Original Article

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Effects of low level laser therapy on grades II and III of diabetic foot ulcers

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Abstract

Objective: To evaluate the effect of Low Level laser Therapy on foot ulcers in diabetic type II based on photographic assessment.

Background data: Researchers have been used low level lasers to enhance wound healing. Ulcers in diabetic patients are in risk of compromised healing, due to reduced microcirculation and the other disorders that may affect wound healing.

Material and Methods: Thirty diabetic type 2 patients, with grade II and III diabetic foot ulcers were treated by low level laser therapy. The mean duration of diabetes was 14.3 years and ulcers were present since average 3.4 months ago. Treatment sessions were performed every other day for 10-15 sessions and then continued two times a week until complete healing or achieving grade 1.

Results: Mean of wounds surface was 43.5 cm^2 (range 0.09- 62.5) before treatment, and was 0.3 cm^2 (range 0-1.7) after about 18 treatment sessions (range 8-46), $P<0.001$. There was no relapse or other problem with ulcers during three months of follow-up. There were no reported side-effects by the patients.

Conclusion: Low level laser therapy could be a safe and effective method for treatment of diabetic foot ulcers. Clinical trials with higher sample size are proposed to evaluate more details about low level laser therapy effectiveness on diabetic wound healing process.

Key words: Low level Laser Therapy, Diabetic Foot Ulcer, Laser Acupuncture, Intravenous Laser

Introduction

According to the American Diabetes Association in 2009, about 23.6 million people in America suffer from diabetes [1]. Diabetic foot ulcers are one of the most common health problems with 1.0-4.1% annual population-based incidence and 4-10% prevalence suggest that the life time incidence may be as high as 25% among patients with diabetes mellitus [2–3]. These ulcers cause considerable morbidity and care expenses, and their significance for the individual and society, is apparent [4-7].

The pathophysiological mechanisms lead to foot ulceration in diabetic patients is not completely clear. Structural deformities, peripheral neuropathy, ischemia, infection, edema, and callus formation are some of the most identified causes lead to diabetic ulcers [8]. Peripheral neuropathy is one of the most important causes [9] which affects more than 50% of diabetic patients older than 60 years [10]. Endothelial dysfunction, reduction of vessel elasticity due to the sclerosis of media and dysfunction of the autonomic vasomotor are the other causal pathways [11-14].

Several surgical and medical options are provided for treatment of diabetic foot ulcers [15]. Low level laser therapy (LLLT) has been suggested as a promising treatment option for open wounds. However, there are few reports on LLLT effectiveness on diabetic wounds.

During past 30 years, low-level lasers have been broadly used in medical fields. Recently, there has been an increase in the clinical applications of low-

level laser irradiation in various therapeutic fields. One of the most important functional aspects of laser therapy is photobiostimulatory effects on various biological systems especially microcirculation. The photobiostimulatory effects is reported based on the effects of low intensity lasers which are described as lasers with less than 500 mW average power [16-19].

Researchers have been tried to use Helium Neon (He-Ne), CO2, and Potassium Titanyl Phosphate. (KTP) lasers in encouraging wound healing in diabetic patients [20]. Carvalho et al (2006) evaluated the effect of He-Ne laser on wound healing in diabetic and non diabetic rats. They showed significant effect of laser on the amount of collagen fibers [21]

In another study, Kawalec et al (2004) used infra red low level laser on diabetic and non diabetic rats [22]. Hawkins et al (2005) showed the effect of LLLT on synthesis of protein and prostaglandins, ATP and fibroblasts, cellular growth and secretion of neurotransmitters. LLLT had significant effect on wound healing in diabetic rats but not on non diabetic ones [23].

Hopkins et al (2004) in triple blinded study with sham laser showed the effect of LLLT on human fibroblast proliferation [24].

Low-level laser irradiation has been shown to accelerate collateral circulation, enhance microcirculation [25] as well as relaxation of vascular smooth muscle [26]. Furthermore, LLLT was reported effective to improve skin circulation in patients with diabetic microangiopathy [27].

