

Efficacy of low level laser therapy on wound healing in patients with diabetic foot ulcers

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Abstract: *Aims and Objectives:* To study the efficacy of low level laser (LLL) on wound healing in Diabetic Foot ulcer and to test the hypothesis that LLLT will promote early healing of Diabetic Foot ulcer. *Materials and Methods:* Patients attending surgical OPD and/or admitted in BLDE (DU) Shri B.M. Patil Medical College Hospital and Research centre, Vijayapur with diabetic foot ulcers (Wagner's Grade I to III) during the period of November 2018-June 2020 were included in the study. A prospective comparative study was conducted with 30 patients to LLLT group (660 and 808 nm laser) and 30 patients to conventional (Saline) dressing group. All the cases were examined on day 1 and day 15. 'Primary efficacy end point' was complete ulcer closure. 'Secondary efficacy end point' include reduction in ulcer surface area over time and time to achieve ulcer closure by either skin grafting or secondary suturing. *Results:* Mean Age of the study group was 56.83 ± 13.8 years with 76.66 % males. Majority of the cases were known diabetic since 5 to 10 years. There was poor glycemic control among the study subjects with mean HbA1c of 8.4%. There was 42% reduction in the size of ulcer among study group. There was average of 7 days i.e. 22% reduction in hospital stay in study group, compared to control group. Three ulcers in LLLT group healed by secondary intention while none in control group. Majority of the cases, ulcer closure was achieved by split thickness skin grafting. *Conclusion:* Low level laser therapy in Diabetic Foot ulcers promotes early healing and reduces the hospital stay.

Keywords: Diabetic Foot Ulcers, Low Level Laser Therapy, Wound Healing.

Introduction

Diabetes mellitus (DM) is one of the main problems in health systems and a global public health threat that has increased dramatically over the past 2 decades. According to epidemiological studies, the number of patients with DM increased from about 30 million cases in 1985, 177 million in 2000, 285 million in 2010, and estimated if the situation continues, more than 360 million people by 2030. The total number of people in India with diabetes is estimated to be around 50.8 million in 2010, rising to 87 million by 2030 according to the International Diabetes Federation (IDF) [1-2].

To date, DFU is considered as a major source of morbidity and the main cause in diabetic patients for hospitalization [1-2]. It is estimated that approximately 20% of hospital admissions among patients with DM are the result of DFU. DFU can

lead to infection of the limb, gangrene of foot, amputation or even death if necessary timely care is not given [2-3].

Low level laser therapy (LLL), also called *soft laser*, is known to supply direct biostimulative light energy to body cells with a wave-length between 600 and 1000 nanometers and power from 5 to 500 mill watts [3-4]. The absorbed laser energy stimulates molecules and atoms of cells but does not cause rapid or significant increase in tissue temperature. Different laser wavelengths have different depths of penetration into human tissue. Red laser has a deeper penetration depth than violet, blue, green, or yellow. Infrared and near infrared light are not visible, but it has been demonstrated to penetrate human tissue deeper than visible red light [5-6].

Low-energy laser radiation was found to have a stimulating effect on cells, and high-energy radiation had an inhibiting effect. The application of lasers to stimulate wound healing in cases of nonhealing ulcers has been recommended. Therefore, the usage of (LLLT) presents itself as being a new therapeutic proposal, seeking the cure of these injuries, the improvement on the quality of life of the affected individuals, as well as the reduction of the costs of the treatment in the health system [7-9].

Aims and Objectives of the study:

1. To study the efficacy of low level laser on wound healing in patients with diabetic foot ulcer in terms of
 - a) Reduction in ulcer size
 - b) Time taken in ulcer healing
 - c) Duration of hospital stay
2. To Test the hypothesis that combined 660 and 808 nm laser phototherapy will promote early healing of diabetic foot ulcers

Material and Methods

The study was conducted at BLDE (Deemed to be university) Shri B.M.Patil Medical College, Hospital and Research Centre, Vijayapur after obtaining ethical clearance from Ethical Committee.

Type 2 DM patients with ulcers of grade I to grade III as per Wagner grading System were included. Patients were selected alternatively into two groups of study and control group on the basis of alternate numbers. The nature of therapy to be given was explained to the patients and written informed consent was obtained from them before enrolment.

Patients in the study group received treatment with LLLT. Ulcer bed with edge was exposed locally with red laser (660nm) and IR laser (808nm) cluster probe. About 2-4J/cm² for 10 minutes delivered on alternate day basis. Saline dressing done for covering after exposure and controls were treated with conventional therapy alone. Course of antibiotic treatment and slough removal was done whenever needed. The size, depth and culture status of the ulcer was assessed on Day 1 and day 15. Duration of stay in hospital noted (Figures 1& 2).

Fig- 1 & 2: LLLT over diabetic ulcer

Fig-1



Fig-2



Sources of Data: Patients admitted in surgery ward or attending OPD with Diabetic foot ulcer (unilateral/bilateral) at BLDE (Deemed to be university) Shri B.M. Patil Medical College, Hospital and Research Centre, Vijayapur from November 2018 to June 2020 were considered in the study.

