

METHICILLIN-RESISTANT STAPHYLOCOCCI ISOLATED FROM PUS SINCE 1992 AND AMINOGLYCOSIDE AND QUINOLONE RESISTANCE IN THESE STRAINS*

Nezihat GÜRLER, Arif KAYGUSUZ, Sabiha KARAYAY,
Kurtuluş TÖRECI

ÖZET

1992 yılından bu yana cerrahatten izole edilen metisiline dirençli stafilokoklar ve bu suşlarda aminoglikozid ve kinolon direnci.

Cerrahatten izole edilen *S.aureus* suşlarında 1992'de %34 (329/954), 1993'de %40 (285/705), 1994'de %36 (195/540), 1995'de %33 (108/324), 1996'nın ilk 6 ayında %30 (45/148); koagülaz negatif stafilokok suşlarında 1992'de %17 (50/289), 1993'de %26 (60/231), 1994'de %16 (41/260), 1995'de %42 (85/204), 1996'nın ilk 6 ayında %24 (27/112) oranında metisilin direnci saptanmıştır.

Ocak 1992 ile Temmuz 1996 arasında izole edilen metisiline dirençli 962 *S.aureus* suşunda gentamisine %76, tobramisine %54, amikasine %33, netilmisine %14, ofloksasine %49, siprofloksasine %43 oranında; aynı dönemde izole edilen metisiline dirençli 263 koagülaz negatif stafilokok suşunda gentamisine %56, tobramisine %51, amikasine %20, netilmisine %10, ofloksasine %48, siprofloksasine %36 oranında direnç gözlenmiştir.

SUMMARY

Methicillin resistance rates were found to be 34% (329/954) in 1992, 40% (285/705) in 1993, 36% (195/540) in 1994, 33% (108/324) in 1995 and 30% (45/148) in 1996 (six months) in *S.aureus*, and 17% (50/289) in 1992, 26% (60/231) in 1993, 16% (41/260) in 1994, 42% (85/204) in 1995, 24% (27/112) in 1996 (six months) in coagulase negative staphylococci isolated from pus specimens.

The aminoglycoside resistance were found to be 76% for gentamicin, 54% for tobramycin, 33% for amikacin, and 14% for netilmicin in 962 methicillin resistant *S.aureus* strains isolated from 1992 to the sixth months of 1996. Of these strains 49% were resistant to ofloxacin and 43% to ciprofloxacin. Of 263 methicillin resistant coagulase negative strains, 56% were resistant to gentamicin, 51% to tobramycin, 20% to amikacin, 10% to netilmicin, 48 % to ofloxacin, 36% to ciprofloxacin.

*Presented at the 10th Mediterranean Congress of Chemotherapy (20-25 October 1996, Antalya).
Istanbul Medical Faculty, Department of Microbiology and Clinical Microbiology, Çapa, Istanbul.

INTRODUCTION

Staphylococcus aureus is one of the most frequently encountered bacteria isolated from pus. The importance of coagulase-negative staphylococci is also increasing as etiological agents due to the increase of invasive procedures such as catheter, shunt and prosthetic device applications.

Methicillin-resistance in staphylococci has a special importance from therapeutic of view as these strains exert resistance to all beta-lactam antibiotics and to many antibiotics from other groups except glycopeptides. Methicillin-resistance was first observed in *S.aureus* in 1961, and since then the isolation of methicillin-resistant *S.aureus* (MRSA) and coagulase-negative staphylococci (MRCNS) are progressively increasing in many part of the World (3,11,16). In some countries, isolation rates as high as 60% were reported for MRSA strains. One the other hand, in some countries, e.g. Denmark, a decrease in the rate of MRSA was also observed in recent years (3,16). Nevertheless, both MRSA and MRCNS strains are among the most important nosocomial pathogens and their infections may end up in death.

In this paper, MRSA and MRCNS strains isolated from pus between January 1992 and July 1996, and their susceptibility to some aminoglycosides and quinolones are presented.

MATERIALS AND METHODS

Isolation and identification of strains were performed by conventional methods and coagulase-positive strains were accepted as *S.aureus*.

Disk diffusion method was used for susceptibility tests. For methicillin susceptibility Mueller-Hinton agar supplemented with cations and 1 µg oxacillin disks, for other tests Mueller-Hinton agar and Oxoid disks were used. The inhibition zones were evaluated according to NCCLS recommendations (10).