Schindle et al. (1999) reported the first diabetic foot which was treated by LLLT. He suggested that this therapeutic method might represent a useful side-effect-free alternative treatment modality for the induction of wound healing in neuropathic diabetic ulcers [28]. Since then, some researchers have been applied low-intensity lasers for treatment of diabetic foot ulcers. But contradictory results have been achieved through different research plans. Cullum et al. (2001) systemically reviewed the available published articles and reported there were no sufficient reliable evidences on contribution of laser therapy in chronic wound healing [29].

There are several methods for laser irradiation, local, intravenous, acupuncture and etc. Unlike the treatment mechanisms of local laser therapy, the medical effects of intravenous laser therapy are determined by predominance of systemic mechanisms as increasing the efficacy of vascular, immune, respiratory, other systems and organs as a whole [30,31].

Apart from standard needle acupuncture, other methods of stimulating acupuncture points are also applied. Due to invention of low power lasers, irradiation laser acupuncture has been introduced into routine treatment methods which are a painless and aseptic technique [32-33].

In our pilot study on seven diabetic foot patients, with grade 2-3 ulcers, we used combination of local LLLT, intravenous laser and laser acupuncture. All patients healed completely after mean 19 sessions of therapy [34].

We report herein a case series of 30 patients with grade II and III diabetic foot ulcers treated with LLLT as an alternative therapeutic method to routine medical conservative treatment.

Material and Methods

Thirty type 2 diabetic (T2DM) patients with grade II and III diabetic foot ulcers, who had conventional therapy and came to laser clinic of Milad Hospital, were recruited voluntarily for this study. Patients with pregnancy, epilepsy, photosensivity and pacemaker were excluded because of laser contraindication [34]. The ulcers were graded as follow: 1-Epidermal ulcers. 2- Dermal ulcers. 3-Muscle involvement [5]. Glycosylated hemoglobin (HbA1C), Fasting Blood Sugar (FBS), Triglyceride (TG), Low-density Lipoprotein (LDL), High-density Lipoprotein (HDL),: LDL-to-HDL ratio (LDL/HDL), Body Mass Index (BMI), Hip-to-waist ratio (HWR) were measured for all patients before treatment(Table 1).

Table 1: Patients overall data

Patients overall data	Mean(SD)	Range
TG	(79)147	50-430
HDL/LDL	(.0.1)0.3	0.17-0.49
HbA1C	(1.3)8.4	6-11
FBS	(57.4)193	71-300
BMI	(3.5)27.6	21.4-38.4
H/W ratio	(0.00)1.07	0.9-1.24
Ulcer area before treatment	(11.11)4.35cm^2	0.9-62.5cm^2
Ulcer area after treatment	(0.3)0.00cm^2	0-1.7cm^2
Ulcer duration	(2.9)3.4 months	0.5-12
Diabetes duration	(7.8)14.3 years	2-30
Treatment sessions	(7.85)17.78	8-46

All patients were under classic conventional treatment for wound including daily wash with normal saline and routine dressing. Wound secretion culture was done before treatment and antibiotic was prescribed according to the antibiogram result. Wound culture was repeated every 2-3 weeks according to the secretions. Debridement was done if needed.

The length and width of the ulcers were measured by one person before and after treatment.
Photographs were taken before and after treatment by digital camera.

We applied LLLT through local contact irradiation of ulcer bed with red light (660 nm, power 25 mW, 1.5 J/cm^2) and ulcer margins with infrared laser (980 nm, power 200 mW, 6 J/cm^2). We used sterile translucent covers to avoid direct contact of probe and ulcer, along with intravenous laser irradiation with red light laser (650 nm, power 1.5 mW) for 15 to 20 minutes, in addition to laser acupuncture with infrared laser (1 J/cm^2) for LI-11, LI-4 SP-6, Pe-6, ST-36 and GB-34 points. Based on the authors past experiences, combination of these three methods (local laser therapy, intravenous laser and laser acupuncture) can be more effective to accelerate wound healing, especially in chronic and non healing wounds.

The LLLT intervention were performed every other day for 10-15 sessions and after that continued two times a week until complete healing were achieved. In total, treatment period was about 1.5-2 months.

