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PREVALENCE AND CHARACTERISTICS OF *STAPHYLOCOCUS AUREUS* ISOLATED FROM INFECTIONS IN NORTHEAST ROMANIA

Dorneanu Olivia[1,2], Miftode Egidia[1,2], Vremeră Teodora[2], E Năstase [2], Filip Olga[2], V Luca [1,2]

1. University of Medicine and Pharmacy "Gr. T. Popa", Iaşi, România
2. Hospital of Infectious Diseases "Sf. Parascheva", Iaşi, România

Abstract. Introduction. Methicillin-resistant *Staphylococcus aureus* (MRSA) is associated with high morbidity and mortality rates. **Materials and methods**. We have tested a total of 89 *S. aureus* strains isolated from blood cultures (25), cerebro-spinal fluid (CSF) (6), pus (48), sputum (3) and urine (10) specimens collected from patients registered in the Infectious Diseases Hospital "Sf. Parascheva" Iaşi, Romania, between 1.01.2006-31.12.2006. The strains have been identified using ID 32STAPH strips and their susceptibility testing was performed using ATB STAPH strips (*bioMerieux*, France). Minimum inhibitory concentrations (MIC) to oxacillin and vancomycin were assessed using E-tests (*AB Biodisk*, Sweden). **Results**. MIC for oxacillin ranged from 0.064 to >256 µg/ml. The prevalence of MRSA in this hospital was 47.1%. Heteroresistance was present in 16.8% strains. MIC for vancomycin was in the susceptible range for all isolates, ranging between 1 to 3 µg/ml. The overall susceptibility of MRSA was: vancomycin 100%, quinupristin-dalfopristin 100%, clindamycin 97%, sulfamethoxazole-trimethoprim 94%, fusidic acid 94%, levofloxacin 50%, erythromycin 19%, gentamicin 9%, tetracycline 9%. **Conclusions**. Quinupristin-dalfopristin and vancomycin remain the first choice therapy for MRSA infections. To preserve their value, their use should be limited to those cases where they are clearly needed. Sulfamethoxazole-trimethoprim, clindamycin and fusidic acid are good alternatives.
Key words: Staphylococcus aureus, oxacillin, MRSA, E-test

Rezumat. Introducere. *Staphylococcus aureus* rezistent la meticilină (SARM) este asociat cu rate crescute de morbiditate şi mortalitate. **Material şi metode**. Au fost studiate 89 tulpini de *S. aureus* izolate din hemoculturi (25), lichid cefalo-rahidian (6), puroi (48), spută (3) şi urină (10), probe recoltate de la pacienţi internaţi în Spitalul Clinic de Boli Infecţioase „Sf Parascheva" Iaşi, România, în perioada 1.01.2006-31.12.2006. Tulpinile au fost identificate folosind galerii ID 32STAPH, iar testarea sensibilităţii lor la antibiotice a fost realizată folosind galerii ATB STAPH (*bioMerieux*, Franţa). Concentraţiile minime inhibitorii (CMI) la oxacilină şi vancomicină au fost evaluate prin E-test (*AB Biodisk*, Suedia). **Rezultate**. CMI pentru oxacilină au avut valori între 0,064 şi >256 µg/ml. Prevalenţa SARM în spital a fost de 47,1%. Heterorezistenţa a fost evidenţiată la 16,8% din tulpini. CMI pentru vancomicină au avut valori între 1 şi 3 µg/ml. Sensibilitatea generală a SARM a fost: vancomicină 100%, quinupristin-dalfopristină 100%, clindamicină 97%, trimetoprim-sulfametoxazol 94%, acid fusidic 94%, levofloxacin 50%, eritromicină 19%, gentamicină 9% şi tetraciclină 9%. **Concluzii**. Quinupristin-dalfopristina şi vancomicina rămân antibiotice de primă intenţie în tratamentul infecţiilor cu tulpini de SARM. Utilizarea lor trebuie limitată la acele cazuri în care acestea sunt realmente necesare. Asociaţia trimetoprim-sulfametoxazol, clindamicina şi acidul fusidic sunt alternative de avut în vedere.
Cuvinte cheie: *Staphylococcus aureus*, oxacilină, SARM, E-test

INTRODUCTION

Staphylococcus aureus is a leading cause of bloodstream and other invasive infections in the world. *S. aureus* has become increasingly resistant to first-line antimicrobial agents in health-care settings (1).

