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Diabetic hand infections and hyperbaric oxygen therapy

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Objective: The aim of this study was to discuss the clinical characteristics and results of hand infections in diabetic patients treated with hyperbaric oxygen therapy (HBOT).

Methods: This retrospective study included 10 patients with diabetes mellitus who underwent HBOT due to hand infections between January 2006 and February 2011.

Results: Amputation was performed at the level of the right hand index finger proximal interphalangeal joint in 1 patient and at the level of the distal phalanx of the left hand middle finger in 1 due to necrotizing soft tissue infection. Ulcers of 8 patients healed completely without amputation.

Conclusion: The addition of HBOT to the standard treatment may contribute to the healing of hand ulcers in diabetics by increasing the tissue oxygenation and correcting the process of disturbed wound healing.

Key words: Amputation; diabetic hand infection; hyperbaric oxygen treatment.

According to the World Health Organization (WHO), 346 million people have diabetes worldwide and the number of diabetics is predicted to double between 2005 and 2030.[1] Foot ulcers are one of the most important complications of diabetes and cause high rates of amputation.[2,3] Hand infections in diabetic patients are observed less frequently than foot infections.

Hand infections related to diabetes have mostly been reported in studies of African origin.[4-8] These ulcers are usually associated with traumas and progress quickly; gangrene of the extremity causes increased rates of morbidity and mortality.[4-9] Hand infections are also seen in the diabetic population outside the tropical regions.[10,11] Hand problems such as limited joint mobility, Dupuytren's contraction and trigger fingers have been reported in diabetic patients. Such problems related with the musculoskeletal system in the hands of diabetic patients could be defined as a syndrome.[12,13]

Risk factors for diabetic hand infection are insect bites and trauma. Tropical diabetic hand syndrome is generally defined by Type 2 diabetes mellitus (DM), female sex, low socioeconomic level, poor glycemic control, presence of neuropathy, previous history of trauma, late admission, severe and deep palmar sepsis, and a high risk of amputation and mortality.[5,7,8,10]

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In the literature, *Staphylococcus aureus* is considered the most common cause of upper extremity necrotizing fasciitis associated with serious mortality and morbidity.[14]

Hyperbaric oxygen therapy (HBOT) is thought to help wound healing by increasing the amount of oxygen in the skin and peripheral tissues via 100% oxygen with more than 1 atm of pressure and also is known to stimulate angiogenesis by high tissue oxygen tension, increase cellular proliferation, minimize necrosis and help in the prevention and treatment of infections.[15-17] Vasoconstriction is another effect of HBOT that decreases edema.[18] The anti-infectious effect of HBOT on ischemic and hypoxic tissue is provided by the correction of low PO2 values. It has a bactericidal effect on anaerobes and microaerophilic aerobes; and it also repairs microbicide effects which are provided by oxidative pathways, regulating macrophage functions and covering oxygen consumption at infected tissues.[19]

Clinical data related to hand lesions of diabetic patients are limited in our country. Only one case presentation referring to the use of HBOT in diabetic hand ulcers was found.[20]

The aim of this study was to report the clinical characteristics and the results of treatment with HBOT in patients with diabetic hand infection.

Patients and methods

This retrospective study included 10 patients (8 males, 2 females) with diabetic hand infection treated with HBOT in addition to the standard methods between January 2006 and February 2011. Mean age was 54.9±7.43 years with a duration of diabetes of 8.7±6.44 years. Diabetes was diagnosed at admission in 2 cases. Eight patients had poor glycemic control during admission despite insulin therapy. Mean HbA1c level was 8.81% (±1.26). Upper extremity neuropathy confirmed with the monofilament test was detected in 3 patients and peripheral arterial disease confirmed by arterial color Doppler ultrasonography (CDU) was detected in 3 patients. Two diabetic subjects were on hemodialysis due to diabetic nephropathy. Although the most common cause of diabetic hand infection (5 patients) was cutting-penetrating injury, minor traumas were responsible in 2 patients. Other etiologic factors were; 1 insect bite, 1 human bite, and 1 ulcer development secondary to thromboembolism. Six patients continued to smoke during treatment. Alcohol addiction was diagnosed in one patient. Clinical characteristics of the study group are summarized in Table 1.

Physical examinations were performed during admission. Biochemical tests were performed by taking samples for routine blood studies before treatment. Deep tissue samples were taken from the ulcers for culture investigation. Daily wound care of all patients were done. Amputations, small debridements, incisions and drainage were performed when necessary.

