Effect of Different Therapeutic Modalities on Healing of Diabetic Foot Ulcers

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Abstract

Background: Diabetic patients are particularly burdened by foot ulcer. About 2.5% of patients with diabetes will develop a foot ulcer each year leads to lower extremity amputation by 15-40 times in diabetics greater than the rate in patients without diabetes mellitus.

Objective: The aim of this study was to determine which therapeutic method out from hyperbaric oxygen therapy (HBO); laser and ultrasound, in addition to medical treatment obtain the best improvement in healing rate of foot ulcers in diabetic patients.

Material and Methods: Forty-five non-insulin dependent diabetic patients of both sexes complicated with foot ulcer grade II. Their age ranged from 60 to 65 years. They were divided into 3 equal groups; group (A) received laser therapy, group (B) received HBO and group (C) received pulsed ultrasound therapy in addition to medical treatment. 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.

Results: There was a statistically significant difference between mean levels of the investigated parameters in laser therapy group and HBO group and laser therapy group and pulsed ultrasound therapy group after treatment, while there was no significant difference between HBO group and pulsed ultrasound therapy group (p<0.05).

Conclusion: It is recommended to use HBO in addition to medical treatment to accelerate healing rate of foot ulcers in diabetic patients.

Key Words: Hyperbaric oxygen (HBO) therapy – Laser – Ultrasound – Diabetic foot ulcer.

Introduction

APPROXIMATELY 15% of diabetic patients develop a foot ulcer during their lifetime, and 20% of these ulcers result in lower extremity amputation. A large majority (84%) of lower extremity amputations in diabetic patients are preceded by a foot ulcer [1]. 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 [2].

Ultrasound can improve tissue repair by increasing protein synthesis, mast cell degranulation and growth factor production, uptake of calcium and fibroblast mobility [4]. Also, Low-level laser therapy is a safe and effective method for treatment of diabetic foot ulcers [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 [4]. Topical HBO and low-energy laser therapies are safe, effective, simple and inexpensive therapies for diabetic foot ulcer and chronic venous ulcer [5].

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

Patients and Methods

Forty-five non-insulin dependent diabetic patients of both sexes with grade II foot ulcer according to Wagner classification [6], their age ranged between 60-65 years, free from renal failure, myocardial infarction, cardiac, respiratory problems or ulcer rather than diabetes and they were divided into 3 equal groups; group (A) received laser therapy; group (B) received HBO and group (C) received the pulsed ultrasound therapy in addition to medical treatment.
A- Evaluated parameters included the following:

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 mm\(^2\) within the wounds tracing were accounted \[7\].

Foot ulcer volume measurement:
Patient was seated in a position according to the site of ulcer allowing complete filling of the ulcer. A 5 cm\(^2\) syringes with removal needle was filled with normal saline \[8\]. The ulcer was injected with saline to measure ulcer volume \[9\].

B- Application methods:

Low intensity 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 (Asa, Australia) was used, its frequency was 50-60 HZ, ulcers were treated for 20 min at intensity of 4 J/cm\(^2\). After application of laser the ulcer was covered with sterile gauze. Patient received three sessions every week for two months.

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/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.

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 90 min 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 between groups \((p<0.05)\).

The analysis of variance was used for comparison between the three groups to analyze the ulcer surface area and volume as measured before treatment and after two months.

Results
Forty-five non-insulin dependent elderly diabetic patients of both sexes complicated with foot ulcer grade II. Their age ranged from 60 to 65 years. Were included into 3 equal groups; group (A) received laser therapy, group (B) received HBO and group (C) received the pulsed ultrasound therapy in addition to medical treatment. 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.

Analysis of variance of ulcer surface area and ulcer volume in the three groups before treatment had a no statistical significant improvement, "F" value was 2.79, \(p<0.05\) \((F_{0.05}=3.23)\) and "F" value was 0.953, \(p<0.05\) \((F_{0.05}=3.23)\) respectively (Tables 1,2).

<table>
<thead>
<tr>
<th>Source of variation</th>
<th>Sum of squares</th>
<th>Degree of freedom</th>
<th>Mean of squares</th>
<th>F-ratio</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Between groups</td>
<td>0.837</td>
<td>2</td>
<td>0.418</td>
<td>2.79</td>
<td>(p&gt;0.05)</td>
</tr>
<tr>
<td>Within groups</td>
<td>6.303</td>
<td>42</td>
<td>0.150</td>
<td></td>
<td></td>
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<tr>
<td>Total</td>
<td>7.14</td>
<td>44</td>
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</table>

Table (1): Analysis of variance of ulcer surface area before treatment in the three groups.

<table>
<thead>
<tr>
<th>Source of variation</th>
<th>Sum of squares</th>
<th>Degree of freedom</th>
<th>Mean of squares</th>
<th>F-ratio</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Between groups</td>
<td>0.204</td>
<td>2</td>
<td>0.102</td>
<td>0.953</td>
<td>(p&gt;0.05)</td>
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<tr>
<td>Within groups</td>
<td>4.96</td>
<td>42</td>
<td>0.107</td>
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<td></td>
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<tr>
<td>Total</td>
<td>4.7</td>
<td>44</td>
<td></td>
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</tbody>
</table>

Table (2): Analysis of variance of ulcer volume before treatment in the three groups.
Analysis of variance of ulcer surface area in the three groups after treatment had a statistical significant improvement, "F" value was 28, \( p < 0.05 \) (\( F_{0.05} = 3.23 \)) (Table 3). The least significant difference of ulcer surface area after treatment between HBO group & laser group and HBO group & ultrasound therapy group was statistical significant difference, but between laser group & ultrasound therapy group wasn’t statistical significant difference (Table 4 and Fig. 1).

