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Original article

IS PHOTOBIOMODULATION AN EFFECTIVE NON-PHARMACOLOGICAL COMPLEMENT TO THE TREATMENT OF DIABETIC NEUROPATHY - A RANDOMIZED, PLACEBO-CONTROLLED TRIAL

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ABSTRACT:

Diabetes is one of the leading causes of health losses among the Bulgarian population. Diabetic neuropathy (DN) occurs in at least 34 % of people with type 1 diabetes after 25 years of disease duration and 20 % - 30 % of newly diagnosed patients with type 2 diabetes, increasing to 50 % after 10 years of disease duration. The treatment of DN is challenging. There is growing interest in non-pharmacological forms of treatment. High-power lasers have increasingly been used in the practice of physical and rehabilitation medicine. However, clinical trials testing their effectiveness in DN are scarce.

Purpose: The aim of this single blinded, placebo-controlled field trial is to investigate the effect of a multiwave locked system (MLS laser) on sensory perception and electroneurographic parameters of sensory and motor nerves in patients with diabetic sensorimotor neuropathy of lower limbs**.**

Material/Methods: A total of 69 patients were randomly assigned laser treatment (n=41) or placebo treatment (n-28) for three weeks, totaling 9 procedural sessions. Vibration sense was measured three times per session. Neurophysiological evaluations were conducted at baseline and on day 90.

Results: On day 21, vibration sense increased bilaterally at all sites in the laser group, with statistically significant differences ($p < 0.05$ for all sites) compared to the placebo group, persisting through day 90. Nerve conduction velocity and amplitude of the sural, peroneal, and tibial nerves improved by day 90 from baseline, with superior results in the sural nerve.

Conclusions: Deep tissue laser therapy can be considered a safe, non-pharmacological adjunct to the standard for managing diabetic neuropathy.

Keywords: diabetes, diabetic neuropathy, electroneurography, laser, non-pharmacological treatment, photobiomodulation, tuning fork,

INTRODUCTION

According to data from the International Diabetes Federation (IDF), in 2021, 61 million people in Europe had diabetes, 36 % of whom were undiagnosed [1]. Europe ranks second globally in terms of the highest average cost of treatment per person with diabetes [1]. Diabetes is also one of the leading causes of health losses among the Bulgarian population. In 2021, it ranked eighth as a cause of disease burden in Bulgaria, resulting in a loss of 113 925.4 Disability Adjusted Life Years (DALYs) [2]. The shift from seventh to eighth position between 2019 and 2021 is attributed to the emergence of Covid-19.

Diabetic peripheral neuropathy occurs in at least 34 % of people with type 1 diabetes after 25 years of disease duration and in at least 20 % - 30 % of newly diagnosed patients with type 2 diabetes, increasing to 50 % after 10 years of disease duration [3].

The pathophysiology of diabetic neuropathy is complex, and its management can be frustrating for both the patient and the physician. Its symptoms are diverse and include numbness, tingling, paresthesias and pain described as different sensations. Neuropathic pain typically intensifies at night, making it a source of not only physical but also psychological impairment, and it is an independent risk factor for depressive symptoms [4]. High pain intensity is associated with insomnia and impairs the quality of life.

Diabetic neuropathy affects small C-fibers (associated with nociception and thermosensitivity) as well as large myelinated Aá and Aâ fibers (functionally associated with balance and pressure) [5]. Damage to small fibers begins early and, when moderately affected, leads to positive results in the 10-g monofilament test and impaired thermal discrimination. When large fibers are involved, physical examination reveals reduced to absent vibration sensation and diminished to absent reflexes [5].

The treatment of diabetic neuropathy is challenging, and research in this area is ongoing. There is growing inter-

est in non-pharmacological forms of treatment due to the limitations of pharmacotherapy. In 2021, an international group of experts reached a consensus on the treatment of painful distal symmetrical polyneuropathy (DSPN), highlighting transcutaneous electrical nerve and muscle stimulation and acupuncture as possible interventions [6]. For patients with refractory painful DSPN who have exhausted other treatment options, spinal cord stimulation is recommended [6].