RESULTS

From 11674 pus specimens, 2671 *S.aureus* (SA) and 1096 coagulase-negative *Staphylococcus* (CNS) strains were isolated. Methicillin-resistance was detected in 962 (36%) of SA and in 263 (24%) of CNS strains. The numbers of staphylococcal isolates and the numbers and percentages of MRSA and MRCNS strains according to the years were show in table 1.

Table 1. The numbers of staphylococcal isolates and the numbers and percentages of MRSA and MRCNS strains.

Year	SA	MRSA		CNS	MRCNS	
	n	n	(%)	n	n	(%)
1992	954	329	(34)	289	50	(17)
1993	705	285	(40)	231	60	(26)
1994	540	195	(36)	260	41	(16)
1995	324	108	(33)	204	85	(42)
1996 (six mo.)	148	45	(30)	112	27	(24)
Total	2671	962	(36)	1096	263	(24)

The numbers and percentages of MRSA and MRCNS strains resistant to gentamicin, tobramycin, amikacin, netilmicin, ofloxacin and ciprofloxacin were shown in table 2.

Table 2. The numbers and percentages of MRSA and MRCNS strains resistant to aminoglycosides and quinolones.

Resistance to	MRSA (n:962)		MRCNS (n: 263)	
	n	(%)	n	(%)
Gentamicin	728	(76)	147	(56)
Tobramycin	523	(54)	133	(51)
Amikacin	317	(33)	52	(20)
Netilmicin		131	(14)	25(10)
Ofloxacin	474	(49)	125	(48)
Ciprofloxacin	410	(43)	95	(36)

DISCUSSION

Methicillin-resistance in staphylococcal isolates creates many problems in the treatment of infections caused by such strains. The proportion of these strains among all staphylococcal isolates are noticeable, especially in hospital settings. The percentages of MRSA strains isolated from pus specimens received from departments of our faculty fluctuated between 30% and 40 % (average 36%) and those of MRCNS between 16% and 42% (average 24%) during 4 1/2 years period. The percentages of methicillin-resistance may show great variations in different hospitals. These variations may due to either technical errors or prevailing of different epidemic strains in some hospitals from time to time. In Turkey the reported percentages varied from 11% to 59% since 1978 (Table 3).

Table 3. Some reports for percentages of MRSA strains in Turkey and in some European countries.

Turkey		European countries (3,16)	
Töreci et al (12) (İstanbul, 1978)	11	Denmark	0.1
Akalin et al (1) (Ankara, 1987)	48	Sweden	0.3
Baykal et al (2) (Ankara, 1988)	28	Netherlands	1.5
Töreci et al (13) (İstanbul, 1988)	31.7	Switzerland	1.8
Gürler et al (6) (İstanbul, 1989)	59	Germany	5.5
Ünal et al (15) (Ankara, 1990)	37	Austria	21.6
Esen et al (5) (Ankara, 1992)	31.8	Belgium	25.1
Karabiber et al (8) (Ankara, 1992)	13	Spain	30.3
Tünger et al (14) (İzmir, 1995)	55	France	33.6
Gürler et al (7) (İstanbul, 1995)	33	Italy	34.4
Kırış et al (9) (Van, 1996)	21		
This study (İstanbul, 1996)	30		

Another aspect of methicillin resistance in staphylococci, which makes the problem worse, is their resistance to other antibiotic groups except glycopeptides. The higher percentages for gentamicin resistance in MRSA and MRCNS strains were well recognized all over the World. But the situation is not confined to gentamicin. As it is shown in table 2, the percentages of resistance to other aminoglycosides and some quinolones are also noticeably high. When the overall results of antibiotic resistance to these antibiotics in staphylococci which isolated in our laboratory (e.g. ref 7) compared with the resistance rates for MRSA and MRCNS strains shown in table 2, these strains were found to be more resistant than others (up to twice in some instances), except for netilmicin resistance in MRSA and MRCNS and for ciprofloxacin resistance in MRCNS strains.

