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Low-Level Laser Therapy for Diabetic Dermopathy in Patients With Type 2 Diabetes: A Placebo-Controlled Pilot Study

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Abstract

Introduction: Diabetic dermopathy (DD) is the most common cutaneous diabetes marker. Few studies have targeted DD using low-level laser therapy (LLLT). This pilot study aimed to evaluate the effect of LLLT on DD in patients with type 2 diabetes (T2D).

Methods: 12 patients with T2D (9 men, 3 women) and bilateral DD were enrolled in this placebo-controlled pilot study, and their ages ranged 50-65 years. One side was subjected to LLLT, three sessions weekly for one month (LLLT side), while the other side received the same treatment protocol with a laser device switched off as a placebo (placebo side). All patients were instructed to receive skincare for both sides, such as debridement, antibiotic creams, and dressings with betadine solution. The diameter of DD lesion and the cutaneous blood flow of the knees and ankles sites were assessed before and after one month at the end of the intervention.

Results: At the baseline, no significant differences existed between LLLT and placebo sides in the DD and skin blood flow at the knee and ankle sites ($P>0.05$). Post-intervention, a significant improvement occurred in DD diameter and the skin blood flow of the knee and ankle sites in the LLLT side ($P<0.05$), while the placebo side showed a significant improvement only in DD diameter ($P<0.05$) and non-significant changes in skin blood flow ($P>0.05$). Comparing both sides, all measures significantly favored LLLT.

Conclusion: The findings of this study indicate that LLLT has beneficial effects on decreasing DD in T2D patients. Also, it was approved that the short term of LLLT is a safe modality to control DD in T2D patients.

Keywords: Diabetic dermopathy; Low-level laser therapy; Skin blood flow; Type 2 diabetes.

Introduction

Skin diseases are generally overlooked and usually underdiagnosed among patients with diabetes, although dermatological complications and numerous skin disorders are common in both insulin- and non-insulin dependent diabetes, such as cutaneous infection, pruritus, diabetic dermopathy (DD), dry skin, and diabetic bullae.[1] DD can be considered the most common cutaneous marker of diabetes and appears on the pretibial areas of both lower limbs with asymmetric distribution.[2]

DD has variously been described as atrophic lesions, shin spots, pigmented pretibial patches, and spotted leg syndrome.[3] It is an inflammation of tiny blood vessels in the skin, with common sites including the shins of tibias or front of the thighs and rarely on the scalp, forearm, or trunk.[4]

Sometimes, dermopathy may be appeared after trauma in non-diabetics.[5] DD has been recorded to appear in between 0.2%-55% of diabetic patients. The lesions affect male patients double as often as female patients.[6] The precise aetiology of DD remains unclear but may result from trauma under heat or cold conditions, infection, injury, or micro-angiopathy in older patients having diabetes for at least 10 to 20 years.[7] DD also appears to be closely linked to high levels of glycosylated haemoglobin.[8] When the lesions are resolved, DD gradually improves with total disappearance or preservation of pigmentation without atrophy.[9]

In recent decades, low-level laser therapy (LLLT) has been used in the management of various pathophysiological conditions such as musculoskeletal disorders, delayed wound healing, and even acute or chronic pain.[10,11] The

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basic principle of LLLT involves photobiomodulation, which affects the content of mitochondrial respiratory chains that enhance ATP synthesis.[12,13] Furthermore, LLLT may improve cell proliferation[14] and have a favourable effect on energy metabolism[15] in addition to enhancing microcirculation[16] and promoting the release of growth factors.[17]

Despite the growing application of LLLT in pathological conditions, studies evaluating the influence of LLLT in the treatment of DD are very limited. Also, given the lack of appropriate and effective treatment modalities for DD, we proposed the present study to evaluate the impact of LLLT on cutaneous blood flow and the diameter of patches in DD patients.

