

ORIGINAL ARTICLE

Evaluation of resistance to fusidic acid in *Staphylococci* isolates

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ABSTRACT

Objectives: Staphylococci were most prominent factors that responsible for skin, soft tissue and foreign body infections. Gaining resistance to methicillin and various antibiotics in these microorganisms over the years increased morbidity and mortality, especially in hospitalized patients. In such situations number of preferred antibiotics was limited. The aim of this study was to investigate in-vitro susceptibility of fusidic acid to clinic isolates of Staphylococci.

Materials and methods: The seventy-seven coagulase negative staphylococci (CNS) and 37 *Staphylococcus aureus* strains isolated from various clinical specimens were included in this study.

Staphylococci were identified with gram stain, catalase and coagulase tests. According to "Clinical and Laboratory Standards Institute (CLSI)" criteria, antimicrobial susceptibility testing was performed by Kirby-Bauer disc diffusion method.

Results: The seventy-four percent of the isolated CNS were defined as methicillin sensitive-CNS (MS-CNS), 26% of the isolated CNS were defined as methicillin resistant (MR-CNS). While 40% of MR-CNS was resistant to fusidic acid, fusidic acid resistance was found to be 24% in MS-CNS.

In methicilline-sensitive *S.aureus* strains fusidic acid resistance rate were detected as 13%; and in methicillin-resistant *S.aureus* strains the rate were 14%.

Conclusion: Susceptibility of fusidic acid in *Staphylococcus aureus* strains were found higher than coagulase-negative staphylococci. Fusidic acid remains as an alternative in the treatment of infections due to staphylococci. *J Microbiol Infect Dis* 2011;1(1):22-25.

Key words: *Staphylococcus aureus*, CNS, fusidic acid, antimicrobial susceptibility

Stafilokok izolatlarında fusidik asit direncinin değerlendirilmesi

ÖZET

Amaç: Stafilokoklar deri ve yumuşak doku enfeksiyonları ile yabancı cisim enfeksiyonlarından sorumlu mikroorganizmalar arasında en önde gelen etkenlerdendir. Bu mikroorganizmaların yıllar içerisinde metisilin ve çeşitli antibiyotiklere direnç kazanması, özellikle hastanede yatan hastalarda morbidite ve mortaliteyi artırmaktadır. Bu durumda tercih edilebilecek antibiyotiklerin sayısı sınırlıdır. Bu çalışmanın amacı klinik örneklerden elde edilen stafilokok izolatlarında fusidik asidin in-vitro etkinliğinin araştırılmasıdır.

Gereç ve yöntem: Çalışmaya çeşitli klinik örneklerden izole edilen 77 Koagülaz Negatif Stafilokok (KNS) izolatı ile 37 *Staphylococcus aureus* suşu dahil edildi.

Stafilokok izolatları; gram boyama, katalaz ve koagülaz testleri ile tanımlandı. Antimikrobiyal duyarlılıkları "Clinical and Laboratory Standards Institute (CLSI)" önerileri doğrultusunda Kirby-Bauer disk difüzyon yöntemi kullanılarak değerlendirildi.

Bulgular: İzole edilen KNS'lerin %74'ü metisiline duyarlı (MS-KNS), %26'sı metisiline dirençli (MR-KNS) olarak tanımlandı. MR-KNS'lerin %40'ı fusidik aside dirençli iken, MS-KNS'lerde fusidik asit direnci %24 olarak saptandı. Metisiline duyarlı *Staphylococcus aureus*'larda fusidik asit direnci %13, metisiline dirençli *Staphylococcus aureus*'larda ise fusidik asit direnci %14 olarak tespit edildi.

Sonuç: *Staphylococcus aureus* suşlarında fusidik asit duyarlılığı Koagülaz Negatif Stafilokok izolatlarına oranla daha yüksek bulundu. Fusidik asit, stafilokokların neden olduğu enfeksiyonların tedavisinde alternatif bir seçenek olarak yerini korumaktadır.

