Effect of Different Therapeutic Modalities on Healing Rate of Diabetic Foot Ulcers

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ABSTRACT

Background and purpose: *About 15% of diabetic patients experience a foot ulcer in their life. Foot ulcers are a major predictor of future lower extremity amputation in patients with diabetes, as about 14 to 24% of patients with foot ulcer require amputation. The purpose of this study was to determine which therapeutic method out from hyperbaric oxygen therapy; laser and ultrasound, in addition to medical treatment obtain the best improvement in healing rate of foot ulcers in diabetic patients.* ***Subjects and methods:*** *Forty-five non-insulin dependent diabetic patients of both sexes complicated with foot ulcer grade II. Their age ranged from 42 to56 years. They were selected from Nasser Institute and randomly assigned into 3 equal groups. Group (1) received laser therapy, group (2) received hyperbaric oxygen therapy and group (3) received the pulsed ultrasound therapy in addition to medical treatment. Measurement of ulcer surface area and volume for all patients in the three groups was done before treatment and after two months at the end of the study.* ***Results:*** *There was a significant difference between group (1) & (2) and group (1) & (3). Where there was no significant difference between group (2) & (3).* ***Conclusion:*** *It is recommended to use hyperbaric oxygen therapy in addition to medical treatment to accelerate healing rate of foot ulcers in diabetic patients.*
Key words: *Hyperbaric oxygen therapy, Laser, Ultrasound, Diabetic foot ulcer and healing rate.*

INTRODUCTION

It was estimated that about 15% of diabetic patients experience a foot ulcer in their life. Foot ulcers are a major predictor of future lower extremity amputation in patients with diabetes. Also, about 14 to 24% of patients with foot ulcer require amputation; therefore it is not surprising that diabetes is the leading cause of non-traumatic lower limb amputation[1,25].

A special problem in diabetic patients is the development of ulcers of the foot. The 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[11].

The most common location for foot ulcers is the planter surface of the foot. These ulcers are often the results of repeated mechanical stress that is not recognized by the patients because of the peripheral neuropathy and loss of protective sensation .In addition the presence of peripheral vascular disease and infection can lead to poor healing of foot wounds and to the development of gangrene[2].

Ultrasound can improve tissue repair by increasing protein synthesis, mast cell degranulation and growth factor production, uptake of calcium and fibroblast mobility[4].

Laser can be used for acceleration of wound healing as the biostimulation of laser accelerate the inflammatory phase of wound healing by altering the levels of various prostaglandins, increasing ATP synthesis by enhancing electron transfer in the inner membrane of the mitochondria and acceleration of collagen and fibroblasts synthesis and vascularization of the healing tissue[5].

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[8,10]. Hyperbaric oxygen therapy for venous ulcers could improve healing at six weeks[15].

The aim of this study was to determine the best therapeutic modality out ultrasound, low intensity laser therapy and hyperbaric oxygen therapy which can accelerate the healing rate in diabetic patients with foot ulcers.

SUBJECTS, MATERIAL AND METHODS

Subjects

Forty-five non-insulin dependent diabetic patients of both sexes (20 female, 25 males) complicated with foot ulcer grade II, according to Wagner classification. Their age ranged from 42 to56 years. They were selected from Nasser Institute.

The patients will randomly assigned into 3 equal groups. Group (1) received laser therapy, group (2) received hyperbaric oxygen therapy and group (3) received the pulsed ultrasound therapy in addition to medical treatment.

Patients will be chosen after medical examination by a physician with no history of other skin abnormalities. They were non insulin dependent diabetes mellitus with full thickness foot ulcer according to Wagner classification grade II[26]. With foot ulcer duration from 1-3 month were selected.

Patients with life threatening disorders as renal failure, myocardial infarction, cardiac or respiratory problems were excluded. Patient suffering from any disorders which leads to ulcer rather than diabetes as varicose vein and trauma were excluded.

