

Evaluation of Low Level Laser Therapy in Reducing Diabetic Polyneuropathy Related Pain and Sensorimotor Disorders

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Abstract- Over the past three decades physicians have used light level laser therapy (LLLT) for the management and the treatment of diabetic peripheral neuropathy and have obtained results that calls for further investigations. This study aimed to investigate the effectiveness of LLLT in treatment of pain symptoms in patients with diabetic polyneuropathy. In this study 60 patients with diabetic peripheral neuropathy were matched based on their sex, age, BMI, type of diabetes, duration of diabetes, and duration of pain, and randomized to case and control groups based on their established scores on the visual analog scale (VAS) and the Toronto clinical scoring system (TCSS). Cases received laser therapy with wavelength of 78 nm and 2.5 j/cm² two times a week, each time for 5 min, for one month. During the same period, controls received sham laser therapy. Comparing the differences between the two groups' VAS and TCSS mean scores before the intervention with that of the 2 weeks and 4 weeks after the intervention we were able to see a statistically significant difference between the two groups ($P < 0.05$). On the other hand, when we compared their VAS and TCSS mean scores 4 weeks and 2 weeks after the intervention we did not find any statistically significant difference between the two groups. We achieved the same results when we examined cases' and controls' pre and post VAS and TCSS scores independent from each other; no improvement in the assessment based on their 2 and 4 weeks comparisons tests. Laser therapy resulted in improved neuropathy outcomes in diabetic patients who received it relative to the group that received sham therapy, evaluating before and after LLLT assessments. Further studies are needed to test types of lasers, as well as different dosage and exposure levels required in different phase of neuropathic care, so as to obtain reproducible results.

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Introduction

Sensual-motional polyneuropathy is one of the most widespread complaints of types I and II diabetes patients. Diabetic peripheral neuropathy or distal symmetric neuropathy (DSP) is a micro vascular disease, which is experienced by many diabetic patients during the course of their diseases due to high blood sugar and chemical changes that occur in the nerves (1). Prevalence of peripheral neuropathy is reported as 30% for hospitalized patients and 20% in community (2).

These patients have painful sensation in their lower extremities especially their feet, toes, and metatarsus, which causes an unpleasant sensation, sleeps disturbance, and at times foot ulcer; gangrene resulting in amputation (3). Pain sensation associated with DSP often intensifies at night and occurs in patient's feet and ankles and can radiate to the toes. Other associated signs

of DSP include allodynia, heat sense disorder, paresthesia, weight lost, anxiety depression, and poor quality of life (1).

DSP often resists conventional pharmacological medicine therapy such as narcotic anti-pain relievers, anticonvulsants, phenothiazine, anti-atheist, opiates and even NSAIDs (non-steroidal anti-inflammatory drugs), the latter of which are rarely used due to their limitations and failure in DSP treatment. In addition, patients who have used these medications have complained of symptoms, such as lethargy, drowsiness, and confusion or unsteadiness, which limit their daily functioning (4).

Although the anti-pain mechanism of low level laser therapy (LLLT) is unknown, over the past three decades physicians have used LLLT as a non-medicine and non-surgical therapy for the management and the treatment of persistent pains in patients complaining of rheumatologic, neurologic, and musculoskeletal

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disorders (5,6), injuries (7), distal and lower extremities diabetic polyneuropathies (8-12), the improvement of microcirculation, as well as that of myocardial contractility and performance capability in diabetic patients (13). In recent decades this technique has also been used in Iran for treatment of various types of pain.

The therapeutic function of LLLT as cited by the results of the aforementioned studies is disputable and deems further investigations. This study aimed to investigate the effectiveness of LLLT in treatment of pain symptoms in patients with diabetic Polyneuropathy.

Materials and Methods

In this matched-pair randomized prospective study, sixty patients presented to Kermanshah diabetes research center to receive care for DSP, consented to be part of this study and were matched based on their sex, age, BMI, type of diabetes, duration of diabetes, and duration of pain. The patients were subsequently randomized to two groups via coin toss.

