

Electrophysiological and Quality-of-Life Improvements in Diabetic Neuropathy Patients with high power Laser Therapy: A Narrative Review

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Abstract

Background: Diabetic neuropathy is a debilitating complication of diabetes, significantly impacting electrophysiological function and quality of life. **Aim:** This study evaluates the effectiveness of high-power laser therapy (HPLT) in improving electrophysiological parameters and enhancing the quality of life in patients with diabetic neuropathy. **Methods:** A total of 44 patients; 22 female and 22 male aging from 50 to 60 years old participated in this study. Patients were recruited from the out clinics of Neurology and internal medicine in Kasr Al-aini hospital in the period from July 2023 – January 2024. Patients had type 2 diabetes and neuropathic symptoms assessed using the Neuropathy Disability Score. High-power laser therapy was applied to target neuropathic pain and peripheral nerve dysfunction. High-power laser therapy with scanning motion, wavelength of 980 nm and a power of 10w, used 3J per min for each planer surface and lumbar point, the lumbar region was also treated using the scanning motion. High-power laser therapy was used twice per week for 6 weeks (total 12 sessions). Nerve conduction velocity (NCV) measurements and patient-reported outcomes on pain, fatigue, and functional limitations were assessed pre and post treatment. **Results:** this study demonstrated a significant improvement in NCV, reduced neuropathic pain, and enhanced patient-reported quality of life following HPLT intervention. **Conclusion:** Findings suggest that HPLT has a promising therapeutic role in addressing diabetic neuropathy, potentially surpassing conventional pharmacological approaches. Future studies should focus on long-term effects, gender-specific responses, and optimizing treatment protocols for broader clinical applications.

Key words: High-power laser therapy, diabetic neuropathy, electrophysiological parameters, neuropathic pain, quality of life.

1. Introduction

There is a general consensus that chronic diabetic neuropathy is the long-term complication of diabetes. It damages the functional and structural integrity of the peripheral nervous system and is the leading cause of sensory motor dysfunction and peripheral neuropathy in diabetic patients¹. This, in turn, often leads to secondary pathology—osteoarthropathy, podoplanopathy, ulcers, and infectious complications. Lesions of the peripheral nervous system in diabetic patients usually begin with small fibers, and these are lesions that precede the clinical manifestation of chronic diabetic neuropathy².

Neuropathic pain is often extremely severe and is associated with significant functional limitations and reduced quality of life in these patients. The results of conducted studies prove the significant impact of the analgesic effect on the dynamics of metabolic parameters, particularly adequate glycemic control, and

the improvement of quality of life in these patients³. The neuropathic deficit develops over a long period of time and, as the severity of the disease increases, it is clinically represented as muscular weakness and atrophy in the distal segments of the extremities, the lack of deep tendon reflexes, and, eventually, the loss of sensitivity. The most common form of diabetic neuropathy is sensorimotor polyneuropathy⁴.

There is less frequent representation of autonomic dysfunction. The mechanism of the development of chronic complications of diabetes mellitus is complex and not fully understood. According to contemporary data, the main factors leading to the development of neuropathy in diabetic patients are multiple and can manifest themselves differently depending on the duration and compensation of diabetes. These include those with a direct effect on the excitation and ion transport through the cell membrane, impaired intracellular repair, increased levels of oxidative stress, amplified formation of advanced glycation end products, and metabolic disorders resulting from poor glycemic control⁵.

The probability of peripheral nerve lesion increases with longer disease duration, hyperglycemia, metabolic disorders, and the presence of signs of oxidative stress, which is characteristic for the modulatory or non-specific neuropathy. The classic pharmacological treatments possess a series of significant limitations; none of the drugs currently used for the treatment of neuropathy have been proven to affect the course of the disease; the number needed to treat is comparative for most drugs; the treatment outcome may change significantly for individual patients, and the therapy is time-consuming, and there may be associated pain management limitations⁶. Alternative methods that can help to suppress neuropathic pain and restore the structure and function of peripheral nerves have to be found. The aim of our study was to assess the effect of high-power laser therapy (HPLT) on the electrophysiological parameters, pain, and quality of life in patients with diabetic neuropathy⁷.