Equipment

A) Evaluation equipment

1- Foot Ulcer Surface Area

Sterilized transparent film put in alcohol solution 70% for 24 hours before application to obtain infection control, fine tipped transparent permanent marker, carbon papers long life made, metric graph papers ($1mm^2$) and white A4 papers[13].

2- Foot Ulcer Volume Measurement

Normal saline and syringe $5cm^3$ were used to measure wound volume[13].

B) Therapeutic Equipments

1- Multiplace decompression chamber (ATC, USA) for the application of hyperbaric oxygen therapy

The chamber accommodates 2 to 14 patients. The chamber was filled with compress air 100% oxygen was applied to patient through a face mask. It was designed to achieve a pressure up to 6mmHg atmospheric pressure and have a chamber lock energy system that allows person to pass through without altering the pressure of inner chamber in case of emergency.

2- Laser (Asa,Australia)

The device emits both Helium-Neon and Infra Red Laser in mixed light. He-Ne of wave length 632.8nm. In this study, He-Ne (scanning) type of laser was used, its frequency is 50-60 HZ, He-Ne power is 8mw, average power equal 6.6 volt, energy density equal 4 jule/cm^2, penetration from 10 to 15mm.

3- Ultrasound

Ultrasound treatment was applied using the Sonosan 100 ultrasonic apparatus which was calibrated by the manufacturer at the start of the study, the size of the treatment head was $5cm^2$.

PROCEDURES

A-Evaluation Procedures

1-Measurement of 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 reliabilitiy.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 mm^2 within the wounds tracing were accounted. The mean of these three measurements was recorded. This method to measure changes of ulcer surface area every month[18].

2-Measurement of Ulcer Volume

Patient was seated in a position according to the site of ulcer allowing complete filling of the ulcer .A $5cm^2$ syringes with removal needle was filled with normal saline. The ulcer was injected with saline to measure ulcer volume[16].

B-Treatment Procedures

All patients received conservative treatment include: medications (antibiotic and hypoglycemic drugs to control hyperglycemia), debridment for removal of microorganism, necrotic tissue and foreign bodies, Irrigation and dressing after irrigation.

Group (1) received hyperbaric oxygen therapy

A medical screening examination is essential to anticipate any 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). A random test of blood sugar was done prior to entering the chamber and any patient with hypoglycemia was provided with a juice.

The patients seated comfortably in air pressured chamber, 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.

Group (2) received laser therapy

The patients were in a comfortable position on an adjustable height bed, and the ulcered leg was putted on a pillow and covered with sterile towels. The patient and the operator used the protective eye glasses using a long arm goniometer; laser cylinder was adjusted to be perpendicular to the ulcer.

Frequency of He-Ne scanning type of laser was used, its frequency was 50-60 HZ, Ulcers were treated for 20min at intensity of $4J/cm^2$. After application of laser the ulcer was covered with sterile gauze. Patient received three sessions every week for two months.

Group (3) received ultrasound therapy

This group received ultrasonic therapy which 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/ cm^2 and the pulse ratio was set at 1:5.The ultrasound head was cleaned with alcohol to avoid any infection transmitted to the patient

Measurement of ulcer surface area and volume for all patients in the three groups was done before treatment and after two months at the end of the study.

Statistical Analysis

The mean values of ulcer surface area and volume were measured and calculated 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 between groups (P<0.05).

RESULTS

Comparative study between the pretreatment values of the three groups

As shown in table (1) , the analysis of variance of ulcer surface area in the three groups pretreatment had a statistical no significant difference "F" value was 2.79, P < 0.05 ($F_{0.05}$ = 3.23).

Table (1): Shows analysis of variance of ulcer surface area before treatment and significance difference of "F" ratio.

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			

Level of significance P < 0.05

As shown in table (2) , the analysis of variance of ulcer volume in the three groups pretreatment had a statistical no significant difference "F" value was 0.953, P < 0.05 ($F_{0.05}$ = 3.23).