To be eligible for the study patients had to be older than 18 years of age, had to be diagnosed with DSP for more than 3 months, had pain sensation related to DSP in both feet, and also scored at least 4 based on the visual analog scale (VAS). Patients who were using medication for their conditions were also eligible for participation in the study, as long as there was no change in their medication regimen four weeks prior to the study. However, patients with malignant disease, patients diagnosed with thyroid disease but not taking any medication, and those with neurological disorders that could interfere with their evaluation were excluded from the study. In addition, pregnant women, patients who had metal objects in their bodies, and patients who used alcohol or psychotropic drugs were removed from the study.

In this study we used laser with wavelength of 78 nm and 2.5 j/cm² for therapy. The laser equipment was calibrated by the manufacture prior to the study. All patients in the study received neurological examination using the VAS and the Toronto clinical scoring system (TCSS) to assess their peripheral neuropathy or diabetic polyneuropathy and the results were registered in the prepared checklist. VAS is an approximately 10 cm long line depicting a spectrum of pain sensation, from, "no pain" at one end to, "extreme pain" at the other end. In this study patients were asked to rate their level of pain from 0 to 10 (11-point scale) on a VAS scale, where, "0" denotes absence of pain and, "10" represents maximum pain. The patient's scores then represent their subjective

assessment of the intensity of pain that they experience. We used TCSS to score patients' degree of neuropathy by clinically assessing: six symptoms (6 points), five sensory tests distally at the toes (5 points), and examining lower-limb reflexes (8 points). TCSS score, therefore, range between a maximum score of 19 and a minimum of 0; the latter indicate no neuropathy.

Subsequently patients were randomized to case and control groups based on their established scores on the VAS and the TCSS. All patients in the case group received laser therapy using laser with wavelength of 78 nm and 2.5 j/cm², two times a week, each time for 5 min, for one month. The same procedure was repeated for patients in the control group; however, this time Sham laser therapy was used in such a way that no output was delivered from the instrument. Two and four weeks after the treatment, the patients were evaluated again by a physician and the results of all their tests were registered in the checklist. Neither the laser therapist, nor the physician evaluator knew how patients were assigned to the study groups (*i.e.*, case and control).

Data analysis

SPSS software (version 11.5) was used for analysis of the obtained data. An independent sample t-test was used to compare mean differences in the VAS and the TCSS scores between the case and control groups before and after the intervention (*i.e.*, 2 and 4 weeks after laser therapy). We also used independent sample t-test, Mann-Whitney non-parametric test; Chi-square and Fisher's exact test whenever appropriate to compare the distribution of the categorical and quantitative variables (*i.e.*, gender, age, duration of diabetes, obesity, HbA_{1C}, height and weight) in the two groups to ensure that the case and control groups were as similar as possible at the beginning of the study, prior to the randomization of and implementation of the intervention. We set the limit for statistical significance at *P*-value > 0.05

Results

There were no differences in the characteristics of the patients at inclusion. Our statistical tests revealed that there were no statistically significant differences between the case (laser therapy) and the control group (sham laser) with respect to gender, age, diabetes duration, HbA_{1C}, height, weights, duration of diabetes and duration of DSP, VAS and TCSS scores at the start of the study, ensuring proper randomization.

Table 1. Range, mean, and standard deviation (SD) of the variables.

Variables	N	%	
Gender			
Male	14	23.3	
Female	46	77.7	
	Range	Mean	SD
Age (yrs)	18-75	56.1	9.43
Height (cm)	148-176	159.37	7.35
Weight (kg)	41-84	66.22	11.62
Duration of diabetes (mo.)	24-360	87.28	125.81
Duration of DSP (mo.)	4-96	24.5	20.2
Duration of HbA1c (mo.)	7.6-14.5	8.6	2.02

Of the 60 patients under the study, the majority 77.7% (n=46) were female. The mean age of participants was 56.1 (SD=9.43). Shortest duration of diabetes disease was 24 months and the longest was 360 months. The duration of DSP was between 4 to 96 months (Table 1).