Photobiomodulation is another promising non-pharmacological approach. The term has been adopted by MeSH (Medical Subject Headings) and supported by NAALT (North American Association for Photobiomodulation Therapy) and refers to "a form of light therapy that uses non-ionizing light sources, including lasers, LEDs, broadband light, in the visible and infrared spectrum". Evidence suggests that low-energy lasers can reduce pain and improve the electroneurographic parameters in motor and sensory nerves of the upper and lower limbs in patients with diabetic neuropathy [7]. In recent years, high-power lasers have increasingly been used in the practice of physical and rehabilitation medicine. However, clinical trials testing their effectiveness in diabetic neuropathy are scarce [7, 8], prompting us to conduct this study.

The aim of our study is to investigate the impact of a multiwave locked system (MLS-laser) on sensation and electroneurographic parameters of sensory and motor nerves in patients with diabetic sensorimotor neuropathy. We hypothesized that the method we developed for work with MLS laser radiation would lead to a therapeutic effect on the subjective indicators and electroneurographic parameters of the sural, peroneal and tibial nerves in the experimental group and that the results would be sustained until the end of the observation period (90 days post treatment). Our hypothesis for the control group was the absence of therapeutic effects on subjective indicators and electroneurographic parameters of the studied nerves.

MATERIALS AND METHODS:

1. Study Design and Population

This study was designed as a single blind, placebo-controlled, parallel-group, randomized field trial. It was conducted in the period 2021-2022 at the Physiotherapy and Rehabilitation Clinic of the University Multi-profile Hospital for Active Treatment "St. Marina" – Varna, among patients with diabetic peripheral neuropathy, confirmed by an abnormal nerve conduction examination.

The criteria for inclusion of the participants in the study were: 1) age over 18 years, 2) duration of diabetes no more than 15 years and HbA1c level < 8.0 %, 3) discontinued intake of symptomatic therapy for neuropathic pain for 24 hours before inclusion in the study 4) no application of a course of physical therapy in the last six months 5) Fitzpatrick skin type I to IV 6) signed informed consent statement.

The exclusion criteria were: 1) age under 18 years, 2) comorbidities contraindicating laser treatment (such as systemic neoplastic, infectious, autoimmune diseases), 3) history of hemorrhages, 4) familial polyneuropathy, 5) pregnancy, 6) chronic alcohol abuse, 7) skin type - V and VI types according to Fitzpatrick, 8) inability to understand and follow study instructions, 9) refusal to sign informed consent regarding therapeutic procedures, 10) unwillingness to participate in treatment for personal reasons, 11) patients undergoing treatment with anticonvulsants or antidepressants.

A total of 100 patients with type 2 diabetes and diabetic neuropathy were screened for eligibility. Of these 82 patients, none met all the inclusion criteria and none of the exclusion criteria and were selected for participation in the study. Of the 82 eligible patients, thirteen refused to take part in the experiment, thus leaving 69 eligible volunteers for randomization.

Randomization was performed using a simple random computer generated sequence. Forty-one participants were allocated to the experimental group (laser treatment) and twenty-eight to the control group (placebo laser treatment). The allocation was concealed, and the participants were blinded to the treatment they received.

2. Methods and Apparatus

The intervention involved the use of an MLS laser, model M6 (fig. 1), manufactured by ASA Laser Company, Italy. The laser is classified as a Class IV near-infrared (NIR) diode laser. The device employs a dual-wavelength approach that synchronizes two emissions: λ-808 nm (in continuous wave mode) and λ-905 nm (in pulsed mode). This approach is based on the principle of synergism, which is hypothesized to enhance therapeutic efficacy and prolong remission periods [9].