Table (2): Shows analysis of variance of ulcer volume before treatment and significance difference of "F" ratio

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			

Level of significance P < 0.05.

Comparative study between the post treatment values of the three groups

As shown in table (3) , the analysis of variance of ulcer surface area in the three groups post treatment had a statistical significant improvement, "F" value was 28, P < 0.05 ($F_{0.05}$ = 3.23).

Table (3): Shows analysis of variance of ulcer surface area after two months (post treatment) in the three groups.

Source of variation	Sum of squares	Degree of freedom	mean of squares	F-ratio	Significance
Between Groups	14.04	2	7.02	28	Sig.
Within Groups	10.5	42	0.25		
Total	25.54	44			

Level of significance P < 0.05

As shown in table (4) and fig. (1), the least significant difference of ulcer surface area after two months (post treatment) between hyperbaric oxygen therapy (HBO) group and laser group and between hyperbaric oxygen therapy (HBO) group and ultrasound therapy (US) group was statistically significant improvement, but between laser group and ultrasound therapy group was not statistically significant improvement.

Table (4): Shows least significance difference ulcer surface area after two months (post treatment) in the three groups.

Program	Stat. values		
	Mean difference ± Standard deviation	L.S.D. "calculated" value	Significance
HBO-Laser	1.15±0.07	1.15	Sig.
HBO-US	1.26±0.05	1.26	Sig.
Laser-US	0.16±0.02	0.16	Non Sig.

HBO -Laser: Hyperbaric oxygen therapy versus Laser HBO-US:Hyperbaric oxygen therapy versus Ultrasound therapy
Laser-US: Laser versus Ultrasound therapy L.S.D. "calculated" value: Least significant difference
L.S.D. "tabulated" value equal 0.56 Sig.: Significant Non Sig.: Non significant

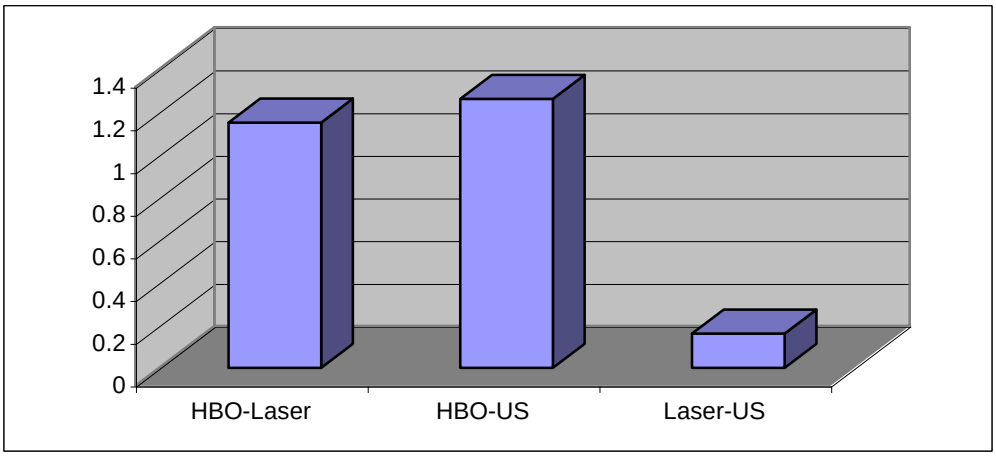

Fig. (1): Shows least significance difference ulcer surface area after two months (post treatment) in the three groups.

As shown in table (5) , the analysis of variance of ulcer volume in the three groups post treatment had a statistical significant improvement, "F" value was 25, $P < 0.05$ ($F_{0.05} = 3.23$).

Table (5): Shows analysis of variance of ulcer volume after two months (post treatment) in the three groups.

