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Effects of Photobiomodulation With Two Wavelengths of 630 and 810 nm on Diabetic Neuropathy

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Abstract

Introduction: Diabetic peripheral neuropathy (DPN) is the most common complication of diabetes patients. Among different therapeutic approaches for treating DPN, low-level laser therapy (LLLT) or photobiomodulation (PBM) is a new promising non-invasive technique. This study aims to evaluate the effect of visible and infra-red LLLT on DPN.

Methods: Sixty DPN patients enrolled in a randomized-controlled study. The patients were randomly divided into the same population of control and laser groups. The patients in the laser group received LLLT with two wavelengths of 630 and 819 nm and conventional therapy, and those in the control group received conventional therapy alone. Irradiation of the patients lasted 15 minutes per session, and it was performed over the surface of each foot three times a week for 12 sessions. The patients were evaluated at baseline and at the end of the study with the Michigan Neuropathy Screening Instrument (MNSI) and microfilament test.

Results: Patients' sensation in the right foot in the monofilament test had increased from 22 (84.6%) to 26 (86.7%) ($P=0.000$), and in the left foot it had increased from 20 (80%) to 25 (86.2%) ($P=0.001$). The mean and standard deviation of the scores of section A of the Michigan questionnaire showed a statistically significant difference between the two groups ($P<0.05$), but the B part scores of the Michigan test did not show a significant difference.

Conclusion: This study showed that the visible and infra-red LLLT significantly improved the symptoms of diabetic neuropathy without any side effects.

Keywords: Diabetic neuropathy; Low-level laser therapy; LLLT; Photobiomodulation.

Introduction

Diabetic neuropathy is one of the most common microvascular complications of diabetes. Diabetic peripheral neuropathy (DPN) is caused by neuronal dysfunction in diabetic patients, and about 50% of the patients develop peripheral neuropathy.[1] DPN symptoms include numbness or pain in extremities and paresthesia that affect patients' quality of life. Distal limb sensory neuropathy is one of the most common manifestations of diabetic neuropathy. DPN is responsible for the incidence of diabetic foot ulcers[2] and amputations,[3] leading to considerable human and economic burden on the healthcare system.[4]

Different approaches for the treatment of DPN include controlling blood glucose levels, appropriate diet, and exercise.[5] Several medications have been used for treating diabetic neuropathy in clinics, but none has completely cured the symptoms. Although there is no effective treatment for diabetic neuropathy, the profound control of blood sugar and reduction of pain and anesthesia by local or systemic methods are the mainstay treatments.

Low-level laser therapy (LLLT) or photobiomodulation (PBM) is a new technique using low-power visible or infra-red laser irradiation. This technique has been proven to modulate positive biological effects, such as inflammation reduction, wound healing promotion, and pain relief.[6,7]

LLLT has also been shown to modulate positive effects on nerve injuries, some nervous system complications,[8,9] and the management of diabetic complications such as foot ulcers.[10] Clinical studies have suggested that LLLT could be a non-pharmacological and non-invasive treatment approach in treating DPN by relieving symptoms and improving nerve function with no side effects.[11] There are also studies reporting the different interactions and biological effects of visible (630-660 nm) and near infra-red (780-980 nm) lasers.[12] Even though LLLT has been proven effective in managing the symptoms of painful DPN patients, there is a lack of published information about the combination effects of visible and infrared lasers. Thus, the objective of the present study is to evaluate the combined effects of visible

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and infrared lasers on patients with painful DPN.

Methods

Study Sample

Sixty DPN patients with a history of peripheral neuropathy, with symptoms including paresthesia and numbness of the hands and feet, pain, and muscle atrophy, enrolled in a randomized-controlled study. They were randomly divided into the same population of control and laser groups.

The patients in the laser group received LLLT and conventional medication administered daily, including gabapentin 300 and vitamin B1 300, and the patients in the control group received only the conventional medication. The patients in the laser and control groups were evaluated as a baseline with the Michigan Neuropathy Screening Instrument (MNSI), microfilament test, and Visual Analogue Scale (VAS).

Low-Level Laser Therapy of Patients

The patients in the LLLT group were irradiated with two wavelengths of visible 630 nm and near infra-red 810 nm. Visible and infra-red lasers operated at pulsed mode with a frequency of 35 Hz, peak power of 100 mW, and spot diameter of 5 mm. Irradiation of the patients lasted 15 minutes per session, and it was performed over the entire surface of each foot three times a week for 12 successive sessions. Each laser's power density per session was 0.35 mW/cm^2, and the corresponding energy density was 32.08 J/cm^2. All the patients were evaluated at the end of the last session. Laser therapy parameters are provided in Table 1.

