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The Use of Hyperbaric Oxygen Therapy the Following Amputation in Patients with Diabetes

Diyabet Hastalarında Amputasyon Sonrası Hiperbarik Oksijen Tedavisi Kullanımı

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Abstract

Objective: Foot ulcers are a frequently seen complication in patients with diabetes, which progress with a long period of hospitalization, a high risk of amputation and amputation stump problems. However, there are very few studies in literature on this subject. Hyperbaric oxygen therapy (HBOT) is an adjuvant treatment method used in cases of diabetic foot ulcers and when wound healing is delayed.

Methods: The aim of this retrospective study was to present and discuss the results of 35 cases that underwent minor amputation because of diabetic foot ulcers and applied HBOT for delayed stump healing.

Results: The patients presented for HBOT at mean 33.1±42.55 days (range, 1-210 days) after amputation. Mean 29.77 (range, 5-45) sessions of HBOT were applied. Clinical healing was obtained without further amputation in 29 (82.86%) cases, further amputation was required in 4 (11.43%) cases and 2 (5.71%) patients terminated the therapy on their own request.

Conclusion: HBOT should be included within a multidisciplinary approach to be able to prevent healing problems following amputation in patients with diabetic foot ulcers.

Keywords: Diabetic foot ulcer, amputation, stump healing, hyperbaric oxygen therapy

Öz

Amaç: Ayak ülserleri diyabet hastalarında sık gözlenen komplikasyonlardan olup, uzun süre hastanede yatış, yüksek amputasyon riski ve amputasyon güdük sorunlarıyla seyredir. Buna karşılık literatürde bu konuda az sayıda çalışma bulunmaktadır. Hiperbarik oksijen tedavisi (HBOT) ise diyabetik ayak ülseri olgularında ve yara iyileşmesinin geciktiği durumlarda kullanılan yardımcı bir tedavi yöntemidir.

Yöntem: Bu retrospektif çalışmanın amacı diyabetik ayak ülseri nedeniyle minör amputasyon yapılan ve güdük iyileşmesi geciktiği için HBOT uygulanan 35 olgunun sonuçlarını tartışmaktır.

Bulgular: Hastalar HBOT'ye amputasyondan 33,1 (1-210±42,55) gün sonra başvurmuştu. Uygulanan ortalama HBOT seansı 29,77 (5-45) idi. Yirmi dokuz olguda (%82,86) amputasyon yapılmadan klinik iyileşme sağlanırken, 4'ünde (%11,43) yeniden amputasyon gerekti. İki hasta ise (%5,71) tedavisini kendi isteği ile sonlandırdı.

Sonuç: Diyabetik ayak ülserlerinde amputasyon sonrası iyileşme sorunlarının önlenmesi için HBOT de multidisipliner yaklaşım içinde yer almalıdır.

Anahtar Kelimeler: Diyabetik ayak ülseri, amputasyon, güdük iyileşmesi, hiperbarik oksijen tedavisi



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Introduction

The prevalence of diabetes is increasing rapidly throughout the world and foot ulcers are the leading cause of morbidity and mortality in these patients⁽¹⁻³⁾. Foot ulcers develop at some point in the life of 25% of patients with diabetes and approximately half of these patients are hospitalized because of foot ulcers, of which 20% will undergo amputation^(4,5). Amputation associated with diabetic foot ulcers is generally applied in patients with more than one diabetic comorbidity⁽⁶⁾. Operation site problems following amputation prolong the length of stay in the hospital and antibiotic use and are a significant cause of morbidity causing further amputations⁽⁵⁻⁷⁾.

Hyperbaric oxygen therapy (HBOT) is a medical treatment method applied to the patient in a completely closed pressure chamber by inhalation of 100% oxygen intermittently at pressures higher than 1 atmosphere^(8,9). With this treatment, the oxygen level dissolved in the plasma increases and anti-edema, antitoxic, and anti-infectious effects are obtained^(10,11). HBOT also accelerates wound healing by increasing fibroblast proliferation, collagen synthesis, expression and fibrillization⁽¹²⁻¹⁵⁾. Angiogenesis formed during this treatment eliminates hypoxia in chronic ulcers. HBOT is widely used in cases of delayed wound healing, primarily in diabetic foot ulcers^(8,13-15).