Materials and Methods

Subjects

This placebo controlled pilot study was conducted from April 2018 to October 2018 at Cairo University Hospitals. Twelve patients (9 males and 3 females) with DD of at least 6-week duration were enrolled in the study. Inclusion criteria were: an age range of 50 to 65 years, a diagnosis of type 2 diabetes (T2D), the asymmetrical distribution of patches bilaterally on the shin of the tibia, the patch's diameter of 2.5 cm or less (2.5 cm), and three patches or more on each side. However, the signs of severing atrophic changes, ischemia, infections, and diabetic foot ulcers were excluded from the study. Prior to undergoing study procedures, each patient underwent a medical history check and an examination of affected areas and peripheral pulses to assess vascularity and circulation.

Outcome Measures

The diameter of DD and cutaneous blood flow were evaluated at the baseline (prior to the first treatment session) and at the end of the study (after session 12). The diameter of DD was measured three times by the same examiner and the mean diameter was recorded in both lower limbs for all patients. Each patient was lying down in a comfortable, relaxed, and well-supported position. Sterile tape was used to measure the greatest diameter of each patch by measuring the length of the line connecting the two farthermost points and passing through the centre of the DD patch.[18]

Cutaneous skin blood flow was measured using a Vasamedic Model 403B laser Doppler device (Vasamedics Inc., St Paul, MN, USA) bilaterally at the knee and ankle for each patient. Laser Doppler measurement is a reliable method for assessing skin blood flow in patients with DD.[19] During measurement, the patient lied in a supine comfortable position at a temperature of 22 to 24°C with both lower limbs well-supported on a pillow for at least 20 minutes prior to the measurement of blood flow. The device was set to scan and obtain readings at two sites: the pretibial area of the leg immediately below the patella (knee) and the dorsal surface of the ankle, between the medial and lateral malleoli (ankle). Knee and ankle blood flow consists mainly of nourishing capillary perfusion with high resistance and poor blood flow.[20] All measurements were performed at a skin temperature of 37°C by a blinded examiner who did not know about the treatment procedures.

Treatment Procedures

Skincare was prescribed for all patients, including debridement, the use of antibiotic creams, and the application of dressings with betadine solution. The patients were requested to avoid trauma or injury of affected areas and to perform twice-daily circulatory exercise training to enhance the range of motion in the ankle and foot, including active ankle movements in the form of dorsiflexion, plantar flexion, inversion, and eversion (10 repetitions each) and the manual self-mobilization of the forefoot joints. Furthermore, all patients received general information on the self-treatment of diabetes, including dietary measures, regular exercise, and continuous care of legs and feet to prevent recurrence or any other complications such as foot ulcers or wounds, skin infection, abscess, and gangrene.[21]

Laser Therapy Protocol

Prior to each treatment session of LLLT, the dressing was removed and the lesions were cleaned with saline to remove creams or ointments and any discharge or debris.

For the LLLT side, one limb received three sessions per week for 1 month using a scanning helium-neon (He-Ne) laser (ASA, Terza-via Alessandro, Italy). Briefly, the patient was placed in a comfortable position; the limb was appropriately positioned, and the affected areas were exposed to LLLT intervention. Protective goggles were used by the patient and the LLLT technician during the session to avoid laser exposure. The distal cylinder of the probe of the scanner was applied perpendicular to the dermopathic patch and the entire patch area was irradiated with a 30-cm distance between the laser probe and patch area. The scanning He-Ne laser was used at a 632-nm wavelength, 25-Hz pulsed frequency, and 20-mW/cm^2 power density, and the duration of irradiation was estimated according to the irradiated area (120 s/1 cm^2) at an energy density of 2.5 J/cm^2.

For the placebo side, this limb received the same laser device but the laser was switched off (no effect), and the lack of a heating effect of the laser meant that the patients were unaware whether the device was operational. Only the patients were blinded about the laser therapy (LLLT or placebo).