Fig. 1. Design of MLS-laser, M6, ASA Laser Company

Laser intervention protocol

The experimental intervention involved a total of nine treatment sessions over three weeks, with one session per day administered every other day (three sessions per week). The treatment protocol was divided into two stages:

Stage 1 (Remote Application): A scan on the plantar of the foot (100–175 cm²) of both lower extremities was performed with the MLS fixed, robotic multi-diode device, positioned 20 cm away from the skin, with a duration of

02:05 (min: sec) to 03:39 (min: sec) depending on the area of the foot. This stage delivered a dose of 2.52 J/cm² per session.

Stage 2 (Contact Application): Seven anatomically relevant areas on each foot (fibular neck, popliteal fossa, medial and lateral malleolus, mid-gluteal fold, and two points on the dorsum of the foot) were treated. Each of these areas (3.14 cm²) was treated using an MLS single-diode handheld applicator in contact with the skin ("contact methodology"), with a duration of 00:30 (min: sec) per point, delivering a dose of 6.04 J/cm² per session, with a cumulative treated area of 21.98 cm².

Both stages used a frequency of 1500 Hz and 100 % intensity. The selected parameters (dose, energy density, duration, and field number) were optimized to ensure safe and effective treatment based on a synthesis of the literature and previous experience [9]. The target areas were selected as biologically active zones for modulating the sciatic nerve, its peripheral branches, and regions commonly affected by diabetic sensorimotor polyneuropathy where peripheral nerves are often compressed or damaged [8, 10].

For the control group, the same methodology was followed. However, the robotic device and handheld applicator were positioned in identical locations without activating the beam, ensuring participant blinding to their treatment group.

3. Assessment Instruments

The following instruments were used to assess the effects of treatment.

1) Rydel-Seiffer tuning fork: used to assess vibration sensation

2) Two-channel electroneurography (ENG) apparatus of Neurosoft, "Neuro-EMG-Micro-2" module: applied for measuring sensory and motor nerve function.

4. Assessment Timeline

Vibration sense was evaluated at three time points: 1) *baseline* - before the start of the treatment), 2) *post-treatment* - immediately after completing the therapeutic course and 3) *follow-up* - 90 days after the start of the therapy.

Nerve conduction studies (NCS) was conducted by a neurologist at two time points: *baseline* - before the start of treatment and *follow-up* – 90 days after the start of the therapy.

5. Assessment Procedure

Vibration Sensation Assessment: The Rydel-Seiffer tuning fork was used to assess vibration sensation in a standardized manner. The examiner held the tuning fork by its proximal end and struck the distal end forcefully against the palm of their opposite hand with consistent intensity for all participants.

The vibration sensation was tested sequentially at three anatomical points: the tibial tuberosity, the medial malleolus and the dorsal aspect of the distal phalanx of the great toe (hallux), just proximal to the nail bed. Prior to testing, the examiner demonstrated the sensation on the dorsal aspect of the participant's hand. Participants were instructed to respond verbally with "Yes" upon initially perceiving the vibration and with "No" when the vibration ceased. The time between the placement of the tuning fork and the participant's "No" response was recorded using the graduated scale (1–8) on the arms of the tuning fork. The level of vibration corresponded to the convergence point of the moving triangles on the tuning fork. If no vibration was felt initially, the duration was recorded as zero. The test was repeated three times per location, and the average value was recorded. Higher vibration thresholds (lower perceived vibration intensities) indicated greater sensory impairment.

Neurophysiological Assessment: The NCS sensory nerve assessment included the measurement of the amplitude of the sensory nerve action potential (SNAP) and the sensory conduction velocity (SCV) of the sural nerve. The NCS motor nerve assessment included the measurement of the amplitude of the total motor action potential (SMAP) and motor conduction velocity (MCV) along the motor fibers of the peroneal and tibial nerves. The study protocol was developed based on the ideas from published research and personal experience [8, 9, 11, 12, 13].

The study protocol was reviewed and approved by Decision No.108/25.11.2021 of the Research Ethics Committee at the Medical University of Varna, Bulgaria. All participants provided written informed consent, and the study adhered to the Declaration of Helsinki guidelines.