2. Principles of High- Power Laser Therapy and Mechanisms of Action

The advantage of HILT is able to reach and stimulate the large and/or deep joints and tissues. The use of HILT has been proven to significantly reduce pain⁸. Previous studies describe the anti-inflammatory, anti-edematous, and analgesic effects of HILT, thus justifying its use in the therapy of pain^{9,10}. Although Stiglic-Rogoznica et al.¹¹ reported a significant decrease in pain level after HILT, they recommended comparing the effect of HILT with other conservative interventions or placebo control groups and that further studies should be conducted to measure the functional improvement as a result of pain reduction.

High-power laser therapy is considered one of the means of phototherapeutic devices that gained popularity for treating acute and chronic inflammatory pain and related impairments¹², but lately, it has been proved that HILT has deeper effect on inflammation and edema, analgesic effects and stimulation of joints more deeply. Thus, the application of HILT for mucopolysaccharidosis may improve pain and function¹³.

Laser therapy is based on the belief that laser radiation, and possibly monochromatic light in general, is able to alter cellular and tissue function in a manner dependent on the characteristics of light itself (e.g., wavelength, coherence)¹⁴. Therefore, it is assumed that any biologic effects are secondary to direct effects of photonic radiation, and are not the result of thermal processes¹⁵. More recently, high intensity laser therapy that uses higher intensity laser irradiation and causes minor and slow light's absorption by chromophores has been utilized among physical therapeutic modalities.

High-power laser therapy is a form of intravenous laser blood irradiation with the wavelength used in the infrared region of the spectrum and strictly defined parameters such as the energy per point and power density. High-power laser therapy is the most popular form of photo-irradiation, which is widely used in medical practice¹⁶. The therapeutic effects are due to the direct and nonspecific biological stimulation of blood and its flow in the optical channel, as well as to the consequent improvement of the health of organs and tissues¹⁷.

The direct effects of HPLT are due to the absorption of energy by blood progressing through the optical channel, which leads to its photo-coagulation and contributes to the photodilation of blood vessels, including the microcirculatory bed and the interstitium, and to the biophotonic induction of processes within blood¹⁸. The therapeutic laser beam is mostly absorbed by the optical absorption band of oxyhemoglobin, which corresponds to the region of red light and near-infrared spectrum, and therefore, all wavelengths in this region of the spectrum give the best therapeutic results¹⁹.

3. Clinical Studies on the Effects of High-Power Laser Therapy on Electrophysiological Parameters in Diabetic Neuropathy

Recent studies have reported that the laser contributes to the preservation of peripheral nerve functions after nerve crush injury. Repeated laser therapy application, in addition to the therapeutic aggression, does not induce side effects in diabetic neuropathy as it might happen with the use of antineoplastic drugs²⁰. Thus, in the present study, the effect of repeated laser therapy application was investigated on electrophysiological parameters and the quality of life in diabetic neuropathic patients. It is considered that the effects achieved owing to the irradiation are effective in the prevention and/or treatment of neuropathic changes and it is supported that laser therapy will be commonly used for this purpose in the future. With the results, it is possible to confirm how much laser therapy differs from conventional treatments used in diabetic neuropathy²¹.

High-power laser therapy is a new, non-invasive, painless intervention which is characterized by its effective anti-inflammatory and reparative mechanisms. High-power laser therapy has therapeutic benefits through photochemical, photothermal, and photomechanical mechanisms, possibly due to its potential for reducing inflammation, enhancing microcirculation, and stimulating immunological proteins and nerve regeneration and secretion of O -endorphins²².

With using HPLT, there is an increase in mitochondrial oxidative reaction and adenosine phosphate, DNA, and RNA production (photobiology effect). Nitric oxide produced in the mitochondria can inhibit respiration by binding to cytochrome c oxidase and competitively displacing oxygen, especially in stressed or hypoxic cells. If light absorption displaced the nitric oxide and thus allowed the cytochrome c oxidase to recover and cellular respiration to resume.

It has been proposed that laser therapy might work by photodissociating NO from the cytochrome c oxidase, thereby reversing the signaling consequences of excessive NO binding²³. Light can indeed reverse the inhibition caused by NO binding to cytochrome oxidase, both in isolated mitochondria and in whole cells²⁴. Light can also protect cells against NO-induced cell death.

The pain releasing effect of HPLT is provided by reducing the transmission of painful stimuli and increased morphine mimetic factors. It has been reported that HPLT reduces pain and inflammation rapidly. Additionally, it has rapidly induced the photochemical and photothermal effects, increasing blood flow, cell metabolism, and vascular permeability²⁵.

