A.G. Salmanov, O.M. Verner

Shupyk National Medical Academy of Postgraduate Education, Kyiv, Ukraine

Prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) in Kyiv Surgical Hospital (Ukraine)

Abstract

Objective — to determine the prevalence of methicillin-resistant strains of *Staphylococcus aureus*, isolated from patients different departments in Kyiv Surgical Hospital.

Materials and methods. Between June 2015 and December 2015, a total of 128 *S. aureus* isolates were collected from the pus samples of the patients with SSI in a surgical hospital in Kyiv, Ukraine. The identification and antimicrobial susceptibility of the cultures were determined, using automated microbiology analyzer VITEK 2 Compact (bioMerieux, France). Susceptibility to antibiotics was determined using VITEK 2 AST-P580 card (bioMerieux, France), which included 20 antibiotics (benzylpenicillin, oxacyllin, cefoxitin, gentamycin, tobramycin, levofloxacin, moxifloxacin, erythromycin, clindamycin, linezolid, teicoplanin, vancomycin, tetracycline, tigecycline, fosfomicin, nitrofurantoin, fusidic acid, mupirocin, rifampicin, and trimethoprim/sulphamethoxazole) and a cefoxitin test, designed for detection of staphylococci resistance to methicillin. Interpretative criteria were those suggested by the Clinical and Laboratory Standards Institute (CLSI).

Results and discussion. Based on antimicrobial susceptibility analysis, the most active antibiotics found in the study were linezolid, tigecycline, and mupirocin, showing growth inhibition of 100 % strains tested. Susceptibility to the other antimicrobials was also on a high level: 99 % of strains were found susceptible to nitrofurantoin and trimethoprim/sulphamethoxazole, 98 % — to fusidic acid, 97 % — to moxifloxacin, 96 % — to teicoplanin, 95 % — to vancomycin and fosfomicin, 93 % — to gentamycin, and 92 % — to tobramycin. Susceptibility to levofloxacin (89 %), tetracycline (88 %), rifampin (87 %), erythromycin (84 %), and clindamycin (79 %) was observed to be some lower. Research of MRSA prevalence in Kyiv Surgical Hospital (Ukraine) shown, that 11 % of staphylococci strains, isolated from patients having nosocomial infections (SSI), had multiple resistance to antibiotics. Resistance *S. aureus* to oxacyllin came up to 19 %. Further, 35.7 % of MRSA strains were resistant only to the group of beta-lactamic antibiotics, while the rest — also to the other classes of antibiotics.

Conclusions. MRSA in surgical hospital, being a subject of the research is considered to be a serious therapeutic and epidemiologic problem. Total prevalence of MRSA in hospital was evaluated as 19 %, varying in every surgical department studied. Antibiotics revealed the most effective for treatment of MRSA infections were linezolid, mupirocin, tigecycline, vancomycine, teicoplanin, moxifloxacin, nitrofurantoin, fusidic acid, and trimethoprim/sulphamethoxazole. Taking into account the constant changes and significant differences of the *S. aureus* resistance levels observed in various regions, the constant monitoring of antibiotic resistance to antimicrobials in every in-patient medical institution is required and on the base of the local obtained results to elaborate the hospital record sheets. Antibiotics application tactics should be determined in accordance with the local data of resistance to them in each surgical in-patient institution. The system of epidemiologic surveillance over microbial resistance should be established on the local, regional, and national levels.

Key words: *Staphylococcus aureus*, surgery, nosocomial infections, antibiotics, antimicrobial resistance, MRSA.

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INTRODUCTION

Humans have been actively using antibiotics to combat infectious agents for more than 70 years. However, the infectious agents' resistance to antimicrobials (antibiotics, antivirals, antiseptics, and disinfectants) is developing quite rapidly, and has become so widespread, that many highly-developed countries consider as a national safety threat [1]. Methicillin-resistant *Staphylococcus aureus* (MRSA) is a multidrug resistant organism that threatens the continued effectiveness of antibiotics worldwide and causes a threat almost exclusively in hospitals and long-term care settings.

The rising prevalence of nosocomial methicillin-resistant *Staphylococcus aureus* (MRSA) and the recent emergence of community-associated MRSA are major clinical, public health, and economic challenges. MRSA is a leading cause of nosocomial pneumonia and complicated skin and soft-tissue infections (cSSTI) [2].