Gentamicin resistance in staphylococci usually caused by the production of APH (2'') + AAC(6') enzyme. This enzyme inactivates all aminoglycoside antibiotics used in the therapy. The strains producing this enzyme are generally found susceptible to aminoglycosides less amenable to modification such as netilmicin, amikacin and tobramycin in in-vitro tests as it is observed in the results given in table 2. Nevertheless, the enzyme diminishes the bactericidal activity of these antibiotics. For this reason, in serious infections caused by gentamicin resistant staphylococcal strains, bactericidal activity can not be attained by combining these antibiotics with beta-lactams, even the strains are found susceptible to other aminoglycosides in in-vitro tests. Thus gentamicin resistant staphylococcal isolates should be accepted resistant to all aminoglycosides including netilmicin, amikacin and tobramycin (4).

REFERENCES

- 1- Akalın HE, Çelik E, Baykal M, Kardeş T: Metisiline dirençli Staphylococcus'ların bazı antibiyotiklere in-vitro duyarlılıkları, *ANKEM Derg 1*: 122 (1987).
- 2- Baykal M, Kanra G, Akalın HE: Stafilokokların çeşitli antibiyotiklere duyarlılıkları, *ANKEM Derg 2*: 106 (1988).
- 3- Boyce JM: Methicillin-resistant Staphylococcus aureus (MRSA): Cost-benefit implications of preventing the spread of MRSA infection during an outbreak *Int Clin Pract Series No.9*: 17 (1994).
- 4- Courvalin P: Interpretive reading of antimicrobial susceptibility tests, *ASM News 58*: 368 (1992).
- 5- Esen N, Köksalan H, Mert A: Staphylococcus aureus suşlarının çeşitli antibiyotiklere in-vitro duyarlılıkları, *ANKEM Derg 6*: 149 (1992).
- 6- Gürler N, Sarpel C, Töreci K, Çetin ET: Muayene maddelerinden izole edilen S.aureus suşlarının kemoterapötiklere duyarlılığı, *ANKEM Derg 3*: 189 (1989).
- 7- Gürler N, Öngen B, Atilla Y, Kaygusuz A, Öksüz L, Töreci K: Gram pozitif koklarda seçimsiz duyarlılık deneylerinde saptanan direnç oranları, *ANKEM Derg 9*: 109 (1995).
- 8- Karabiber N, Emekdaş G, Türet S: Çeşitli klinik örneklerden izole edilen Staphylococcus aureus suşlarında vankomisin, metisilin, ampisilin+sulbaktam ve amoksisilin+klavulanat duyarlılığı, *ANKEM Derg 6*: 149 (1992).
- 9- Kırış M, Berktaş M, Bozkurt H, Yavuz MT, Dalkılıç AE: Sağlık personelinde nazal Staphylococcus aureus taşıyıcılığı ve izole edilen suşların antibiyotik duyarlılığı, *ANKEM Derg 10*: 135 (1996).
- 10- National Committee for Clinical Laboratory Standards: *Approved Standard M2-A5*, NCCLS, Villanova (1993).
- 11- Peterson LR: Quinolone resistance in Gram positive bacteria, *Infect Dis Clin Pract 3*: S127 (1994).

- 12- Töreci K, Çetin ET, AngÖ: The antibiotic susceptibility of 7726 bacterial strains isolated from clinical specimens, *Current Chemotherapy* (Eds: W Siegethaler, R Lüthy), Proceedings of the 10th International Congress of Chemotherapy, vol 1, p 553, Am Soc Microbiol, Washington (1978).
- 13- Töreci K, Gürler N, Çalangu S, Sarpel C, Eraksoy H, ÖzsütH, Çetin ET: Methicillin resistance in *Staphylococcus aureus* strains isolated in Istanbul, *ANKEM Derg* 2: 265 (1988).
- 14- Tünger A, Ulusoy S, Özkan F, Yamazhan T, Saydam C, Özinel MA, Tokbaş A: Deri ve yumuşak doku infeksiyonlarında saptanan başlıcbakteriler ve antibiyotik duyarlılıklarının araştırılması, *ANKEM Derg* 9: 122 (1995).
- 15- Ünal S, Korten V, Gür D, Akalın HE, Baykal M: Klinik örneklerden izole edilen *Staphylococcus aureus* suşlarında methicillin direnci, *ANKEM Derg* 4: 235 (1990).
- 16- Voss A, Milatovic D, Wallrauch-Schwarz C, Rosdahl VT, Braveny I: Methicillin-resistant *Staphylococcus aureus* in Europe, *Eur J Clin Microbiol Infect Dis* 13: 50 (1994).