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Hyperbaric oxygenation in prevention of amputations of diabetic foot

Hiperbarična oksigenacija u prevenciji amputacija dijabetičkog stopala

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Abstract

Background/Aim. Diabetic foot is the term for the pathological changes on foot in patients with diabetes. It is caused by diabetic angiopathy, polyneuropathy and osteoarthropathy. The treatment is complex and long-term and often leads to the loss of the extremity. The appliance of hyperbaric oxygen therapy (HBOT) has a lot more important place in adjuvant treatment of this disease. The aim of this study was to determine the influence of HBOT on the wound healing in comparison with the conventional treatment, the possibility of shortening the time of the treatment in patients with diabetic foot. **Methods.** In a five-year period a retrospective-prospective multicentric study, involving 60 patients with diabetic foot divided into two groups, was performed. The first group (group A) consisted of 30 patients treated by combined therapy (with medications, surgical therapy and HBOT). All the patients were receiving HBOT in the Special Hospital for Hyperbaric Medicine, CHM Hollywell-Neopren in Belgrade. The control group (group B) also consisted of 30 patients treated with medications and surgical therapy, but without HBOT. **Results.** The demographic data, the types of diabetes, as well as the Wagner classification stage of diabetic ulcers and radiography scans of changes in bones were equal in both groups. The median healing time of the Wagner grade III ulcer in the group A was 37.36 days [mean ± standard deviation (SD) = 65.6 ± 45.8 days], and in the group B 99.78 days (mean ± SD = 134.8 ± 105.96 days) and it was statistically significant (p = 0.074). The median time of recovery in patients of the group A with the Wagner grade IV was 48.18 days (mean ± SD = 49.7 ± 33.8 days), and in the group B 85.05 days (mean ± SD = 86.7 ± 71.6 days) and that was statistically significant (p = 0.121). The foot amputations were performed in both groups in 3 (10%) patients. In the group A there were no high amputations, whereas in the group B there were 4 (13.33%) below-knee amputations and 4 (13.33%) above-knee amputations which was highly statistically significant ($p < 0.0001$). **Conclusion.** In this study, HBOT definitely showed positive adjuvant role in the treatment of diabetic foot. For the good treatment result it is essential the timely and successful surgical treatment of the ulcer and the use of bandage with the healing dressings. In case of the clear signs of local infection, the antibiotic therapy according to the antibiogram is necessary.

Key words:
diabetic foot; hyperbaric oxygenation; amputation; wound healing.

Apstrakt

Uvod/Cilj. Dijabetičnim stopalom nazivamo patološke promene na stopalu kod bolesnika koji boluju od šećerne bolesti, a uzrokovane su dijabetičkom angiopatijom, polineuropatijom i osteoartropatijom. Lečenje je kompleksno i dugotrajno i često dovodi do gubitka esktremiteta. Primena hiperbarične oksigene terapije (HBOT) ima sve značajnije mesto u adjuvantnom lečenju ovog oboljenja. Cilj ovog rada bio je utvrđivanje uticaja HBOT na efikasnije zarastanje rane u poređenju sa konvencionalnim lečenjem i mogućnost skraćenja vremena lečenja bolesnika sa dijabetičkim stopalom. **Metode.** U petogodišnjem periodu urađena je retrospektivno-prospektivna multicentrična studija, koja je obuhvatila 60 bolesnika podeljenih u dve grupe. Prva grupa (grupa A) od 30 bolesnika lečena je kombinovanom terapijom (medikamentoznom, hirurškom i HBOT). Svi bolesnici dobijali su HBOT u Specijalnoj bolnici za hiperbaričnu medicinu, CHM Hollywell-Neopren u Beogradu. Kontrolna grupa (grupa B), takođe od 30 bolesnika sa dijabetičkim stopalom, lečena je medikamentozno i hirurški, ali bez HBOT. **Rezultati.** Demografski podaci, tip dijabetesa,