Among the multiresistant bacteria MRSA is a major cause of HAIs in the EU. In 2008, over 380,000 HAIs due to selected antibiotic-resistant bacteria, including those of the bloodstream, lower respiratory tract, skin or soft tissues and urinary tract, were estimated to be acquired annually in hospitals of the EU Member States, Iceland and Norway. Overall, MRSA accounts for 44 % of these HAIs, 22 % of attributable extra deaths and 41 % of extra days of hospitalisation associated with these infections. [3]. MRSA is the most common multidrug-resistant pathogen causing nosocomial infections in Europe. There are about 132,000 cases of MRSA in German hospitals each year. MRSA is found in about 18 % to 20 % of all inpatient-derived culture specimens that are positive for *S. aureus* [4].

Estimates indicate that there are approximately 170,000 MRSA infections in European healthcare systems each year, causing more than 5,000 fatalities, more than 1 million additional inpatient days, and additional costs of approximately € 380 million [5, 6].

MRSA is at present the most commonly identified antibiotic-resistant pathogen in many parts of the world with a prevalence between 25 and 50 % in most parts of America, Australia and southern Europe [7, 8]. In 2005, 19,000 deaths associated with MRSA strains were reported in the USA [9]. Although infection rates are decreasing, MRSA infections were estimated to affect more than 150,000 patients in the EU alone in 2010 [5]. Until recently, vancomycin and daptomycin have been the only effective treatment for methicillin-resistant pathogens [10]. But in 1997, the first vancomycin-intermediate-resistant *S. aureus* strains were isolated, followed by reports of vancomycin-resistant ones in 2003 [11, 12]. Cases of daptomycin-resistant MRSA have also been described [13, 14]. Consequently, the need for new antibiotics for the treatment of these multi-resistant bacteria arises. In a global priority list released by the WHO in 2017, development of antibiotics against MRSA is given the second highest priority [15].

The global spread of MRSA over the past 20 years has become a major worldwide public health concern [16, 17]. In some areas of the world, MRSA prevalence is very high, for example, in Latin American countries prevalence is estimated to be > 80 % [18]. In other regions the prevalence is rising. Australia experienced an increase from 12 % in 2000 to 19 % in 2013 [19]. In India proportions of 41—80 % were observed in 2008—2012. Although the mean prevalence of MRSA is decreasing in Europe, the United States and Canada, the prevalence of MRSA is still high in most countries, ranging from 15 % to 45 % [18]. In Ukraine proportions of 33.8—48.1. % were observed in 2008—2014 [20—22].

The WHO declared year 2011 a year of a campaign, directed against antimicrobial resistance, under the following motto: «No action today, no cure tomorrow». The global strategy of combating antimicrobial resistance is directed to guarantee efficacy of such vital preparations as antibiotics, not only for the present generation, but for the future ones as well. Thus, monitoring of antimicrobial resistance is an extremely important measure that allows studying the extent of the problem, as well as forecasting its future developments. The European Antimicrobial Resistance Surveillance System (EARSS-Net), created in 1999, is considered to be the biggest system of monitoring and controlling of antimicrobial resistance in the world. It provides with official, well-grounded, and comparative data regarding the resistance of 7 types of indicative bacteria in Europe: *Streptococcus pneumoniae, Staphylococcus aureus, Escherichia coli, Enterococcus faecalis* and *Enterococcus faecium, Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. Unfortunately, nowadays Ukraine is not a part of this system, because it's outside the European Community. The absence in Ukraine of systematic microbiological monitoring of antimicrobial resistance, the lack of local multi-center researches and relevant data, related to resistance issues, especially worrying specialists.

MRSA is considered to be so-called «problematic» microorganisms, since it demonstrates

high frequency of associated resistance to beta-lactamic antibiotics, aminoglycosides, erythromycin, imipenem, and clindamycin [20]. This phenomenon considerably narrows the range of antimicrobials, used for the treatment of infections, caused by staphylococci, while the latter belong to major causes of opportunistic infections, including nosocomial. Diseases, caused by MRSA, are treated by glycopeptide antibiotics (first of all, vancomycin), that are considered to be the most efficient for the moment. However, glycopeptides, in comparison with beta-lactams, have a deficiency, which is bacteriostatic action to staphylococci. Moreover, wide use of vancomycin has facilitated the formation of resistance to it among S. aureus. All this allows considering utilization of glycopeptides as suboptimal alternative, when treating infections caused by staphylococci, and efforts are to be directed on prevention of further spreading of MRSA. According to the global experience, the implementation of infection control system is the most efficient remedy, directed on prevention of MRSA spreading in healthcare facilities. This may explain, to some extent, such a huge difference in MRSA prevalence in various countries.