Method of data collection: The patients were allocated alternatively into study and control groups. And while allocating cases, age of the patient, duration of DM and size of the ulcer were matched. A proforma was used to collect all the relevant data from the patients. A detailed history was taken; thorough clinical examination and investigations were performed on all the patients included in the study. All the cases were followed up till discharge and subsequently for a follow-up till wound healing. "Primary efficacy endpoint" was complete ulcer closure and "Secondary efficacy endpoint" was time taken to achieve ulcer closure by either secondary suturing or skin grafting.

Study Design: Prospective interventional study.

Sample Size: On the basis of a study, the anticipated mean \pm SD of Ulcer area at day 1

vs Ulcer area at day 15 was 13.74 ± 11.88 and 3.97 ± 5.41 resp. the minimum sample size is 25 per group with 95% level of significance and 90% power.

Formula used was;

$$N = 2[(Z_{1-\alpha/2} + z_{\beta}) * Sd]^2$$

$Z_{1-\alpha/2}$ Level of significance=95%

$Z_{1-\beta}$ power of the study=90%

d=clinically significant difference between two parameters

S= Common standard deviation

Statistical analysis: Data represented using Mean \pm SD, percentages and diagrams. Significant difference between quantitative data found using unpaired t-test/ Wilcoxon signed rank test to compare with the control group. Significant difference between quantitative data was found using paired t-test/ Wilcoxon paired signed rank test to compare day1 result with day15 result. Significant difference between Qualitative data was found using Chi-square or Fisher's Exact test.

Inclusion Criteria: Diabetic foot ulcers that come under Wagner's grade I to III.

Exclusion criteria:

- Patients on medications such as corticosteroids, immunosuppressants or chemotherapy
- Diabetic patients with foot ulceration resulting from electrical and radiation burns
- Pregnant or nursing mothers.
- Case of diabetic foot ulcers with skin cancer.
- Those with clinical signs of ischemia and ABI less than 0.7
- Patients associated with critical illness that need intensive care.

Description of the procedure step by step: All patients admitted to the surgical ward and/or attending Surgery OPD were subjected to detailed evaluation, complete haemogram and HbA1c levels. Detailed workup of the diabetic foot was done. Ulcer size was calculated by obtaining the impression of ulcer floor on a sheet of cellophane paper and then transferring the imprint onto a graph paper OR by multiplying the largest length of the ulcer by the second largest length

perpendicular to it. Depth was described as deep if full-thickness skin was involved and superficial if not extending till subcutaneous plane. The ulcer size was measured on day 1 and day 15. (Figures 4&5, 6&7) Patients with evidence of slough were subjected to repeated surgical debridement. Objective assessment of vascularity was done by careful palpation of peripheral pulses. Systemic antibiotics were administered based on culture sensitivity reports. Insulin/oral hypoglycaemic agents (OHA) used to maintain a good glycaemic control. Adequate glycaemic and infection control achieved. LLLT was commenced. (Figures 1 & 2).

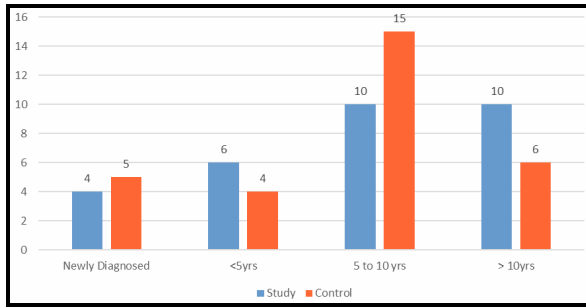
The dose of exposure calculated to deliver 2–4 J/cm² at 100 mW, 5 kHz, from a distance of 10cm, alternate day for 15 days. Both the patients and administrators wore laser safety goggles to prevent damage to their eyes. The ulcer floor and edge were exposed to laser. The ulcer was covered with Saline dressing. Pressure off-loading was carried out in patients with plantar ulcers. Simultaneously, these patients were educated about various aspects of Diabetes Mellitus treatment including dietary restrictions, exercise and foot care in order to prevent recurrence.

Results

Total of 60 patients were included in this study. Patients were selected alternatively into two groups of study and control group on the basis of alternate numbers. In this study, it was noted that about 60% of the patients in study group and 56.7% of patients included in the control group belong to the age group of 60+ years of age suggesting that diabetic foot ulcers are more common in older age groups. The mean age of the patients in years included in this study were 56.83 ± 13.8 and 58.53 ± 13.15 for the study group and control group respectively.

The sex ratio of the patients included in the study showed a male preponderance with 87 % of patients included in the study being males. Majority of patients presented with chronic history of diabetes, maximum number of patient among both study group and control group had history of diabetes for duration 5 to 10 years (Figure 3).

Fig-3: distribution of patients based on the duration of diabetes



The mean BMI of the patients included in this study were 27.8 and 26.5 respectively for study group and control group respectively, which was comparably same in both groups. There was also poor glycemic control among the study subjects with mean FBS of 182mg/dl and post prandial blood sugars of 212.6 mg/dl. Also the mean HbA1c was 8.463% indicating, poor glycemic control as the major cause of ulcers and poor healing (Table 1).

