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## Efficacy of low level laser therapy on peripheral neuropathy in type 2 diabetes mellitus

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The prevalence of type 2 diabetes mellitus (T2DM) is rapidly rising worldwide. It has been associated with many micro-vascular and macro-vascular complications1. Among all the complications, peripheral neuropathy is considered to be the most common with prevalence 60 to 65% and 11% patients with diabetic neuropathy complaining of pain2, where 50% of all the inpatient admissions are due to foot complications caused by peripheral neuropathy (DPN)3,4

DPN is a result of injury to the Vasa nervorum, axons and atrophy of the axons leading to tissue damage5. All nerve fibres may be injured, but small myelinated and unmyelinated fibre's that transmit pain and temperature are most affected6. In association with injury to the nerves, reduced microcirculation of the blood is responsible for the development of ulcers, and infections of skin and bone in T2DM subjects with long duration of diabetes mellitus7. In many subjects with diabetic neuropathy, pain will develop as a symptom localized to the lower extremities, primarily the soles and toes8. Evidences suggest that long term complications of diabetes mellitus are associated with depressive symptoms, the neuropathic pain considered to be one of the major cause for the depression9,10.

Current therapy for DPN is purely aiming to symptomatic relief of the pain through various drug administration. These drugs are effective, but often associated with central nervous system side effects and do not retard the advancement of the underlying neuropathy11. Other than pharmacological treatment, non-pharmacological management have also been suggested, including acupuncture12, infrared therapy13, and various electrotherapies, including transcutaneous electrical nerve stimulation (TENS) 14, and spinal cord electro stimulation 15. The efficacy of most conservative treatment options for painful DPN is still little known. Among the different alternatives for treatment, low-level laser therapy (LLLT) may hold the potential to induce a biostimulational effect on the nervous system16,17,18,19

The typical aetiology of DPN pain starts with injury to a peripheral nerve, the majority of research into the management of DPN pain is focused on the nerves themselves. Various clinical and observational research studies on peripheral nerve injuries used LLLT because it promotes microcirculation in the irradiated area, increases nerve functional activity increases the rate of axon growth and myelinisation and improves regeneration of the injured nerve20, 21,22,23. In addition, LLLT has also been used for the handling of other diabetic complications, such as foot ulcers24, diabetic microangiopathy and wound healing25. Therefore the objective of this study is to evaluate the effect of LLLT on pain intensity and foot skin microcirculation in patients with painful DPN.

**Methods:** After abstaining approval by the Institutional Ethical Committee (IEC) and informed written consent from the subjects, 19 T2DM subjects were screened for DPN in an outpatient setting using Michigan Neuropathy Screening Instrument (MNSI), Vibration Perception Threshold (VPT) using Biothesiometer and DPN was assessed using Visual Analog Scale (VAS). Subjects with T2DM with clinically detected DPN on analgesics, antidepressants were recruited in the study and medications remained unchanged for at least 2weeks. Subjects with malignancy, thyroid disease or other neurological problems, pregnancy, old fractures of lower leg, metallic implants and alcohol or drug abuse were excluded from the study. The detailed clinical evaluation was done to identify the evidence of dry skin, callus formation, fissures, ulceration or deformities like hammer toes, overlapping toes, hallux valgus, prominent metatarsal heads. MNSI was administered following clinical evaluation consist of two components.During the examination, subject's foot was inspected for abnormalities in the foot. Each foot with any abnormality received a mark of 1. Each foot was also examined for ulcers and each foot with an ulcer receives a score of 1. The ankle reflexes were elicited. If the reflex is present and it's scored as 0, the reflex designated as present with reinforcement and was scored as 0.5. If the reflex is absent and is scored as 1. Vibration sensation tested same as above mention in VPT. Vibration is scored as present if the subject was able to feel within 8Mv and scored as 0, if the subject is able to sense from 15mv- 24mv scored as 0.5 and if the subject was not able to feel or feel in within an above 25mv was scored as 1. The total potential score is 8 and, in the published score algorithm, a score  $\geq 2.5$  is considered presence of DPN.

The vibration threshold was examined using Biothesiometer with the subject in supine lying and the result is recorded and >25mVolts is considered presence of DPN Temperature of the foot was examined using Infrared thermal imaging was done using infrared thermal camera (GUIDE \* EASIR-4, Wuhan Guide Infrared Co., Ltd., China) with sensitivities of 0.08 and 0.010C, a