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stadijum dijabetičkih rana prema Wagner-u i nalazi radiografskih promena na kostima bili su jednaki u obe grupe. Medijana vremena za sanaciju rane III stadijuma po Wagner-u u grupi A iznosila je 37,36 dana [srednja vrednost ± standardna devijacija (SD) = 65,6 ± 45,8 dana], a u grupi B 99,78 dana (srednja vrednost ± SD = 134,8 ± 105,96 dana) (p = 0,074). Bolesnici u IV stadijumu po Wagner-u u grupi A imali su medijanu vremena za sanaciju rane od 48,18 dana (srednja vrednost ± SD = 49,7 ± 33,8 dana), a u grupi B 85,05 (srednja vrednost ± SD =86,7 ± 71,6 dana) (p = 0,121). Amputacije stopala bile su izvršene u obe grupe kod tri (10%) bolesnika. U grupi A nije bilo ni jedne visoke amputacije, a u grupi B su bile izvršene četiri (13,33%) potkolene i četiri (13,33%) natkolene amputacije, što je bilo visoko statistički značajno (p < 0,0001). **Zaključak.** HBOT u ovoj studiji kao i kod većine drugih autora definitivno je pokazala pozitivnu adjuvantnu ulogu u lečenju dijabetičkog stopala. Za dobar rezultat lečenja potrebna je pravovremena i sukcesivna hirurška obrada rane i zavoj lekovitim oblogama. U slučaju pojave jasnih znakova lokalne infekcije potrebna je antibiotska terapija prema antibiogramu.

Ključne reči:
dijabetesno stopalo; hiperbarična oksigenacija; amputacija; rana, zarastanje.

Introduction

Diabetic foot is the term for the pathological changes on foot caused by ischaemia as a consequence of microangiopathy, the late notice of soft tissue damage and slow ulcer healing as a result of polyneuropathy as well as the uneven pressure of footwear due to the deformation of foot because of diabetic osteoarthropathy [1, 2]. The curing demands a complex multimodal treatment, including regulation of glycaemia, antibiotic therapy, local treatment of the ulcer, as well as surgical or endovascular revascularization in patients with macro-occlusive artery disease. The healing of diabetic foot ulcer is longterm and in 60% of patients it lasts about one year. All this is accompanied by high treatment costs and additional social problems [3]. In the most of European countries 10% of health care costs are expended on diabetes treatment, and 68% of those are spent on the curing the disease complications.

In the newer literature hyperbaric oxygen therapy (HBOT) has a lot more significant place in an adjuvant treatment of this disease [4]. HBOT means a breathing 100% oxygen in a special chamber, in higher ambient pressure conditions (2.0–2.9 Kpa), determined by the particular protocols. The oxygen content in plasma increases from 0.3 to 5.62 volume percents. The average number of treatments is 20 (from 15 to 30). In normal conditions haemoglobin-bound oxygen is transported to the cells in erythrocytes. In the hyperbaric pressure conditions, according to the laws of physics, there is the increased dissolution of molecular oxygen in plasma which enables the oxygen supply even there where the blood vessels are narrowed (the capillary lumen is smaller than the erythrocytes' diameter) or occlusive [5, 6]. In patients with diabetic foot HBOT ameliorates the peripheral tissue oxygen supply, and in addition to that oxygen has antibacterial (for anaerobic flora it is bactericidal), anti-inflamatory and imunosuppressive effects [7, 8]. These effects are made by the inhibition of prostaglandins, interfereon gamma (IFNG), interleukin-1 and interleukin-2 [9]. The hyperbaric oxygenation is beneficial for wound healing due to stimulation of fibroblast proliferation and differentiation, and rapid collagen synthesis [10, 11]. The neovascularization is stimulated and the energy metabolism of peripheral cells is increased.

The aim of this study was to determine the significance of HBOT as an adjuvant therapy that may influence on: the efficient healing of diabetic foot ulcer in comparison to the conventional type of treatment (with medications and surgical treatment); the possibility of shortening the time of diabetic foot healing and reducing the treatment costs in patients with diabetic foot.

Methods

In a five-year period a retrospective-prospective multicentric study was conducted which involved 60 patients divided into two groups. The first group (group A), consisted of 30 patients, was treated by combined therapy (with medications, surgical therapy and HBOT). There were 25 patients from the Clinic for Surgery "Zvezdara" in Belgrade and the rest 5 of them were from The Clinic for the Vascular and Endovascular Surgery, Clinical Center of Serbia, Belgrade. All the patients were receiving HBOT in Special Hospital for Hyperbaric Medicine, CHM Hollywell-Neopren in Belgrade.