Statistical Analysis

All data are presented as means ± SD. A Kolmogorov–Smirnov test was used to assess the normality of data. Inferential statistics assessed the changes in outcome measures using a two-tailed Student's *t* test (a paired *t* test was used to estimate the differences in each side and an independent-samples *t* test was used to estimate the differences between the LLLT and placebo sides). Data analysis was performed using SPSS software version 23.0 (IBM Corp., Armonk, NY, USA). Values of $P<0.05$ were considered statistically significant for all analysed measures.

Results

From April 2018 to October 2018, 15 patients with T2D and DD were enrolled in the study, and 12 of these patients (9 males and 3 females) with a mean age of 58±6.7 years completed the study program. Three patients withdrew from the study (one patient did not attend regular treatment and two patients discontinued for no specific reason) as presented in the study flowchart (Figure 1). The baseline and clinical characteristics of the study participants are presented in Table 1.

At the beginning of the study program (pre-intervention), no significant differences in baseline clinical characteristics were observed between the LLLT and placebo sides in the diameter of DD and cutaneous blood flow at the knee and ankle. By the end of the treatment (post-intervention), a significant improvement in DD diameter and blood flow was observed for both the knee and ankle areas in the LLLT side compared with the baseline ($P<0.05$), as shown in Table 2. The placebo side showed a significant improvement in DD diameter ($P<0.05$), while the difference in blood flow for the knee and ankle was not significant. There were significant overall differences between the two sides in DD diameter ($P=0.002$) and cutaneous blood flow at the knee and ankle areas ($P=0.019$ and $P=0.009$ respectively) at the end of the study (Table 2).

Discussion

This pilot study was performed to assess the therapeutic effects of LLLT on DD in patients with T2D. The main findings of the study were a reduction in DD diameter and improvement of cutaneous blood flow in the treated side following 4 weeks of LLLT, whereas a reduction in DD diameter without any change in leg cutaneous blood flow was observed in the placebo side. A comparison between the treated and placebo sides showed a significant treatment benefit associated with LLLT.

Given the prevalence of DD, the current placebo-controlled pilot study addressed an important clinical issue. The patients in this study presented with typical symptoms of DD,[22] including reddish patches on the front of both legs with dark coloration associated with atrophic lesions with insufficient blood supply and metabolic disruption.[23]

Our study results were in line with those from previous studies indicating that LLLT is an effective modality for chronic wounds in patients with diabetes[24] and showed clinical effects on controlling skin complications in diabetic patients.[25] LLLT at a wavelength of 632.8–1000 nm and energy of 5 J/cm^2 has been shown to have a beneficial role in reducing inflammation, cell proliferation, collagen synthesis, tissue repair, and wound healing.[10, 26,27]

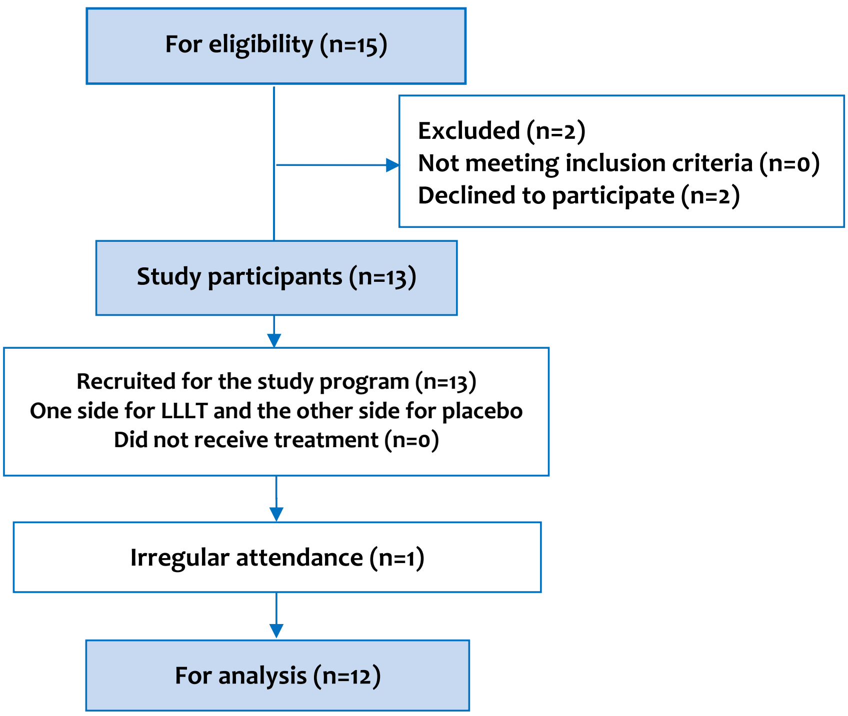

Figure 1. The Flowchart of the Study.

