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ABSTRACT

Objectives: The survey of trends in multidrug resistance among most common pathogens in intensive care unit (ICU) is very important task for the purpose of determination of actual empiric regimen of therapy. The aim of our study was to document changes in resistance patterns of ICU pathogens isolated from respiratory specimens between 2006 and 2012.

Methods: Susceptibility data of all clinical respiratory isolates (BAL and tracheal aspirate) collected in ICU departments of 18 Russian hospitals in 2006 and 2012 were analysed. Species identification and antimicrobial susceptibility testing were performed by automatic system and standart disk-diffusion method. Susceptibility to antibiotics was interpreted according to CLSI guidelines.

Results: A total of 2133 and 5055 isolates from lower respiratory tract were analysed in two periods, 2006 and 2012. The proportion of prevalent Gram-negative microorganisms wasn't changed from 2006 to 2012 (79.9 and 83.0%). Among Gram-positive microorganisms S.aureus was dominated, and its rate was diminished from 18.4% in 2006 to 14.5% in 2012, as well as MRSA rate decreased from 60.7 to 42.0%. Among Gram-negative isolates about half were Enterobacteriaceae (40.6%) and 42.2% were nonfermenting microorganisms in 2012. The most common pathogens among Gram-negatives were Klebsiella pneumoniae (24.0%) and Acinetobacter spp. (24.3%) followed by *P.aeruginosa* (16.2%), *Proteus* [1]. The therapeutic challenges that have arisen because spp. (6.6%) and *E.coli* (6.5%). The resistance rate of *E.coli* of heightened antimicrobial resistance among gramand *Klebsiella* spp. to 3rd generation of cephalosporins (68.6 and 89.5%) and ciprofloxacin (74.9 and 78.0%) in 2012 was very high and did not changed in comparison with 2006. During the 6 year period resistance of gramnegatives to imipenem was considerably elevated: from 0 to 3.9% (*E.coli*), from 1.6 to 9.9% (*Klebsiella* spp.), from 7.9 to 60.6% (Acinetobacter spp.). The most strains of Acinetobacter spp in 2012 were MDR, the rate of nonsusceptibility to ceftazidime, ampicillin/sulbactam, cefoperazone/sulbactam, amikacin, ciprofloxacin was 83.5, 79.6, 49.5, 84.0, and 89.8% respectively. The minimal rate of resistance among E.coli, Klebsiella spp. and Acinetobacter spp. was detected to tigecycline – 5.0, 4.8 and 6.4%.

Conclusion: Increasing rate of resistance to most antibiotics among gram-negative ICU pathogens is a matter of great concern. At present in Russian ICUs the best available option of empiric treatment seems to be tigecycline but its use in nosocomial respiratory tract infections is limited by approved indications.

INTRODUCTION AND PURPOSE

Antimicrobial therapy management is impossible without knowledge of current data about the microbiological landscape and etiological structure of infections and the resistance level of both community-acquired and hospital-acquired pathogens. The problem of bacterial resistance became particularly actual and disturbing in XXI century because of wide spread of carbapenemresistant gram-negative and vancomycin-resistant grampositive microorganisms in the hospitals. This problem is doubling by the spread of the pathogens with typical nosocomial resistance phenotype like ESBL-producing *E.coli* and *Klebsiella* spp. and community-acquired MRSA in the community.

The continuously evolving antibacterial resistance of some gram-negative microorganisms (Klebsiella spp., E.coli, Proteus spp., Acinetobacter spp.) has led to the emergence of clinical isolates susceptible to only one class of antimicrobial agents and eventually to pandrugresistant isolates, i.e. resistant to all available antibiotics negative pathogens have been exacerbated by the stagnation in development of novel antimicrobial agents to treat these pathogens [2-3]. Since the late 90-s in Russian hospitals there was a high prevalence of ESBL-producing Enterobacteriaceae, MBL-producing *P.aeruginosa* and MRSA. The emergence of ESBL wasn't adequate observed and these strains of Enterobacteriaceae rapidly became endemic in the majority of hospitals. The most important task now is promptly detecting the emergence of carbapenemases amongEnterobacteriaceaeandAcinetobacteriatoprevent the spread of these highly multi-resistant pathogens. The study of trends in multidrug resistance (MDR) among

