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The Resistance Rates of Different Antimicrobials in Staphylococci Isolated from Intensive Care Units

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Purpose: The aim of this study is to determine the resistance ratios of staphylococci to antimicrobial agents in intensive care units that might be useful from therapeutic and epidemiological points of view.
Methods: Staphylococcus spp. were isolated from different specimens and identified according to conventional methods. Antimicrobial susceptibility test was performed by disk diffusion method according to proposals of NCCLS.
Results: The incidence of resistance is higher among coagulase-negative staphylococcus (CNS) than *Staphylococcus aureus*. The antimicrobial resistance of 58 strains of CNS isolates was 29% teicoplanin, 51% ciprofloxacin, 58% gentamicin, 63% for each of co-trimoxazole and clindamycin, 79% erythromycin, 86% oxacillin and 96% penicillin. The multiple antimicrobial resistances were revealed by 96% of CNS isolates. The multiple antimicrobial resistance was also observed in *S. aureus* isolates but less than CNS (78%). Of 32 *S. aureus* isolates, 12% co-trimoxazole, 25% teicoplanin, 46% erythromycin, 50% clindamycin, 68% gentamicin, 71% ciprofloxacin, 81% oxacillin and 100% penicillin were resistant. No resistance to vancomycin was observed.
Conclusion: The findings revealed an increase in incidence of resistance and multiple antimicrobial resistant strains to commonly used antimicrobials in intensive care units. Therefore, prudent policy in prescribing and using of antibiotics is indispensable.

Key Words: *Staphylococcus aureus*, CNS, Antibiotic Resistance, Intensive Care Units

Yoğun Bakım Ünitelerinden Izole Edilen Stafilokok'ların Farklı Antibiyotiklere Direnç Oranları

Amaç: Çalışmamızın amacı antimikrobiyal ajanlara karşı stafilokokların direnç oranlarını incelemektir. Bu epidemiyolojik ve tedavi açısından faydalı olabilir.
Yöntem: Farklı numunelerden izole edilen Stafilokok'lar geleneksel yöntemlerle tanımlandı. Antibiyotiklere duyarlılık testi NCCLS önerilerine göre disk diffüzyon yöntemi ile yapıldı.
Sonuçlar: Koagulaz negatif stafilokok'larda antibiyotiklere (KNS) direnç oranı *S. aureus*'dan daha yüksek bulundu. Ellisekiz koagulaz negatif stafilokok suşunun %29'u teikoplanine, %51'i siprofloksasine, %58'i gentamisine, %63'ü ko-trimaksazol ve klindamisine, %79'u eritromisine, %96'sı penisiline, %86'sı oksasiline dirençli bulundu. Bu suşların %96'sı çoğul dirence sahipti, *S. aureus*'da da çoğul direnç gözlendi, ancak CNS'den daha düşüktü (%78). Otuziki *S. aureus* suşunun, %12'si ko-trimaksazole, %25'i teikoplanine, %46'sı eritromisine, %50'si klindamisine, %68'i gentamisine, %71'i siprofloksasine, %81'i oksasiline ve tümü penisiline dirençli saptandı. Vankomisine direnç gözlenmedi.
Tartışma: Antibiyotik kullanımının yaygın olduğu yoğun bakım ünitelerinde, dirençte ve çoğul dirençte artış vardır. Bu nedenle ihtiyatlı antibiyotik kullanım politikalarının uygulanması gereklidir.

Anahtar Kelimeler: *Staphylococcus aureus*, KNS, Antibiyotik Direnci, Yoğun Bakım Üniteleri.

Staphylococci are present as normal flora of different human body sites. They may opportunistically be important human pathogens that cause high morbidity and mortality under appropriate conditions.[1] Patients in intensive care units are usually immunocomprimised and are at high risk of developing serious staphylococcal illnesses.[1] Particularly staphylococci resistant strains are commonly implicated in these diseases. High consumption of antibiotics such as broad-spectrum beta-lactams, quinolones and others in hospital wards particularly in intensive care units led to development of multiple antimicrobial resistances which in turn brings forward serious therapeutic dilemmas.[2] The antimicrobial resistant pattern greatly varies among hospital and even wards.[2] Our work was aimed to determine antimicrobial resistance profile of many strains staphylococci isolat in intensive care wards of Turgut Ozal Medical Centre in order to achieve correct therapeutic addressing.

MATERIALS AND METHODS

Clinical specimens submitted from intensive care units were blood, cerebrospinal fluids, pus, wound swabs and urine. They were cultured on routine media including blood agar. Suspected colonies were stained with Gram stain and *Staphylococcus* spp. were identified according to catalase test, tube coagulase and its resistance to bacitracin. For antimicrobial susceptibility test, disk diffusion method was performed according to instructions of the National Committee for Clinical Laboratory standards (NCCLS) particularly for methicillin. The following antimicrobial disks (Oxoid) were used: Oxacillin, penicillin, erythromycin, clindamycin, teicoplanin, vancomycin, gentamicin, co-trimoxazole and ciprofloxacin.