Table 1. Baseline and Clinical Characteristics of the Study Participants

Variables	Mean ± SD (n = 12)
Age	58 ± 6.7
Gender (M/F)	9/3
BMI (kg/m^2)	28 ± 3.5
Duration of type II diabetes (y)	9.7 ± 2.6
Duration of dermopathy (wk)	5.6 ± 2.3
HbA1c (%)	7.4 ± 1.6
Dermopathy diameter (cm)	2.3 ± 0.7
Blood flow (mL/min)	
Knee	1.4 ± 0.2
Ankle	1.2 ± 0.1

Abbreviations: SD, standard deviations; M, males; F, females; BMI, body mass index; HbA1c, glycohemoglobin.
Significant at *P* value <0.05.

Table 2. Mean Differences Between Pre- and Post-intervention in the LLLT and Placebo Sides

Variables	LLLT Side Mean±SD	Placebo Side Mean±SD	*P* Value
Dermopathy diameter (cm)			
Pre-	2.3±0.7	2.3±0.8	0.999
Post-	0.8±0.2	1.3±0.5	0.004
P value	<0.0001	0.001	
Blood flow (mL/min)/100 g of tissue			
Knee			
Pre-	1.4±0.2	1.4±0.2	0.999
Post-	1.7±0.4	1.5±0.1	0.019
P value	0.0298	0.137	
Ankle			
Pre-	1.2±0.1	1.1±0.1	0.227
Post-	1.5±0.3	1.2±0.2	0.009
P value	0.0034	0.136	

Abbreviations: SD, standard deviations; LLLT: low-level laser therapy.
Significant at *P* value <0.05.

Frangez et al previously verified the positive effects of a He-Ne laser at wavelengths of 625, 660, and 850 nm for 8 weeks on skin microcirculation and chronic wounds in patients with and without diabetes,[24] while Arunachalam et al showed that LLLT at a wavelength of 830 nm and power density of 0.1 W reduced pain, improved tissue perfusion, and promoted revascularization.

The physiological mechanism of LLLT appears to be attributable to a photochemical effect. LLLT at a wavelength of 600–900 nm radiates photons, leading to an increase in cytochrome oxidase which stimulates the production of ATP and improves cellular metabolic oxidation[13,28] as well as contributing to decrease erythrocyte aggregation and increase blood microcirculation.[29] LLLT enhances cell proliferation, activates mitochondrial respiration, and releases various molecules such as interleukins, cytokines, and growth factors which promote fibroblast proliferation and revascularization.[14,30]

This study included some strengths; its findings support a novel approach to the management of skin disorders with LLLT in patients with diabetes and recommend the application of laser therapy to achieve beneficial clinical effects. Also, it highlights the importance of LLLT to get better results in T2D patients with DD. Moreover, the findings motivate physician's referral of those patients to the physiotherapy clinic.

The main limitation of this study is the small number of the study's participants. Also, the recruited patients with DD may not be representative of other patients in future studies. Finally, this study lacks a long follow-up period. Hence, further studies are required to provide a clear understanding of the DD lesion so that the optimal therapeutic modality can be identified. Furthermore, studies with larger study populations and longer follow-up periods should be carried out.

Conclusion

The findings of this study indicate that LLLT has beneficial effects on decreasing DD in T2D patients. Also, it was approved that a short term of LLLT is a safe modality to control DD in T2D patients.