The control group (group B), also consisted of 30 patients, was treated with medications and surgical therapy, but without HBOT. Twenty three patients were treated in the Clinic for Surgery "Zvezdara" in Belgrade and the remaining 7 patients in the Clinic for the Vascular and Endovascular Surgery, Clinical Center of Serbia, Belgrade.

Only the patients with diabetic foot in whom magistral arteries were passable and surgical or endovascular revascularization was not indicated, as proved by non-invasive examination (Color duplex sonography – CDS, Ankle brachial index – ABI), were included in the study. Before the treatment, radiography scans were made to all the patients and the wound smear was taken for the bacteriological examination.

The inclusion criteria for the study were: palpable pedal pulses; an ancle-brachial index (ABI) higher than 0.75; three-phase spectrogram on pedal arteries.

The surgical interventions were performed in both groups depending on the type of diabetic foot lesions and with: ulcers – necrectomia; phlegmons – incision, contra-incision, drainage; osteomyelitis – incision, contra-incision, sequestrectomia; gangrene – necrectomia or amputation.

The transplantation of skin (Thiersch) was performed in a few patients with the amputation of foot in the joint line (Chopart or Lisfranc) in order to shorten the healing period.

The complete recovery considered the state of full epithelialization of the wound or recovery of inflammatory changes (the soft tissue and the bone). In patients with the amputation the recovery considered the full healing of the amputation stump.

Statistical analysis

Descriptive statistics were used for the processing demographic and clinical characteristics of patients in both groups. Categorical variables were compared by using χ^2 test. Continuous variables were compared by ANOVA test, or Median test (for variables without normal distribution). A significance of 0.05 was required. Means ± standard deviations (SD) and medians with the corresponding 95% confidence intervals (CI) were estimated. Analyses were performed using SPSS for Windows, Version 22 (SPSS, Inc., Chicago, IL).

Results

Patients characteristics in both groups are presented in Tables 1 and 2.

The Group A was treated by combined therapy (with medications, surgical therapy and HBOT), and the Group B was treated in the same way, but without HBOT. It was shown that there were no statistically significant differences in demographic data between patients in the Groups A and B (Table 3).

In the group A there were 11 patients with type 1 diabetes and 19 with type 2 diabetes. In the control group there were 12 patients with type 1 diabetes and 18 with type 2 diabetes. There was no statistically significant difference between groups regarding diabetes type. Among 30 patients in the group A, 12 were with the Wagner grade III ulcers and 18 with the Wagner grade IV ulcers. In the control group (group B) there were 10 patients with ulcers of the grade III in the Wagner classification system, and 20 with the Wagner grade IV ulcers (Table 3).

Based on the foot radiography, the patients were divided into subgroups with osteoporosis, osteoarthropathy, osteomyelitis and the normal finding of foot bones. In the group A the normal result was found in 50% of the patients, and in the group B in 60% of the patients (Table 3).

The most frequent pathological result was osteomyelitis, which was diagnosed in 30% of the patients in the group A and in 26.67% of the patients in the group B. Radiography results of foot bones did not differ significantly between groups.

The type of surgical intervention depended on the local result (Table 3). Incision and drainage were performed in 5 patients in total, in the group A in 3 (10%) patients, whereas in the group B in 2 (6.7%) patients.

Necrectomia was the most frequent intervention in the group A (in 17 patients or 56.7%) while in the group B just in 3 (10%) patients. The finger amputations were conducted in 7 (23.3%) patients of the group A and in 14 (46.7%) patients of the group B. The foot amputations (transmetatarsal, in Chopart and Lisfranc's joint line) were performed in 3 (10%) patients in each the group. There were no high amputations in the group A, but there were 4 (13.3%) below-knee and 4 (13.3%) above-knee amputations in the group B ($p < 0.0001$).

In this study the mean (± SD) healing time of the Wagner grade III ulcer in the group A was 65.6 (± 45.8) days whereas in the group B it was 134.8 (± 105.96) days ($p = 0.074$).

In the group A, the patients with the Wagner grade IV ulcers had the mean time of healing 49.7 (± 33.8) days, and in the group B 86.7 (± 71.6) days ($p = 0.121$) (Tables 4).