There are few studies in the literature related to healing of the amputation stump site in patients with diabetes. Therefore, this study aimed to present the treatment results of patients applied with HBOT because of delayed healing following amputation due to diabetic foot ulcers.

Materials and Methods

This retrospective study included the data of 35 patients with diabetes who applied with HBOT for operation site complications following a minor amputation due to diabetic foot ulcers between 01.01.2017 and 31.12.2020. On presentation, the necessary consultations were made; laboratory and radiological tests and culture-antibiogram examinations of deep tissue samples were performed. HBOT was applied in a Barotech multi-person pressure chamber in our clinic, as a single session each day of 120 min at 2.4 ATA (absolute atmosphere), 5 days a week.

Approval for the study was granted by the Clinical Research Ethics Committee of University of Health Sciences Turkey, İzmir Tepecik Education and Research Hospital (decision no: 2021/02-46, dated: 22.02.2021).

Statistical Analysis

Statistical analyses were performed using Statistical Package for the Social Sciences version 18.0 for Windows. Categorical variables were expressed as numbers or percentages, whereas continuous variables were expressed as mean±standard deviation.

Results

The evaluation was made of 35 patients, comprising 29 (82.86%) males and 6 (17.14%) females with a mean age of 60.7±9.78 years. All the patients were diagnosed with type 2 diabetes and 94.3% were under intensive insulin treatment. The clinical characteristics of the patients are shown in Table 1.

The micro-organisms most often determined in the deep tissue cultures were *Pseudomonas aeruginosa* (62.5%), *Staphylococcus aureus* (29.2%) and others (*E. coli* and *Klebsiella*) (8.3%). The patients received mean 29.77 (range, 5-45) sessions of HBOT and no complications were observed during the therapy sessions. Following the treatment, clinical healing was obtained without any additional surgical intervention in 29 (82.86%) cases (Figure 1a-e), further amputation was required in 4 (11.43%) cases and 2 (5.71%) patients terminated the treatment on their own request.

Discussion

More than 60% of all non-traumatic lower extremity amputations are applied to patients with diabetes and diabetics have a risk of amputation 6-10-fold higher than non-diabetics^(16,17). Major complications following amputation are stump infection, pain, tissue necrosis, edema, osteomyelitis, hematoma, opening of the stump and further amputations^(6,7). There are very few data in the literature related to wound healing following amputation. In a retrospective study of 101 cases with diabetes and vasculopathy, it was reported that these patients had a high risk of complications because of ulceration and gangrene of transmetatarsal amputation and the most important cause of morbidity was end-stage renal failure⁽¹⁸⁾. In another study, the stump infection was reported in 22% of lower extremity amputations, opening of the stump was observed in 16% of the amputations, and these complications significantly prolonged the length of stay in the hospital and required a longer period of broad-spectrum antibiotics in late stump infections including osteomyelitis⁽¹⁹⁾. There are also studies in literature that have reported that prophylactic antibiotic uses reduced stump infections and re-amputation rates and shortened the length of stay in the hospital⁽¹⁹⁻²¹⁾.

