

Hyperbaric Oxygen Therapy Versus Ultrasound on Healing of Diabetic Foot Ulcers

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Abstract: Approximately 15% of diabetic patients develop a foot ulcer during their lifetime and 20% of these ulcers result in lower extremity amputation. The aim of this study was to compare the healing rate of foot ulcers after hyperbaric oxygen therapy (HBO) versus ultrasound therapy. Forty-five non-insulin dependent diabetic patients complicated with foot ulcer grade II were participated. They were of both sexes. Their age ranged from 35 to 50 years. They were divided into 3 equal groups; group (A) received ultrasound therapy in addition to medical treatment, group (B) received HBO in addition to medical treatment and group (C) received medical treatment only. Measurements of ulcer surface area and volume for all patients in the three groups were done before treatment and after two months at the treatment program also laboratory analysis of Leptin, HBA1c %, WBCs, CRP, HDL, LDL and TG as done to confirm that all groups were homogenous and to be sure that the diabetes was under control as it is an important factor for healing of the diabetic foot ulcer. There was a statistically significant difference between mean levels of the investigated parameters in the HBO group and ultrasound group & HBO group and medical group. Where there was no significant difference between ultrasound group & medical treatment group ($p < 0.05$). Therefore, HBO in addition to medical treatment accelerates healing rate of foot ulcers in diabetic patients.

Key words: Hyperbaric oxygen (HBO) therapy · Ultrasound therapy · Diabetic foot ulcer

INTRODUCTION

Diabetic foot ulcers appear to be due to abnormal pressure distribution secondary to diabetic neuropathy, vascular disease with diminished blood supply contributes to the development of the ulcers and infections are common often with multiple organisms [1].

The most used and validate foot ulcer classification system is the Maggitt-Wagner System. Also, Maggitt-Wagner classification has been shown to give an accurate guide to risk of amputation, the grade of foot ulcer is included in 6 grades: grade (0) there is no open lesion, may have deformity or cellulites, grade (1) there is Superficial diabetic ulcer (partial/full thickness ulcer), grade (2) there is Ulcer extension to tendon or capsule without osteomyelitis, grade (3) there is Deep ulcer with osteitis, abscess and osteomyelitis, grade (4) there is Partial foot gangrene and grade (5) there is Whole foot gangrene [2].

Ultrasound can improve tissue repair by increasing protein synthesis, mast cell degranulation and growth

factor production, uptake of calcium and fibroblast mobility [3]. Hyperbaric oxygen therapy (HBO) is defined as a treatment in which patients breathe 100% oxygen intermittently under a pressure of greater than sea level or one atmosphere HBO for venous ulcers could improve healing at six weeks. Topical HBO and low-energy laser therapies are safe, effective, simple and inexpensive therapies for diabetic foot ulcer and chronic venous ulcer [4].

The aim of this study was to determine the best therapeutic modality out of HBO and ultrasound which can accelerate the healing rate in diabetic patients with foot ulcers.

MATERIALS AND METHODS

Subjects: Forty-five non-insulin dependent diabetic patients of both sexes with grade II foot ulcer according to Meggitt-Wagner classification [5], their age ranged between 35-50 years, free from renal failure, myocardial infarction, cardiac, respiratory problems or ulcer rather than diabetes and included and selected randomly into

3 equal experimental groups; Group (A) received ultrasound therapy in addition to medical treatment, group (B) received HBO in addition to medical treatment and group (C) received medical treatment only.

Inclusion criteria were no history of other skin abnormalities, non insulin dependent diabetes mellitus, full thickness foot ulcer according to Wagner classification grade II and foot ulcer duration from 1-6 month. However, exclusion criteria were life threatening disorders as renal failure or myocardial infarction, disorders which leads to ulcer rather than diabetes as varicose vein and trauma, cardiac problem or respiratory problems and medical problem includes: sinusitis, ear problem and hypoglycemia as hyperbaric oxygen therapy increases metabolism and patient with diabetes may experience a low blood sugar (hypoglycemia).

Informed consent was obtained from all participants. If any adverse effects had occurred, the experiment would have been stopped. This study was applied at King Abdulaziz Teaching Hospital However, no adverse effects occurred and so the data of all the participants were available for analysis.