The first control examination was carried out immediately after the healing process was finished, the second one was after a month and later on, the examinations were carried out in three months. In case of deterioration of the local result the examinations were carried out more frequently.

In patients treated with HBOT the most common side effects were discomfort and ear pain (17–20%) and claustrophobia (13%). The cases of pneumothorax and neurological disturbances were not noticed.

Ten patients from the group A had some problems after healing of diabetic foot lesions: one patient – foot pain and discomfort during walking; five patients – ulcer appearing at the different place on the same foot, or ulcer appearing on the other foot; four patients – foot deformation after the surgical interventions and discomfort during walking; four patients died within a year; 7 patients did not come for the control examination and their state was not known.

Discussion

The reasons for the bad outcomes of the diabetic foot ulcer healing are combined influences of ischaemia with hypoxia of soft tissues, prolonged wound healing due to existing polyneuropathy and propensity to infection [12]. Many authors report about positive influence of oxygen therapy in hyperbaric conditions on the healing or reducing the major complications of diabetic foot ulcer. In this study the effects of treatments on the Wagner grades 3 and 4 ulcers in two groups of patients with diabetic foot were compared [13]. The first group of 30 patients was treated with HBOT and medication and surgical methods (group A), whereas the the control group (group B) was treated with medication and surgical methods in the same way, but without HBOT.

In regards to significant parameters, this study showed the positive influence of HBOT on diabetic foot ulcer healing, especially in regard to the most important result – high amputation. Moreover, there were no above-knee and below-knee amputations whereas there were 8 amputations in the control group and that was highly significant ($p < 0.0001$).

The most patients in the group A well tolerated HBOT. The most common side effects were discomfort and ear pain (17–20%) and after that claustrophobia (13%). The cases of pneumothorax and neurological disturbances were not noticed.

Table 1

Demographic and clinical characteristic of patients treated by conventional therapy + hyperbaric oxygen therapy (HBOT) – the group A

Patients	Gender	Age	Diabetes Type	Ulcer grade (wagner)	Foot x ray scan at the beginning of the study	Treatment before entering the study	Surgical intervention	Number of HBOT treatments	Healing Period
1	M	65	I	3	*Osteolysis dig. V ped. l. dex. Osteoporosis digitorum ped. dex.*	30 days	*Amputatio dig. V Inciharacteristics sio, contraincisio et drainage ped. l. dex.*	30	150 days
2	M	69	I	4	*Osteomyelitis dig. II, III et IV ped. l. dex.*	30 days	*Amputatio ped. l. dex. (Chopart)*	20	120 days
3	M	64	II	3	/	7 days	*Incisio et contraincisio ped. l. sin.*	20	21 days
4	M	67	II	4	*Osteoporosis ped. dex.*	5 days	*Amputatio hal. l. dex. Necrectomia et incisio*	20	31 days
5	M	64	II	4	*Osteomyelitis hall. l. dex. St. p. fracturam hall. l. dex.*	4 days	*Incisio et contraincisio hall. l. dex. Necrectomia*	30	20 days
6	M	30	II	3	/	15 days	*Necrectomia*	30	40 days
7	F	64	II	3	*Osteomyelitis dig. V et osteoporosis gravis ped. dex.*	10 days	*Amputatio ped. dex. (Lisfrank) Thiersch*	30	130 days
8	F	71	II	4	/	35 days	*Necrectomia ped. l. sin.*	30	25 days
9	M	61	II	4	/	5 days	*Necrectomia et incisio ped. l. sin.*	30	90 days
10	M	50	II	4	*Osteolysis dig. II ped. l. sin. DOAP ped. l. sin. Fractura patologica digitorum ped. l. sin.*	5 days	*Incisio et contraincisio ped. l. sin. Necrectomia*	30	45 days
11	M	70	I	4	*Osteomyelitis dig. IV ped. dex.*	30 days	*Amputatio dig. IV ped. l. sin.*	15	15 days
12	M	73	II	4	/	10 days	*Amputatio dig. IV ped. l. dex.*	20	30 days
13	F	61	I	4	/	120 days	*Amputatio ped. l. sin. (Chopart) Thiersch*	20	130 days
14	M	74	II	3	*Osteomyelitis hall.dex. DOAP ped. l. dex.*	10 days	*Incisio et contraincisio hall. l. dex.*	20	35 days
15	M	63	I	4	*DOAP pedis l. dex.*	5 days	*Amputatio hall. dex.*	20	30 days