Michigan Neuropathy Screening Test

The Michigan neuropathy screening test, composed of two parts of A and B, is used in this study. Section A of the test includes 15 questions to be completed by the patient (numbness, burning pain, tenderness, muscle cramps, tingling sensation, pain in the legs due to contact with sheets, open wound, feeling of weakness, aggravation of symptoms at night, history of diabetic neuropathy, foot pain when walking, cracked or dry skin of the foot, history of foot amputation, diagnosis of water temperature, & feeling of feet while walking). Each Yes response to questions 1–6, 8–12, and 14–15 is assumed to be one point, and any No response to questions 7 and 13 is considered one point. A total score of seven or above is assumed to be abnormal.

The B section of the test, generally completed by a health professional, evaluates the appearance of the foot symptoms such as foot tremors, reflexes, wounds, infection, and dry skin. A higher score indicates a worse condition (Maximum 10 points). The existence of abnormality in each foot has a score of 1 and an ulcer also receives the same score of 1.

If the reflex is absent, the Jendrassik maneuver must be performed, and if present, the reflex is designated as present with reinforcement and is scored 0.5. If absent, the reflex is designated as absent and is scored 1.

Vibration sensation was tested in the great toe by a 128-Hz tuning fork. If the examiner senses the vibration on his or her hand for longer than 10 seconds, the vibration is present with a score of 0, reduced if sensation presented for ≥ 10 with a score of 0.5, and absent with a score of 1 (no vibration sensation). To ensure that the patient responds to vibration and not pressure, the examiner should check the patient's response to a non-vibrating tuning fork. Scores from two parts of the test were added to obtain a total score for each patient.

Table 1. Laser Parameters.

Parameters	Unit
Type of laser	Diode
Wavelength	630 & 810 nm
Emission mode	Pulsed
Frequency	35 Hz
Duty cycle	7%
Delivery system	Straight handpiece
Spot area at the tissue	0.196 cm^2
Treatment time per session	15 min
Number of sessions	12
Peak Power	100 mW
Average power	7mW
Power density per session	35 mW/cm^2
Energy density per session	32.08 J/cm^2

Monofilament Test

In this test, the patient's foot must be supported on a flat, warm enough surface while applying the filament vertically and briefly (less than one second) with constant pressure. When the filament is bent, a force of 10 grams is applied. Eight correct answers out of 10 are considered normal. The number of correct answers from 1 to 7 indicates a decreased feeling, and no correct answer is a sign of loss of feeling.

Data Analysis

Data were analyzed by SPSS package version 20. The Kolmogorov-Smirnov test was used to evaluate the normal distribution of data. The paired samples *t* test was used to compare the groups.

Results

The demographic characteristics of all the patients are provided in Table 2. The paired t-test and Mann-Whitney U test showed no significant difference between the control and study groups concerning mean age, sex, diabetes mellitus (DM) duration, HbA1c, Insulin No, oral

Table 2. Demographic Characteristics of Patients

Variable	Laser Group	Control Group	*P* Value
Age, (Mean ± SD)	55.57 ± 8.685	56.30 ± 7.521	0.328
Gender, No. (%)			0.121
Male	18 (60.0%)	12 (40.0%)	
Female	12 (40.0%)	18 (60.0)	
DM duration, (Mean ± SD)	12.200 ± 8.887	13.872 ± 10.548	0.207
FBS (mg/dL), (Mean ± SD)	188.80 ± 65.939	150.17 ± 20.728	< 0.001
HbA1c (%), (Mean ± SD)	9.4947 ± 2.19652	8.3600 ± 1.51466	0.065
Insulin, No. (%)	21 (70%)	23 (76.7%)	0.559
Oral drug, No. (%)	16 (53.3%)	12 (40.0%)	0.301

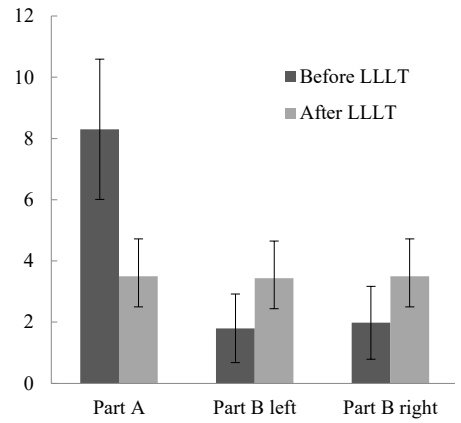

Figure 1. Scores of the A and B parts of the Michigan test before and after LLLT

drug number, frequency of nephropathy, retinopathy, and ischemic heart disease ($P > 0.05$).

Section A of the Michigan test contains parameters of pain, flushing, and pain during walking, sores, gait weakness, open sores, and history of neuropathy. In the LLLT group, this score significantly decreased from 8.30 ± 2.29 to 3.50 ± 1.22 after 12 sessions of laser treatment ($P = 0.000$).