Trends in Antibiotic Resistance among Respiratory Isolates from ICU: Multicentre Study in Russian Hospitals, 2006-2012 (ERGINI Study)

the most common pathogens isolated from patients The Gram-positive microorganisms were represented in intensive care unit (ICU) is very important task to predominantly by S.aureus. The portion of S.aureus was moderately decreased since 2006 from 18.4 to 14.5% determine an actual empiric regimen of antimicrobial therapy. The aim of our study was to document changes (tabl. 2). in resistance patterns of ICU pathogens isolated from respiratory specimens between 2006 and 2012. The first Table 2. Gram-positive and Gram-negative respiratory part of microbiological ERGINI study familiarized with isolates in two periods blood pathogens in ICU departments was presented elsewhere previously [4].

MATERIAL AND METHODS

multicentre retrospective We conducted the microbiological study in medical or surgical ICU departments of 18 emergency multifields hospitals from 12 cities of Russian Federation (Barnaul, Ekaterinburg, Kazan, Krasnodar, Moscow, Surgut, Toliatty, Uljanovsk, Vladivostok, Volgograd, Yakutsk, Yaroslavl). Special-ICUs like hematologic, cardiological, purpose transplantologist, neonatal didn't include in the study.

Susceptibility data of all bacterial clinical respiratory isolates (BAL or tracheal aspirate) collected in 2006 and 2012 were analysed.

Species identification and antimicrobial susceptibility testing were performed by automatic system and standard disk-diffusion method in each centre. Susceptibility to antibiotics was interpreted in accordance with CLSI criteria.

RESULTS

A total of 2133 and 5055 isolates from lower respiratory tract were analysed in two periods, 2006 and 2012, among them gram-negative microorganisms were predominant. Proportion of Gram-positive and Gramnegative pathogens did not significantly change from 2006 till 2012 (tabl.1).

Table 1. Microorganisms collected from lower respiratory tract in ICU departments in 2006 and 2012

Period, year	2006	2012
Total number of strains	2133	5055
Gram-positive	428 (20.1%)	860(17.0%)
Gram-negative	1705 (79.9%)	4195 (83.0%)

Microorganisms	2006 (n = 2133)	2012 (n = 5055)				
Gram-positive isolates						
Staphylococcus aureus	392 (18.4%)	183 (14.5%)				
Streptococcus pneumoniae	16 (0.8%)	93 (1.8%)				
Streptococcus pyogenes	20 (0.9%)	35 (0.7%)				
Gram-negative isolates						
P.aeruginosa	529 (24,8%)	817 (16,2%)				
<i>Klebsiella</i> spp.	385 (18,0%)	1214 (24,0%)				
Acinetobacter spp.	348 (16,3%)	1228 (24,3%)				
E.coli	100 (4,7%)	328 (6,5%)				
Proteus spp.	80 (3,8%)	333 (6,6%)				
Enterobacter spp.	78 (3,8%)	119 (2,4%)				
S.maltophilia	47 (2,2%)	51 (1,0%)				
Other	138 (6,5%)	105 (2,0%)				

The changes in resistant patterns of S. aureus are presented in tabl.3. MRSA rate decreased from 60.7% in 2006 to 42.0% in 2012. The same tendency in reduction of resistance was demonstrated for clindamycin, rifampin and levofloxacin. The total susceptibility of Staphylococci was detected to linezolid and vancomycin.

Table 3. Resistance rate (%) of Staphylococcus aureus collected from lower respiratory tract in 2006 and 2012

Antibiotics	Oxacillin		Clindamycin		Rifampin		Levofloxacin	
	2006	2012	2006	2012	2006	2012	2006	2012
S.aureus	60.7	42.0	61.6	39.1	49.4	31.4	50.6	33.9

Among Gram-negative isolates about half were Enterobacteriaceae (40.6%) and 42.2% were nonfermenting microorganisms in 2012.