Table 1 (continued)

Patients	Gender	Age	Diabetes Type	Ulcer grade (wagner)	Foot x ray scan at the beginning of the study	Treatment before entering the study	Surgical intervention	Number of HBOT treatments	Healing Period
16	M	51	II	3	*Osteomyelitis hall. sin.*	30 days	*Amputatio hall. et incisio ped. l. sin.*	30	60 days
17	F	80	I	4	/	19 days	*Necrectomia ped. l. dex.*	20	60 days
18	M	64	II	3	*Osteomyelitis hall. sin.*	45 days	*Incisio Amputatio hall. sin.*	15	20 days
19	F	65	II	3	/	15 days	*Incisio ped. l. sin.*	10	30 days
20	M	70	I	3	/	7 days	*Incisio Necrectomia ped. l. dex.*	20	30 days
21	M	66	II	4	*Osteoporosis ped. dex.*	10 days	*Necrectomia ped. l. dex.*	20	60 d days
22	M	50	II	4	/	60 days	*Necrectomia ped. l. dex.*	20	20 days
23	M	57	I	3	*Osteomyelitis phal. dis. hall. l. sin.*	15 days	*Incisio et contraincisio hall. sin. Extirpatio phal. dist. hall. ped. l. sin.*	30	120 days
24	F	69	I	4	/	3 days	*Necrectomia ped. l. sin.*	10	62 days
25	M	46	I	4	/	30 days	*Necrectomia hall. l. dex.*	30	60 days
26	M	43	II	4	/	150 days	*Necrectomia hall. l. dex.*	20	21 days
27	F	75	II	4	*Osteoporosis ped. l. dex.*	180 days	*Necrectomia dig. V ped. dex.*	30	30 days
28	M	66	II	4	*Osteomyelitis hall. dex.*	10 days	*Necrectomia hall. l. dex.*	30	45 days
29	M	72	I	3	/	120 days	*Necrectomia ped. l. dex.*	20	90 days
30	M	60	II	3	/	10 days	*Necrectomia ped. l. sin.*	30	61 days

In the Group A, 24 patients were treated as the inpatients, whereas 6 patients were outpatiently treated. The number of HBOT treatments depended on the Wagner classification grade of ulcers as well as on the approval of the treatment extension by National Health Insurance Fund; DOAP – *A. dorsalitis pedis.*

Table 2

Demographic and clinical characteristic of patients in the control gropu treated by conventional therapy only (the group B)

Patients	Gender	Age	Diabetes Type	Ulcer grade (wagner)	Foot x ray scan at the beginning of the study	Treatment period before entering the study	Surgical intervention	Healing Period
1	M	58	I	3	*Osteomyelitis ped. l. sin. Arthodesim mediotarsalis l. sin.*	720 days	*Amputatio ped. l. sin. (Chopard) Thiersch*	150 days
2	M	64	II	3	/	7 days	*Amputatio dig. IV ped. dex.*	244 days
3	M	71	II	4	*Osteomyelitis dig. II ped. l. sin*	31 days	*Amputatio dig. II et III ped. l. sin.*	240 days
4	M	73	II	4	/	30 days	*Amputatio hall. l. sin.*	120 days
5	F	74	I	3	*DOAP gr. III ped. l. sin.*	15 days	*Amputatio dig. IV ped. l. sin.*	38 days
6	M	58	II	3	/	10 days	*Amputatio transmetatharsalis ped. l. dex.*	360 days
7	M	69	I	4	*Osteomyelitis hall. dex.*	153 days	*Amputatio hall. l. dex.*	81 days
8	M	62	I	4	/	7 days	*Amputatio dig. I–III ped. dex.*	91 days
9	M	83	II	4	/	30 days	*Amputatio cruris l. sin.*	35 days
10	M	52	II	4	/	7 days	*Amputatio femoris l. dex.*	26 days
11	M	65	I	4	/	30 days	*Amputatio femoris l. sin.*	15 days
12	M	63	II	4	*DOAP ped. l. sin. Osteoporosis ped. l. sin.*	75 days	*Incisio et contraincisio ped. l. sin. Necrectomia ped. l. sin.*	126 days
13	M	50	I	3	/	15 days	*Amputratio dig. IV ped. dex.*	60 days
14	M	46	II	4	/	21 days	*Amputatio hall. l. sin.*	66 days
15	F	71	II	4	*Osteomyelitis dig. II ped. dex.*	21 days	*Amputatio dig. II ped. dex.*	121 days

