ANTIMICROBIAL RESISTANCE OF *STAPHYLOCOCCUS AUREUS* NOSOCOMIAL BLOOD ISOLATES IN RUSSIAN ICUS

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ABSTRACT

Background. *S. aureus* is a common cause of bacteremia. Due to high mortality the early administration of effective therapy based on the data on antimicrobial susceptibility is crucial.

Objectives. To evaluate the susceptibility of nosocomial strains of *Staphylococcus aureus* isolated from blood in ICUs in different parts Russia.

Methods. A total of 143 *S.aureus* strains isolated in 2004-2005 from patients with bacteremia hospitalized in ICUs in different parts of Russia, were studied. Antimicrobials tested: chloramphenicol (CHL), ciprofloxacin (CIP), clindamycin (CLI), co-trimoxazole (CTX), erythromycin (ERY), fusidic acid (FUS), gentamicin (GEN), levofloxacin (LEV), linezolid (LNZ), oxacillin (OXA), rifampin (RIF), tetracycline (TET), vancomycin (VAN). Antimicrobial susceptibility testing was performed by agar dilution method according to CLSI/NCCLS guidelines (2006).

Results. Results of susceptibility testing are presented in the table.

Conclusions. 1) high rate of MRSA (86%) was found that do not allow to use beta-lactams in ICU patients with staphylococcal bacteremia; 2) the most active antimicrobials with all strains susceptible were vancomycin and linezolid; 3) other antimicrobials with high in vitro activity were fusidic acid and co-trimoxazole. 4) high rates of resistance to fluoroquinolones, aminoglycosides, lincosamides, tetracyclines and chloramphenicol were revealed.

Antimicrobial	I/R, %	MIC$_{50}$/MIC$_{90}$, mg/L	MIC ranges, mg/L
CHL	0.7/62.9	64/64	4-128
CIP	4.9/58.0	16/64	0.125-128
CLI	0/47.6	0.06/512	0.03-512
CTX	0/8.4	0.06/2	0.03-8
ERY	2.1/60.8	512/512	0.125-512
FUS	0/0	0.125/0.25	0.015-0.25
GEN	0.7/58.7	128/512	0.25-512
LEV	11.2/36.4	2/8	0.125-16
LNZ	0/0	2/2	0.5-2
OXA	0/86.0	64/256	0.25-512
RIF	2.8/26.6	0.015/64	0.015-256
TET	0/54.6	64/256	0.125-256
VAN	0/0	1/1	0.25-2

INTRODUCTION

Bacteremia caused by *Staphylococcus aureus* continues to be a common problem worldwide. In the pre-antibiotic era the associated death rate for this condition was as high as 82%. Even with antimicrobial drug treatment, mortality rates remain high, especially for infections caused by oxacillin-resistant strains (ORSA).

Antimicrobial drug resistance in *S. aureus* arose early after the development of antimicrobial agents and continues to evolve. An increased prevalence of oxacillin-resistant strains that display resistance not only to all beta-lactams, but frequently also to other classes of antibiotics is the core problems. The problem of antimicrobial resistance is particularly warring in patients with severe infections, accompanied by bacteremia, because of patient's conditions and very high mortality rate when inappropriate initial antimicrobials are used. In Russia, as in majority of other countries, at least nosocomial strains are frequently oxacillin resistant and resistant to majority of other antimicrobials. This resistance limits the choice of potentially efficacious agents and results in frequent use of glycopeptides. The reliance on vancomycin causes difficulties because vancomycin has been shown to be less effective than antistaphylococcal β-lactams (e.g., oxacillin) in treating severe infections caused by *S. aureus*.

There is a common knowledge that every country, region and hospital needs local epidemiological data on resistance pattern. At the same time in Russia it is impossible to summarize separate data from diverse laboratories all over the country due to variety of standards applied for susceptibility testing. Simple application of features from foreign studies may lead to serious mistakes due to significant differences in antibiotic prescribing policy which is very likely to cause a noticeable discrepancy in resistance patterns. So, the aim of this study was to determine in vitro activity of antimicrobials towards *S. aureus* isolated from blood of patients hospitalised in ICUs in different regions of Russia.