6. Statistical analysis

Qualitative variables were summarized with absolute values and percentages, and quantitative variables with mean and SD, or median and IQR, depending on their distribution. The distribution of variables was assessed with the Kolmogorov – Smirnov test. Baseline comparisons between the experimental and control groups were performed using independent sample t-tests, Mann-Whitney tests or chi-square tests, as appropriate. Differences were considered significant at p-values < 0.05.

Treatment effectiveness was assessed by comparing the study's outcomes before and after the intervention (on the 21st and 90th days) for both the experimental and the control groups applying the Wilcoxon signed-rank test, or ANOVA, in pre-test-post-test design. Comparisons of the effects between the experimental and control groups were performed with Kruskal-Wallis or ANOVA tests. Differences were considered significant at an alpha level<0.05. Analysis were performed with IBM SPSS version 26.0 (Chicago, IL, USA).

RESULTS:

Of the 69 participants who fulfilled the inclusion and exclusion criteria and were randomized, in total, 41 participants received MLS-laser therapy (experimental group), and 28 participants received placebo laser therapy (control group) over three weeks.

The baseline demographic and clinical characteristics for both groups are summarized in Table 1. No statistically significant differences were observed between the experimental and control groups in terms of age, diabetes duration, neuropathy duration and diabetes treatment at baseline ($p>0.05$).

Table 1. Main characteristics of experimental and control groups.

	Experimental group	Control group	p value
Participants number	41	28	
Male, n (%)	21 (51.2)	15 (53.6)	0.848
Age, years	61 (55.0-68.5)	61.5 (54.3-72.0)	0.957
Height, cm	169 (165.0-176)	169.5 (163.0-175.8)	0.884
Weight, kg	90 (73.5-100.0)	89 (73.3-100.0)	0.739
Diabetes duration, years	10 (7.0-13.5)	10.5 (7.2-15.0)	0.512
Neuropathy duration, years	5 (2.5-7.0)	7 (3.0 -8.8)	0.586
HbA1c % before intervention	7 (6.2-7.95)	6.95 (6.1-8.0)	0.811
HbA1c % 90th day after intervention	7 (6.2-8.00)	7.1 (6.1-8.0)	0.884
Insulin therapy (%)	9 (22.0)	4 (14.3)	0.424

* Quantitative variables are presented with a median value and IQR

1. Vibration sense

Baseline:

At baseline, no statistically significant differences were observed between the experimental and control groups in vibration sense measurements across all three locations (tibial tuberosity, medial malleolus, and distal phalanx of the great toe) on both lower limbs ($p > 0.05$ for all comparisons). The lowest mean baseline values in both groups were recorded at the distal phalanx of the great toe (hallux), bilaterally, while the highest mean values were observed at the tibial region, bilaterally in both groups (table 2).

Post-treatment (21st day):

By the end of the treatment course, mean vibration sense values in the control group increased bilaterally at all sites compared to baseline. However, these changes were not statistically significant, except for the medial malleolus on the left side ($p < 0.05$). In contrast, the experimental group showed significant improvements in vibration sense at all measurement sites bilaterally, with greater increases compared to the control group ($p < 0.05$ for all sites).

These results indicate a clinically meaningful improvement in vibration sense for participants in the experimental group, while improvements in the control group were minimal and inconsistent (table 2).

Follow-up (90th Day)

At the 90th day follow-up, the control group demonstrated decreases in mean vibration sense values at all sites bilaterally, compared not only to the post treatment (21st day) values but also below baseline levels. These reductions were statistically significant ($p < 0.05$), indicating a regression in vibration sense.

In the experimental group, values demonstrated sustained improvement. At the medial malleolus, vibration sense values were preserved bilaterally at levels comparable to the 21st day. At the tibial tuberosity, there was a slight decrease bilaterally compared to the 21st day, but the values remained above baseline. At the distal phalanx of the great toe, values showed a further increase bilaterally, surpassing both the 21st day and baseline measurements.

These findings suggest that the experimental group experienced durable improvements in vibration sense, while the control group showed a reversal to baseline levels or worse (table 2).

Table 2. Vibro-sensitivity measurements at baseline, 21 days and 90 days post-treatment.