Levels of resistance to oxacyllin may differ in various medical institutions of the same country, and even in various departments of the same medical facility. Thus, according to some sampling studies, conducted in Ukraine, MRSA prevalence in the country in 2010—2014 came up to 9.7—55.6 % [20].

Resistance of staphylococci to beta-lactamic antibiotics is associated with their ability to create beta-lactamases. Staphylococcal beta-lactamases are a homogeneous group of enzymes having actually no differences regarding their main properties. All of them have similar substrate profiles, and besides, they hydrolyze natural and semi-synthetic penicillins (excluding methicillin and isoxazolilpenicillins: oxacyllin, cloxacillin, and dicloxacillin). Staphylococcal beta-lactamases are efficiently inhibited by clavulanate, sulbactam, and tazobactam. Beta-lactamases production is inducible, and its quantitative description obviously depends upon the number of plasmids' copies, carrying beta-lactamases' production gene [23].

The nature of staphylococci resistance to oxacyllin has been described in 1980s. Resistance to oxacyllin is related to acquisition of additional penicillin-binded protein, PBP2a (can be also indicated as PBP2'), with a decreased affinity to beta-lactamic antibiotics. PBP2a protein is encoded by mecA gene that is a part of movable

genetic element «staphylococcal chromosomal cassette mec», which origin is unknown. Complete homology detected between mecA gene, and another gene of one penicillin-binded protein Staphylococcus sciuri, however, does not allow to establish the origin of oxacyllin resistance gene, since S. sciuri is susceptible to beta-lactams. Viability of MRSA in the presence of beta-lactamic antibiotics can be explained by maintaining of functional activity of PBP2a protein, while other penicillin-binded proteins are not active in the presence of beta-lactams [23].

Currently several mechanisms of staphylococci resistance to oxacyllin are established. Classic resistance to oxacyllin is caused by PBP2a production, subdivided within a cell population to homogeneous and heterogeneous types. Strains, that are resistant due to PBP2a production, are typically also resistant to beta-lactamic and other antibiotics. In this case, a combination of beta-lactamic antibiotic and beta-lactamase inhibitor does not eliminate strain's resistance to beta-lactams. Another type of resistance to oxacyllin is caused by beta-lactamases' hyper-production. Such strains do not have multiple resistance to other classes of antibiotics, and loose their resistance to beta-lactams in presence of beta-lactamases' inhibitors. If a strain is resistant to oxacyllin due to a modified PBP production, it's not going to have multiple resistance to various classes of antibiotics, neither cross-resistance to all the beta-lactams. However, beta-lactamases' inhibitors are not efficient in such a case. The specificity of MRSA antimicrobial resistance, actually resulting in difficulties in treatment of SSI, causes the need of conducting a microbiological monitoring of MRSA prevalence, in order to develop effective approaches of its control.

The aim of this study was to determine the prevalence of methicillin-resistant strains of Staphylococcus aureus, isolated from patient's different departments in Kyiv Surgical Hospital.

MATERIALS AND METHODS

This work is a microbiological research, to study the prevalence of methicillin-resistant Staphylococcus aureus strains, isolated from patients of Kyiv Surgical Hospital. The investigation included the analysis of 128 strains of conditionally pathogenic microorganisms from biological material obtained from patients with clinical symptoms. The clinical sample consisted of laboratory-diagnosed SSIs that emerged no less than 48 hours after a surgery. Bacterial strains obtained for a second time from the

same patients were not subject to analysis. Analysis of biological material and interpretation of results were performed in accordance with the approved rules for clinical material selection, analysis and interpretation of results.

Primary identification of isolated cultures was made in bacteriology lab by routine manual methods, based on valid local regulatory documents. Totally, 128 strains of staphylococci were taken and all were subjected to re-identification in the reference lab. Of them, 100 strains of *S. aureus* were selected for the further investigation.