MATERIALS AND METHODS

A total of 143 clinical strains of *S. aureus* isolated from patients with nosocomial infections hospitalized in ICUs in 24 hospitals in 16 cities in different parts of Russia, were included in the study: Voronezj, Ekaterinburg (2 centers), Kazan, Krasnodar (2 centers), Krasnoyarsk (2 centers), Moscow (4 centers), Novosibirsk, Omsk, Perm, Saint Petersburg (2 centers), Smolensk, Tomsk, Tyumen, Ufa, Chelyabinsk, and Yaroslavl. Geographical distribution of centres participating in the study presented in the Figure 1.

Figure 1. Geographical distribution of centres participating in the study.

Susceptibility testing was performed by agar dilution method according to CLSI/NCCLS recommendations (2006). Double series dilutions in Muller-Hinton agar (Beckton Dickinson, 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), linezolid (Pharmacia, USA), moxifloxacin (Bayer, Germany), mupirocin (GSK, UK), oxacillin (Sigma, Germany), rifampicin (Fluka, Germany), tetracycline (Sigma, Germany), trimethoprim/sulfamethoxazole (Sigma, Germany), vancomycin (Eli Lilly, USA). Susceptibility testing results were interpreted in accordance with CLSI/NCCLS recommendations (2006) with the exception of fusidic acid and lincomycin for which the recommendations of Antibiotic Committee of French Microbiological Society (Comitee de l'Antibiogramme de la Societe Francaise de Microbiologie, 2004) were used. *S. aureus* ATCC 29213 was used as a control strain for susceptibility testing.

RESULTS

The most frequently (52.4%) strains of *S. aureus* were isolated from blood of the patients with diagnosis "sepsis" without the indication of specific site of infection. The most common source of bacteremia when indicated were skin and soft tissue infections (16.1%), pneumonia (15.4%), and intra-abdominal infections (9.1%). Structure of clinical diagnoses is presented in the Figure 2.

IAI - intra-abdominal infections; BJI - bone and joint infections; CAI - catheter-associated infections; UTI - urinary tract infections; SSTI - skin and soft tissue infections.

Figure 2. Structure of clinical diagnoses in patients with *S. aureus* bacteremia.

Figure 3. Results of susceptibility testing.

Susceptibility rates to different antimicrobials, as well as MIC$_{50}$, MIC$_{90}$, and MIC ranges are shown in the Figure 3. The rates of cross-resistance to different antimicrobials presented in the Table 1.

The prevalence of ORSA among all tested strains was 86.0% and differs significantly depending on the centre participating in the study. Among all tested antimicrobials the most potent were linezolid, vancomycin, and fusidic acid with all strains susceptible to these agents. Sulfamethoxazole/trimethoprim have also shown the high in vitro activity - only 8.4% of strains were non-susceptible to this agent. High activity of vancomycin and linezolid corresponds to the data from all other studies available in the literature. High rates of resistance were noted to other groups of antimicrobials tested which basically correlate with available in the literature data on susceptibility of *S. aureus* isolated in ICUs.

Table 1. Cross-resistance to different antimicrobials.

CONCLUSIONS

- Very high rate of ORSA (86.0%) was found that makes very doubtful the role of β-lactams in empiric treatment of staphylococcal bacteraemia in Russia.
- The most active systemic antimicrobials with all strains susceptible were linezolid, vancomycin and fusidic acid.
- The only other systemic antimicrobial with high *in vitro* activity was sulfamethoxazole/trimethoprim with 8.4% of strains non-susceptible.
- High rates of resistance to lincosamydes, macrolides, tetracyclines, fluoroquinolones, aminoglycosides, and chloramphenicol were detected.