Efficacy of Low Level Laser Therapy on Wound Healing in Patients with Chronic Diabetic Foot Ulcers—A Randomised Control Trial

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Abstract

Introduction

The number of cases of diabetes mellitus (DM) worldwide is estimated to be around 150 million. This is predicted to double by 2025 with the greatest number of cases in China and India [1, 2]. Diabetic foot ulcer (DFU) is a serious complication of DM and is the single most important risk factor for lower limb amputations. More than 60% of all non-traumatic lower limb amputations are due to DFU complications [3]. Risk factors for DFUs include males, DM of more than 10 years' duration, peripheral neuropathy, abnormal foot structure, peripheral arterial disease, smoking, previous history of ulcers or amputations, and poor glycaemic control. About 15% of patients with DM are likely to develop foot ulcers during their lifetime and about 6–40% of them may require an amputation [4].

Although the fundamental pathophysiological factors leading to DFUs remain incompletely understood, the triad of neuropathy, ischaemia, and infections is commonly considered the most important [5]. These ulcers show decrease in both angiogenic response and deficient growth factors resulting in delayed healing [6]. Non-healing DFUs are resistant to conventional treatment [7]. Several adjuvant therapies which have been tried to stimulate healing process are ultrasound, laser therapy, and other forms of photobiomodulation, electrical stimulation, hyperbaric oxygen, and vacuum-assisted closure [8, 9].

Low-level laser therapy (LLLT) also called low-intensity laser therapy (LILT) or low-energy photon therapy (LEPT) has received clearance from the United States Food and Drug Administration. The clinical efficacy of LLLT in wound healing has been reported [10]. It has been found to significantly decrease the time of wound healing [11, 12].

We conducted a study to assess the efficacy of LLLT in Indian patients with chronic DFUs [13].

Materials and Methods

This study was conducted over a period of 2 years from February 2008 to February 2010 at a tertiary level teaching hospital after obtaining ethical clearance from Institutional Ethics Committee. Type 2 DM patients with Meggitt-Wagner grade I DFUs of at least 4 weeks' duration were included. Those with clinical signs of ischaemia and ankle brachial pressure index (ABI) less than 0.9 were excluded from the study. Sample size was 68. Patients were randomised into two groups of 34 each on the basis of computer-generated numbers. The nature of therapy to be given was topically explained to the patients and written informed consent was obtained from them before enrolment.

All patients were admitted to the surgical ward and were subjected to detailed evaluation. A complete haemogram and renal and liver function tests were carried out in all patients. Patients with fasting blood sugar (FBS) levels measured on two occasions 24 h apart between 90 and 200 mg/dL with glycosylated haemoglobin (HbA1c) levels between 6% and 9% were included. Ulcer area was calculated by obtaining the impression of ulcer floor on a sheet of cellophane paper and then transferring the imprint onto a graph paper. The ulcer size was measured on day 0 and day 15. Patients with evidence of slough were subjected to repeated surgical debridement before starting the treatment. Objective assessment of vascularity was done by careful palpation of peripheral pulses and calculation of ABI. Colour Doppler imaging of the arterial circulation of lower limbs was performed in patients with feeble or absent pulsations. Presence of osteomyelitis was determined with the help of plain radiographs and they were excluded from the study.

Systemic antibiotics were administered based on culture sensitivity reports. Insulin/oral hypoglycaemic agents (OHA) as advised by the physician/endocrinologist were used to maintain a good glycaemic control. Once adequate glycaemic and infection control had been achieved, LLLT was commenced.

Patients in the study group received treatment with LLLT along with conventional or standard therapy, and those in control group received only conventional treatment in the form of daily wet saline or betadine dressings, antibiotic treatment, contact cast immobilization and slough excision as and when required. An LLLT device with a multidiode cluster probe (Thor International Ltd) (Fig. 1) was used in the study [8]. Figure 2 shows an LLLT cluster probe being used to treat foot ulcers. On the basis of the ulcer size, the duration of exposure was calculated to deliver 2–4 J/cm^2 at 60 mW, 5 kHz, daily for 15 days. The ulcer floor and edge were irradiated. The ulcer was then covered with conventional moist dressing.