The identification and antimicrobial susceptibility of the cultures were determined, using automated microbiology analyzer VITEK2 Compact (bioMerieux, France). Following Gram-staining of the cultures, their identification was made using a VITEK2 GP card (bioMerieux, France), which consisted of 64 biochemical tests, to identify Gram-positive cultures. Susceptibility to antibiotics was determined using VITEK2 AST-P580 card (bioMerieux, France), which included 20 antibiotics and a cefoxitin test, designed for detection of S. aureus resistance to methicillin. VITEK2 Compact analyzer is able to determine susceptibility to antibiotics, with an indication of minimum inhibitory concentrations (MICs), estimated by means of serial dilutions. The results obtained were analyzed using a built-in VITEK2 Advanced Expert System™ (AES), intended for interpretation of antibiogram and determination of anti-microbial resistance profiles of microorganisms studied. In general, susceptibility of staphylococci strains to the following antibiotics was analyzed: benzylpenicillin, oxacyllin, cefoxitin, gentamycin, tobramycin, levofloxacin, moxifloxacin, erythromycin, clindamycin, linezolid, teicoplanin, vancomycin, tetracycline, tigecycline, fosfomicin, nitrofurantoin, fusidic acid, mupirocin, rifampicin, and trimethoprim/sulphamethoxazole. Interpretative criteria were those suggested by the Clinical and Laboratory Standards Institute (CLSI) [24].

Data obtained were transferred for further analysis into computer software WHONET 5.1 (Copyright 1989—2001, World Health Organization. All rights reserved. Freeware downloadable from http://www.who.int/drugresistance/whonetsoftware/en/). The analysis of statistical data was performed using Microsoft Excel. Personal IBM-computer, running Microsoft Windows, was used during the study.

RESULTS AND DISCUSSION

100 strains of *S. aureus* were selected for the research. Analyzing the cases, when the

primary identification was not confirmed by the re-identification in a reference lab (catalase and coagulase tests, Gram staining, and automated identification), we highlighted two error types: 1) related to subjective impact of lab personnel, and 2) occurred due to specific biological properties of microorganisms.

As an example of the 1st type of errors, one could take the cases, when strains primarily identified as *S. aureus*, actually reacted negatively on catalase, which is not typical for Micrococaceae. Also discrepancies with the identification due to contamination of staphylococci cultures by outside microflora were found. These cases clearly demonstrate that in local microbiology laboratories much higher attention must be paid to internal quality control of the operations, performed in the labs.

Regarding the 2nd type of errors, some strains reacted positively on coagulase, but biochemically were different from *S. aureus*, and some strains were coagulase-negative, while biochemically identified as *S. aureus*. It proves once more, that a coagulase test is not to be used as the only criteria to differentiate types of *S. aureus* from all the other types of staphylococci, despite this test is very common in local labs.

As a result of studying of staphylococci tested strains susceptibility to antibiotics it was established, that based on antimicrobial susceptibility analysis, the most active antibiotics found in the study were linezolid, tigecycline, and mupirocin, showing growth inhibition of 100 % strains tested (Table 1).

Susceptibility to the other antimicrobials was also on a high level: 99 % of strains were found susceptible to nitrofurantoin and trimethoprim/sulphamethoxazole, 98 % — to fusidic acid, 97 % — to moxifloxacin, 96 % — to teicoplanin, 95 % — to vancomycin and fosfomicin, 93 % — to gentamycin, and 92 % — to tobramycin. Susceptibility to levofloxacin (89 %), tetracycline (88 %), rifampin (87 %), erythromycin (84 %), and clindamycin (79 %) was observed to be some lower. Resistance to oxacyllin came up to 19 %. Interestingly, benzylpenicillin, which is currently not used for treatment of staphylococcal infections anymore, was shown to be ineffective in 72 % of strains, which still suggests the usefulness of this antibiotic for patient treatment, based on the individual antibiogram data.

At first glance, taking into account the fact, that levels of antimicrobial resistance of tested strains of *S. aureus* did not exceed 21 %, it seems quite easy to choose any of the above-mentioned antibiotics

Table 1

Antimicrobial susceptibility of *S. aureus* isolates from different departments of Kyiv Surgical Hospital (Ukraine)

Antibiotic	Division by susceptibility, %		
	Resistant	**Moderately resistant**	**Susceptible**
Cefoxitin	14	0	86
Benzylpenicillin	72	0	28
Oxacyllin	19	0	81
Gentamycin	8	0	92
Tobramycin	7	0	93
Levofloxacin	2	9	89
Moxifloxacin	2	1	97
Erythromycin	16	0	84
Clindamycin	21	0	79
Linezolid	**0**	**0**	**100**
Teicoplanin	4	0	96
Vancomycin	5	0	95
Tetracycline	12	0	88
Tigecycline	**0**	**0**	**100**
Fosfomicin	5	0	95
Nitrofurantoin	1	0	99
Fusidic acid	1	1	98
Mupirocin	**0**	**0**	**100**
Rifampin	8	5	87
Trimethoprim/sulphamethoxazole	1	0	99

(excepting benzylpenicillin) to treat staphylococcal infections of any localization. However, analysis of antimicrobial resistance profiles revealed that some strains were resistant to 9—13 antibiotics, belonging to 6—10 classes of antimicrobials. This considerably limits the choice of antibiotics useful for treatment of infections, despite of low levels of resistance among staphylococci in general (Table 2).

