Antimicrobial Resistance in Nosocomial Strains of *Enterobacter* spp. Isolated in Intensive Care Units (ICUs) in Russia: Results of Multicentre Study

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ABSTRACT

Objective: To evaluate the antimicrobial resistance and cross-resistance rates of nosocomial strains of *Enterobacter* spp. isolated in ICUs in different parts of Russia.

Methods: This study has been carried out in 10 ICUs of 9 cities in different parts of Russia. Only strains of clinical significance isolated in patients with hospital-acquired infections have been included. The antimicrobial susceptibility testing has been performed with Etest® (AB Biodisk) to 12 following antimicrobials: piperacillin (PP), piperacillin/tazobactam (PTc), amoxicillin/clavulanate (XL), cefuroxime (XM), cefotaxime (CT), ceftriaxone (TX), ceftazidime (TZ), imipenem (IP), gentamicin (GM), amikacin (AK), ciprofloxacin (CI) and co-trimoxazole (TS). Interpretation of the results has been done according to the NCCLS standards. Strains with intermediate resistance have been included in the "resistant" group.

Results: 82 nosocomial strains of *Enterobacter* spp. have been isolated in this study. Antimicrobial resistance rates were as follows: PP - 69.5%; PTc - 63.4%; XL - 87.8%; XM - 81.7%; CT - 59,8%; TX - 57.3%; TZ - 56.1%; IP - 0%; GM - 41.5%; AK - 3.7%; CI - 4.9%; TS - 12.2%. Among the 46 TZ-resistant strains, the lowest cross-resistance rates have been observed to imipenem (0%), amikacin and ciprofloxacin (4.3%), co-trimoxazole (10.6%).

Conclusions: The most active antimicrobials in this study were IP, AK and CI which can be considered as the drugs of choice for the empirical therapy of nosocomial infections in ICUs caused by *Enterobacter* spp. which has been also underlined by the lowest cross-resistance rates with ceftazidime for these drugs. At the same time, comparatively low level of resistance of TS and cross-resistance rate with ceftazidime leads to suggestion about the possibility of usage of this drug for the therapy of the above mentioned infections.

INTRODUCTION AND PURPOSE

Among the nosocomial infections in intensive care units (ICUs), around 50-60% are caused by gram-negative bacteria. The importance of *Enterobacter* spp. as a nosocomial pathogen has been recognised recently. The antimicrobial resistance which is of the main concerns lead not only to decrease of clinical efficacy of commonly used antibiotics, but also to decrease in cost-effectiveness of treatment. The development of nosocomial infections in patients hospitalised in ICUs require the immediate initiation of the most effective (from different points of view) therapy. The local structure and phenotypes of resistance unique to the particular regions are the most important determinants in the rational choice of antimicrobials and selection of latter for antibiotic formularies.

To determine the extent of the infections caused by *Enterobacter* spp. and antimicrobial resistance to the most commonly used antimicrobial this study has been performed.

METHODS

Eighty-two strains of *Enterobacter* spp. isolated from patients with nosocomial infections in 10 UCUs from 9 cities in different regions of Russia have been included in this study. The strains were identified with API20E systems (bioMerieux, France). Susceptibility testing was performed with Etest (AB BIODISK, Sweden) to 12 most commonly used antimicrobials: piperacillin, amoxicillin/clavulanae, piperacillin/tazobactam, cefuroxime, cefotaxime, ceftriaxone, ceftazidime, imipenem, gentamicin, amikacin, ciprofloxacin, co-trimoxazole.

Testing was performed on Mueller-Hinton II agar according NCCLS guidelines. Interpretation of the results has been carried out in connection with NCCLS standards. Strains with intermediate susceptibility have been included in the 'resistant' category. Data analysis and calculation of cross-resistance rates have been done using SAS 6.11 software (SAS Institute, Germany).

RESULTS

At total of 82 nosocomial strains of *Enterobacter* spp. have been isolated in this study.

The antimicrobial susceptibility patterns are presented in table below:

Table. Antimicrobial susceptibility patterns of *Enterobacter* spp. (N=82) and antimicrobials usage priority scales

Antimicrobial	R,%	MIC_{50}	MIC_{90}	MIC range	Usage priority according R rates	Usage priority according MIC_{90}
Piperacillin	70	> 256	> 256	2 - 256	10	11
Piperacillin/tazobactam	63	> 256	> 256	1 - 256	9	11
Amoxicillin/clavulanate	88	64	128	0.5 - 128	12	5
Cefuroxime	82	128	128	2 - 128	11	5
Cefotaxime	60	64	128	0.25 - 128	8	5
Ceftriaxone	57	64	128	0.25 - 128	7	5
Ceftazidime	56	64	128	0.25 - 128	6	5
Imipenem	0	0.5	2	0.125 - 4	1	2
Gentamicin	42	2	128	0.5 - 128	5	5
Amikacin	4	2	4	1 - >256	2	3
Ciprofloxacin	5	0.125	0.5	0.06 - 8	3	1
Co-trimoxazole	12	0.25	64	0.13 - 64	4	4

According to the resistance rates and MIC_{90} of *Enterobacter* spp. to tested antimicrobials the usage priority rates were calculated (see table).

Penicillins and their combinations with beta-lactamases inhibitors showed poor activity against nosocomial strains of *Enterobacter* spp. and should not be used for the empirical therapy of hospital-acquired infections caused by this pathogen.

More than 50% of strains were resistant to II-III generations cephalosporins that leads to consideration to restrict usage of this class of antimicrobials in ICUs with high frequency of nosocomial infections caused by *Enterobacter* spp.

The most active of the tested antimicrobials were imipenem, amikacin and ciprofloxacin the rates of resistance to which have not exceeded 0%, 4% and 5%, respectively. Notably, among the 46 ceftazidime-resistant strains, the lowest cross-resistance rates have been observed to imipenem (0%), amikacin, ciprofloxacin (4.3%), co-trimoxazole (10.6%).

CONCLUSION

- Imipenem, amikacin and ciprofloxacin can be considered as the drugs of choice for the empirical therapy of nosocomial infections in ICUs caused by *Enterobacter* spp. For these drugs the lowest cross-resistance rates with ceftazidime has also been noted.
- Comparatively low level of resistance to co-trimoxazole and associated-resistance rate with ceftazidime leads to suggestion about the possibility of usage of this drug for the therapy of the above mentioned infections.