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ARAŞTIRMA YAZISI / RESEARCH ARTICLE

CERRAHİ DEBRİDMAN İHTİYACI OLAN DİYABETİK AYAKLI HASTALARDA ANTİBİYOTİK DİRENÇ DURUMU

ANTIBIOTIC RESISTANCE STATUS IN PATIENTS WITH DIABETIC FOOT REQUIRED SURGICAL DEBRIDEMENT

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ÖZET

AMAÇ: Bu çalışmanın temel amacı, diyabetik ayak sebebiyle yara debridmanı yapılan hastalardan elde edilen örneklerdeki mikroorganizmalar ile antibiyotik direnci veya duyarlılığı arasındaki ilişkiyi değerlendirmektir.

GEREÇ VE YÖNTEM: Bu retrospektif çalışmada 2013 - 2018 yılları arasında iki ayrı merkezde diyabetik ayak nedeniyle debridman yapılan hastalar değerlendirildi. Hastaların yaş, cinsiyet gibi demografik verileri kaydedildi. Diyabetik ayak yaralarından alınan derin doku örneklerinden izole edilen mikroorganizma ve antibiyogram sonuçları kaydedildi.

BULGULAR: Diyabetik ayak nedeniyle debridman yapılan 84 hasta (47 erkek, 37 kadın) çalışmaya dahil edildi. Yaşları 26 ile 87 arasında değişmekte olup, ortalama yaş 63.2 ± 16 idi. 44 (% 53) numunede bakteri üremesi (29 gram-pozitif ve 15 gram-negatif) tespit edildi. En fazla izole edilen mikroorganizmalar sırasıyla Staphylococcus aureus ve Escherichia coli idi. İzole edilen stafilokoklardan sadece biri metisiline dirençliydi. Escherichia coli'den biri geniş spektrumlu beta-laktamaz (ESBL) (+) idi.

SONUÇ: Diyabetik ayak enfeksiyonunda izole edilen bakteriler gram (-) ve gram (+) özellikte olup, tedavi planlanırken bu durum göz önünde bulundurulmalıdır.

ANAHTAR KELİMELER: Diyabetik ayak, Antibiyotik direnci, Debridman

ABSTRACT

OBJECTIVE: The main purpose of this study is to evaluate the relationship between microorganisms and antibiotic resistance or susceptibility in samples obtained from patients with wound debridement due to diabetic foot.

MATERIAL AND METHODS: In this retrospective study patients who underwent debridement for the diabetic foot in two separate referral centers between 2013 and 2018 were evaluated. Demographic data of patients including age, gender were collected. The microorganism and antibiogram results isolated from deep tissue samples taken from diabetic foot wounds were recorded.

RESULTS: 84 patients (47 male, 37 female) who underwent debridement surgery due to diabetic foot were included in the study. Their ages ranged from 26 to 87 years and the mean age was 63.2 ± 16 years. Bacterial growth (29 gram-positive and 15 gram-negative) was detected in 44 (53%) samples. The most isolated microorganisms were Staphylococcus aureus and Escherichia coli, respectively. Only one of the staphylococci isolated in the cultures was methicillin resistant one of the Escherichia coli was extended-spectrum beta-lactamase (ESBL) (+).

CONCLUSIONS: Bacteria isolated in diabetic foot infection have gram (-) and gram (+) characteristics, and this should be taken into consideration when planning the treatment.