Table 1. Clinical characteristics of the patients

	Minimum	Maximum	Mean ± SD
Age (years)	47	66	60.7±9.34
Duration of DM (years)	0 ^a	45	23.7±11.07
Duration of the wound (weeks)	1.43	34.29	16.67±11.45
Post-op admission (days)	1	210	33.1±42.55
HbA1c (mg/100 mL)	5.3	16	9.4±2.60
White blood count	6.16	16.58	11.49±2.82
Erythrocyte sedimentation rate	9.00	125.00	67.50±25.62
C-reactive protein	1.40	288.80	70.90±68.65
HBOT session	5	45	29.90
	Number	%	
Sex			
Female	6	17.14	
Male	29	82.86	
Type of DM			
Type 1	0	0.0	
Type 2	35	100.0	
Type of DM treatment			
OAD	2	5.7	
Insulin	33	94.3	
Neuropathy	35	100.0	
Retinopathy	25	71.4	
End-stage renal failure	3	8.6	
Smoking	27	77.1	
Coronary arterial disease	21	60.0	
Peripheral arterial disease	18	51.4	
Results			
Clinical healing	29	82.86	
Further amputation	4	11.43	
Terminated treatment	2	5.71	
DM: Diabetes mellitus, HbA1c: Glycosylated haemoglobin, OAD: Oral antidiabetic drug, 0 ^a : Means undiagnosed diabetes mellitus before foot ulcer, SD: Standard deviation, HBOT: Hyperbaric oxygen therapy			

Armstrong et al.⁽³⁾ reported that the leading factors preventing healing within 1 year in 77% of diabetic foot ulcers were advanced end-organ disease (congestive heart failure, peripheral artery disease, or end-stage renal failure requiring renal replacement therapy) and the inability to walk independently. In the same study, it was stated that 40% of these ulcers recurred within 1 year, 60% within 3 years, and 65% within 5 years, and therefore it would be more appropriate to say remission rather than recovery. Natcher reported that minor amputations in cases of diabetic foot ulcers were effective for both preserving the extremity and for

reducing morbidity and mortality, but stump complications were not mentioned in that study⁽²²⁾.

There are several studies in the literature related to the use of HBOT for treating diabetic foot ulcers⁽²³⁻³⁰⁾. Some of these are prospective, randomized controlled studies that have reported that the addition of HBOT to standard treatments has shortened the healing period and the length of stay in the hospital. In several studies, extremity ischemia has been shown to be the most important factor determining the development of diabetic foot ulcers and poor prognosis for the healing of ulcers that have developed^(31,32). A meta-analysis