Analysis of variance of ulcer volume in the three groups after treatment had a statistical significant improvement, "F" value was 25, \( p < 0.05 \) (\( F_{0.05} = 3.23 \)) (Table 5). The least significant difference of ulcer volume after treatment between HBO group & laser group and HBO group & ultrasound therapy group was statistical significant difference, but between laser group & ultrasound therapy group wasn’t statistical significant difference (Table 6).

**Table (3): Analysis of variance of ulcer surface area after treatment in the three groups.**

<table>
<thead>
<tr>
<th>Source of variation</th>
<th>Sum of squares</th>
<th>Degree of freedom</th>
<th>Mean of squares</th>
<th>F-ratio</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Between groups</td>
<td>14.04</td>
<td>2</td>
<td>7.02</td>
<td>28</td>
<td>( p &lt; 0.05 )</td>
</tr>
<tr>
<td>Within groups</td>
<td>10.5</td>
<td>42</td>
<td>0.25</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>25.54</td>
<td>44</td>
<td></td>
<td></td>
<td></td>
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</table>

**Table (4): Least significance difference ulcer surface area after treatment in the three groups.**

<table>
<thead>
<tr>
<th>Program</th>
<th>Mean difference ± L.S.D.</th>
<th>Statistical values</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBO-Laser</td>
<td>1.12 ± 0.05</td>
<td>1.12 ( p &lt; 0.05 )</td>
</tr>
<tr>
<td>HBO-US</td>
<td>1.24 ± 0.06</td>
<td>1.24 ( p &lt; 0.05 )</td>
</tr>
<tr>
<td>Laser-US</td>
<td>0.12 ± 0.01</td>
<td>0.12 ( p &gt; 0.05 )</td>
</tr>
</tbody>
</table>

**Table (5): Analysis of variance of ulcer volume after treatment in the three groups.**

<table>
<thead>
<tr>
<th>Source of variation</th>
<th>Sum of squares</th>
<th>Degree of freedom</th>
<th>Mean of squares</th>
<th>F-ratio</th>
<th>Significance</th>
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<tbody>
<tr>
<td>Between groups</td>
<td>14.03</td>
<td>2</td>
<td>7.02</td>
<td>25</td>
<td>( p &lt; 0.05 )</td>
</tr>
<tr>
<td>Within groups</td>
<td>11.76</td>
<td>42</td>
<td>0.28</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>25.79</td>
<td>44</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

**Table (6): Least significance difference ulcer volume after treatment in the three groups.**

<table>
<thead>
<tr>
<th>Program</th>
<th>Mean difference ± L.S.D.</th>
<th>Statistical values</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBO-Laser</td>
<td>1.12 ± 0.05</td>
<td>1.12 ( p &lt; 0.05 )</td>
</tr>
<tr>
<td>HBO-US</td>
<td>1.24 ± 0.06</td>
<td>1.24 ( p &lt; 0.05 )</td>
</tr>
<tr>
<td>Laser-US</td>
<td>0.12 ± 0.01</td>
<td>0.12 ( p &gt; 0.05 )</td>
</tr>
</tbody>
</table>

**Fig. (1): Mean difference of ulcer surface area after treatment in the three groups.**

**Discussion**

The results of this study indicated that there was a significant improvement in values of ulcer surface area and volume for all patients in the three groups after treatment. There was a statistically significant difference between mean levels of the investigated parameters in laser therapy group & HBO group and laser therapy group & pulsed ultrasound therapy group after treatment. Where there was no significant difference between HBO group & pulsed ultrasound therapy group.

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 [10]. Low intensity laser therapy of 4 J/c m\(^2\) increased the cell number about three to six folds compared to control cultures [11]. 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 [3].

Ultrasound may work at several levels in the early stages of healing, it may decreases edema, increases blood flow, increases the delivery of oxygen & macrophages to the area, stimulates collagen deposition and remodeling [12]. 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/cm$^2$ with pulsed frequency of 20% [13]. Ultrasound therapy applied at pulsed mode, frequency 3 MHz, intensity 0.5 w/cm$^2$, duration of 5 minutes per session and for three weeks can promote healing of diabetic foot ulcers [12].

Tissue hypoxia can be a significant factor in the etiology of non-healing foot ulcers in diabetic patients. Through its correction of peripheral ischemia, HBOT may be useful in promoting healing when other modalities fail. 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 [1]. White blood cells that fight the infection in the ulcer use 20 times more oxygen when they are killing bacteria [2]. High oxygen levels make red blood cells more flexible which enable them to get through the capillaries and get to where are needed [14].

The difference in the percentage of improvement in healing rate between laser, 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 [15].

Conclusion:

Hyperbaric oxygen therapy improves rate of healing of diabetic foot ulcers and had better results than laser and ultrasound.

Acknowledgment:

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References