KEYWORDS: Diabetic foot, Antibiotic resistance, Debridement

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INTRODUCTION

Diabetes Mellitus (DM) is the most common disease in the world. According to World Health Organization (WHO) data, there were 422 million people with diabetes worldwide in 2014 and this number will reach 642 million in 2040. The number of diabetic patients was 3 million in the 2000s in Turkey and in 2030 it will be estimated to be about 6.5 million according to the WHO reports. However, in until 2014, the number of patients had already exceeded the expected numbers and there were 7 million people with diabetes in 2014 (1). This metabolic disease is associated with acute and chronic complications. More than 1 million people undergo lower limb amputation due to diabetes each year and 85% of these patients have diabetic ulcers. The prevalence of lower extremity amputations in diabetic patients ranged from 0.2% to 4.8% (2). Early diagnosis and effective treatment are important for diabetic foot ulcers that cause such significant morbidity. A multidisciplinary approach with branches such as orthopedics, infectious diseases and cardiovascular surgery is necessary for the treatment of diabetic foot wounds, which are caused by the addition of infection to complications such as neuropathy secondary to diabetes and peripheral circulatory disorder. For proper treatment planning, culture should be taken first, and appropriate anti-biotherapy should be started with antibiograms after isolation of the active microorganism. Contamination is often encountered in culture swab specimens and the ideal management of this situation is to take deep tissue culture during debridement of the diabetic wound. By means of debridement, more appreciate results are obtained by eliminating microorganisms colonized on the surface (3 - 6). The main purpose of this study was to evaluate the relationship between microorganisms isolated from diabetic foot infection (DFI) and antibiotic resistance or susceptibility.

MATERIALS AND METHODS

In this retrospective study patients who underwent debridement for a/the diabetic foot in two separate referral centers between 2013 and 2018 were evaluated. Patients with insufficient records, history of immunosuppressive drug use or disease, and who are were under anti-biotherapy were excluded from the study. Our study consisted of patients who had no history of antibiotic use recently. A total of 84 patients who underwent debridement surgery due to diabetic foot were included in the study. Demographic data of patients including age, gender was collected. The microorganism and antibiogram results isolated from microbiological specimen cultures of deep tissue samples taken from diabetic foot wounds were recorded. All the patients included in the study were cultured by taking samples from deep tissue under sterile conditions during surgical intervention.

First-generation cephalosporins were preferred for empirical treatment until the culture results. In the patients who growth bacteria in cultures, treatment planning was made according to the grade of the susceptibility of bacteria to antibiotics. The patients who did not grow bacteria in cultures were treated with regular wound debridement and dressing.

Statistical Analysis

Statistical analysis was performed using the MedCalc Statistical Software version 12.7.7 (MedCalc Software bvba, Ostend, Belgium). The normality of continuous variables was investigated by Shapiro-Wilk's test. Descriptive statistics were presented using mean (SD; standard deviation) for continuous variables. For comparison of 2 non-normally distributed groups, student's t-test was used. The χ^2 test was used for categorical variables and expressed as observation counts (and percentages).

Ethical Committee

This retrospective study was conducted in accordance with the Helsinki Declaration after having the approval of the institutional ethical review board (Erzincan Binali Yıldırım University Faculty of Medicine, Clinical Trials Ethical Review Board) (Approval Number: 33216249-604.01.02-E.49620).

RESULTS

A total of 84 patients were included in the study and were retrospectively reviewed. There were 47 male and 37 female patients. Their ages ranged from 26 to 87 years and the mean

age was 63.2 ± 16 years. Bacterial growth was detected in 44 (53%) samples. No growth was detected in 39 (46.9%) patients **(Table 1)**. 29 gram-positive (65.9%) and 15 gram-negative (34.09%) bacteria were isolated from the cultures. The most isolated microorganisms were Staphylococcus aureus and Escherichia coli **(Table 2)** respectively. Only one of the staphylococci isolated in the cultures was methicillin resistant and one of the Escherichia coli was extended-spectrum beta-lactamase (ESBL) (+).

Table1: Demographic data of patients

Gender	
Female	47
Male	37
Mean age	63,2 ±16
Culture results	
Positive	44
Negative	39

Table 2: Microorganisms isolated from culture

Microorganism	Number
Achromobacter species	1
Acinetobacter baumannii	1
Enterococcus faecalis	1
Escherichia coli	6
Morganella morganii	1
Proteus mirabilis	2
Proteus penneri	1
Proteus vulgaris	1
Pseudomonas aeruginosa	1
Serratia marcescens	1
Staphylococcus aureus	22
Staphylococcus epidermidis	2
Koagülaz Negatif Staphylococcus	1
Streptococcus dysgalactiae	1
Streptococcus pyogenes	2

Antibiotic resistance status was determined by dividing gram positive bacteria into 5 groups. Trimethoprim sulfamethoxazole (TMP / SMX) and vancomycin resistance were examined in all 5 groups, and none of the gram-positive bacteria was found to be resistant **(Table 3)**.