HbA1c (%)	Study Group		Control group		Mean difference (%)	Mann Whitney U test	P value
	Mean	±SD	Mean	±SD			
HbA1c	8.463	1.816	8.386	1.057	0.077(0.91%)	U=358.500	P=0.452
Insignificant							

	Study Group		Control group		Mean difference (%)	Mann Whitney U test	P value
	Mean area cm ²	±SD	Mean area cm ²	±SD			
1 st day	57.17	57.357	60.73	35.821	3.56(5.86)	U=335.500	P=0.090
15 th Day	30.233	34.8541	42.200	27.3602	11.97(28.36%)	U=251.500	P=0.003*
*: Highly significant							

Although the initial mean wound area for the study group was more compared to the control group, on day 15, it is lower than the control group (p < 0.001). Healing rate of the ulcers in this study when compared between the conventional dressing was found to be statistically significant with healing of more than 40% in the study group and P value of <0.001(Table 2) (Figures 4&5, 6&7).

The average healing time in study was 24.93±3.38 days while control was 31.97±3.596 days which is significant P<0.001.3 cases showed complete healing of ulcer by secondary intention in this study, while no ulcer in control group healed completely. It was also observed that the study group was on average taken up 7 days (p<0001) early for skin grafting as compared to the control group. In this study there was reduction in the hospital stay by mean duration of 7.04 days i.e 22.02% which is highly significant (Table 3).

Case-1; Fig-4&5:Depicting progress over 15 days following application of LLLT.



Case-2; Fig 6 & 7: Depicting progress over 15days following application of LLLT

Fig-6: Day 15



Fig-7: Day 1



Table-3: Comparison of Hospital stay (Days) between study and control groups							
Hospital stay (Days)	Study Group		Control group		Mean difference (%)	Mann Whitney U test	P value
	Mean	±SD	Mean	±SD			
Hospital stay (Days)	24.93	3.383	31.97	3.596	7.04(22.02%)	U=7.803	P<0.001*

*: Highly significant

Discussion

Diabetic foot ulcers are the most common complications of diabetes mellitus and conventional wound healing therapies are not that much effective for DFUs and if proper treatment is not given to the DFUs they may herald severe complications. Wound healing can be initiated by treating with a beam of electromagnetic radiations or laser. In the existing literature, few studies are available in this area [10-12]. The current study was aimed to assess the adequacy of a treatment modality with LLLT for diabetic foot ulcers.

The mean age of the patients in years included in this study were 56.83±13.8 and 58.53±13.15 for the study group and control group respectively. This is found to be in slightly higher with the mean age of patients as in different similar studies conducted like 52.1±8.940 years noted in Lenifa Priyadarshini M. J. et al 2018[13].

The sex ratio of the patients included in the study showed a male preponderance with 87 % of patients included in the study being males. Other similar studies also noted high number of male patients included in the study with 88% in David

Armstrong et al [14] and 82.4 % in Lindy Begg et al 2016[15].

The mean BMI of the patients included in this study were 27.8 and 26.5 respectively for study group and control group respectively, which was comparably same in both groups. Therefore, it predicts higher incidence among people with increased BMI. Almost all the patients in the study were above the normal BMI range. Similar studies also show high BMI among the study subjects indicating obesity as a risk factor for development of diabetic foot ulcers.

In our study, majority (42%) had Sterile cultures, followed by 30% has S. aureus, followed by 16% had pseudomonas, followed by 8% had streptococci, and 4% had E.coli. Study by Chalya et al [16] showed that Eight out of 12 (66.7%) cultured specimens had positive bacterial growth within 48 hours of incubation while 4 (33.3%) had negative bacterial growth. One out of 8 cultured specimens (12.5%) had pure bacterial growth while seven (87.5%) had polymicrobial bacterial growths. Staphylococcus aureus was

the most frequent microorganism isolated 4 (50.0%), followed by Escherichia coli 3 (37.5%) and Klebsiella pneumoniae 2; (25.0%). Pseudomonas spp and Proteus spp were the least bacteria isolated.

The mean reduction in the ulcer size in the study after 15 days was 42%. (Table 2) This is similar to the LLLT studies conducted by other studies by Priyadarshini LMJ et al [13] and R. K. Mathur et al [3] of 39% and 41% respectively. In the study, a combination of 660nm and 808nm wavelength of Low level laser was used. Lenifa Priyadarshini M. J et al [13] used single wavelength 660nm low level laser and another study by R. K. Mathur et al [3] also used a single wavelength 660nm low level laser in their study. Both studies reported a mean reduction of 39% and 40% reduction in size of ulcer by the end of 15th day. This is comparable to this study which reported 42% reduction.

In this study there was reduction in the hospital stay by mean duration of 7.04 days i.e 22.02%

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Conflicts of interest: There are no conflicts of interest.

Conclusion

In conclusion, the wounds in subjects treated with LLLT contracted significantly more compared to those who were not treated ($p < 0.001$), 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. Due to its stimulatory effect, LLLT can be used to treat chronic wounds, including diabetic ulcers.

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