Among gram-negative isolates three microorganisms -Klebsiella spp., Acinetobacter spp. and P.aeruginosa were dominated (altogether from 59.1 to 64.5% in two periods), but their ratio has been changed in comparative periods. The value of *P.aeruginosa* in etiology of nosocomial pneumonia was significantly decreased by 9%, whereas Klebsiella spp. and Acinetobacter spp. extended their portions by 6 and 8%.

The Top 4 pathogens responsible for 79% of cases of nosocomial pneumonia in 2012 were:

- Acinetobacter spp.
- Klebsiella spp.
- P.aeruginosa
- Staphylococcus aureus

The changes in resistant patterns of gram-negative microorganisms are presented in tabl.4. The resistance rate of E.coli and Klebsiella spp. to 3rd generation of cephalosporins (68.6 and 89.5%) and ciprofloxacin (74.9 and 78.0%) in 2012 was very high and did not change in comparison with 2006. The high resistance level of Enterobacteriaceae to cephalosporins was nearly exclusively owing to wide spread of ESBL in Russian hospitals during last 15 years. The high resistance rate of *E.coli* and *Klebsiella* spp. was detected also to ampicillin/ sulbactam, cefepime and amikacin as well, however some reduction of resistance to latter antibiotic was registered, especially in *Klebsiella* spp.

Table 4. Non-susceptibility rate (%) of Gram-negative microorganisms collected from lower respiratory tract in 2006 and 2012

Antibiotics/ Microorganisms			<i>E.coli</i> ((n=428)	<i>Acinetobacter</i> spp. (n=1576)		P.aeruginosa (n=1346)	
	2006	2012	2006	2012	2006	2012	2006	2012
Ampicillin/ sulbactam	88,4	90,5	72.5	52.3	53,2	79,6	NA	NA
Ceftazidime	84,4	88,6	63,3	66,7	90,2	83,5	57,2	44,4
Cefotaxime	87,3	89,5	76,8	68,6	NA	NA	NA	NA
Cefepime	80,9	91,0	66,3	71,3	86,5	82,6	51,1	47,2
Cefoperazone/ sulbactam	38,6	45,6	6,2	21,4	27,2	49,5	43,6	51,8
Imipenem	1,6	9,9	0	3,9	7,9	60,6	51,5	42,9
Meropenem	1,4	10,3	0	3,0	12,1	77,6	49,9	58,4
Amikacin	58,2	27,9	39,8	22,3	62,1	84,0	65,6	54,5
Ciprofloxacin	74,6	78,0	62,6	74,9	90,5	89,8	80.0	70.1
Tigecycline	-	4,8	-	5,0	-	6,4	NA	NA

During the 6 year period resistance of gram-negatives to imipenem was considerably elevated: from 0 to 3.9% (E.coli), from 1.6 to 9.9% (Klebsiella spp.), from 7.9 to

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60.6% (*Acinetobacterspp.*). The same tendency is obviously true for meropenem. The most strains of Acinetobacter spp in 2012 were MDR, the rate of non-susceptibility to ceftazidime, ampicillin/sulbactam, cefoperazone/ sulbactam, amikacin, ciprofloxacin was 83.5, 79.6, 49.5, 84.0, and 89.8% respectively. The minimal rate of resistance among *E.coli*, *Klebsiella* spp. and *Acinetobacter* spp. was detected to tigecycline – 5.0, 4.8 and 6.4%.

Pseudomonas aeriginosa is conventionally characterized as MDR.

CONCLUSION

Increasing rate of resistance to most antibiotics among gram-negative ICU pathogens from lower respiratory tract is a matter of great concern.

At present in Russian ICUs the best available option of empiric treatment seems to be tigecycline but its use in nosocomial respiratory tract infections is limited by approved indications.

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