Results

Thirty diabetic T2DM patients with grade II and III diabetic foot ulcers were recruited for this study (mean age 61.77, range 46-76). The mean period of diabetes was 14.3 years (range 2-30, SD 7.8) and the mean value for glycosylated hemoglobin (HbA_1C) also was 8.4mg/dl (range: 6-11, SD: 1.3). The ulcers were emerged from average 3.4 months ago (range 0.5-12, SD 2.9). Mean wound's area before treatment was 43.5 cm^2 (range 0.09-62.5), and after about 18 sessions of treatment 0.3 cm^2 (range 0- 1.7), Wilcoxon-signed test showed $P<0.001$. Total outcome measures can be reached by table 1. All ulcers were completely healed with exception of three patients who quitted from the study. Mean of therapeutic sessions in these three patients were 19. The surface of their ulcers was about 1.5-2.64 cm^2 at the ending session but all of these ulcers reduced to grade I. The lower extremity blood supply was assessed by doppler sonography. 17 patients (53.1%) normal, in 10 patients (31.3%) decreased and in 5 patients (15.6%) cut off. There was no significant difference between three groups based on doppler report (normal flow, decreased, and cut off) and number of therapeutic sessions.

There was no relapse or other problem with ulcers during three months of follow-up. There was no compliance reported by the patients.

In Spearman's rho test for evaluating the relation between laser sessions with HbA1c (as blood sugar control indicator), BMI (as body mass indicator), diabetes duration, ulcer duration, age and wound surface before treatment ,$P>0.05$ which is statistically insignificant.

A: before treatment

B: After treatment

Discussion

Low Level Lasers have been evaluated as a non-invasive treatment for wound healing. This effect, called “photostimulation” or “biostimulation”, produces non-destructive effects on tissues at the cellular level [32]. The exact pathophysiological

mechanisms for this treatment have not yet been elucidated. However, ATPase activity changes, long-term erythrocytes membrane proteins as well as lipid bi-layer structural changes, changes in membrane ion pumps activities [35], changes in neutrophils through activation of tyrosine kinase and phospholipase C [22], dose-dependent priming of polymorphonuclear leukocytes [36] have all been mentioned as cellular mechanisms for application of low intensity laser irradiation.

It seems that laser irradiation increases cell and fibroblast proliferation, collagen synthesis, stimulates macrophages, releases cytokines, modulates the production of growth factors and develops new blood vessels [19, 37-38].

In a randomized control trial by Ataie-Fashtami et al on 16 diabetic foot patients, healing rate in laser group was reported 70% versus 33.3% in placebo group. The difference between the groups in Javid study was not statistically significant, which might happen because of small numbers in each group [39].

Laser clinical trials in wound healing have lots of structural and methodological defects [40]. There is no evidence for positive effect of LLLT on wound healing in some studies which may due to defect in the study designs, sample sizes or insufficient irradiated dosage. [29, 41, 42]. For example in two studies by Lagan and Fernando, chronic ulcers were categorized too [43, 44].

Our study is new because of combination of three laser therapy methods including: local LLLT, intravenous laser and laser acupuncture.

For better evaluation of the relationship between the parameters, more studies with control group and more sample size are necessary.

Conclusion

Effective cure of all diabetic ulcers in 1.5-2 months give a magnificent approach to open a new horizon in treatment of diabetic foot ulcers as already known to be refractory chronic ulcers.

This study is a case series report and lack of control group is a limitation for this research. More clinical and experimental studies may necessary to describe a distinct laser profile for treatment of diabetic foot ulcers.

Although the aim of our study was not evaluating the effect of LLLT on resistant ulcers, but it affect the surface area and grading of the ulcers. Our patients had chronic diabetic foot ulcers and had received several kind of treatment, but the exact kind of therapies was not cleared. According to the results, the grading of the ulcers for all patients after nearly 18 sessions were 0 (complete healing) to 1 (small epidermal ulcers).Patients with ulcer grade 1 were those that stopped their treatment because the ulcer was so small.

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