RESULTS

The antimicrobial resistance pattern of *Staphylococcus* strains was shown in table 1. The antimicrobial resistance pattern of 32 isolates of *Staphylococcus aureus* against 9 antimicrobial agents was recorded. They were all resistant to penicillin. The resistance pattern to other antimicrobial agents was shown in table 1. In regard to CNS strains, they were more resistant than *Staphylococcus aureus* to each tested antimicrobial agent except vancomycin to which none of the strains was resistant. The rate of resistance to penicillin was 100%, 96% among *Staphylococcus aureus* and CNS strains respectively. The resistance profile of CNS isolates to other antimicrobials was also shown in table 1. The number of CNS strains resistant to three or more antibiotics was 48 (96%). This number among *Staphylococcus aureus* was 25 (78%). It was worth mentioning that all multiple resistant *Staphylococcus* strains were resistant to oxacillin except one strain. Moreover, oxacillin resistance was the most frequently observed among multiple resistant CNS strains.

Table 1. The numbers and rates of resistance of staphylococci isolated from intensive care units to different antimicrobials.

	S.aureus (32)		CNS(58)		Total (90)	
	No	%	No	%	No	%
Oxacillin	26	81	50	86	76	84
Penicillin	32	100	56	96	88	97
Gentamicin	22	68	34	58	56	62
Ciprofloxacin	23	71	30	51	53	58
Co-trimoxazole	4	12	37	63	41	45
Clindamycin	16	50	37	63	53	58
Erythromycin	15	46	46	79	61	67
Teicoplanin	8	25	17	29	25	27
Vancomycin	0	0	0	0	0	0

DISCUSSION

Increase in the ratio of resistant staphylococci to antimicrobial agents is of primary importance particularly in intensive care units where general health conditions of patients deteriorated when proper therapy of infections due to such organisms failed.[3] The high frequency of antibiotic resistance among staphylococci in current study is in accordance with other studies.[3,4] Results also showed that the rate of resistance differed considerably between *S. aureus* and CNS. The latter was more resistant than the former. This is consistent with other studies.[5,6] Table 1 showed that among CNS isolates 86% were resistant to oxacillin, 58% to gentamicin, 51% to ciprofloxacin and 29%to teicoplanin. These values indicated that resistance rates among our strains are higher than those reported by Jarlov and Hoiby.[2] They found that the resistant rates were 56% to methicillin, 51% to gentamicin, 28% to ciprofloxacin and 5% to teicoplanin.[2] However, resistant rates in our hospital were lower than values of other hospitals.[5] Moreover, methicillin resistance was the most frequently observed among multiple resistant CNS strains. This may indicate the misuse and high consumption of broad-spectrum beta-lactams. The increase in antibiotic resistance among staphylococci renders therapy of staphylococcal infections more difficult and problematic particularly in patients of intensive care units. Ciprofloxacin resistance may be due to single clonal mutation in DNA gyrase a & b subunits and topoisomerase subunits among staphylococci and depends on type of species.[7] It was found that methicillin resistant *Staphylococcus aureus* are more resistant to ciprofloxacin than methicillin resistant CNS strains except for *Staphylococcus hemolyticus*.[8,9] In current study, 81%, 86% of *Staphylococcus aureus* and CNS strains were resistant to oxacillin respectively. Of these 71%, 51% were resistant to ciprofloaxcin respectively. For our knowledge, the exact mechanism of such difference is not well understood but it can be underlined that methicillin resistant staphylococci was most probably associated with resistance to other antibiotics.[9] On the mean time, this may indicate that the usefulness of ciprofloxacin against *Staphylococcus aureus* was more limited than CNS strains. Concerning teicoplanin, the resistant rates of 25%, 29% among *Staphylococcus aureus* and CNS strains necessitate confirmation by minimum inhibitory concentration (MIC) determination for its precise efficacy establishment. In a study by Goldstein et al [10] 1.7% of CNS strains was found to be resistant to teicoplanin by agar dilution method.

Fortunately, all the examined strains were sensitive to vancomycin. The same result was obtained in similar studies in Brazilan, Kuwait and Malaysian hospitals.[4-6,11,12] This displays the significance of vancomycin which should be recommended in therapy of multiple resistant staphylococci despite the high cost of this antibiotic. Although a vancomycin resistant strain was reported in many parts of world, such strain fortunately has not yet emerged in Turkey.[13] Moreover, our study showed that there were numerous multiple resistant strains among staphylococci. The increase in ratio of multiple resistant strains among staphylococci limits physician right in selecting appropriate drug for proper therapy. This resistance problem within staphylococci and other pathogens exists today globally as consequence of uncontrolled unwise use of antibiotics as well as partly due to the incorporation of antibiotics in animal feeds.[14] In conclusion, performance of antimicrobial susceptibility is necessary due to common multiple antimicrobial resistance and widespread of important staphylococcal infections. There has been also an imperative need to detect changes in antimicrobial resistance profiles that exert consequently an important impact on empirical therapy of serious staphylococcal infections.

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