007 / 67

RESULTS OF RUSSIAN COUNTRY-WIDE SURVEILLANCE OF ANTIMICROBIAL RESISTANCE OF NOSOCOMIAL GRAM-NEGATIVE BACTERIA (NGNB) FROM 28 INTENSIVE CARE UNITS (ICUs)

L. Stratchounski, G. Reshedko, O. Stetsiouk, O. Kretchikova, E. Riabkova,
Institute of Antimicrobial Chemotherapy, Smolensk, Russian Federation

L. Stratchounski,
Institute of Antimicrobial Chemotherapy,
P.O. Box 5, 214019,
Smolensk, Russian Federation
Tel: +7 0812 611301 or +7 0812 611327
Fax: +7 0812 611294
E-mail: str@antibiotic.ru
http://www.antibiotic.ru

ABSTRACT

Objective: To evaluate the prevalence and antimicrobial resistance of NGNB from Russian ICUs. **Methods:** Minimal inhibitory concentrations of amoxicillin/clavulanate (XL), piperacillin (PP), piperacillin/tazobactam (PTc), cefuroxime (XM), cefotaxime (CT), ceftazidime (TZ), imipenem (IP), gentamicin (GM), amikacin (AK), ciprofloxacin (CI) were determined by Etest (AB Biodisk, Sweden). Interpretation of results was performed according to NCCLS guidelines, 2000. **Results:** A total of 2664 aerobic NGNB were isolated in 28 ICUs in 15 Russian cities during 1997-99. Predominant pathogens were *Pseudomonas aeruginosa* (30%), *Escherichia coli* (18%), *Klebsiella pneumoniae* (15%), *Proteus* spp. (10%), *Enterobacter* spp. (8%), *Acinetobacter* spp. (7%). Other species accounted for 12% in total. Resistance (I+R) rates (%) were:

	P. aeruginosa (n=798)	*E. coli* (n=489)	*K. pneumoniae* (n=389)	*Proteus* spp. (n=263)	*Enterobacter* spp. (n=203)	*Acinetobacter* spp. (n=184)
XL	-	36	56	33	90	-
PP	45	41	68	38	45	76
PTc	30	6	30	9	29	58
XM	-	19	57	51	63	-
CT	-	11	38	21	29	85
TZ	11	8	34	7	25	64
IP	19	0	0	0	0	0
GM	61	21	56	43	24	72
AK	7	2	9	3	3	9
CI	29	8	13	9	6	32

Decreased activity of PP and GM against the majority of NGNB was alarming, as well as high resistance to CI in *P. aeruginosa* and *Acinetobacter* spp. Significant differences in prevalence and resistance patterns were revealed among participating centers. **Conclusion:** AK, TZ were the most active against *P. aeruginosa*; AK, IP - against other NGNB in Russian ICUs. Existing geographical differences underline the necessity of obtaining the local data.

INTRODUCTION AND PURPOSE

Nosocomial infections are of great importance in hospitals worldwide. Due to severity they often require the empirical treatment that should be based on the local epidemiological data. In spite of emerging role of gram-positive bacteria and fungi in the etiology of nosocomial infections, gram-negative bacteria still cause about 23-76% of different nosocomial infections in intensive care units (Fridkin et al., 1997). The purpose of our study was to evaluate the prevalence and resistance patterns of nosocomial gram-negative bacteria (NGNB) in Russian intensive care units (ICUs).

MATERIALS AND METHODS

Participating centers collected approximately 100 consecutive aerobic NGNB each from patients with documented nosocomial infection during 1997-1999. Duplicate isolates were excluded from the study. Isolated strains were identified in local laboratories using standard biochemical tests. Strains were transferred to central laboratory in Smolensk where reidentification of 100% bacteria was performed. Collected strains were stored at –70^{0}C. Minimal inhibitory concentrations (MICs) of piperacillin (PP), piperacillin/ tazobactam (PTc), cefuroxime (XM), cefotaxime (CT), ceftazidime (TZ), imipenem (IP), gentamicin (GM), amikacin (AK), ciprofloxacin (CI) were determined by Etest (AB Biodisk, Sweden). Interpretation of results was performed according to NCCLS guidelines, 2000. Intermediate strains were included into the "resistant" category. *E. coli* ATCC 25922 and *P. aeruginosa* ATCC 27853 were used as quality control strains for susceptibility. Data management and statistical analysis were performed with M-lab® software (Institute of Antimicrobial Chemotherapy, Smolensk, Russia).

RESULTS

Twenty eight ICUs from 15 Russian cities took part in the study. Location of participating cities is shown on the Fig 1.

Figure 1. Geographical location of participating cities.