Table 2 (continued)

Patients	Gender	Age	Diabetes type	Ulcer grade (Wagner)	Foot x- ray scan at the beginning of the study	Treatment period before entering the study	Surgical intervention	Healing Period
16	M	55	II	4	*DOAP ped. l. sin.*	15 days	*Amputatio dig. V ped. sin.*	61 days
17	M	65	II	3	*Osteomyelitis dig. V ped. sin.*	120 days	*Incisio et contraincisio ped. l. sin.*	90 days
18	F	51	II	4	/	10 days	*Amputatio dig. IV ped. dex.*	60 days
19	M	67	I	3	*Osteomyelitis hall. l. sin.*	30 days	*Amputatio cruris l. sin.*	28 days
20	F	76	I	4	/	35 days	*Amputatio ped. l. dex. (Chopart)*	210 days
21	M	53	I	4	*Osteoporosis ped. l. sin.*	30 days	*Amputatio cruris l. sin.*	21 days
22	M	49	II	3	*Osteomyelitis metatharsalis V ped. l. sin.*	15 days	*Incisio et curettage ped. l. sin.*	180 days
23	M	78	II	4	/	60 days	*Amputatio femoris l. dex.*	18 days
24	M	66	II	4	*Osteomyelitis hall. dex.*	60 days	*Amputatio hall. dex.*	51 days
25	F	71	II	4	/	10 days	*Amputatio dig. II ped. l. sin.*	100 days
26	F	68	I	4	/	15 days	*Amputatio dig. II ped. l. dex.*	240 days
27	F	70	I	4	/	90 d days	*Amputatio femoris l. dex.*	34 days
28	F	82	II	3	/	7 days	*Incisio, contraincisio et necrectomia ped. l. dex.*	48 days
29	M	79	I	4	/	360 days	*Amputatio cruris l. dex.*	18 days
30	M	37	II	3	/	7 d days	*Necrectomia ped. l. dex.*	150 days

All the patients in the control group were admitted to the hospital, and the duration of their stay depended on the healing period; DOAP – *A. dorsalitis pedis.*

Table 3
Summary of patients demographic characteristics, diabetes mellitus (DM) type and the ulcer grade (Wagner classification)

Characteristics	Group A	Group B	*p*
Number of patients	30	30	
Age (years), mean ± SD	62.67 ± 10.71	64.20 ± 11.35	0.592
median	64.5	65.5	
range	30–80	37–83	
Gender, n (%)			
female	7 (23)	8 (27)	0.766
male	23 (77)	22 (73)	
Type of DM, n (%)			
I	11 (37)	12 (40)	0.791
II	19 (63)	18 (60)	
Wagner classification, n (%)			
3	12 (40)	10 (33.3)	0.592
4	18 (60)	20 (66.7)	
Radiographic findings, n (%)			
without pathological result	15 (50.0)	18 (60.0)	
osteoarthropathy	1 (3.3)	3 (10.0)	0.262
osteomyelitis	9 (30.0)	8 (26.7)	
osteoporosis	5 (16.7)	1 (3.3)	
Intervention type, n (%)			
incision	3 (10.0)	2 (6.7)	
necrectomia	17 (56.7)	3 (10.0)	0.0001
finger amputation	7 (23.3)	14 (46.7)	
foot amputation	3 (10.0)	3 (10.0)	
high amputation	0 (0.0)	8 (26.7)	

Group A – patients treated by combination of conventional therapy + hyperbaric oxygen therapy (HBOT); Group B – patients treated by conventional therapy only; SD – standard deviation.