Analysis of the profiles for strains resistant to 6 and more classes of antibiotics demonstrated, that all the strains were resistant to oxacyllin, suggesting previously shown evidences on multiple antimicrobial resistance among staphylococci, resistant to oxacyllin.

Oxacyllin-resistant strains were found not to have identical susceptibility to cefoxitin, and therefore, different mechanisms of resistance to oxacyllin were presumed. Thus, oxacyllin-resistant strains were also resistant to cefoxitin due to beta-lactamases hyper-production, while cefoxitin-resistant strains were also resistant to oxacyllin due to production of PBP2a, or the other modified PBP, which was impossible to differentiate without use of molecular methods of analysis.

MRSA antimicrobial resistance profiles, excepting differences in resistance to cefoxitin, had some other diversity. 35.7 % of MRSA strains were found to be resistant only to beta-lactamic antibiotics: penicillin, cefoxitin, and oxacyllin. Such an MRSA phenotype is specific for non-nosocomial strains of *S. aureus*, or for strains, resistant due to modified penicillin-binded proteins (not PBP2a). Other strains, except of anti-beta-lactam resistance, were resistant to other classes of antibiotics, and such a phenotype is considered to be specific for nosocomial MRSA.

Besides the differences in antimicrobial resistance phenotypes, nosocomial and non-nosocomial MRSA are very well known for their differences in genotypes, e.g., non-nosocomial MRSA contains a staphylococcal cassette chromosome SCCmec, type IV, which cannot be found in nosocomial staphylococcal strains. In addition, most non-nosocomial strains of MRSA are typical of Panton-Valentine leukocidin (PVL) production, while oxacyllin-resistant nosocomial strains of *S. aureus*, express this feature much less frequently.

It should be highlighted, that when isolating MRSA, particular attention should be paid to the choice of antibiotic, prescribed for treatment. Having analyzed MRSA resistance levels to antibiotics, our data allowed us to determine the

Table 2
Profiles of resistance to antibiotics among *S. aureus* strains

Combination of resistance determinants to antibiotics	Number of resistance determinants	Number of antibiotics classes at resistance profile	Percentage of *S. aureus* strains, %
Not detected	0		22
Y	1	1	1
L	1	1	1
P	1	1	40
GT	2	1	1
PY	2	2	1
PL	2	2	4
PO	2	1	1
PED	3	3	4
CPO	3	1	5
DTVR	4	4	2
ODVR	4	4	1
PEDY	4	4	3
PLED	4	4	1
PGTE	4	3	1
CPOF	4	2	1
CPODF	5	3	1
CPODFR	6	4	3
POEDTVYSR	9	6	1
POGTLEDYR	9	7	1
CPOGTLEDYR	10	7	2
CPOGTLMEYR	10	6	1
CPOGTLMEDYR	11	7	1
POGMEDTVYNSRH	13	10	1

Note. C — cefoxitin; P — penicillin; O — oxacyllin; G — gentamycin; T — tobramycin; L — levofloxacin; M — moxifloxacin; E — erythromycin; D — clindamycin; J — teicoplanin; V — vancomycin; Y — tetracycline; F — fosfomicin; N — nitrofurantoin; S — fusidic acid; R — rifampicin; H — trimethoprim/sulphamethoxazole.

antibiotics, that can be chosen for treatment of staphylococcal infections (Table 3).

MRSA resistance levels, in comparison with resistance of all analyzed *S.aureus* strains in general, were higher, and therefore, the list of antibiotics to be effective used for MRSA treatment, had more limitations. Except of linezolid, mupirocin, and tigecycline, that no strain demonstrated resistance to, MRSA indicated quite high levels of susceptibility to nitrofurantoin and trimethoprim/sulphamethoxazole (both 94.7 %), fusidic acid (89.4 %), and moxifloxacin (84.2 %). These antibiotics could be the preparations of choice for the treatment of MRSA-caused infections.

It is important to specifically note low levels of MRSA susceptibility to glycopeptide antibiotics, vancomycin and teicoplanin (vancomycin — 15.8 %, and teicoplanin — 10.5 %), that no strain quite recently demonstrated resistance to, and that were

typically chosen for treatment of infections, caused by MRSA. Isolation of such strains suggested, that staphylococci have acquired resistance to vancomycin, and that it is greatly important to find new antibiotics, active against MRSA.