Emergence and dissemination of methicillin- resistant *Staphylococcus aureus* (MRSA) in Europe is becoming alarming because these strains usually show multiple resistances to antimicrobial agents.

Another concern is *S. aureus* resistance to vancomycin, although reported only in the United States of America. Infections with *S. aureus* with heterogeneous intermediate resistance to vancomycin (hVISA) are emerging. Detection of these infections, their prevalence, clinical characteristics and significance are controversial (2).

These are reasons for which knowing the resistance profile of MRSA has a great impact on medical practice. The objective of our study was to asses the prevalence of *S. aureus* infections, the methicillin resistance rate in *S. aureus* and the susceptibility patterns of the isolated strains in the Infectious Diseases Hospital "Sf. Parascheva" from Iaşi, Romania.

MATERIALS AND METHODS

We have tested a total of 89 *S. aureus* strains isolated from blood cultures (25), cerebro-spinal fluid (CSF) (6), pus (48), sputum (3) and urine (10) specimens collected from patients registered in the Infectious Diseases Hospital "Sf. Parascheva" Iaşi, România, between 1.01.2006-31.12.2006. The strains have been screened by the coagulase test and definitively identified using ID 32STAPH strips.

Available *S. aureus* isolates were characterized by antimicrobial-susceptibility testing, performed using ATB STAPH strips (*bioMerieux*, France).

Minimum inhibitory concentrations (MIC) to oxacillin and vancomycin were assessed on Mueller-Hinton agar, using E-test strips (*AB Biodisk*, Sweden).

RESULTS AND DISCUSSION

The prevalence of MRSA within the hospital was 47.1% for the year 2006. Heteroresistance was present in 16.8% strains and could be only detected by the E-test macromethod, but not with ATB STAPH strips.

European studies show an overall oxacillin resistance rate for *S. aureus* of 26.7% for *S. aureus* and 77% for coagulase-negative staphylococci. There is a great variation of MRSA rate between countries, the resistance level ranging from over 40% in Great Britain, Belgium, Greece, Ireland, and Island to only 0.6% in Sweden (4).

Methicillin-resistant *S. aureus* infections have been confined to healthcare centers for decades. However, MRSA infections are increasingly seen in young healthy individuals with no exposure to healthcare centers (6).

Both in Europe and United States of America there is a dramatic raise in the number of reports showing the increase of MRSA prevalence in community-associated infections. Before 2000, in USA, the number of

MRSA strains isolated from skin and soft tissue infections was very low (3%) and raised in some regions to 30% and then to 64% between 2001-2004 (3).

Minimum inhibitory concentration (MIC) for oxacillin ranged from 0.064 to >256 μg/mL. A high proportion of strains (30,7%) showed oxacillin MICs of >256 μg/mL. MIC for vancomycin was in the susceptible range for all isolates, ranging from 1 to 3 μg/mL. MIC_{50} and MIC_{90} values for the tested strains are shown in table 1.

Table 1. Oxacillin and vancomycin MIC_{50} and MIC_{90} for *S. aureus* strains

Minimum inhibitory concentration	Oxacillin	Vancomycin
MIC_{50}	1 μg/mL	1.5 μg/mL
MIC_{90}	>256 μg/mL	2 μg/mL

In European studies the vancomycin resistant enterococci (VRE) have a relatively high rate, more than 15% *Enterococcus faecium* strains being resistant to vancomycin. The distribution of VRE maximum prevalence is similar to that of MRSA, indicating that the two resistance phenotypes might be epidemiologically correlated (4).