Ethical Considerations

Ethical approval was received from the Institutional Scientific Review Committee (approval no. PT-018-024). All patients provided written informed consent prior to participation.

Conflict of Interests

The authors declare that there is no conflict of interest.

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References

1. Wang YR, Margolis D. The prevalence of diagnosed cutaneous manifestations during ambulatory diabetes visits in the United States, 1998–2002. *Dermatology*. 2006;212(3):229-34. doi: 10.1159/000091249.
2. Fisher ER, Danowski TS. Histologic, histochemical, and electron microscopic features of the shin spots of diabetes mellitus. *Am J Clin Pathol*. 1968;50(5):547-554. doi: 10.1093/ajcp/50.5.547.
3. Murphy RA. Skin lesions in diabetic patients: the "spotted-leg" syndrome. *Lahey Clin Found Bull.* 1965;14(1):10-4.
4. Fowler MJ. Microvascular and macrovascular complications of diabetes. *Clin Diabetes*. 2008;26(2):77-82. doi: 10.2337/diaclin.26.2.77.
5. Shemer A, Bergman R, Linn S, Kantor Y, Friedman-Birnbaum R. Diabetic dermopathy and internal complications in diabetes mellitus. *Int J Dermatol*. 1998;37(2):113-5. doi: 10.1046/j.1365-4362.1998.00273.x.