Evaluative Measures

Laboratory Analysis: Blood sample after fasting for 12 hours was taken from each patient in clean tubes containing few mg of K₂EDTA, centrifuged and plasma was separated and stored frozen at -20° used for estimation of plasma leptin level by immunoradimetric assay (IRMA) and glycosylated hemoglobin (HBA_{1c}) using colorimetric method, plasma lipid profile includes Triglycerides, HDL and LDL. Also, Acetic acid for white blood cells (WBCs) and Avitex RF for C - reactive protein (CRP). ADVIA 120 (by Bayer) was used for detection of WBCs.

Foot Ulcer Surface Area: Sterilized transparency will be placed directly over the ulcer and ulcer area was traced with a fine tipped indelible pen. Three tracing of each ulcer was made by the same investigator to establish measurement reliability. Then the traced transparency film was placed over carbon paper with a white paper in between and transcribed the tracing onto metric of graph paper. To calculate surface area the numbers of mm² within the wounds tracing were accounted [6].

Foot Ulcer Volume Measurement: Patient was seated in a position according to the site of ulcer allowing complete filling of the ulcer. A 5cm² syringes with removal needle was filled with normal saline [7]. The ulcer was injected with saline to measure ulcer volume [8].

Intervention Measures

Ultrasound Treatment: The ultrasonic therapy (Sonosan 100) was applied to the intact skin surrounding the wound using coupling gel for contact for 5 minutes 3 times per week, for a total period of two months, treatment was delivered at a frequency of 3 MHZ, at spatial average intensity of 0.5 w/ cm² and the pulse ratio was set at 1:5. The ultrasound head was cleaned with alcohol to avoid any infection transmitted to the patient.

Hyperbaric Oxygen Therapy: The patients seated comfortably in air pressured chamber (Multiplace decompression chamber, ATC, USA) and breathe oxygen through a face mask within the chamber for 90min at 2.5 absolute temperature air (ATA). Treatment was applied 5 days per week for 8 weeks.

Statistical Analysis: The mean values of ulcer surface area and volume were measured before treatment and after two months at the end of the study for the three groups, then the analysis of variance was used for comparison among groups, least statistical significant difference was used as a *post hoc test* if ANOVA revealed statistical significant difference (p<0.05). Statistical analyses were carried out using SPSS for Windows Version 10.0 (SPSS, Inc., Headquarters, 233 South Wacker Drive, Chicago, USA).

RESULTS

The three groups were considered homogeneous regarding the mean values of ulcer surface area and ulcer volume in the three groups (Table 1 and 2). Also, the demographic variables and chemical analysis included Leptin, HBA_{1c} %, WBCs, CRP, HDL, LDL and TG were present in Table 3. Analysis of variance of ulcer surface area in the three groups after treatment had a statistical significant improvement (Table 4). The post hoc comparison test revealed that the significant difference was found between groups A and B as well as between groups A and C (Table 5).

Analysis of variance of ulcer volume in the three groups after treatment had a statistical significant improvement (Table 6). The post hoc comparison test revealed that the significant difference was found between groups A and B as well as between groups A and C (Table 7).

Table 1: Mean value of demographic data and chemical analysis for participants in the three groups

Variables	Ultrasound therapy group	Hyperbaric oxygen therapy group	Medical Treatment group
Age (year)	47.13±4.62	50.23±4.24	49.98±5.19
BMI (kg/m ²)	28.12±5.26	28.78±5.61	28.53±5.94
Duration of Ulcer (month)	4.8±2.12	5.1±2.15	5.74±1.89
C-reactive protein (mg/l)	14.74 ± 3.56	15.13 ± 3.21	14.70 ± 3.56
White blood cell count (×10 ⁹ l ⁻¹)	9.15 ± 2.82	9.26 ± 2.55	9.19 ± 2.64
HbA1c (%)	8.10 ± 2.17	8.02 ± 2.43	8.22 ± 2.33
Leptin (ng/ml)	39.53± 6.94	39.64± 6.46	39.28± 6.27
HDLc (mg/dl)	35.81 ± 2.57	35.55 ± 2.28	36.14 ± 2.63
LDLc (mg/dl)	136.22± 14.96	135.21± 15.10	135.59± 14.42
TG (mg/dl)	158.81± 13.05	158.15± 13.65	158.05± 14.11

Table 2: Analysis of variance of ulcer surface area before treatment in the three groups