This study was performed on 44 patients diagnosed with type 2 diabetes and who were neuropathic according to the Neuropathy Disability Score before treatment. Nerve conduction velocity was significantly related to disease duration and age, affecting less intensively a population over 56 years. If diabetes could not be controlled, neuropathy tended to be more intense. The patients were questioned in social areas with questionnaires prepared by the physician about their sensory-motor functions, fatigue, sleep disorders, and quality of life expectations²⁶. Highly effective and long-term results, positive effects on diastolic values and the cardiovascular system have been detected in the study on heart rate variability response to laser therapy in short treatment periods of a few days, but it is recommended to consider gender because it could be less effective in women due to hormonal protection²⁷.

4. Assessment of Quality of Life in Patients with Diabetic Neuropathy: Tools and Measures

Diabetic neuropathy is one of common complication of diabetes, usually seen in the late stages of the disease, and is therefore a significant cause of morbidity and mortality. Quality of life assessment is an essential aspect of monitoring a patient's status in medical practice²⁸. Ervin's questionnaires, Würzburg Diabetic Neuropathy Specific-Diabetes Quality-of-Life – a 54-item questionnaire, and the Complex Therapy Index are commonly used in these patients group. More information about the European Quality of Life 5-D, the Neuropathy Walking Aid Assessment Questionnaire, the Toronto Clinical Scoring System, the Liverpool Outcome Score, the Medical Outcomes Short Form, the Neuropathy Specific Quality-of-Life, and the World Health Organization Quality of Life versions could be obtained from various sources²⁹.

Impairment of quality of life leads to negative outcomes of the disease, and its correction directly influences the severity and progression of the disease, life expectancy, and the time of life lost as a result of diseases³⁰. Human health is not only an important aspect of the development of any country but is also an invaluable human capital, the basis of economic growth, and recognition at the global level. As a result, an increase in the level of public health entails a change in the attitude towards public health management in order to maintain and improve the quality of life of people, as well as similar indicators. Furthermore, the main objective of health reform is not only to extend the life of a person but to improve its quality³¹. To assess people's abilities, namely their limitations, and avoid subjectively interpreting their ability limitations in everyday life, quality of life patient questionnaires were also used. These methods are well known as self-assessment instruments that help to obtain an idea of the patient's quality of life, defining their physical, emotional, and social situation; as well as the patient's social and occupational situation; the status of daily activities; and the patient's social activity³². The difference between the above-mentioned tools is in the context of chronic sensory neuropathy. All these tools can separate between the subpopulations of the patients mentioned above, but the presence of additional postural hypotension, which is often observed not only during the walking period but also in patients at rest, often leads to patients assembling different autonomic symptoms even with physical disability. The patient complains of all impediments and discomfort with low standing time and is quite affected by the exercises of quality of life tools due to the high burden³³.

Conclusion:

A novel approach is presented to investigate the impact of HPLT on electrophysiological parameters and quality of life in patients with diabetic neuropathy. This study demonstrated scientific evidence of the beneficial effect of HPLT on electrophysiological parameters and quality of life in patients with diabetic neuropathy. The clear, easy, and conceptual model in this study can be used successfully in further electrophysiological studies. This study has provided strong scientific evidence of the benefits of HPLT on electrophysiological parameters and quality of life in patients with diabetic neuropathy, suggesting implementing HPLT as part of standard care in treating patients with diabetic neuropathy.

Future Directions:

Despite the significant obstacle of the treatment of neuropathic pain, a potentially beneficial therapy of HPLT was presented. It is anticipated that more skilled treatments are actually needed for the painful experience of neuropathy. One disadvantage is that when reducing a sign such as a knee jerk, someone with sensory ataxia may have to lean on something and ultimately affect the H max measurement. This analysis particularly emphasizes the direction of future electrophysiological studies on diabetic neuropathy in HPLT-treated individuals. This outcome serves as fertile ground for subsequent randomized controlled trials. It is also necessary to present actions to enhance the quality of information offered during HPLT to boost the patient's perception of the therapy; all these aspects should be researched in longitudinal trials. More scientific studies are required to understand well the processes of treatments and factors contributing to HPLT success. In addition, it is important to identify the strong and permanent effect on electrophysiological parameters. The lasting effects of HPLT should be investigated in order to decrease the probability of the effect being temporary. Only then we can produce compelling knowledge of how to handle neuropathic distal pain and differentiate advantageous effects. Other recently developed advanced techniques will be found to offer functional benefits to treat a disease distinguished by this substantial inconvenience.