	Baseline	21 days post treatment	90 days post treatment	p value (within groups)
Tibia left				
Experimental group	4.9 (1.53)	6.0 (1.15)	5.7 (1.38)	0.001
Control group	4.7 (1.46)	5.0 (1.50)	4.6 (1.46)	0.13
p value (b/w groups)	0.559	0.009	0.001	
Maleol left				
Experimental group	4.6 (2.13)	5.6 (1.96)	5.6 (1.92)	<0.001
Control group	4.4 (1.95)	4.6 (2.00)	4.2 (1.89)	0.026
p value (b/w groups)	0.543	0.028	0.002	
Toe left				
Experimental group	4.3 (2.32)	5.4 (2.31)	5.7 (2.12)	<0.001
Control group	4.1 (2.32)	4.2 (2.30)	4.0 (2.30)	0.056

p value (b/w groups)	0.699	0.033	0.004	
Tibia right				
Experimental group	4.7 (2.07)	5.9 (1.66)	5.8 (1.60)	< 0.001
Control group	4.8 (1.80)	4.9 (1.80)	4.6 (1.74)	0.078
p value (b/w groups)	0.927	0.028	0.006	
Maleol right				
Experimental group	4.5 (2.10)	5.6 (1.89)	5.6 (1.89)	< 0.001
Control group	4.4 (1.86)	4.5 (1.94)	4.3 (1.84)	0.136
p value (b/w groups)	0.622	0.01	0.003	
Toe right				
Experimental group	4.1 (2.42)	5.1 (2.44)	5.3 (2.34)	< 0.001
Control group	4.1 (2.24)	4.3 (2.21)	4.0 (2.27)	0.165
p value (b/w groups)	0.825	0.076	0.015	

2. Electrophysiological results

At baseline, there were no statistically significant differences between the experimental and control groups in sensory conduction velocity (SCV) and sensory nerve action potential (SNAP) amplitude of the sural nerve ($p>0.05$ for both parameters, table 3). The two indicators were abnormal values (reduced SCV and amplitude). On the 90th day, sural nerve SCV and SNAP amplitude increased in the experimental group and decreased in the control group.

Table 3. Sural nerve electrophysiological measurements.

Parameter	Group	Before experiment median (IQR)	90 days after experiment median (IQR)	p value
SNAP				
n. Suralis left	Experimental group	2.6 (4.10)	3.8 (5.20)	<0.001
	Control group	2.5 (4.55)	2.2 (4.23)	<0.001
	p value	0.98	0.046	
n. Suralis right	Experimental group	2.7 (2.85)	3.3 (4.84)	<0.001
	Control group	2.4 (4.00)	2.0 (2.83)	<0.001
	p value	0.66	0.028	
SCV				
n. Suralis left	Experimental group	42.9 (7.23)	46.8 (14.60)	<0.001
	Control group	43.7 (12.38)	42.1 (10.48)	<0.001
	p value	0.497	0.012	
n. Suralis right	Experimental group	43.3 (8.03)	46.6 (12.50)	0.001
	Control group	43.0 (8.94)	40.55 (8.73	<0.001
	p value	0.579	0.019	

At baseline, no statistically significant differences were observed between the experimental and control groups for motor conduction velocity (MCV) or the amplitude of the compound muscle action potential (SMAP) of the peroneal nerve ($p > 0.05$ for both parameters, table 4). Both groups demonstrated reduced MCV and SMAP values, consistent with motor nerve dysfunction associated with diabetic sensorimotor polyneuropathy (DSPN).

On the 90th day of the study, the SMAP amplitude increased in the experimental group compared to baseline values. In contrast, the control group exhibited a significant decline in SMAP amplitude from baseline, indicating a progressive deterioration in motor nerve function. Between-group comparisons on the 90th day did not reveal a statistically significant difference in SMAP amplitude ($p > 0.05$).