Table 3: Antibiotic resistance of gram-positive bacteria isolated from cultures

	Enterococcus faecalis (n: 1)	Staphylococcus aureus (n: 22)	Staphylococcus Epidermidis (n: 2)	Coagulase(-) Staphylococcus (n: 1)	Streptococcus Dysgalactiae (n: 1)	Streptococcus pyogenes (n:2)
Ciprofloxacin	1	0	0	0	-	-
Levofloxacin	1	0	0	-	0	0
TPM/SMX*	**0**	**0**	**0**	**0**	**0**	**0**
Daptomycin	0	0	0	0	-	-
Vancomycin	**0**	**0**	**0**	**0**	**0**	**0**
Gentamicin	-	1	0	0	-	-
Ampicillin Sulbactam	-	0	-	-	-	-
Linezolid	-	**0**	**0**	**0**	**0**	**0**
Benzyl Penicillin (Pen G)	-	18	0	1	-	-
Teicoplanin	-	0	0	0	-	-
Erythromycin	-	3	0	1	-	-
Clindamycin	-	2	0	1	0	0
Tetraskelion	-	5	0	1	1	0
Tigecycline	-	0	0	-	-	-
Fosfomycin	-	0	1	-	-	-
Nitrofurantoin	-	0	0	-	-	-
Fusidic Acid	-	1	1	-	-	-
Mupirocin	-	0	-	-	-	-
Cefoxitin	-	0	-	0	-	-
Rifampin	-	1	0	0	-	-
Oxacillin	-	**1**	0	0	-	-
Quinupristin/ dalfopristin	-	0	-	-	-	-
Moxifloxacin	-	-	0	-	-	-
Cefotaxime	-	-	-	-	0	0
Ampicillin	-	-	-	-	-	0

*Trimethoprim Sulfamethoxazole

When the antibiogram results of gram-negative bacteria were examined, ciprofloxacin, ampicillin and ceftriaxone resistance were found in 50% of Escherichia coli. When the antibiogram for Acinetobacter baumannii was examined, it was found that it was only sensitive to trimethoprim sulfamethoxazole and no antibiotic resistance was observed in the antibiogram for pseudomonas aeruginosa **(Table 4)**.

Table 4: Antibiotic resistance of gram-negative bacteria isolated from cultures

	Achromobacter species (n: 1)	Acinetobacter baumannii (n: 1)	Escherichia coli (n: 6)	Morganella morganii (n: 1)	Proteus mirabilis (n: 2)	Proteus penneri (n: 1)	Proteus vulgaris (n: 1)	Pseudomonas aeruginosa (n: 1)	Serratia marcescens (n: 1)
Ciprofloxacin	1	1	3	0	1	-	-	0	1
Levofloxacin	0	-	2	0	-	-	-	0	-
TMP/SMX	0	0	2	0	1	0	-	-	1
Gentamicin	1	1	2	0	1	0	0	0	-
Ampicillin Sulbactam	-	1	1	-	-	-	-	-	-
Tigecycline	-	-	0	-	-	1	1	-	-
Fosfomycin	-	-	0	-	-	-	-	-	-
Nitrofurantoin	-	-	0	-	-	-	-	-	-
Cefoxitin	-	1	0	-	-	-	-	-	-
Ampicillin	-	-	3	1	1	1	1	-	-
Amikacin	1	1	0	0	0	-	-	0	-
Piperacillin Tazobactam	0	1	1	0	0			0	0
Piperacillin	-	-	1	0	-	-	-	-	-
Ticarcillin Clavulanic Acid	0	1	2	-	-	-	-	-	-
Cefepime	0	1	1	0	-	-	-	0	-
İmipenem	0	1	0	0	-	-	-	0	0
Meropenem	0	1	0	0	-	-	-	0	0
Ceftazidime	0	1	2	0	-	0	0	0	-
Aztreonam	1	-	0	-	-	-	-	0	-
Cefuroxime Sodium	-	1	1	-	1	1	1	-	-
Cefuroxime Acetyl	-	1	1	-	1	1	1	-	-
Colistin	-	1	0	-	2	-	1	-	-
Tobramycin	-	-	0	0	-	-	-	-	-
Ceftriaxone	-	-	3	-	-	-	-	-	1
Ertapenem	-	-	0	-	-	-	-	-	-
Amoxicillin Clavulanate	-	-	1	1	1	1	0	-	1
Cefixime	-	-	0	-	-	-	-	-	-
Cefazolin	-	-	1	-	-	-	1	-	-
Netilmicin	-	-	-	0	-	-	-	-	-
Azithromycin	-	-	-	0	-	-	-	-	-

