9	57.1	10.3	1.3	1.4	0.3	4.6	1.9				
Moxifloxacin*	5.3	21.3	53.6	10.3	1.1	1.4	1.6	3.5	1.9						

Susceptible
Intermediate
Resistant

* No recommendations for interpretation of susceptibility testing results available

Conclusions

- The overall rate of methicillin-resistance was 35.9%.
- The most potent antimicrobials were linezolid, vancomycin and fusidic acid, to which no resistant strains were found, followed by quinupristin/dalfopristin, mupirocin and co-trimoxazole with rates of resistance lower than 5%.
- Macrolides, lincosamydes, tetracyclines and chloramphenicol should not be used for the empiric therapy of nosocomial wound infections caused by *S. aureus.*