Regarding MCV, the experimental group demonstrated a significant increase in MCV from baseline on both sides, with the improvement being more pronounced on the left. Meanwhile, the control group exhibited a reduction in MCV bilaterally, with the decrease being statistically significant. When comparing the two groups on the 90th day, a significant difference in MCV was observed on the left side ($p < 0.05$), favoring the experimental group. However, no significant difference was found between the groups on the right side ($p > 0.05$).

Table 4. Peroneal nerve electrophysiological measurements.

Parameter	Group	Before experiment median (IQR)	90 days after experiment median (IQR)	p value
SMAP				
n. Peroneus left	Experimental group	3.9 (2.00)	4.6 (2.26)	<0.001
	Control group	4.2 (2.27)	3.9 (2.18)	<0.001
	p value	0.569	0.189	
n. Peroneus right	Experimental group	4.0 (2.13)	4.6 (2.38)	<0.001
	Control group	4.2 (2.45)	3.8 (2.41)	<0.001
	p value	0.666	0.16	
MCV				
n. Peroneus left	Experimental group	42.6 (9.46)	45.2 (8.74)	<0.001
	Control group	44.0 (5.65)	41.8 (6.48)	<0.001
	p value	0.622	0.002	
n. Peroneus right	Experimental group	44.2 (6.73)	45.4 (6.52)	0.002
	Control group	44.4 (5.46)	43.1 (6.02)	<0.001
	p value	0.937	0.065	

At baseline, no statistically significant difference was observed between the experimental and control groups for either MCV or SMAP of the tibial nerve ($p > 0.05$ for both parameters, table 5). On the 90th day, SMAP amplitude exhibited distinct trends between the two groups, but no statistically significant differences were detected. On the left side, the SMAP amplitude kept its baseline values for both groups. On the right side, the SMAP amplitude showed a slight increase in the experimental group and a decrease in the control group, although these changes were not statistically significant.

For MCV, a significant difference emerged between the groups on the 90th day. In the experimental group, tibial MCV increased from baseline values, reflecting improved motor conduction along the tibial nerve. In contrast, the control group experienced a decrease in tibial MCV over the same period, indicative of progressive motor nerve dysfunction. This significant divergence between the groups highlights the potential efficacy of the intervention in preserving and enhancing motor nerve conduction.

Table 5. Tibial nerve electrophysiological measurements.

Parameter	Group	Before experiment median (IQR)	90 days after experiment median (IQR)	p value
SMAP				
n. Tibialis left	Experimental group	5.5 (4.72)	5.5 (5.93)	<0.001
	Control group	5.0 (5.02)	4.9 (4.77)	<0.001
	p value	0.898	0.208	
n. Tibialis right	Experimental group	5.1 (5.78)	6.2 (6.07)	<0.001
	Control group	5.0 (5.83)	4.2 (5.53)	<0.001
	p value	0.779	0.094	
MCV				
n. Tibialis left	Experimental group	42.2 (8.65)	44.8 (7.45)	<0.001
	Control group	42.1 (9.55)	41.7 (8.83)	<0.001
	p value	0.903	0.016	
n. Tibialis right	Experimental group	42.0 (10.15)	43.2 (9.20)	<0.001
	Control group	41.5(8.48)	40.0 (5.93)	<0.001
	p value	0.575	0.007	

Laser wavelength and dose are critical factors for the success of biostimulation. Infrared stimulation has demonstrated significant positive effects on nerve regeneration due to its ability to penetrate deeply into tissue [9, 14]. Although the literature provides strong evidence of laser therapy's efficacy on nerve function, the optimal dose remains a subject of debate, with experimental studies showing significant effects across a range of dosages [14].

Studies have shown that the 128-Hz tuning fork tested at fewer number of sites has the same accuracy as the monofilament [15] and that the tuning fork test was a more reproducible, accurate and sensitive test in diabetic neuropathy [15]. The Rydel-Seiffer tuning fork test is inexpensive, simple, painless and can be performed by non-specialists; therefore, we conducted it three times. Consistent with the literature, our findings show a reduction in the vibration perception threshold across all measurement sites following laser therapy [12, 16].