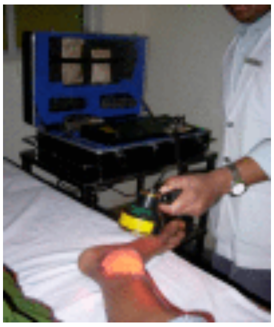

Fig. 1

An LLLT device with a multidiode cluster probe (Thor International Ltd) used in the study

Fig. 2

An LLLT cluster probe being used to treat foot ulcers

Pressure off-loading was carried out in patients with plantar ulcers. Healing or per cent reduction in the size of the ulcer over a period of 15 days after commencement of LLLT was recorded as the end point of the study. Simultaneously, these patients were also educated about various aspects of DM including dietary restrictions, exercise, and foot care in order to prevent recurrence. Statistical analysis of data was carried out using standard '*t* test', and *p* value was calculated. Both the patients and administrators wore laser safety goggles to prevent damage to their eyes.

Results

A total of 68 patients were included in the study. Male to female ratio was 3:1. Mean age of the patients was 50.94 years in the control group and 54.35 years in the study group. No significant difference was found between two groups in the demographic characteristics and risk factors as summarized in Tables 1and and22.

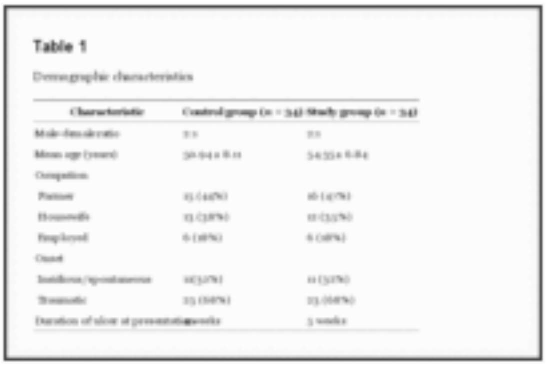
Table 1

Table 1

Demographic characteristics

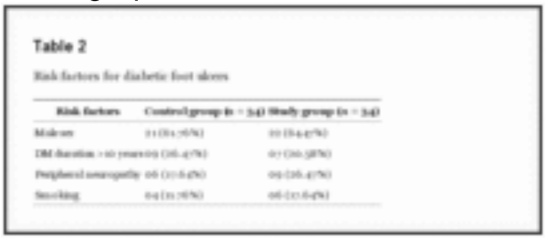
Table 2

Table 2

Risk factors for diabetic foot ulcers

The mean FBS levels among controls were 129.80 ± 3.42 mg/dL (range 90–172 mg/dL) and 120.50 ± 4.51 (range 90–187 mg/dL) in the study group ($p = 0.105$). The mean HbA1c levels in the control group were 7.39 ± 0.05 (range 6.9–8%) and 7.42 ± 0.05 (range 7–8%) in the study group ($p = 0.686$), suggesting no biochemical differences between two groups.

Median duration of ulcer at the time of enrolment in the study was 4 weeks in control and 5 weeks in study groups. Median duration of oral hypoglycaemic agents intake was 10 years in the control group and 5 years in the study group ($p = 0.51$), while that of insulin intake was 6.5 months in the control group and 4 months in the study group.

Mean initial size of the ulcer was 2747.17 mm^2 in the control group and 2608.03 mm^2 in the study group ($p = 0.361$). All ulcers in both groups belonged to Meggitt-Wagner grade I and had a depth of 5 mm. There was no significant difference between the two groups (Table 3).

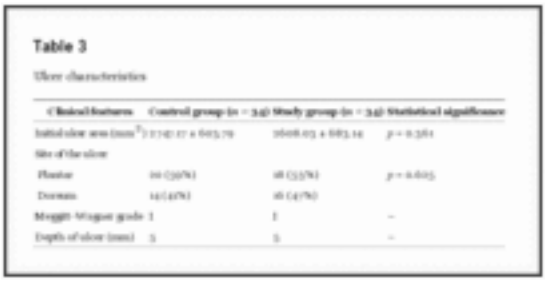
Table 3

Table 3

Ulcer characteristics

After completion of 15 days of therapy, the final area was 2424.75 mm^2 in the control group and 1564.79 mm^2 in the study group ($p = 0.218$). Mean reduction in ulcer area was 322.44 ± 85.84 mm^2 in the control group and 1043.20 ± 266.62 mm^2 in the study group, and this difference between the two groups was statistically significant ($p < 0.010$) (95% confidence interval = 624.91–816.73) (Table 4).