Since strains investigated have been received from different departments located in one surgical hospital, it was interesting to establish the prevalence of MRSA in different regions of Ukraine. According to the results of our study, the prevalence of MRSA by departments: Surgery — 36.4 %; Trauma — 25.0 %; ICU — 16.7 %, Urology — 9.1 %; in Ophthalmology there was no MRSA. However, the information provided may not reflect, in our opinion, the real MRSA prevalence in the country due to impact of several factors, the most important of which was small selection of strains. Thus, we actually made our research using a total selection of 100 strains, having from every department just 20 strains of *S. aureus*.

Table 3
Susceptibility of oxacyllin-resistant *S. aureus* to antibiotics

Antibiotic	Division by susceptibility, %		
	Resistant	Moderately resistant	Susceptible
Cefoxitin	73.7	0	26.3
Gentamycin	31.6	0	68.4
Tobramycin	26.3	0	73.7
Levofloxacin	10.5	15.8	73.7
Moxifloxacin	10.5	5.3	84.2
Erythromycin	36.8	0	63.2
Clindamycin	57.9	0	42.1
Linezolid	**0**	**0**	**100.0**
Teicoplanin	10.5	0	89.5
Vancomycin	15.8	0	84.2
Tetracycline	36.8	0	63.2
Tigecycline	**0**	**0**	**100.0**
Fosfomicin	26.3	0	73.7
Nitrofurantoin	5.3	0	94.7
Fusidic acid	5.3	5.3	89.4
Mupirocin	**0**	**0**	**100.0**
Rifampin	42.1	15.8	42.1
Trimethoprim/sulphamethoxazole	5.3	0	94.7

To combat the spreading of strains, resistant to antibiotics, one should have, first of all, reliable data about the status of this problem in each region, hospital, and even in every department. Implementation of standardized methods to receive this information, as well as introduction of efficient sanitary and hygienic approaches to control and decrease the prevalence of problematic microorganisms is of great importance, and should be based on the close cooperation between experts, both microbiologists, clinicians, and epidemiologists.

CONCLUSIONS

1. Based on our data, the prevalence of *S. aureus* strains, resistant to oxacyllin, is about 19 % in Kyiv Surgical Hospital.

2. Among studied strains, 11 % of *S. aureus* had 5—13 resistance determinants to 3—10 classes of antibiotics, thus demonstrating multiple resistance.

3. 35.7 % of MRSA strains demonstrated resistance to the only group of beta-lactamic antibiotics, the other were resistant also to the other classes of antibiotics.

4. Currently, among the most active antibiotics, that can be used for treatment of oxacyllin-resistant *S. aureus* isolated from patients of surgical departments, there are linezolid, mupirocin, tigecycline, vancomycine, teicoplanin, moxifloxacin, nitrofurantoin, fusidic acid, and trimethoprim/sulphamethoxazole.

5. Considerable differences in the MRSA prevalences among strains, isolated from patients of different departments of surgical hospital, presuppose clarification by further determination of staphylococcal resistance to methicillin, using more isolates.

Prospects of further studies presuppose determination of MRSA proliferation progress among agents, causing pyoinflammatory infections, in particular, nosocomial infections in hospitals of different types, and finding ways of prevention of these diseases.

Conflicts of interest
Authors declare no conflicts of interest.

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ПОШИРЕНІСТЬ МЕТИЦИЛІН-РЕЗИСТЕНТНИХ ШТАМІВ *STAPHYLOCOCCUS AUREUS* (MRSA) У КИЇВСЬКІЙ МІСЬКІЙ ХІРУРГІЧНІЙ ЛІКАРНІ (УКРАЇНА)

А.Г. Салманов, О.М. Вернер

Національна медична академія післядипломної освіти імені П.Л. Шупика, Київ, Україна

Резюме

Мета роботи — вивчити поширеність метицилін-резистентних штамів *Staphylococcus aureus* (MRSA), виділених від пацієнтів, госпіталізованих у хірургічні відділення Київської міської хірургічної лікарні.