At baseline, the distal phalanx of the great toe exhibited the lowest average vibration sense values and the highest thresholds. By the 90th day, this location demonstrated a statistically significant improvement in vibration sense, surpassing the progress observed by the 21st day.

This improvement may reflect enhanced nerve regeneration and repair over time. Conversely, the tibial region showed a slight increase in vibration perception thresholds on the 90th day compared to the 21st day. This may be attributed to the relatively greater reduction in thresholds in this region at the end of the treatment compared to the other two sites.

The increase, though not significant in terms of vibration sense, observed at the end of the treatment course in the control group may be attributed to the psychological effect of more frequent meetings with the study physician between baseline and day 21. Concern for the patient's condition can foster an expectation of improvement.

NCS was employed as an objective and quantitative method to assess peripheral nerve function. Other studies similar to ours have conducted NCS only post-treatment without tracking long-term effects [8, 11, 13]. These studies demonstrate the effectiveness of laser therapy in terms of electrophysiological parameters of peripheral nerve function. The fact that NCS requires an experienced neurologist, access to neurology laboratory, and causes discomfort to the patient, led us to conduct it twice (before the start of treatment and 90 days after the start of the therapy). Our results confirm the findings from previous studies on laser therapy's effects on sensory nerve action potential (SNAP) and conduction velocity (SCV) of the sural nerve [11, 13]. In alignment with Khamseh et al., our study found a 9 % increase in SCV on the left and 7.6 % on the right after treatment, comparable to their reported 4.4 % and 8.9 %, respectively [13]. Yamany and Sayed documented even larger improvements in SCV (32 %) and SNAP (23 %) of the suralis nerve in the laser therapy group, alongside declines in the placebo group [11]. These findings support the superior responsiveness of sensory nerves like the sural nerve to laser therapy, potentially due to their peripheral location and the scanning application targeting the foot's surface.

For motor nerve function, our results align with previous studies reporting increases in motor conduction velocity (MCV) of the tibial and peroneal nerves following laser therapy [8, 11]. Notably, Yamany and Sayed [11] observed that the therapeutic effects of laser therapy manifest more prominently in sensory nerves than in motor nerves, possibly due to the peripheral initiation of laser-induced biostimulation. The transcutaneous or direct stimulation of peripheral sensory nerves through the plantar application of the laser likely contributes to analgesic effects by blocking neurotransmission along A-δ and C fibers to the posterior horn of the spinal cord [11, 17].

The observed improvements in NCS parameters for both sensory and motor nerves in the experimental group can be attributed to the biostimulatory effects of laser therapy on the nervous system. Mechanistically, laser therapy induces Schwann cell proliferation, stimulates nerve metabolism, promotes myelination, and facilitates axonal regeneration [18, 19]. Beyond the immediate positive outcomes reported by other authors, our study highlights the sustained or even enhanced therapeutic effects at the 90th day, indicating the long-term benefits of laser therapy in DSPN management.

This study's limitations include a relatively small sample size, which may restrict the generalizability of the findings. Future research should involve larger, multicenter samples to validate these results. Additionally, comparative studies assessing laser therapy against other physical modalities such as iontophoresis, transcutaneous electrical nerve stimulation (TENS), and magnetotherapy could provide valuable insights. Exploring the combined application of laser therapy with kinesitherapy may also yield synergistic effects, further enhancing therapeutic outcomes in DSPN.

CONCLUSION:

The application of NIR laser, combining two wavelengths (808 nm and 905 nm), led to a statistically significant reduction in the vibration perception threshold and improvements in nerve function, as evidenced by enhanced electroneurographic parameters of the sural, tibial and peroneal nerves. These findings indicate improved sensory and motor function of the lower limbs.

Given its non-invasive nature, high safety profile (with no adverse effects reported), and efficacy, deep tissue laser therapy can be considered a safe, non-pharmacological adjunct to the standard for managing painful diabetic peripheral neuropathy. Further research with larger cohorts is warranted to validate these results and explore their integration into broader therapeutic protocols.

Abbreviations:

MLS - Multiwave locked system

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