Our results indicated no statistically significant differences in the pre intervention VAS mean scores ($P=0.978$) between the two study groups (*i.e.*, case group that received laser therapy, and the control group that received sham laser). However, when we compared the differences between the two groups' VAS mean scores before the intervention (mean=8.17, SD=2.13) with that of the 2 weeks (mean=6.2, SD=2.18) and 4 weeks (mean=5.9, SD=2.18) after the intervention we were able to see a statistically significant difference between the two groups ($P<0.0001$). On the other hand, when we compared their VAS mean scores 4 weeks (mean=5.9) and 2 weeks (mean=6.2) after the intervention we did not find any statistically significant difference between the two groups. ($P=0.830$). Furthermore, mean differences in TCSS scores, between the two groups prior to the intervention were not statistically significant ($P=0.122$), nevertheless, the difference 2 weeks (mean=7.9, SD=1.98) and 4 weeks (mean=7.87, SD=2.04) after the intervention in comparison with prior to intervention (mean=9.93, SD=2.44) were statistically significant ($P<0.0001$)

(Table 2). Comparing the mean TCSS scores 4 weeks after the intervention (mean=7.87) with 2 weeks post intervention (mean=7.9) did not result in any statistically significant differences ($P=0.853$).

As for the findings in the case group, (*i.e.*, the positive laser group) mean VAS scores 2 and 4 weeks after the intervention compared with the scores before the intervention were significant ($P<0.0001$). Also, mean VAS scores 4 weeks after the intervention compared with 2 weeks after the intervention were statistically significant ($P<0.012$). In addition, comparing the mean TCSS scores in this group 2 and 4 weeks after the intervention with the scores before the intervention resulted in statistically significant differences ($P<0.0001$). However, mean differences between the TCSS scores 2 and 4 weeks after the intervention were not significant ($P=0.792$).

In the control group with sham laser therapy, mean differences in the VAS scores 2 and 4 weeks after the intervention compared with the mean scores before the intervention were not statically significant ($P=0.881$). In addition, the mean TCSS scores 2 and 4 weeks after the intervention in comparison with the scores before the intervention did not result in any statistically meaningful differences ($P=0.821$). Similarly, the differences between the mean scores 2 and 4 weeks after the sham laser therapy were not significant ($P=0.841$).

Table 2. VAS and TCSS average and standard deviation (SD) before and 2 and 4 weeks after intervention for case and control group

	Ave. Before	Ave. 2 weeks	Ave. After 4 weeks	SD Before	SD 2 weeks	SD After 4 weeks
VAS	8.17	6.2	5.9	135.2	188.2	2.187
TCSS	9.93	7.9	7.87	2.447	1.989	2.047

Discussion

This was a matched pair randomized prospective study in which we aimed to evaluate the role of LLLT for treatment of sensual-motional polyneuropathy measured by the VAS and the TCSS scores among a sample of diabetic patients receiving care from a diabetic clinic in Kermanshah. Our findings revealed that, in general laser therapy with wavelengths of 78 nm and 2.5 j/cm² and duration of two times-a-week each time for 5 minutes, for one month shown statistically significant effects in reducing neuropathic pain in the intervention group 2 and 4 weeks post LLLT. Although this is encouraging, further analysis revealed that this difference remains significant between the two groups only when pre laser therapy scores were measured with post laser therapy scores. In another words, we were not able to detect any statistically significant improvement in the neuropathic outcomes between the two groups once they were compared based on their 2 and 4 weeks post assessments. We found similar findings when we analyzed the VAS and the TCSS assessments of the case and control groups, independently, *i.e.*, within their own group. In that regard, we found positive results with pre and post comparisons in the case group, but not such improvement in the control group. Also, no improvement was shown in the neuropathic assessment of the cases and controls based on their 2 and 4 weeks comparisons tests.