Source of variation	Sum of squares	Degree of freedom	mean of squares	F-ratio	Significance
Between Groups	14.03	2	7.02	25	Sig.
Within Groups	11.76	42	0.28		
Total	25.79	44			

Level of significance $P < 0.05$

As shown in table (6) and fig. (2), the least significant difference of ulcer volume after two months (post treatment) between hyperbaric oxygen therapy (HBO) group and laser group and between hyperbaric oxygen therapy (HBO) group and ultrasound therapy (US) group was statistically significant improvement ,but between laser group and ultrasound therapy group was not statistically significant improvement.

Table (6): Shows least significance difference ulcer volume after two months (post treatment) in the three groups.

Program	Stat. values		
	Mean difference ± Standard deviation	L.S.D. "calculated" value	Significance
HBO-Laser	1.12±0.05	1.12	Sig.
HBO-US	1.24±0.06	1.24	Sig.
Laser-US	0.12±0.01	0.12	Non Sig.

HBO -Laser: Hyperbaric oxygen therapy versus Laser HBO-US: Hyperbaric oxygen therapy versus Ultrasound therapy
Laser-US: Laser versus Ultrasound therapy L.S.D. "calculated" value: Least significant difference
L.S.D. "tabulated" value equal 0.59. Sig.: Significant Non Sig.: Non significant

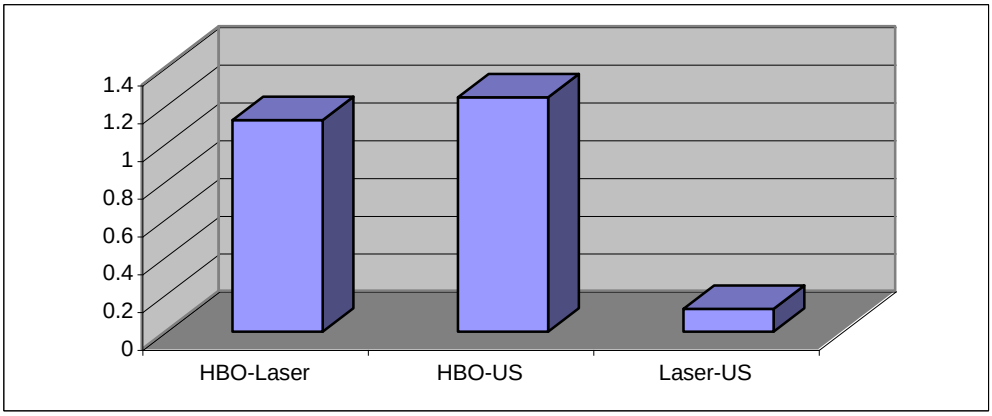

Fig. (2): Shows least significance difference ulcer volume after two months (post treatment) in the three groups.

DISCUSSION

Helium-Neon laser was the effective type of irradiation that lead to complete healing within 17 days with low dose 1 J/c m^2 than Ga-As laser with the same dose on wound healing for 20 rates[21].

Helium-Neon laser can penetrate in the granulation tissue 2.5 times higher than its penetration in the normal skin which gives the advantage of using He-Ne laser in treating ulceration and non-healing wounds[14]. Low intensity laser therapy of 4 J/c m^2 increased the cell number about three to six folds compared to control cultures[19].

After total of 16 sessions of low intensity laser therapy using a 670nm diode laser administered within four weeks period, the ulcer healed completely .During a follow up period of nine months, there was no recurrence of the ulcers even though the patients' metabolic condition remained unstable[22].

Ultrasound may work at several levels in the early stages of healing, it may decreases edema and increases blood flow .Secondarily increases the delivery of oxygen and macrophages to the area .In the later stages of healing, ultrasound may stimulates collagen deposition and remodeling[17].

Full thickness excised skin wound treated with low intensity ultrasound (0.1 w/c m^2) for 5 minutes, three times a week during the first two weeks after injury led to production of a strong elastic scar tissue[20]. Ultrasound therapy increases intracellular calcium and permeability of cell membrane which lead to faster tissue healing was shown to occur in human tissue in cultured medium at intensities of 0.5 to 0.75 w/c m^2 with pulsed frequency of 20%[3].