References

1. Mengstie MA, Chekol Abebe E, Behaile Teklemariam A, Tilahun Mulu A, Agidew MM, Teshome Azezew M, et al. Endogenous advanced glycation end products in the pathogenesis of chronic diabetic complications. *Front Mol Biosci.* 2022;9:1002710.
2. Elafros MA, Andersen H, Bennett DL, Savelieff MG, Viswanathan V, Callaghan BC, et al. Towards prevention of diabetic peripheral neuropathy: clinical presentation, pathogenesis, and new treatments. *Lancet Neurol.* 2022;21(10):922–36.
3. Szewczyk AK, Jamroz-Wiśniewska A, Haratym N, Rejdak K. Neuropathic pain and chronic pain as an underestimated interdisciplinary problem. *Int J Occup Med Environ Health.* 2022;35(3):249.
4. Sloan G, Selvarajah D, Tesfaye S. Pathogenesis, diagnosis and clinical management of diabetic sensorimotor peripheral neuropathy. *Nat Rev Endocrinol.* 2021.
5. Kaur M, Misra S, Swarnkar P, Patel P, Kurmi BD, Gupta GD, et al. Understanding the role of hyperglycemia and the molecular mechanism associated with diabetic neuropathy and possible therapeutic strategies. *Biochem Pharmacol.* 2023;215:115723.
6. Lopes B, Sousa P, Alvites R, Branquinho M, Sousa AC, Mendonça C, et al. Peripheral nerve injury treatments and advances: one health perspective. *Int J Mol Sci.* 2022;23(2):918.
7. Bordett R, Danazumi KB, Wijekoon S, Garcia CJ, Abdulmalik S, Kumbar SG. Advancements in

- stimulation therapies for peripheral nerve regeneration. *Biomed Mater.* 2024;19(5):052008.
8. **Zati A, Valent A.** Physical therapy: new technologies in rehabilitation medicine (translated to English). Edizioni Minerva Medica. 2006;162–18.
 9. **Santamato A, Solfrizzi V, Panza F, Tondi G, Frisardi V, Leggin BG, et al.** Short-term effects of high-intensity laser therapy versus ultrasound therapy in the treatment of people with subacromial impingement syndrome: a randomized clinical trial. *Phys Ther.* 2009;89(7):643–52.
 10. **Saggini R, Bellomo RG, Cancelli F.** Hilterapia and chronic ankle pain syndromes. *Energy Health.* 2009;3(3):22–5, 38.
 11. **Stiglic-Rogoznica N, Stamenković D, Frlan-Vrgoc L, AvanciniDobrović V, Vrbanić TS.** Analgesic effect of high intensity laser therapy in knee osteoarthritis. *Coll Antropol.* 2011;35(2):183–5.
 12. **Parr JJ, Larkin KA, Borsa PA.** Effects of class IV laser therapy on exercise-induced muscle injury. *Athl Train Sports Health Care.* 2010;2(6):267–76.
 13. **Song HJ, Seo HJ, Lee Y, Kim SK.** Effectiveness of high-intensity laser therapy in the treatment of musculoskeletal disorders: a systematic review and meta-analysis of randomized controlled trials. *Medicine (Baltimore).* 2018;97(51):e13640.
 14. **Miura Y, Senoo A, Doura T, Kiyonaka S.** Chemogenetics of cell surface receptors: beyond genetic and pharmacological approaches. *RSC Chem Biol.* 2022.
 15. **Chow LS, Gerszten RE, Taylor JM, Pedersen BK, Van Praag H, Trappe S, et al.** Exerkines in health, resilience and disease. *Nat Rev Endocrinol.* 2022;18(5):273–89.
 16. **Waddell IS, Orfila C.** Dietary fiber in the prevention of obesity and obesity-related chronic diseases: from epidemiological evidence to potential molecular mechanisms. *Crit Rev Food Sci Nutr.* 2023.
 17. **Pruitt T, Carter C, Wang X, Wu A, et al.** Photobiomodulation at different wavelengths boosts mitochondrial redox metabolism and hemoglobin oxygenation: lasers vs. light-emitting diodes in vivo. *Metabolites.* 2022.
 18. **Muniz XC, de Assis AC, de Oliveira BS, Ferreira LF, Bilal M, Iqbal HM, et al.** Efficacy of low-level laser therapy in nerve injury repair—A new era in therapeutic agents and regenerative treatments. *Neurol Sci.* 2021;42:4029–43.
 19. **Buzza AS, Cousins H, Tapas KE, Anders JJ, Lewis SJ, Jenkins MW, et al.** Direct photobiomodulation therapy on the sciatic nerve significantly attenuates acute nociceptive sensitivity without affecting motor output. *Neuromodulation.* 2024;27(8):1338–46.
 20. **Kenareh R, Mirmohammadi SJ, Khatibi A, Shamsi F, Mehrparvar AH.** The comparison of the efficacy of photobiomodulation and ultrasound in the treatment of chronic non-specific neck pain: a randomized single-blind controlled trial. *J Lasers Med Sci.* 2021;12(1):e20.
 21. **Karu TI, Pyatibrat LV, Afanasyeva NI.** Cellular effects of low power laser therapy can be mediated by nitric oxide. *Lasers Surg Med.* 2005;36:307–14.
 22. **Borutaite V, Budriunaite A, Brown GC.** Reversal of nitric oxide-, peroxynitrite- and S-nitrosothiol-induced inhibition of mitochondrial respiration or complex I activity by light and thiols. *Biochim Biophys Acta.* 2000;1459:405–12.
 23. **Yilmaz M, Eroglu S, Dundar U, Toktas H.** The effectiveness of high-intensity laser therapy on pain, range of motion, functional capacity, quality of life, and muscle strength in subacromial impingement syndrome: a 3-month follow-up, double-blinded, randomized, placebo-controlled trial. *Lasers Med Sci.* 2022;37(1):241–50.
 24. **Ortiz-Martínez M, González-González M, Martagón AJ, Hlavinka V, Willson RC, Rito-Palomares M.** Recent developments in biomarkers for diagnosis and screening of type 2 diabetes