Матеріали і методи. Досліджено 128 клінічних штамів *S. aureus*, виділених від пацієнтів з інфекціями в ділянці хірургічного втручання в період з червня до грудня 2015 р. Ідентифікацію виділених культур і визначення чутливості до антибіотиків проводили за допомогою автоматизованого мікробіологічного аналізатора VITEK 2 Compact та карти VITEK 2 AST-P580 (bioMerieux, Франція), яка охоплювала 20 антибіотиків (бензилпеніцилін, оксацилін, цефокситин, гентаміцин, тобраміцин, левофлоксацин, моксифлоксацин, еритроміцин, кліндаміцин, лінезолід, тейкопланін, ванкоміцин, тетрациклін, тигециклін, фосфоміцин, нітрофурантоїн, фузидинова кислота, мупіроцин, рифампіцин і триметоприм/сульфаметоксазол) і тест цефокситину, призначений для виявлення стійкості стафілококів до метициліну. Для оцінки результатів чутливості до антибіотиків використовували критерії, запропоновані Інститутом клінічних та лабораторних стандартів США (CLSI).

Результати та обговорення. Аналіз чутливості *S. aureus* до протимікробних препаратів виявив, що найактивнішими антибіотиками були лінезолід, тигециклін і мупіроцин, які продемонстрували пригнічення росту 100 % тестованих штамів. Чутливість до інших протимікробних препаратів також була високою: 99 % штамів були чутливі до нітрофурантоїну і триметоприму/сульфаметоксазолу, 98 % — до фузидинової кислоти, 97 % — до моксифлоксацину, 96 % — до тейкопланіну, 95 % — до ванкоміцину і фосфоміцину, 93 % — до гентаміцину і 92 % — до тобраміцину. Відзначено зниження чутливості до левофлоксацину (89 %), тетрацикліну (88 %), рифампіцину (87 %), еритроміцину (84 %) і кліндаміцину (79 %). Дослідження поширеності MRSA в Київській міській хірургічній лікарні показало, що 11 % штамів *S. aureus*, виділених від пацієнтів з нозокоміальною інфекцією (SSI), мають множинну стійкість до антибіотиків. Загальна поширеність MRSA в лікарні становила 19 %, показники у хірургічних відділеннях відрізнялися. Крім того, 35,7 % штамів MRSA були стійкі лише до групи β-лактамних антибіотиків, решта — до інших класів антибіотиків.

Висновки. Антибіотикорезистентність клінічних штамів *S. aureus* в досліджуваному хірургічному стаціонарі — важлива терапевтична та епідеміологічна проблема. Найбільшою активністю до клінічних штамів MRSA володіли лінезолід, мупіроцин, тигециклін, ванкоміцин, тейкопланін, моксифлоксацин, нітрофурантоїн, фузидинова кислота та триметоприм/сульфаметоксазол. З огляду на постійну зміну рівня резистентності штамів *S. aureus*, що спостерігається в усіх регіонах світу, необхідно проводити постійний моніторинг антибіотикорезистентності у кожному стаціонарі та на підставі отриманих локальних даних розробити лікарняний формуляр антибіотиків. Політика використання антибіотиків у кожному хірургічному стаціонарі має визначатися залежно від локальних даних щодо резистентності до протимікробних препаратів. Доцільно налагодити систему епідеміологічного нагляду за мікробною резистентністю на локальному, регіональному та національному рівнях.

Ключові слова: *Staphylococcus aureus*, хірургія, нозокоміальні інфекції, антибіотики, антибіотикорезистентність, MRSA.

РАСПРОСТРАНЕННОСТЬ МЕТИЦИЛЛИН-РЕЗИСТЕНТНЫХ ШТАММОВ *STAPHYLOCOCCUS AUREUS* (MRSA) В КИЕВСКОЙ ГОРОДСКОЙ ХИРУРГИЧЕСКОЙ БОЛЬНИЦЕ (УКРАИНА)

А.Г. Салманов, О.М. Вернер

Национальная медицинская академия последипломного образования имени П.Л. Шупика, Киев, Украина

Резюме

Цель работы — изучить распространенность метициллин-резистентных штаммов *Staphylococcus aureus* (MRSA), выделенных от пациентов, госпитализированных в хирургические отделения Киевской городской хирургической больницы.

Материалы и методы. Исследованы 128 клинических штаммов *S. aureus*, выделенных у пациентов с инфекциями в области хирургического вмешательства в период с июня по декабрь 2015 г.

Идентификацию выделенных культур и определение чувствительности к антибиотикам проводили с помощью автоматизированного микробиологического анализатора VITEK 2 Compact и карты VITEK 2 AST-P580 (bioMerieux, Франция), которая включала 20 антибиотиков (бензилпенициллин, оксациллин, цефокситин, гентамицин, тобрамицин, левофлоксацин, моксифлоксацин, эритромицин, клиндамицин, линезолид, тейкопланин, ванкомицин, тетрациклин, тигециклин, фосфомицин, нитрофурантоин, фузидиновая кислота, мупироцин, рифампицин и триметоприм/сульфаметоксазол) и тест цефокситина, предназначенный для выявления устойчивости стафилококков к метициллину. Для оценки результатов чувствительности к антибиотикам использовали критерии, предложенные Институтом клинических и лабораторных стандартов США (CLSI).