DISCUSSION

Diabetic foot infections are one of the leading medical and socioeconomic problems in the world. In the literature, it is seen that the frequency of DFI increases with the age. In our study, the mean age of the patients was 63 and 50% of patients were 65 years old or over. In patients without early and appropriate treatment, the results are catastrophic and end up with amputation. The most important guide for the proper treatment planning is the culture results of the infected diabetic wound and the antibiograms made according to these results (7).

Empirical antibiotic treatment is recommended according to the severity of the infection and the microorganism that is likely to grow until the culture and antibiogram results of the patients are obtained. In addition, it is accepted as a general rule that empirical treatment should cover gram (+) cocci in patients who do not have a recent history of anti-biotherapy (8). However, in a study conducted in India, it was reported that 60% of microorganisms iso-

lated in DFI were gram (-) bacilli (9). In the study conducted by Kara et al., gram (-) bacilli were isolated at a higher rate. However, the average wound duration of the patients included in the study was 30 days and there was a history of antibiotic use or hospitalization (8). In recent studies, it has been observed that the frequency of gram (+) microorganisms is increased and especially staphylococcus aureus, coagulase negative Staphylococci, Streptococci, Enterococci and Corynebacterium species are isolated (4, 10). Our study consisted of patients who had no history of antibiotic use recently, and when the results of culture were examined, it was found that 29 of 44 patients with culture-positive (65.9%) produced gram (+) cocci. Although methicillin-resistant Staphylococcus aureus (MRSA) is known as a common microorganism in patients with a history of hospitalization, it is also seen in community-acquired cases. Tentolouris et al. investigated the prevalence of MRSA in infected and non-infected diabetic foot wounds and the most commonly isolated microorganism was gram (+) staphylococcus aureus. It was found that 50% of these microorganisms obtained from culture were MRSA (11). In our study, 22 Staphylococcus aureus were isolated and only 1 (4.5%) of them was found to be MRSA.

In 2007, Örmen et al. reported that 60% of microorganisms isolated from patients with DFI consisted of gram (-) bacteria and the ESBL (+) ratio was determined to be 16% (12). When the data published in the same clinic in 2014 were examined, it was seen that ESBL (+) ratio increased twice. Such high rates were explained by the hospitalization history of the patients and the use of broad-spectrum antibiotics (8). Motta et al. found 6% ESBL (+) in enteric microorganisms isolated from DFI and pointed out the increase in resistant gram (-) bacteria isolation in community-acquired infections (13). In our study, gram-negative bacteria were isolated in 15 (34.09%) of 44 patients with culture-positive, and one of them was ESBL (+).

DFI causes serious complications and should be managed with a multidisciplinary approach. In these patients, wound classification should be prioritized in order to make appropriate treatment planning. However, since our study was planned retrospectively, classification protocols could not be reached in the archive records examined. However, we included deep tissue samples taken during the surgical procedure under sterile conditions. Empirical treatment of DFI should affect gram-negative bacteria as well as gram-negative positive bacteria. We detected the main limitation of our study. The flora in the hospitals included in the study may be different from other cities or hospitals. Therefore, each hospital should determine its flora diversity.

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