Ultrasound therapy applied at pulsed mode, frequency 3 MHz, intensity 0.5 w/c m^2, duration of 5 minutes per session and for three weeks can promote healing of diabetic foot ulcers[24].

Hyperbaric oxygen therapy increases tissue oxygenation and amplifies the oxygen gradient along the periphery of ischemic wounds, oxygen gradient has been demonstrated to be an important stimulus to angiogenesis and wound healing[12].

Increased oxygen delivery to the tissue with HBO therapy may prevent tissue damage by decreasing tissue lactic acid level and maintain the ATP level; this may help preventing tissue damage in ischemic wounds and reperfusion of injured tissues[7].

Elevation of oxygen tension in hypoxic wound ulcers enhances neutrophil oxidative killing of bacteria and stimulates fibroblast proliferation, collagen production, revascularization and epithelization .In addition, oxygen is directly toxic to anaerobic organisms[6,11]. Bacterial activity is inversely proportional to tissue oxygen supply .Elevation of wound oxygen tension may be as effective as antibiotic administration[10].

White blood cells that fight the infection in the ulcer use 20 times more oxygen when they are killing bacteria .Also, the more oxygen the more efficiently the repair of the connective tissues .New capillaries means more blood gets to the site of the ulcer which accelerates healing . High oxygen levels make red blood cells more flexible which enable them to get through the capillaries and get to where are needed[7].

Hyperbaric oxygen therapy is effective in accelerating the healing rate and shortening hospitalization time than ultrasound in diabetic foot ulcers[9].

The difference in the percentage of improvement in healing rate between laser, ultrasound and hyperbaric oxygen therapy was high which means that hyperbaric oxygen therapy is faster as increased level of oxygen increased resistance to infection, decreased level of lactic acid and maintained level of ATP. Hyperbaric oxygen affected immune system and vascular tone leading to release of collagen and fibroblast and vascular growth factors by macrophages[8,23].

Finally, Hyperbaric oxygen therapy improves rate of healing of diabetic foot ulcers and had better results than laser and ultrasound but it can not be applied for all cases and still laser and ultrasound are the safe modality to produce nearly similar effects in treating diabetic foot ulcers.

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الملخص العربى

تأثير طرق علاجية مختلفة على معدل ألتئام قرح القدم السكرى

تعتبر قرح القدم السكرى من أهم أسباب البتر لمرض السكر الغير معتمدين على الأنسولين لذلك تهدف هذه الدراسة إلى معرفة تأثير طرق علاجية مختلفة على معدل ألتئام قرح القدم السكرى. أجرى البحث على خمسة و أربعين مريضا من مرضى السكر الغير معتمدين على الأنسولين يعانون من قرح بالقدم تراوحت اعمارهم بين 42- 56 سنة مقسمين إلى ثلاث مجموعات متساوية. المجموعة الأولى تلقت العلاج بالاكسيجين تحت الضغط والمجموعة الثانية تلقت العلاج بالليزر والمجموعة الثالثة تلقت العلاج بالموجات فوق الصوتية بالإضافة إلى العلاج الطبى . أظهرت النتائج وجود فروق ذات دلالة إحصائية فى قياس مساحة وعمق القرح بين مرضى المجموعه الاولى والثانيه و الاولى والثالثه فى حين لم يوجد فروق ذات دلالة إحصائية بين مرضى المجموعه الثانيه والثالثه .لذلك توصى الدراسه بإستخدام العلاج بالأكسجين تحت الضغط ضمن برنامج العلاج الطبى لقرح القدم السكرى .

الكلمات الدالة: العلاج بالأكسيجين تحت الضغط –الليزر- الموجات فوق الصوتيه – قرح القدم السكرى.