Anahtar kelimeler: *Staphylococcus aureus*, KNS, fusidik asit, antimikrobiyal duyarlılık

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INTRODUCTION

Staphylococci are cause of many nosocomial and community acquired infections with high rates of morbidity and mortality all over the world. Antimicrobial resistance in *Staphylococcus aureus*, especially methicillin-resistant *S.aureus* (MRSA) isolates remain a major problem all over the world.^{1,2}

Fusidic acid is a narrow-spectrum antibiotic derived from *Fusidium coccineum* used in *S.aureus* infections treatment for 40 years. Fusidic acid shows antibacterial activity by inhibiting bacterial protein synthesis. It is effective especially for methicillin-resistant staphylococci, particularly against many gram-positive aerobic and anaerobic bacteria. The basic indications for fusidic acid are systemic treatment of staphylococcal infections, MRSA infection and colonization and topical treatment of skin infections in atopic dermatitis. Studies have showed that fusidic acid may be a good alternative in *S.aureus* infections including nosocomial infections that pose difficulties in treatment.³

In present study, in-vitro susceptibilities of a variety of staphylococcal strains isolated from clinical specimens to fusidic acid were investigated.

MATERIALS AND METHODS

The seventy-seven coagulase negative staphylococci (CNS) and 37 *Staphylococcus aureus* strains isolated from various clinical specimens that had been sent to Infectious Diseases and Clinical Microbiology laboratory in Kırıkkale University Hospital had been included in this study. The samples were inoculated in 5% blood agar medium and incubated at 37°C for 18-24 hours. Staphylococci were identified by gram stain, catalase and coagulase tests. Methicillin resistance was determined by incubation of oxacillin disk (1 µg) on Mueller-Hinton agar medium at 35°C for 24 hours. Oxacillin inhibition zone diameter >13 mm strains were evaluated as susceptible, <10 mm the strains were resistant. Antimicrobial susceptibility testing was performed by Kirby-Bauer disc diffusion method in accordance with the recommendations of "Clinical and Laboratory Standards Institute (CLSI)".⁴ Susceptibility of fusidic acid was evaluated in accordance with the standards proposed by France of Microbiology and

Antibiogram Committee; zone diameter was >22 mm considered as susceptible, 15-21 mm as intermediate, <15 mm as resistance.⁵

In present study, the control strain of *S.aureus* ATCC 29213 standard strain was used.

RESULTS

The seventy-seven CNS and 37 *S.aureus* strains were included in this study. The seventy-four percent isolate of CNS's were defined as MS-CNS, 26% isolate of CNS's were defined as MR-CNS. While 40% of MR-CNS was resistant to fusidic acid and fusidic acid resistance was found to be 24% in MS-CNS.

Fusidic acid resistance was detected to be 13% in MSSA, while fusidic acid resistance was detected to be 14% in MRSA (Table 1).

DISCUSSION

Fusidic acid is a steroid-like structured antibiotic isolated from fungi called *Fusidium coccineum* in 1962 and the only member of fusidan class used in the clinic. Fusidic acid shows antimicrobial effects mainly by inhibiting protein synthesis as a result of interfering elongation factor G. Because of this specific mechanism, it has been reported that it has very low probability of cross-resistance action with other groups of antibiotics.⁶

Fusidic acid susceptibility is high against both methicillin-resistant, and methicillin-sensitive *Staphylococcus* strains as in-vitro. Therefore, these properties make it an important antibiotic in the per oral treatment of mild and moderate staphylococcal infections caused by methicillin-resistant strains.^{3,6} It is obvious that efficiency of orally given fusidic acid is unreliable in cases of endocarditis, sepsis, pneumonia. Even if fusidic acid is detected to be sensitive in-vitro, glycopeptide drugs are to be preferred in MRSA sepsis or endocarditis. Fusidic acid is a drug that is used in mild to moderate uncomplicated infections, however severe infections can be treated by oral route as in combination with other antibiotics.⁶

In our country several studies have been done about fusidic acid resistance related to staphylococci.