Source of variation	Sum of squares	Degree of freedom	Mean of squares	F-ratio	Significance
Between Groups	0.837	2	0.418	2.79	Non Sig.
Within Groups	6.303	42	0.150		
Total	7.14	44			

Table 3: Analysis of variance of ulcer volume before treatment in the three groups

Source of variation	Sum of squares	Degree of freedom	Mean of squares	F-ratio	Significance
Between Groups	0.204	2	0.102	0.953	Non Sig.
Within Groups	4.96	42	0.107		
Total	4.7	44			

Table 4: Analysis of variance of ulcer surface area after treatment in the three groups

Source of variation	Sum of squares	Degree of freedom	Mean of squares	F-ratio	Significance
Between Groups	16.23	2	8.115	31	P< 0.05
Within Groups	11.16	42	0.26		
Total	27.39	44			

Table 5: Least significance difference ulcer surface area after treatment in the three groups

Statistical values			
Program	Mean difference ± Standard deviation	L.S.D. value	Significance
HBO-Ultrasound	1.34±0.15	1.34	P< 0.05
HBO-Medical treatment	1.12±0.18	1.57	P< 0.05
Ultrasound-Medical treatment	0.86±0.11	0.68	P> 0.05

HBO - Ultrasound: Hyperbaric oxygen therapy versus Ultrasound

HBO- Medical treatment: Hyperbaric oxygen therapy versus Medical treatment

Ultrasound - Medical treatment: Ultrasound versus Medical treatment

Table 6: Analysis of variance of ulcer volume after treatment in the three groups

Source of variation	Sum of squares	Degree of freedom	Mean of squares	F-ratio	Significance
Between Groups	12.25	2	6.125	24	P< 0.05
Within Groups	10.71	42	0.255		
Total	22.96	44			

Table 7: Least significance difference ulcer volume after treatment in the three groups

Program	Statistical values		
	Mean difference ± Standard deviation	L.S.D. value	Significance
HBO-Ultrasound	1.51±0.18	1.47	P< 0.05
HBO-Medical treatment	1.42±0.19	1.65	P< 0.05
Ultrasound-Medical treatment	0.75±0.16	0.72	P> 0.05

HBO - Ultrasound: Hyperbaric oxygen therapy versus Ultrasound

HBO- Medical treatment: Hyperbaric oxygen therapy versus Medical treatment

Ultrasound - Medical treatment: Ultrasound versus Medical treatment

DISCUSSION

The results of this study indicated that there was a significant improvement in values of ulcer surface area and volume in the three groups after treatment which means that both ulcer surface area and volume were reduced. Laboratory analysis of Leptin, HbA1c %, WBCs, CRP, HDL, LDL and TG as done to confirm that all groups were homogenous and to be sure that the diabetes was under control as it is an important factor for healing of the diabetic foot ulcer. There was a statistically significant difference between mean levels of the investigated parameters in HBO group & ultrasound therapy group and HBO group & medical treatment group after treatment. Where there was no significant difference between ultrasound therapy group & medical treatment group.

Ultrasound may work at several levels in the early stages of healing, it may decrease edema, increase blood flow, increase the delivery of oxygen & macrophages to the area, stimulate collagen deposition and remodeling [9]. Ultrasound therapy increases intracellular calcium and permeability of cell membrane which lead to faster tissue healing at intensities of 0.5 to 0.75 w/c m² with pulsed frequency of 20% [10]. Ultrasound therapy applied at pulsed mode, frequency 3 MHz, intensity 0.5 w/c m², duration of 5 minutes per session and for three weeks can promote healing of diabetic foot ulcers [9].

HBOT promotes healing in a variety of ways; it promotes the formation of new vessels required for wound healing and increases fibroblast proliferation and collagen production, its bactericidal and bacteriostatic effects on both aerobic and anaerobic bacteria [11, 12]. High oxygen levels make red blood cells more flexible which enable them to get through the capillaries and get to where are needed [13].

The difference in the percentage of improvement in healing rate between ultrasound and HBO was high which means that HBO is faster as increased level of

oxygen increased resistance to infection, decreased level of lactic acid and maintained level of ATP. HBO affected immune system and vascular tone leading to release of collagen and fibroblast and vascular growth factors by macrophages [14, 15].

CONCLUSION

It is recommended to use HBO in addition to medical treatment to accelerate healing rate of foot ulcers in diabetic patients, also, further researches were needed to study the effects of other modalities that may help healing of diabetic foot ulcers.

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