Hyperbaric oxygen therapy was applied in a multiplace chamber (Hiperbot Model 101; Hiperbot Ltd. Şti, Istanbul, Turkey). None of the patients had any contraindication to HBOT. The starting time of the patient's HBOT was an average of 40±29 days after injury. Each treatment session lasted 120 minutes with 2.4 ATA (atmosphere absolute) pressure. Sessions were carried out once a day and 6 days a week. Informed consent was obtained from all patients.

For statistical analysis, Pearson's chi-square and Fisher's exact tests were used where appropriate. P values of less than 0.05 were accepted as statistically significant. Statistical evaluations were performed using SPSS for Windows v.13 (SPSS Inc., Chicago, IL, USA) software.

Results

All patients had edema, hyperemia, pain and limitation of movement in the hands at the initial examination. Most cases had a purulent discharge. Deep tissue infection was expanded to the bones and tendons in 5 cases. There was localized gangrene in the finger of 2 cases and deep ulcer without bone involvement in three. According to the Wagner classification, 2 of the ulcers were Wagner Grade 2, 5 were Grade 3 and 3 were Grade 4 ulcers (Table 2).

The main pathogen detected in the deep tissue samples was *Staphylococcus aureus*. The second most common agent, pseudomonas, was considered to be resultant from hospital infections related to previous surgical interventions.

Six patients received treatment as outpatients and 4 were treated and followed in the hospital due to systemic infectious findings.

Patients had undergone a total of 5 surgical interventions. Eight recovered without amputation, minor amputation was performed in two. In these 2 patients, gangrene was detected in the right hand index finger in one of the newly diagnosed DM cases and necrotizing infection in the deep tissues in the other. The level of amputation was at the proximal interphalangeal (PIP) joint of the right hand index finger in one and the distal phalanx of the left hand middle finger in the other case.

Hyperbaric oxygen therapy was begun an average

Table 1. Clinical characteristics of the patients.

	Minimum	Maximum	n	Mean±SD
Age (years)	43	67		54.90±7.43
Duration of diabetes mellitus (years)	0	20		8.70±6.44
Duration of the wound (days)	10	90		40.40±28.99
HbA1C (mg/100 ml) (on presentation)	6.9	10.7		8.81±1.26
HBOT sessions	13	60		35.30±14
Duration of follow-up (months)	2	48		18.80±15.01
Sex				
Male			8	
Female			2	
Type of diabetes mellitus				
Type 1 diabetes mellitus			0	
Type 2 diabetes mellitus			10	
Type of diabetes mellitus treatment				
Insulin			8	
Oral anti-diabetes drugs			2	
Neuropathy				
Yes			3	
No			7	
Nephropathy				
Yes			2	
No			8	
Retinopathy				
Yes			6	
No			4	
Peripheral arterial disease				
Yes			3	
No			7	
Smoking				
Yes			6	
No			4	
Alcohol				
Yes			1	
No			9	

HBOT: Hyperbaric oxygen therapy; SD: Standard deviation.

Table 2. Clinical symptoms of the patients.

Clinical description	Wagner Grade	Patients	
		n	%
Deep ulcer with no bone involvement	2	2	20
Deep ulcer with bone involvement	3	5	50
Localized hand gangrene	4	3	30
Extensive hand gangrene	5	0	0

of 40±29 days after injury and no statistical significance was found between the starting time and prognosis (p=0.231). HBOT was continued until healing was completed. Total epithelialization of the ulcer area was accepted as healed, either with surgical or nonsurgical secondary closure. Patients underwent an average of 35.3±14 HBOT sessions. An increased number of sessions was related with increased Wagner scores of wounds and delayed admission to medical management. None of the patients developed any complication

related to HBOT during treatments and all ulcers were healed.

Discussion

While hand infections are a serious complication of diabetes, few studies related to diabetic hand ulcers have been published in the literature. Hand infections are seen most frequently in tropical countries.[4-8] The majority of subjects were females in studies conducted in rural areas of Africa due to their activity in farming and were, thus, more exposed to traumas whereas males were more affected in urban areas.[7]

As in the literature, the main cause of ulcers in our study were cutting-penetrating injuries and minor traumas.[4,7,9] In one patient with previously undiagnosed DM, the etiology was an insect bite (Fig. 1). Cases in subtropical African countries are also mostly associated with insect bites, bee stings and human bites.[4,7,9]

The admission rates of healthy individuals for measurement of blood glucose levels are very low in our country. For this reason, two patients in our study were not aware of their diabetes before onset of their hand infection. Diagnoses were made incidentally in examinations performed due to prolonged treatment of the hand infection and intensive insulin treatment was initiated. One of the reported poor prognostic factors for diabetic hand ulcers in the literature is late admission for treatment.[4,8-10,21] In Coppini and Best's study, it was reported that neuropathy may lead to anesthetic hand ulcers in diabetics.[22] In our study, peripheral polyneuropathy was detected with a monofilament test in 3 patients.