In a study carried out with 144 MSSA isolates and 71 MRSA isolates, Baysal et al.⁷ have reported that 4 (3%) MSSA isolates and 8 (11%) MRSA isolates were resistant to fusidic acid. In

a multi-center study, Altun et al.⁸ detected fusidic acid resistance as 3% in total 202 MRSA isolates (Table 2). In a comprehensive study with 1,080 staphylococci strains isolated from wound, Oz-

can et al.⁹ detected MR-CNS strains were the most fusidic acid-resistant strains and resistance rate as 30%. In same study resistance of MSSA strains was quite low (3%).

Table 1. This is distribution of Staphylococcus strains fusidic acid resistance rates.

Bacteria		n (%)	Fusidic acid resistant strains n (%)
CNS (n=77)	MS-CNS	57 (74)	14 (24)
	MR-CNS	20 (26)	8 (40)
<i>S.aureus</i> (n=37)	MSSA	30 (81)	4 (13)
	MRSA	7 (19)	1 (14)

Table 2. Fusidic acid resistance rates of staphylococcal strains isolated in our country, in some studies.

	Year	MSSA (%)	MRSA (%)	MS-CNS (%)	MR-CNS (%)
Erdemoglu et al. ¹⁵	2000	3.2	7.7	10.8	14.9
Baysal et al. ⁷	2003	2.8	11.3	-	-
Yazgi et al. ¹⁶	2003	6	7.6	10.9	15.7
Altun et al. ⁸	2003	0	3	0	13
Sengoz et al. ⁶	2004	1	9	21	33
Celen et al. ¹⁷	2005	3	6	20	3
Dogruman Al et al. ¹⁸	2005	-	-	11	39
Nergiz et al. ¹⁹	2007	-	-	-	28
Eksi et al. ²	2008	2.4	9.2	-	-
Mert Dinc et al. ²⁰	2009	-	98.6	-	-
Yaman et al. ³	2010	4	6	-	-

MSSA: Methicillin-sensitive *S.aureus*, **MRSA:** Methicillin-resistant *S.aureus*

MS-CNS: Methicillin-sensitive coagulase-negative staphylococci, **MR-CNS:** Methicillin-resistant coagulase-negative staphylococci

In a study of Ulug et al.¹⁰ resistance to fusidic acid has been found as 4.3% in methicillin-sensitive *S.aureus* strains, 16.7% in methicillin-resistant *S.aureus* strains, 0% in methicillin-sensitive coagulase-negative staphylococci, 36% in methicillin-resistant coagulase-negative staphylococci, however in none of the strains vancomycin, and teicoplanin resistance have been observed.

The presence of high sensitivity ratios of Staphylococcus strains to fusidic acid, suggested that this drug may be a viable option in the treatment of staphylococcal chronic osteomyelitis.

In a comprehensive study with 1,152 *S.aureus* strains in nine hospitals of Ireland, methicillin sus-

ceptibility has been found as 85% and fusidic acid susceptibility has been found as 96%.¹¹

Coombs et al. have applied alone and combined therapy to 20 patient who had acute orthopedic infection with CNS and they have received successful results in all patients.¹²

In recent years, some overseas studies have shown that fusidic acid resistance has increased compared to previous years. In a study conducted by Mc Laws et al.¹³ *S.epidermidis* strains obtained from clinical isolates have been found as highly resistant to fusidic acid. Fusidic acid resistance in community-acquired *S.aureus* strains has been found as 88.9% in a study by Katopodis et al.¹ In

our study, it was detected that fusidic acid susceptibility of *S. aureus* strains was higher than the susceptibility of coagulase-negative staphylococci. Fusidic acid remains as an alternative option in the treatment of staphylococcal infections.

In conclusion, the increase of inappropriate antibiotic use causes increase of multiple-resistant bacterial infections. On the other hand, although being in use for many years, because of low resistance rates to fusidic acid, it is seen as a good option for the treatment of MRSA and MSSA infections. Because of the high efficiency in MS-CNS, MR-CNS, MRSA, MSSA infections; fusidic acid may be a preferred option in the treatment of uncomplicated mild to moderate infections.

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