ANTIMICROBIAL RESISTANCE OF NOSOCOMIAL STRAINS OF *ENTEROCOCCUS* SPP. IN RUSSIA

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Introduction and Purpose

Enterococci are normal inhabitants of the gastrointestinal tract of humans and animals. At the same time enterococci are the well-recognised cause of infections in human, especially in inpatients with corresponding risk factors. *E. faecalis* is a predominant pathogen that accounts for more than 75% of all cases of enterococcal infections, followed by *E. faecium* as a cause of remaining 15-25% of cases. Other enterococci are rarely isolated from clinical specimens.

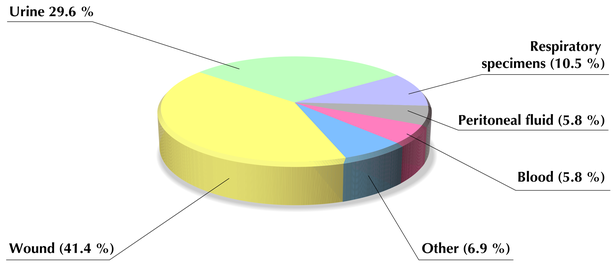
Enterococci possess several virulence factors, including adhesion-promoting factors and haemolysin/bacteriocin production. But the most important virulence factor of enterococci is the resistance to antimicrobial drugs among which the most important are high level aminoglycoside resistance, ampicillin resistance and, most recently, glycopeptide resistance. There are very limited data on antibiotic resistance of enterococci in Russia. So, the aim of our study was to determine the rates of antimicrobial resistance in nosocomial strains of *Enterococcus* spp. in Russia.

Methods

A total of 362 clinical strains of *Enterococcus* spp. isolated in 2000-2001 from patients hospitalized in 15 hospitals in different parts of Russia (Fig. 1) - 4 in Central region (Moscow, Ryazan, Smolensk), 2 in North-West region (St.-Petersburg), 2 in South region (Krasnodar), 2 in Volga region (N. Novgorod, Kazan), 2 in Ural region (Ekaterinburg), 3 in Siberia (Krasnoyarsk, Novosibirsk, Tomsk), were included in the study. Majority of patients (60.5%) included in the study were hospitalized in surgical units, 18.2% - in neonatal units, 16% and 5.3% in ICU and general medical units, respectively. Structure of clinical material from which the studied strans were isolated presented in the Figure 2. Antimicrobials tested included ampicillin (AMP), gentamicin (GEN), streptomycin (STR), vancomycin (VAN), teicoplanin (TEI), linezolid (LNZ), tetracycline (TET), chloramphenicol (CHL), ciprofloxacin (CIP), levofloxacin (LEV), moxifloxacin (MOX), quinupristin/dalfopristin (QD). Antimicrobial susceptibility testing was performed by agar dilution method. The susceptibility testing and interpretation of the results were performed according to the NCCLS guidelines (2002). *E. faecalis* ATCC 29212 was used as a control.

Fig. 1. Centres participating in the study

Fig. 2. Clinical specimens from which the studied strains were isolated



Results

Two hundred seventy three out of 362 strains (75.4%) were *E. faecalis*, 59 (16.3%) - *E. faecium*, 30 (8.3%) - *Enterococcus* spp. (*E. durans, E. raffinosus, E. gallinarum, E. avium*). Results of susceptibility testing are presented in the Figure 3 and Table 1.

The most potent antimicrobials were glycopeptides (vancomycin and teicoplanin) and linezolid with no non-susceptible strains found.

The alarmingly high rates of resistance to aminoglycosides (gentamicin and streptomycin) were detected in both *E. faecium* and *E. faecalis*: 69.5% of *E. faecium* strains were resistant to both aminoglycosides tested, 44.7% and 51.6% of *E. faecalis* strains were resistant to gentamicin and streptomycin, respectively. Ampicillin resistance was documented for 66.1% of *E. faecium* and 7% of E. faecalis. Chloramphenicol ant tetracycline were not active against 55.6% and 68.0% of tested strains, respectively. Fluoroquinolones differ in their activity: the most active was moxifloxacin with MIC_{50}/MIC_{90} 0.5/8 mg/l, followed by levofloxacin (MIC_{50}/MIC_{90} 2/8 mg/l), the least active was ciprofloxacin with MIC_{50}/MIC_{90} 2/32 mg/l.

Fig. 3. Non-susceptibility (R + I) of tested strains to antimicrobials, %.

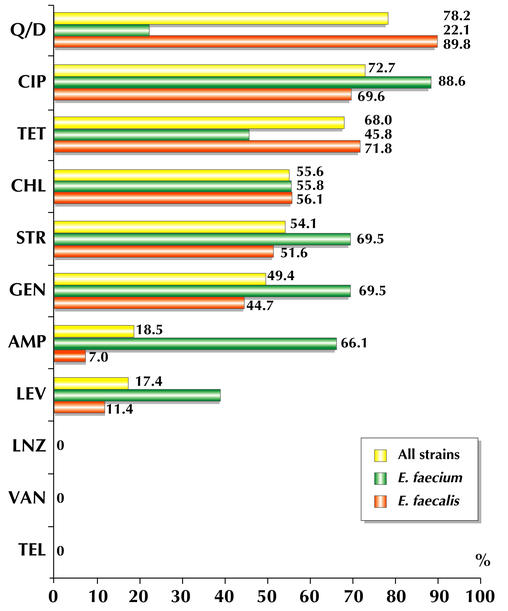


Table 1. Susceptibility testing results.

Antimicrobial	All strains (n=362)		*E. faecalis* (n=273)		*E. faecium* (n=59)	
	I+R, %	MIC50/MIC90	I+R, %	MIC50/MIC90	I+R, %	MIC50/MIC90
AMP	18.5	2/64	7	2/4	66.1	32/128
GEN	49.4	256/4096	44.7	64/4096	69.5	4096/4096
STR	54.1	4096/8192	51.6	2048/8192	69.5	8192/8192
VAN	0	1/2	0	1/2	0	1/2
TEI	0	0,5/1	0	0.25/1	0	0.5/1
LNZ	0	2/2	0	2/2	0	2/2
QD	78.2	8/16	89.7	8/16	22.1	0.5/8
TET	68	64/128	71.8	64/128	45.8	1/128
CHL	55.8	16/64	56.1	32/64	55,8	16/64
CIP	72.7	2/32	69.6	2/8	88.1	2/32
LEV	17.4	2/8	11.4	2/4	39.1	2/32
MOX	N/A	0,5/8	N/A	0.5/2	N/A	2/8

Conclusion

- As far as no strains non-susceptible to vancomycin have been detected, resistance to glycopeptides seems not yet to be a problem of great importance in Russia.
- Considering that no resistance to linezolid has been found, this agent can be use as an alternative to glycopeptides for the treatment of nosocomial enterococcal infections.
- The most important problems determined are the high frequencies of resistance to ampicillin in E. faecium and to aminoglycosides in both *E. faecalis* and *E. faecium* that make questionable the adequacy of administration of combination of penicillins with aminoglycosides for the empiric therapy of severe nosocomial enterococcal infections.
- Other tested antimicrobials such as fluoroquinolones, tetracycline and chloramphenicol can be administered for the therapy on nosocomial enterococcal infections only in the case of microbiologically proven susceptibility of particular strain.