Table 4

Outcome of the study

Results	Control group (n = 34)	Study group (n = 34)	Statistical significance
Initial ulcer area (mm^2)	[illegible]	[illegible]	[illegible]
Final ulcer area (mm^2)	[illegible]	[illegible]	[illegible]
Mean reduction in ulcer area (mm^2)	[illegible]	[illegible]	[illegible]

Table 4

Outcome of the study

Discussion

Diabetic foot ulcers pose a major healthcare problem as a significant cause of morbidity, mortality, and financial burden [14]. The healing process in DFUs is arrested in the stage of inflammation, and it is not known why it does not progress further. Decades of intense research have not unravelled the mystery of wound healing completely. However, it is evident that wound healing involves several biological processes at cellular and molecular levels. The research on wound healing targets the cellular and subcellular biomodulation [15–19]. The healing properties of LLLT are likely to be due to photobiomodulation resulting in increased granulation tissue, fibroblast proliferation, collagen synthesis, neovascularization, and early epithelialization, the important changes observed in LLLT-treated wounds. Low doses of laser are stimulative and higher doses are suppressive. Among the various non-invasive treatment modalities, LLLT is gaining increasing interest. Research findings to date based on animal, human, and in vitro studies have shown that LLLT can play a useful role in healing chronic diabetic ulcers resistant to conventional treatment [20–28].

A study by Hopkins et al. has reported results in 22 healthy subjects and shown 55% greater wound contraction in cases as compared to controls [29]. Gupta et al. have demonstrated a significantly greater reduction ($p < 0.002$) in the surface area of leg ulcers treated with red light and infrared light than in sham-irradiated controls. The leg ulcers were given three treatments per week for 10 weeks, by which time LLLT-treated ulcers showed an average reduction in surface area of 193.0 mm^2, whereas in controls it was only 14.7 mm^2 [30].

In our study, 34 ulcers treated with LLLT showed significant reduction in percentage wound area, that is, 40.24 ± 6.30 mm^2 compared to 11.87 ± 4.28 mm^2 in control groups ($p < 0.001$, $Z = 7.08$). These results show significant benefit following the use of LLLT.

In conclusion, the wounds in subjects treated with LLLT contracted significantly more than the wounds in the non-treated group (40.24% vs 11.87%, $p < 0.001$), which indicates that LLLT is an effective modality to facilitate wound contraction in patients suffering from diabetes and can be used as an adjunct to conventional mode of treatment (dressings and debridement) for healing of diabetic wounds.

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Low-intensity laser irradiation improves skin circulation in patients with diabetic microangiopathy.

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Abstract

OBJECTIVE:

Diabetic foot problems due to angiopathy and neuropathy account for 50% of all nontraumatic amputations and constitute a significant economic burden to society. Low-intensity laser irradiation has been shown to induce wound healing in conditions of reduced microcirculation. We investigated the influence of low-intensity laser irradiation by means of infrared thermography on skin blood circulation in diabetic patients with diabetic microangiopathy.

RESEARCH DESIGN AND METHODS:

Thirty consecutive patients with diabetic ulcers or gangrenes and elevated levels of glycosylated hemoglobin were randomized by blocks of two to receive either a single low-intensity laser irradiation with an energy density of 30 J/cm2 or a sham irradiation over both forefoot regions in a double-blind placebo-controlled clinical study. Skin blood circulation as indicated by temperature recordings over the forefoot region was detected by infrared thermography.

RESULTS:

After a single transcutaneous low-intensity laser irradiation, a statistically significant rise in skin temperature was noted ($P < 0.001$ by ANOVA for repeated measurements), whereas in the sham-irradiated control group, a slight but significant drop in temperature ($P < 0.001$) was found. Subsequently performed contrasts for comparison of measurements before and after irradiation revealed significant temperature increases at 20 min of irradiation time ($P < 0.001$), at the end of the irradiation ($P < 0.001$), and 15 min after stopping the irradiation ($P < 0.001$). In the sham-irradiated feet, the drop in local skin temperature was not significant at 20 min ($P = 0.1$), but reached significance at the end of the sham-irradiation procedure ($P < 0.001$) and 15 min after the end of sham irradiation ($P < 0.001$).

CONCLUSIONS:

The data from this first randomized double-blind placebo-controlled clinical trial demonstrate an increase in skin microcirculation due to athermic laser irradiation in patients with diabetic microangiopathy.