Table 4
Treatment period before entering the study and the healing period in patients with diabetic foot

Treatment period (days)		n	Mean ± SD	95% CI		Min.	Max.
				lower bound	upper bound		
Group A							
before entering the study	Wagner 3	12	26.2 ± 31.7	6.0	46.3	7.0	120.0
	Wagner 4	18	39.5 ± 54.0	12.7	66.3	3.0	180.0
	Total	30	34.2 ± 46.2	16.9	51.4	3.0	180.0
healing period	Wagner 3	12	65.6 ± 45.8	36.5	94.7	20.0	150.0
	Wagner 4	18	49.7 ± 33.8	32.8	66.5	15.0	130.0
	Total	30	56.0 ± 39.1	41.4	70.6	15.0	150.0
Group B							
before entering the	Wagner 3	10	94.6 ± 222.4	-64.5	253.7	7.0	720.0
study	Wagner 4	20	54.5 ± 80.1	17.0	92.0	7.0	360.0
	Total	30	67.9 ± 141.2	15.2	120.6	7.0	720.0
healing period	Wagner 3	10	134.8 ± 106.0	59.0	210.6	28.0	360.0
	Wagner 4	20	86.7 ± 71.6	53.2	120.2	15.0	240.0
	Total	30	102.7 ± 85.9	70.7	134.8	15.0	360.0

SD – standard deviation; CI - confidence interval.

Baroni et al. [14] were among the first who published treatment outcomes with HBOT. In their study, when comparing the two groups of patients (the group treated with HBOT and the group without receiving HBOT) the statistical analysis using χ^2 test demonstrated highly significant difference ($p = 0.001$) in favour of HBOT. In regards to the most significant parameter, the limb amputation, HBOT drastically reduced the percentage of amputations. These results coincide with our experience.

Kalani et al. [15] from Karolinska Hospital, Stockholm, Sweden, in their study followed-up the treatment results of two groups of patients with diabetic foot (treated with and without HBOT) during 3 years. Seventy six percent of patients treated with HBOT had healed ulcer lesion and intact skin, whereas in the group of patients treated conventionally that effect was obtaind in 48% of the patients. The amputation had to be performed just in 12% of the patients in the HBOT group and in 33% of the conventionally treated patients [15].

The mechanisms by which HBOT acts positively on diabetic foot ulcer healing are the reducing of wound exudate and stimulation of granulation process. The values of partial oxygen pressure in the wound surrounding during HBOT may indicate the future treatment outcome. There is positive correlation between transcutanous oxygen pressure (TcPO2) values and the speed of the wound size and exudate reduction, and epithelialization [16]. A negative correlation between TcPO2 values and parameters of wound healing was determined in the group of patients whose treatment ended with high amputations [17].

The authors who have compared the patients with the Wagner grades III and IV diabetic foot ulcer conclude that HBOT after 30 sessions greatly contributes to prevention of amputations and the healing of the wound by epithelialization, but an antibiotic therapy has alsorole in the healing process [18].

In comparison with the results of Fedorko et al. [19] who randomly chosen 103 patients divided into two groups (49 in the HBOT group and 54 in the control group), our results are far better regarding amputations. They had 22.4% of high amputations in each group. In HBOT group 11 out of 49, and in the control group 13 out of 54 patients with the Wagner grades III and IV diabetic foot ulcer had underwent amputations.

Conclusion

HBOT definitely has positive adjuvant role in managing diabetic foot. For the optimal treatment results successful surgical ulcer treatment is necessary and the use of bandage with the healing dressings, as well as the treatment with HBOT. In case of the clear signs of local infection, antibiotic therapy according to the antibiogram is necessary.

The medical practitioners, the patients and policy creators should define good clinical practice guidelines of Shared Decision Making for appliance of hyperbaric oxygen therapy as the additional treatment for diabetic foot management. The future researches should be aimed at the improvement of methods for choosing patients, testing various protocols of treatment and improvement of trust in those assessments. The routine implementation of transcutaneous oximetry imposes itself as a simple, cheap and reliable method for early assessment of HBOT efficacy and the patients are not needlessly exposed to the efforts which exist at some degree (arrival from their home to Centre for baromedicine or organizing transport from their hospital to the Centre). The special problem is the treatment cost which should be paid by the Health Insurance Fund without interference with ethical principles that every patient should have the same right on treatment if that treatment is a proper one.

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