6. Danowski TS, Sabeh G, Sarver ME, Shelkrot J, Fisher ER. Shin spots and diabetes mellitus. *Am J Med Sci.* 1966;251(5):570-5. doi: 10.1097/00000441-196605000-00011.
7. Bauer M, Levan NE. Diabetic dermangiopathy. A spectrum including pigmented pretibial patches and necrobiosis lipoidica diabeticorum. *Br J Dermatol.* 1970;83(5):528-35. doi: 10.1111/j.1365-2133.1970.tb15736.x.
8. Van Hattem S, Bootsma AH, Thio HB. Skin manifestations of diabetes. *Cleve Clin J Med*. 2008;75(11):772-87. doi: 10.3949/ccjm.75.11.772.
9. Port M. Diabetic dermopathy: a controversy in dermatology. *J Am Podiatry Assoc*. 1982;72(8):418-23. doi: 10.7547/87507315-72-8-418.
10. Nambi SG, Kamal W, George J, Manssor E. Radiological and biochemical effects (CTX-II, MMP-3, 8, and 13) of low-level laser therapy (LLLT) in chronic osteoarthritis in Al-Kharj, Saudi Arabia. *Lasers Med Sci*. 2017;32(2):297-303. doi: 10.1007/s10103-016-2114-5.
11. Enwemeka CS, Parker JC, Dowdy DS, Harkness EE, Sanford LE, Woodruff LD. The efficacy of low-power lasers in tissue repair and pain control: a meta-analysis study. *Photomed Laser Surg.* 2004;22(4):323-329. doi: 10.1089/pho.2004.22.323.
12. Lins RD, Dantas EM, Lucena KC, Catão MH, Granville-Garcia AF, Neto LG. Biostimulation effects of low-power laser in the repair process. *An Bras Dermatol.* 2010;85(6):849-855. doi: 10.1590/s0365-05962010000600011.
13. Tantawy SA, Abdelbasset WK, Kamel DM, Alrawaili SM, Alsubaie SF. Laser photobiomodulation is more effective than ultrasound therapy in patients with chronic nonspecific low back pain: a comparative study. *Lasers Med Sci.* 2019;34(4):793-800. doi: 10.1007/s10103-018-2665-8.
14. Gao X, Xing D. Molecular mechanisms of cell proliferation induced by low power laser irradiation. *J Biomed Sci*. 2009;16(1):4. doi: 10.1186/1423-0127-16-4.
15. Karu T. Photobiology of low-power laser effects. *Health Phys*. 1989;56(5):691-704. doi: 10.1097/00004032-198905000-00015.
16. Schindl A, Merwald H, Schindl L, Kaun C, Wojta J. Direct stimulatory effect of low-intensity 670 nm laser irradiation on human endothelial cell proliferation. *Br J Dermatol*. 2003;148(2):334-336. doi: 10.1046/j.1365-2133.2003.05070.x.
17. Peplow PV, Chung TY, Ryan B, Baxter GD. Laser photobiomodulation of gene expression and release of growth factors and cytokines from cells in culture: a review of human and animal studies. *Photomed Laser Surg.* 2011;29(5):285-304. doi: 10.1089/pho.2010.2846.
18. Bonner R, Nossal R. Model for laser doppler measurements of blood flow in tissue. *Appl Opt*. 1981;20(12):2097-2107. doi: 10.1364/AO.20.002097.
19. Wigington G, Ngo B, Rendell M. Skin blood flow in diabetic dermopathy. *Arch Dermatol.* 2004;140(1):1248-1250. doi: 10.1001/archderm.140.10.1248.
20. Rowell LB. Reflex control of the cutaneous vasculature. *J Invest Dermatol.* 1977;69(1):154-166. doi: 10.1111/1523-1747.ep12497938.
21. Romano G, Moretti G, Di Benedetto A, Giofrè C, Di Cesare E, Russo G, et al. Skin lesions in diabetes mellitus: prevalence and clinical correlations. *Diabetes Res Clin Pract.* 1998;39(2):101-6. doi: 10.1016/s0168-8227(97)00119-8.
22. Ragunatha S, Anitha B, Inamadar AC, Palit A, Devarmani SS. Cutaneous disorders in 500 diabetic patients attending diabetic clinic. *Indian J Dermatol.* 2011;56(2):160-164. doi: 10.4103/0019-5154.80409.
23. Mendes AL, Miot HA, Haddad Junior V. Diabetes mellitus and the skin. *An Bras Dermatol*. 2017;92(1):8-20. doi: 10.1590/abd1806-4841.20175514.
24. Frangez I, Cankar K, Frangez HB, Smrke DM. The effect of LED on blood microcirculation during chronic wound healing in diabetic and non-diabetic patients—a prospective, double-blind randomized study. *Lasers Med Sci*. 2017;32(4):887-894. doi: 10.1007/s10103-017-2189-7.
25. Tantawy SA, Abdelbasset WK, Kamel DM, Alrawaili SM. A randomized controlled trial comparing helium-neon laser therapy and infrared laser therapy in patients with diabetic foot ulcer. *Lasers Med Sci.* 2018;33(9):1901-1906. doi: 10.1007/s10103-018-2553-2
26. Andrade FS, Clark RM, Ferreira ML. Effects of low-level laser therapy on wound healing. *Rev Col Bras Cir*. 2014;41(2):129-133. doi: 10.1590/s0100-69912014000200010.
27. Arunachalam LT, Sudhakar U, Janarthanam AS, DAS NM. Effect of low level laser therapy on revascularization of free gingival graft using ultrasound doppler flowmetry. *J Indian Soc Periodontol.* 2014;18(3):403-407. doi: 10.4103/0972-124X.134592.
28. Keshri GK, Gupta A, Yadav A, Sharma SK, Singh SB. Photobiomodulation with pulsed and continuous wave near-infrared laser (810 nm, Al-Ga-As) augments dermal wound healing in immunosuppressed rats. *PLoS One*. 2016;11(11):e0166705. doi: 10.1371/journal.pone.0166705.
29. Walski T, Drohomirecka A, Bujok J, Czerski A, Wąż G, Trochanowska-Pauk N, et al. Low-level light therapy protects red blood cells against oxidative stress and hemolysis during extracorporeal circulation. *Front Physiol*. 2018;9:647. doi: 10.3389/fphys.2018.00647.
30. Gkogkos AS, Karoussis IK, Prevezanos ID, Marcopoulou KE, Kiryakidou K, Vrotsos IA. Effect of Nd:YAG low level laser therapy on human gingival fibroblasts. *Int J Dent*. 2015;2015:258941. doi: 10.1155/2015/258941.