The literature shows the impact of laser therapy in reducing neuropathy is mixed. For example, Aigner *et al.* reported that low laser therapy (LLT) was ineffective in management of whiplash injuries (7). Bingol *et al.* tested the therapeutic effectiveness of LLT on 40 patients who complained of shoulder pain (5). The intervention group during a period of 2 weeks received 10 sessions of one minute laser therapy with a frequency of 2000 Hz at tuberculum majus and minus, bicipital groove, and anterior and posterior faces of the capsule. However, they found no significant improvement in pain, active range, and algometric sensitivity in the laser treatment group, compared with the control group who received the placebo laser and the same exercise regimen as the intervention group. On the other hand, in a double blind study Venanico *et al.* were able to show improvement in pain (measured by VAS) among 30 patients presenting with temporomandibular joint (TMJ) pain and mandibular dysfunction (6). In their study, the intervention group received infrared laser (780 nm, 30 mW, 10 s, 6.3 J/cm²) at three TMJ points and were evaluated throughout six sessions and 15, 30 and 60

days after the end of the therapy. LLT, however, did not show similar results for improvement in the range of mandibular movements and TMJ pressure pain threshold (6).

The positive effect of LLLT as an alternative or in combination with medication in offering some relief to patients with DSP has been reported in earlier studies by Bodnar *et al.* (13), and Kalinina *et al.* (8). Bodnar *et al.* study showed that Laser therapy promotes compensation, has an antiatherogenic, antioxidant, immunomodulating effect in diabetic patients (13). In Kalinia's study, evaluation of patients with diabetic polyneuropathy showed that the group with laser exposure in comparison with the placebo had more pronounced restoration of functional state of nervous fibers than conventional therapy (8).

Results of more recent investigations in the use of LLLT for treatment of DSP show a positive trend but call for more investigations. In a randomized, double-blind control trial Zinman *et al.* presented all 50 DSP patients in the study with sham therapy over 2 weeks in the baseline period before giving biweekly sessions of Low Intensity Laser Therapy (LILT) for 4 weeks to the DSP patients and sham therapy to the control group (12). They reported improvement in weekly mean pain scores (VAS) of both groups during sham treatment (baseline) and an additional reduction in weekly mean pain scores, after the 4-week intervention in the LILT group. However, LILT had no effect on the Toronto Clinical Neuropathy Score, sympathetic skin response, or quantitative sensory testing. The investigators concluded that their results did not provide statistically significant evidence to support LILT for treatment of painful symptoms in DSP patients (12). In a randomized control trial Peric investigated the influence of LILT on spatial perception threshold and electroneurographic parameters in 45 patients with painful DPN (10). Study results indicated a favorable effect of this treatment in patients with painful DPN; however, it was concluded that further investigation is needed. In conclusion, in this study we found that laser therapy resulted in improved neuropathy outcomes in diabetic patients who received it relative to the group that received sham therapy, evaluating before and after LLLT assessments. However, no such improvement was obtained in the assessment of the cases and controls based on their 2 and 4 weeks comparisons tests. Nevertheless this is an encouraging trend, suggesting that LLLT has the potential to offer relief for DSP. However, we need to have more randomized trials with larger sample sizes to test types of lasers and dosage levels required in

different phase of neuropathic care, so as to obtain reproducible results. Also, additional human studies are needed to test different exposure levels that may result in more pronounced restoration of the improved state while avoiding photo-bio inhibitory and other side-effects. LLLR results of studies using Wistar rat suggest a dose-effect in the relationship between local pain relief and laser therapy (3,14). In addition, more studies are needed to examine the extent to which radiation or heat is responsible for the therapeutic effect of LLLT (14).

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