Wang et al.[11] reported recovery rates of 76% and no amputation was recorded. In this study, 2 patients (12%) died of respiratory failure and as a result of uremia after discharge and 2 discharged themselves because of economic difficulties. Gill et al. reported that prompt amputation was one of the treatment choices in tropical diabetic hand ulcers.[10] In their 26-patient series, Benotmane et al. recorded 23.1% minor amputation as a result of treatment of upper extremity infections in diabetic

Fig. 1. **(a-c)** Serial clinical photos throughout hyperbaric oxygen therapy of a 48-year-old man treated for his diabetic hand ulcer due to insect bites and **(d)** the final result. The patient worked as an archeologist and was not diagnosed with diabetes mellitus previously. [Color figure can be viewed in the online issue, which is available at www.aott.org.tr]

patients, 53.8% recovery without an amputation and 19.2% death.[23]

Treatment principles in tropical diabetic hand syndrome are defined as hospitalization and hand elevation, intravenous antibiotic treatment and optimal glycemic control. In our study, hospitalization was required for minor amputation in 2 patients and intravenous antibiotic therapy due to systemic infections in four. Insulin therapy was initiated for blood sugar control in outpatient follow-up. Antibiotherapy was regulated when needed. Recovery is much slower in diabetic patients than non-diabetics and requires more frequent surgical intervention.

Limited data on the usage of HBOT in the treatment of diabetic hand ulcers has been reported in the literature.[20] The effects of HBOT on impaired wound healing are due to fibroblastic activity, collagen production, release and fibrillation, angiogenesis, epithelialization, and osteogenesis by activating osteoblastic and osteoclastic activities in bone tissue.[15,19] The effectiveness of HBOT in infections occurs in three ways; by bactericidal or bacteriostatic effects on certain microorganisms, increasing the effectiveness of some antimicrobial or antibiotic agents, and enhancing host defense mechanisms (especially microbicide effects of polymorphonuclear leukocytes).[15,19] Antimicrobial effects of HBOT on *Staphylococcus aureus* and *Pseudomonas aeruginosa* have also been detected in *in vivo* studies. It is also well known that HBOT enhances activity of antibacterial agents, particularly quinolones, aminoglycosides, beta-lactam antibiotics, vancomycin and teicoplanin through various mechanisms.[19,24,25]

The anti-infection effects of HBOT provide infection control through the bacteriostatic and bactericidal effects on certain microorganisms. The antimicrobial effects of HBOT on *Staphylococcus aureus* and *Pseudomonas aeruginosa* is well known. In our study, the isolated pathogens in the deep tissue cultures from ulcers of patients were *Pseudomonas aeruginosa* as nosocomial infection and *Staphylococcus aureus*. Although there was a resistance against previous several anti-infective agents, infection regression after adjuvant HBOT can be explained by the anti-infective effect of HBOT. Synergism with antibacterial agents such as aminoglycosides, quinolones, beta-lactam antibiotics, vancomycin and teicoplanin also contributes to the anti-infective effect of HBOT. Indeed, the most commonly used anti-bactericidal agents in our study were beta-lactam antibiotics and quinolones according to the antibiograms. The required surgical interventions were planned after the infection was controlled.

As a result, the anti-infectious effects of HBOT on ischemic-hypoxic tissue are due to the correction of low PO_2 values through the bactericidal effect on anaerobes and microaerophilic aerobes; the repairing microbicide effects provided by oxidative pathways; regulating macrophage functions; and increased covering oxygen consumption at infected tissues.[19]

The limited number of cases in our study was not sufficient for statistical analysis. Additionally, there are not enough studies in the literature on the treatment of diabetic hand ulcers with HBOT. Ulcers were successfully treated by glycemic control with insulin treatment, appropriate antibiotics, wound care and HBOT. In the 2 patients requiring minor amputations, diabetes was only diagnosed at admission for their hand lesions.

In conclusion, the addition of HBOT to standard therapies is a safe method for the treatment of hand infections in diabetic patients due to its anti-infective effects. Controlled studies with larger series are required for further analysis.

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