Результаты и обсуждение. Анализ чувствительности *S. aureus* к противомикробным препаратам показал, что наиболее активными антибиотиками были линезолид, тигециклин и мупироцин, продемонстрировавшие ингибирование роста 100 % тестируемых штаммов. Чувствительность к другим противомикробным препаратам также была высокой: 99 % штаммов были восприимчивы к нитрофурантоину и триметоприму/сульфаметоксазолу, 98 % — к фузидиновой кислоте, 97 % — к моксифлоксацину, 96 % — к тейкопланину, 95 % — к ванкомицину и фосфомицину, 93 % — к гентамицину и 92 % — к тобрамицину. Выявлено снижение чувствительности к левофлоксацину (89 %), тетрациклину (88 %), рифампицину (87 %), эритромицину (84 %) и клиндамицину (79 %). Исследование распространенности MRSA в Киевской хирургической больнице показало, что 11 % штаммов *S. aureus*, выделенных у пациентов с нозокомиальными инфекциями (SSI), имеют множественную устойчивость к антибиотикам. Общая распространенность MRSA в больнице составляла 19 %, показатели в хирургических отделениях отличались. Кроме того, 35,7 % штаммов MRSA были устойчивы только к группе β-лактамных антибиотиков, остальные — к другим классам антибиотиков.

Выводы. Антибиотикорезистентность клинических штаммов *S. aureus* в исследуемом хирургическом стационаре — важная терапевтическая и эпидемиологическая проблема. Наиболее эффективными для лечения инфекций MRSA были линезолид, мупироцин, тигециклин, ванкомицин, тейкопланин, моксифлоксацин, нитрофурантоин, фузидиновая кислота и триметоприм/сульфаметоксазол. Учитывая постоянное изменение уровня резистентности нозокомиальных штаммов *S. aureus* в разных регионах мира, необходимо проводить постоянный мониторинг за антибиотикорезистентностью в каждом стационаре и на основании полученных локальных данных разработать больничный формуляр антибиотиков. Политика использования антибиотиков в каждом хирургическом стационаре должна определяться в зависимости от локальных данных относительно резистентности к противомикробным препаратам. Необходимо организовать систему эпидемиологического надзора за микробной резистентностью на локальном, региональном и национальном уровнях.

Ключевые слова: *Staphylococcus aureus*, хирургия, внутрибольничные инфекции, антибиотики, антибиотикорезистентность, MRSA.

Адреса для листування

04112, Україна, м. Київ, вул. Дорогожицька, 9
Національна медична академія післядипломної
освіти імені П.Л. Шупика, кафедра мікробіології,
епідеміології та інфекційного контролю
Тел. роб. +38 (044) 205-49-67
E-mail: mozsago@gmail.com
Салманов Айдин Гурбанович

Address for correspondence

04112, Ukraine, Kyiv, 9 Dorohozhytska St.
Shupyk National Medical Academy of Postgraduate
Education, Department of Microbiology,
Epidemiology and Infection Control
Tel./fax +38 (044) 205-49-67
E-mail: mozsago@gmail.com
Aidyn Salmanov

Інформація про авторів

Салманов А.Г. — д. мед. н., професор, завідувач
кафедри мікробіології, епідеміології та інфекцій-
ного контролю Національної медичної академії
післядипломної освіти імені П.Л. Шупика, голова
Всеукраїнської асоціації інфекційного контролю
та антимікробної резистентності, національний
координатор з антимікробної резистентності
та інфекційного контролю

Вернер О.М. — к. мед. н., доцент кафедри
мікробіології і епідеміології, начальник
навчального відділу Національної медичної
академії післядипломної освіти імені П.Л. Шупика

About the authors

Aidyn Salmanov — MD, Professor, Head of the
Department of Microbiology, Epidemiology and
Infection Control of Shupyk National Medical Academy
of Postgraduate Education, President of Ukrainian
Association of Infection Control and Antimicrobial
Resistance, National Coordinator of Antimicrobial
Resistance and Infection Control

Olga Verner — MD, PhD, Associate Professor of the
Department of Microbiology and Epidemiology, Head
of the Educational Department of Shupyk National
Medical Academy of Postgraduate Education