In total 2664 NGNB isolated from 2306 specimens from 2187 patients were included in the study. The studied specimens were skin and soft tissue specimens (760/33.0%), low respiratory tract specimens (575/24.9%), urine (383/16.6%), abdominal samples (305/13.2%), blood (74/3.2%) and others (209/9.1%). The most common pathogens isolated were *P. aeruginosa* (798/29.9%), *E. coli* (489/18.3%), *K. pneumoniae* (389/14.6%), *Proteus* spp. (263/9.9%), *Enterobacter* spp. (203/7.6%), *Acinetobacter* spp. (184/6.9%), while *Serratia* spp. (108/4.0%), *Stenotrophomonas* spp. (35/1.3%), *Citrobacter* spp. (34/1.3%), *Flavobacter* spp. (22/0.8%), *Morganella* spp. (20/0.8%) and other NGNB (119/4.6%) were infrequent pathogens. Distribution (%) of species with respect to site of infection is presented in Table 1. Table 2 shows resistance rates (%), Tables 3-4 - MIC_{50}/MIC_{90} and MIC ranges of predominant pathogens.

Table 1. Pathogens distribution (%) in different infection sites.

Microorganisms (n=2664)	Skin and soft tissue	Respiratory tract	Urinary tract	Abdomen	Blood	Other sites
P. aeruginosa (n=798)	300 (37.6%)	236 (29.6%)	115 (14.4%)	54 (6.7%)	12 (1.5%)	81 (10.2%)
E. coli (n=489)	135 (27.6%)	58 (11.9%)	142 (29.0%)	91 (18.6%)	10 (2.1%)	53 (10.8%)
K. pneumoniae (n=389)	91 (23.4%)	157 (40.3%)	48 (12.3%)	26 (6.7%)	17 (4.4%)	50 (12.9%)
Proteus spp. (n=263)	138 (52.5%)	40 (15.2%)	47 (17.9%)	26 (9.9%)	4 (1.5%)	8 (3.0%)
Enterobacter spp. (n=203)	76 (37.4%)	42 (20.7%)	29 (14.3%)	20 (9.9%)	7 (3.4%)	29 (14.3%)
Acinetobacter spp. (n=184)	54 (29.3%)	45 (24.5%)	12 (6.5%)	33 (17.9%)	9 (4.9%)	31 (16.9%)
Serratia spp. (n=108)	19 (17.7%)	48 (44.4%)	12 (11.1%)	9 (8.3%)	9 (8.3%)	11 (10.2%)
Stenotrophomonas spp. (n=35)	3 (8.5%)	23 (65.7%)	1 (2.9%)	1 (2.9%)	2 (5.7%)	5 (14.3%)
Citrobacter spp. (n=34)	10 (29.4%)	2 (6.0%)	6 (17.6%)	6 (17.6%)	0 (0.0%)	10 (29.4%)
Flavobacter spp. (n=22)	1 (4.5%)	15 (68.2%)	0 (0.0%)	0 (0.0%)	1 (4.5%)	5 (22.8%)
Morganella spp. (n=20)	8 (40.0%)	2 (10.0%)	6 (30.0%)	2 (10.0%)	0 (0.0%)	2 (10.0%)
Other microorganisms (n=119)	32 (26.9%)	31 (26.1%)	16 (13.4%)	14 (11.8%)	6 (5.0%)	20 (16.8%)

Table 2. Resistance (%) of predominant pathogens.

	P. aeruginosa (n=798)	*E. coli* (n=489)	*K. pneumoniae* (n=389)	*Proteus* spp. (n=263)	*Enterobacter* spp. (n=203)	*Acinetobacter* spp. (n=184)
XL	-	35.8	56.0	32.7	89.7	-
PP	44.7	40.9	68.4	37.6	44.8	75.5
PTc	29.7	6.3	30.1	8.7	29.1	58.2
XM	-	19.2	57.3	51.3	63.1	-
CT	-	11.0	37.5	20.9	29.1	84.8
TZ	11.2	7.8	33.7	6.9	24.6	63.6
IP	18.8	0.0	0.0	0.0	0.0	0.0
GM	61.3	20.9	55.8	43.3	24.1	71.7
AK	6.7	2.2	9.0	3.4	2.5	8.7
CI	28.9	8.4	12.9	8.7	5.9	31.5

Table 3. MIC_{50}, MIC_{90} and MIC ranges of *P. aeruginosa*, *E. coli* and *K. pneumoniae*.