Section B of the Michigan test examines the parameters of vibration, reflex, wound, infection, dry skin, and overall appearance of the foot. Any increase in the scores in this section indicates the recovery of symptoms. In the LLLT group, the section B scores significantly increased from 1.87 ± 1.12 to 3.44 ± 1.21 for the left leg ($P = 0.000$) and also increased significantly from 1.98 ± 1.19 to 3.50 ± 1.22 for the right leg ($P = 0.000$).

Among the patients in the LLLT group, eight patients did not have any sensations in the right monofilament nerve before laser treatment; four patients felt some sensations after laser therapy intervention. The patients' sensation in this nerve had increased from 22 (84.6%) to 26 (86.7%) ($P = 0.000$). Similarly, the patient's sensation in the right monofilament nerve had increased from 20 (80%) to 25 (86.2%) ($P = 0.001$).

Scores of the A and B parts of the Michigan test before and after LLLT are compared in Figure 1. Part A of the Michigan test includes symptoms such as the sensation of pain, numbness or pain in extremities, paresthesia, pain during walking, and the presence of an open sore. Any decrease in scores of part A of the test indicates the healing of symptoms. The mean score of part A reduced from 8.30 ± 2.29 to 3.50 ± 1.22 after LLLT, indicating the positive effect of LLLT on symptoms listed in part A of the test. Part B of the Michigan test includes symptoms such as deformities, fissures, and ulceration. Any increase in scores of the B part of the test indicates the healing of symptoms. The mean score of part B of the left side of the test increased from 1.87 ± 1.12 to 3.44 ± 1.21 after LLLT. The mean score of part B of the right side of the test increased from 1.98 ± 1.19 to 3.50 ± 1.22 after LLLT, indicating a positive effect of LLLT on symptoms of part B of the test.

Discussion

Different approaches for the treatment of DPN reveal limited therapeutic effects and side effects. In searching for an alternative treatment, LLLT or PBM seems to be an efficient treatment approach with no reported side effects.

The major parameters of LLLT protocols used by different studies include the wavelength of the laser (nm), the power output of the laser (W), the spot size of the laser beam (cm^2), the energy density (J/cm^2), and irradiation time.[12,13] Energy density depends on power, spot size, and treatment time. Hence, wavelength and energy density are the two main parameters affecting the effectiveness of LLLT.

The positive effects of LLLT on treating the symptoms of DPN were reported in different investigations, which agree with the results of this study.[8,9,12-17] On the other hand, in the study by Zinman et al about the effects of LLLT on DPN patients, no significant improvement was observed in the Toronto Clinical Neuropathy Score, nerve conduction velocity, and sensory tests.[18]

Due to the lack of standardization in the protocols used by different investigators, there is considerable confusion about the effectiveness of LLLT. All studies using the LLLT for treating DPN could be divided into two categories using single wavelength or multiple wavelengths in the visible or near infra-red region of light spectra.

There is considerable heterogeneity among all published literature regarding the wavelength of the laser, energy density, treatment time, and the number of sessions that could be the source of the heterogeneity among the obtained results. The wavelengths of lasers used in the visible region fall in the range of 630-660 nm, and for infra-red lasers, there is a span of 780-905 nm.[12,19] Several studies employ two wavelengths.[13,15,20] However, there is only one study using two wavelengths in the visible and infra-red region of light spectra[13] with wavelengths of 632

and 850 nm, which is in agreement with the results of this study. One study using LED light with a wavelength of 780 nm reports the positive effects on the symptoms of DPN patients.[21]

Different LLLT responses might be due to the different energy densities in the range of 2.5-10 J/cm^2 and different irradiation times.[8,9,13,15-17] The energy density used in the current study is higher than those used in other studies. Some studies reported the neuroprotective effects of transcranial LLLT for treating decreased cerebrovascular perfusion in brain ischemia patients, increased neural metabolism, and cerebral blood flow.[22,23] Therefore, the effectiveness of LLLT in treating DPN symptoms could be explained by the instantaneous presence of two main mechanisms of nerve injury healing and increased tissue perfusion in lower extremities. The limitation of the present study was the incomplete treatment sessions of some patients which excluded from the study.

Conclusion

LLLT is a safe non-pharmacological treatment approach with no side effects and has the potential to be a modality of choice in the care of patients with diabetic neuropathy. Further studies are recommended to standardize the parameters of this new treatment approach for DPN patients.

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Authors' Contribution

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Visualization: Faraj Tabeie, Sahar Tavakoli.
Writing–original draft: Sahar Tavakoli, Faraj Tabeie.
Writing–review & editing: Faraj Tabeie.

Competing Interests

There are no conflicts of interest to be declared by the authors.

Ethical Approval

This randomized controlled study has been registered in the registry of clinical trials (identifier: IRCT20201009048972N1; https://www.irct.ir/trial/51648), and the design has been ethically approved by the university ethical committee IR.UMSHA.REC.1396.525. The patients who participated in the study were assured that their information would remain confidential. They gave individual written informed consent to clinical data collection, analysis, and the use of those data for research.

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