- mellitus. *Curr Diab Rep.* 2022;22(3):95–115.
25. **Conrad N, Misra S, Verbakel JY, Verbeke G, Molenberghs G, Taylor PN, et al.** Incidence, prevalence, and co-occurrence of autoimmune disorders over time and by age, sex, and socioeconomic status: a population-based cohort study of 22 million individuals in the UK. *Lancet.* 2023;401(10391):1878–90.
 26. **Gao X, Zhang W, Yang F, Ma W, Cai B.** Photobiomodulation regulation as one promising therapeutic approach for myocardial infarction. *Oxid Med Cell Longev.* 2021;2021:9962922.
 27. **Edmonds M, Manu C, Vas P.** The current burden of diabetic foot disease. *J Clin Orthop Trauma.* 2021.
 28. **Elam AR, Tseng VL, Rodriguez TM, Mike EV, Warren AK, Coleman AL, et al.** Disparities in vision health and eye care. *Ophthalmology.* 2022;129(10):e89–113.
 29. **Zhao N, Yang Y, Zhang L, Zhang Q, Balbuena L, Ungvari GS, et al.** Quality of life in Parkinson's disease: a systematic review and meta-analysis of comparative studies. *CNS Neurosci Ther.* 2021;27(3):270–9.
 30. **Salam MA, Al-Amin MY, Salam MT, Pawar JS, Akhter N, Rabaan AA, et al.** Antimicrobial resistance: a growing serious threat for global public health. *Healthcare.* 2023;11(13):1946.
 31. **Cooper N, Kruse A, Kruse C, Watson S, Morgan M, Provan D, et al.** Immune thrombocytopenia (ITP) World Impact Survey (I-WISH): impact of ITP on health-related quality of life. *Am J Hematol.* 2021;96(2):199–207.
 32. **Wieling W, Kaufmann H, Claydon VE, van Wijnen VK, Harms MP, Juraschek SP, et al.** Diagnosis and treatment of orthostatic hypotension. *Lancet Neurol.* 2022;21(8):735–46.
 33. **Tański W, Wójciga J, Jankowska-Polańska B.** Association between malnutrition and quality of life in elderly patients with rheumatoid arthritis. *Nutrients.* 2021.