	P. aeruginosa (n=798)			*E. coli* (n=489)			*K. pneumoniae* (n=389)		
	MIC_{50}	MIC_{90}	MIC range	MIC_{50}	MIC_{90}	MIC range	MIC_{50}	MIC_{90}	MIC range
XL	-	-	-	6	32	0.75-256	16	64	0.125-256
PP	32	256	0.25-256	3	256	0.19-256	256	256	0.75-256
PTc	16	256	0.25-256	1.5	8	0.25-256	4	256	0.5-256
XM	-	-	-	4	128	0.5-256	16	256	0.75-256
CT	-	-	-	0.094	12	0.016-256	3	256	0.023-256
TZ	3	12	0.094-256	0.38	6	0.025-256	3	128	0.094-256
IP	3	8	0.125-32	0.25	0.38	0.016-3	0.25	0.5	0.064-2
GM	96	256	0.064-256	1	64	0.25-256	16	256	0.25-256
AK	4	12	0.25-256	2	3	0.5-256	2	16	0.38-256
CI	0.38	32	0.023-32	0.016	0.38	0.004-32	0.064	2	0.008-32

Table 4. MIC_{50}, MIC_{90} and MIC ranges of *Proteus* spp., *Enterobacter* spp. and *Acinetobacter* spp.

	Proteus spp. (n=263)			*Enterobacter* spp. (n=203)			*Acinetobacter* spp. (n=184)		
	MIC_{50}	MIC_{90}	MIC range	MIC_{50}	MIC_{90}	MIC range	MIC_{50}	MIC_{90}	MIC range
XL	6	48	0.38-256	192	256	1-256	48	256	0.25-256
PP	1.5	256	0.094-256	3	256	0.5-256	192	256	2-256
PTc	0.5	4	0.094-256	3	256	0.5-256	48	256	0.016-256
XM	12	256	0.25-256	16	256	1.5-256	256	256	1-256
CT	0.032	256	0.016-256	0.38	256	0.032-256	64	256	0.064-256
TZ	0.19	3	0.025-256	0.75	256	0.125-256	24	96	0.25-256
IP	0.5	2	0.023-4	0.38	1	0.125-3	0.38	1	0.064-4
GM	2	256	0.047-256	1	256	0.125-256	24	256	0.023-256
AK	2	6	0.19-256	2	3	0.75-48	2	12	0.125-256
CI	0.032	0.75	0.006-32	0.032	0.5	0.004-32	0.75	32	0.006-32

DISCUSSION

Among β-lactams PP, XL and XM showed low activity against all NGNB. PTc exhibited high acitvity against *E. coli* and *Proteus* spp. but about one third of *P. aeruginosa*, *K. pneumoniae* and *Enterobacter* spp. were resistant. CT was active mainly against *E. coli* while its activity was quite poor against other species. TZ was the most active β-lactam against *P. aeruginosa* whereas IP possessed decreased activity against this pathogen. No strains of *Enterobacteriaceae* and *Acinetobacter* spp. resistant to IP were revealed. Generally AK was much more active than GM against all tested NGNB. CI had quite poor activity against non-fermenting bacteria, showing also decreased activity against *Enterobacteriaceae*.

We observed significant inter-hospital and inter-regional variations in the resistance rates. The observed resistance rates of *P. aeruginosa* in different cities were 0-47.5% for IP; 0-69.2% for TZ; 0-41.7% for AK; 0-84.4% for CI. Resistance rates of *E. coli* to PTc varied between 0-35.7%, to AK - 0-57.1%; to CI - 0-85.7%; of *K. pneumoniae* to PTc were 0-72.3%; to AK - 0-69%; to CI - 0-61.1%. At the same time in 9 Moscow centers resistance of *P. aeruginosa* also varied considerably; for IP variations were 0-36.9%; for TZ - 0-31.3%; for AK – 0-41.7%; for CI – 0-84.4%. The similar situation was observed with antibiotic resistance rates of other pathogens.

CONCLUSIONS

1. *P. aeruginosa*, *K. pneumoniae*, *E. coli*, *Proteus* spp., *Enterobacter* spp. and *Acinetobacter* spp. were the predominant gram-negative nosocomial pathogens in Russian ICUs.

2. TZ, AK were the most active against *P. aeruginosa*; IP and AK - against other NGNB in Russian ICUs.

3. Due to the high resistance rates of NGNB to PP, XL, XM and GM these drugs should not be recommended for the treatment of nosocomial infections caused by these pathogens.

4. Significant inter-regional and inter-hospital differences in the prevalence and resistance patterns of NGNB emphasize the vast need for local epidemiology data.

ACKNOWLEDGMENTS

The survey was supported by Merck, Sharp and Dohme Idea, Inc. We also thank all participating laboratories for submitting nosocomial strains.