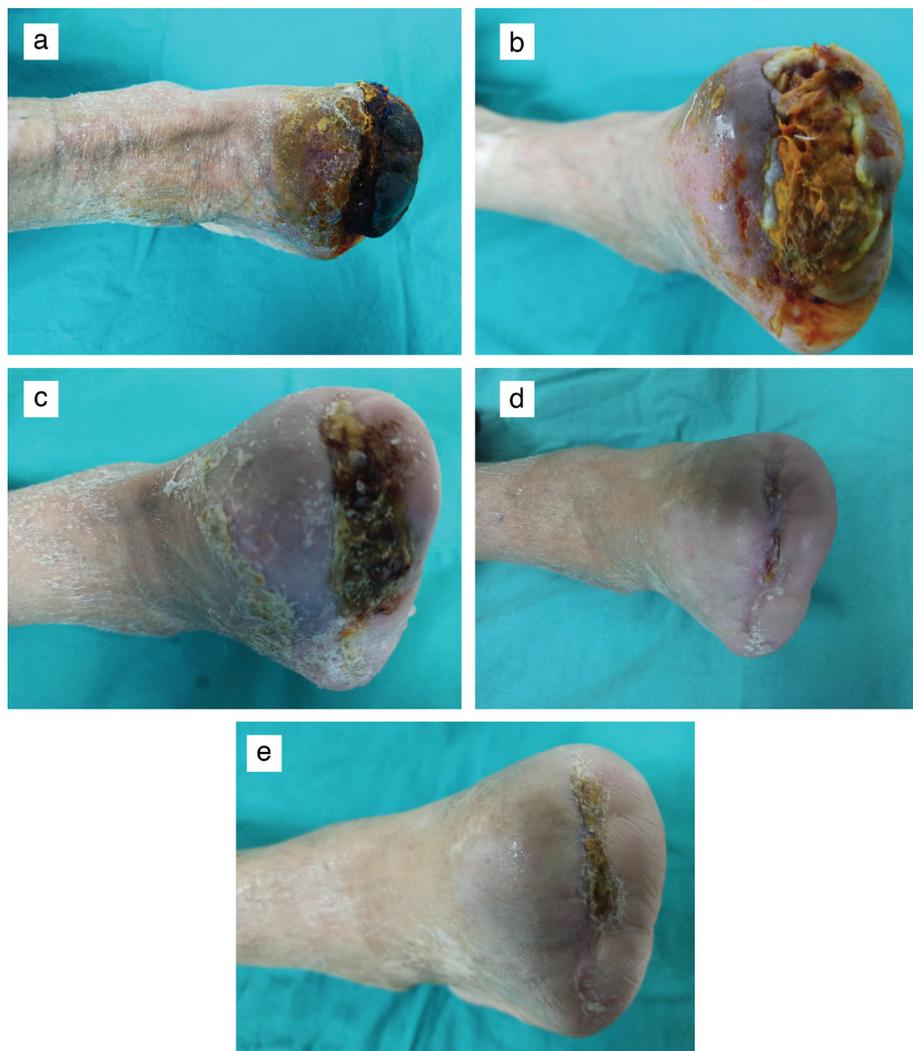


Figure 1. Stump necrosis after transmetatarsal amputation in a type-II DM. a) HBOT 0 (admission). b) HBOT 10th session c) HBOT 30th session. d) HBOT 45th session. e) Control after one month of treatment

published in 2021 reported that HBOT was effective in the full healing of diabetic foot ulcers and significantly reduced rates of major amputation and could therefore effectively be used as an adjuvant treatment for these ulcers⁽³³⁾. Another systematic review presented a high level of evidence that when HBOT was included within a multidisciplinary wound care program, the risk of amputation was decreased in cases with diabetic foot ulcers complicated by surgical infection⁽³⁴⁾. In another review, a significantly high rate of recovery was recorded for diabetic foot ulcers treated with HBOT and the major amputation rate was found to be significantly low⁽³⁵⁾. In a previous retrospective study of 184 patients by the present authors, the major amputation rate was recorded as 4.9% in diabetic foot ulcers treated with HBOT⁽²⁷⁾. In another meta-analysis that investigated the efficacy of HBOT in diabetic foot ulcers with arterial insufficiency, the addition of HBOT to

standard treatments was reported to be helpful in reducing amputation rates⁽³⁶⁾. The efficacy of HBOT investigated according to the Wagner classification in another study and the treatment was determined to significantly increase wound healing in grade 3 and 4 ulcers⁽³⁷⁾.

Study Limitations

This study has some limitations. The most important one is the absence of the control group. Thus, randomization could not be realized. Moreover our study had a retrospective design.

Conclusion

In the current retrospective study of 35 patients, clinical healing was obtained without any further amputations

in 29 cases and in 4 cases, re-amputation was required. No statistically significant difference was determined between the recovered group and those who required further amputation regarding age, duration of diabetes, and laboratory values, whereas the patients with further amputation were seen to have presented later with advanced end-organ failure (hemodialysis because of end-stage renal disease, congestive heart failure, and occlusions at the level of femoral and popliteal arteries shown on angiography). There was no difference between the two groups with respect to the number of HBOT sessions applied.

Although conducted retrospectively with a limited number of patients, the results of this study with findings in the literature demonstrate that the addition of HBOT to standard treatments can contribute to the healing of stump complications following amputation. Nevertheless, there is a need for further prospective, controlled studies on this subject.

Ethics

Ethics Committee Approval: Approval for the study was granted by the Clinical Research Ethics Committee of University of Health Sciences Turkey, İzmir Tepecik Education and Research Hospital (decision no: 2021/02-46, dated: 22.02.2021).

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: F.A., M.İ., E.E.Ö., A.K., Design: F.A., M.İ., E.E.Ö., A.K., Data Collection or Processing: F.A., M.İ., E.E.Ö., A.K., Analysis or Interpretation: F.A., M.İ., E.E.Ö., A.K., Literature Search: F.A., M.İ., E.E.Ö., A.K., Writing: F.A., M.İ., E.E.Ö., A.K.

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