In vancomycin intermediate *S. aureus* (VISA) resistance seems to be a consequence of peptidoglycan synthesis alteration, but vancomycin resistant *S. aureus* (VRSA) receives an additional resistance by the transfer of plasmids containing operon *vanA* from vancomycin resistant *Enterococcus faecalis* (5).

Resistance to oxacillin is more frequent in *S. aureus* strains isolated from invasive infections (57.9-60% resistant strains) comparing to those isolated from localized infections (48.3-50% resistant strains) (fig. 1).

All strains have proved their susceptibility to teicoplanine, vancomycin and quinupristin-dalfopristin.

The overall susceptibility of MRSA was: vancomycin 100%, quinupristin-dalfopristin 100%, clindamycin 97%, sulfamethoxazole-trimethoprim 94%, fusidic acid 94%, levofloxacin 50%, erythromycin 19%, gentamicin 9%, and tetracycline 9%. Methicillin susceptible *S. aureus* (MSSA) showed increased susceptibility to antibiotics comparing to MRSA strains (fig 2).

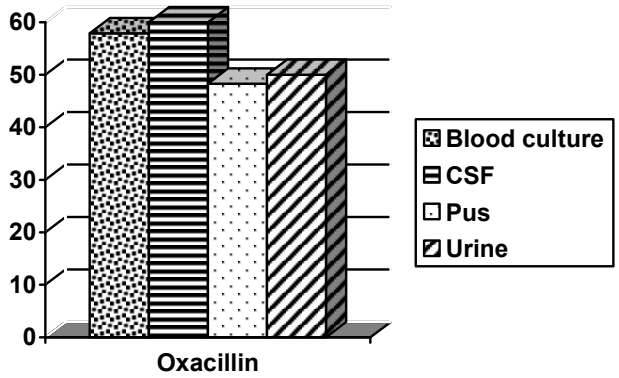

Fig. 1. Compared resistance to oxacillin (% of resistant strains) according to the clinical specimen.

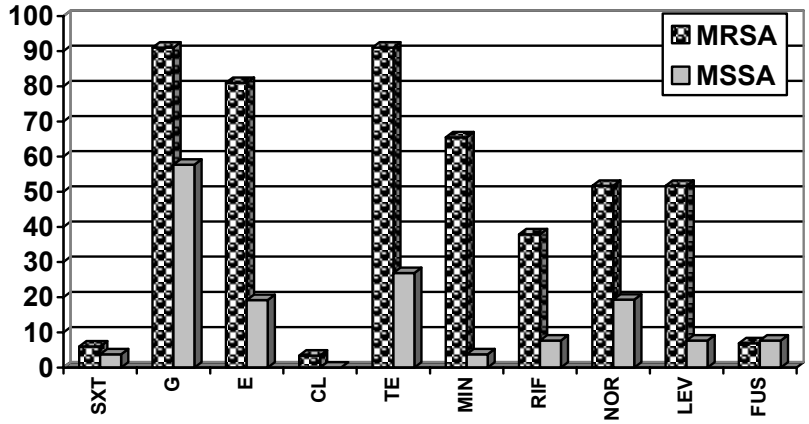

Fig. 2. Compared resistance to antibiotics (% of resistant strains) of MRSA and MSSA strains (SXT = sulfamethoxazole-trimethoprim; G = gentamicin; E = erythromycin; CL = clindamycin; TE = tetracycline; MIN = minocycline; RIF = rifampicine; NOR = norfloxacin; LEV = levofloxacin; FUS = fusidic acid)

CONCLUSIONS

- Quinupristin-dalfopristin and vancomycin remain the first choice therapy for MRSA infections. To preserve their value, their use should be limited to those cases where they are clearly needed. Sulfamethoxazole-trimethoprim, clindamycin and fusidic acid are good alternatives.
- In order to prevent and control MRSA outbreaks successfully, the restrictive antibiotic policy must be followed with strict infection prevention measures.

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