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ORIGINAL ARTICLES

Efficacy of low level laser therapy on painful diabetic peripheral neuropathy

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Background & aims: Diabetic peripheral neuropathy (DPN) accounts for most common complications of T2DM. Painful DPN is associated with functional limitation & poor quality of life. Therefore, objective of the study is to find the effect of low level laser therapy on painful diabetic peripheral neuropathy (DPN) in type 2 diabetes mellitus (T2DM)
Materials & methods: The study design is pre-post observational design. After obtaining ethical clearance and informed consent, 19 T2DM subjects were screened and confirmed for peripheral neuropathy in an outpatient setting with biochemical parameter, pain scale and Michigan Neuropathy Screening Instrument (MNSI). Low Level Laser therapy was irradiated through scanning mode with dosage of 3.1J/cm^2 on the plantar and dorsum of the foot and 3.4j/cm^2 with contact method for 10days and all subjects were reassessed at the end of the 10 day. Descriptive statistics and paired' test was used to analyze the pre-post finding within the group. Level of significance was set at $p<0.05$
Results: The result analysis showed significant reduction in Pain using VAS scale (6.47 ± 0.84 to 1.21 ± 0.78 ($p<0.001$), MNSI (5.52 ± 1.26 to 2.71 ± 0.97 (<0.001). In addition we observed significant reduction in Vibration perception threshold (32.68 ± 6.08 to 24.84 ± 4.29 (<0.001) and a significant increase in the temperature from baseline to post intervention (30.01 ± 2.11 to 31.75 ± 1.03 ($p<0. 001$).
Conclusion: In the present study, Low level laser therapy was found to be effective in type 2 DM with peripheral neuropathy.

Key words: Type 2 diabetes mellitus · Peripheral Neuropathy · Pain · Low Level Laser Therapy

Introduction

The prevalence of type 2 diabetes mellitus (T2DM) is rapidly increasing worldwide. It has been associated with many micro-vascular and macro-vascular complications. [1)] Among all the complications, peripheral neuropathy is considered to be the most common. [2)] It is estimated that the prevalence of peripheral neuropathy in T2DM patients is approximately 25-50% in developing countries. [3)] Diabetic peripheral neuropathy (DPN) accounts for more hospitalization than all the other complications of T2DM. Painful DPN is associated with functional impairment & poor quality of life. [4, 5)]

Painful DPN is a result of injury to the Vasa nervorum, axons and atrophy of the axons leading to tissue damage. [6)] All nerve fibres may be injured, but small myelinated and unmyelinated fibres that transmit pain and temperature are most affected. [6)] In association with injury to the nerves, reduced microcirculation is responsible for the loss of protective sensation and atrophy of intrinsic foot muscles which later leads to

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development of foot complications like callus, ulcers, and infections of skin and bone in T2DM subjects with long duration of diabetes mellitus. [7] In many subjects with diabetic neuropathy, pain develops as a symptom localized to the lower extremities, primarily the soles and toes. [8]

Current therapy for painful DPN is aiming to symptomatic relief through various drug administrations. These drugs are effective, but often associated with systemic side effects and do not retard the advancement of the underlying neuropathy. [9] Other than pharmacological treatment, non-pharmacological management have also been used, including acupuncture [10], infrared therapy [11], and various electrotherapies, including transcutaneous electrical nerve stimulation (TENS) [12], and spinal cord electro stimulation. [13] The efficacy of most conservative treatment options for painful DPN is still needs to be investigated. Among the electrotherapy modalities, low-level laser therapy has been used to manage nerve injuries and other pathologies of the nerve because it hold the potential to induce a biostimulational effect on the nervous system. [14 - 16] In addition, low-level laser therapy has also been used in the management of diabetic complications such as foot ulcers. [17] Even though low-level laser therapy is found to be very effective in nerve regeneration, there is a dearth of literature on effect of low-level laser therapy on painful DPN in T2DM population. Therefore the objective of the present study is to evaluate the effect of low-level laser therapy on Type 2 DM subjects with painful DPN.

Materials & methods

After obtaining Institutional Ethical Committee (IEC) clearance and informed written consent, 19 T2DM subjects on oral hypoglycaemic agents were recruited based on inclusion and exclusion criteria. The neuropathy evaluation was performed using Michigan Neuropathy Screening Instrument (MNSI), Vibration Perception Threshold (VPT) using Biothesiometer. Pain was assessed using Visual Analogue Scale (VAS), temperature was assessed using Infrared Thermal Imaging. Subjects with malignancy, thyroid disease, other neurological conditions, pregnancy, were excluded from the study.

Following detailed base line evaluation, all 19 subjects were treated with two separate low level laser therapy equipment. The EC laser wave length of 632.8 nm with dosage of 3.1J/cm^2 and Thor Laser wave length of 660nm & 850 nm with dosage of 3.4J/cm^2 and power density of 50-150 mW/cm^2. The EC laser was treated with scanning mode with duration of nine minute on the plantar and dorsum of foot **(Figure-1)** and Thor Laser probe was used with contact method over popliteal fossa **(Figure-2)** and over the neck of fibula for 10 days and all subjects were reassessed at the end of the 10th day by using following outcome measures, VAS, MNSI, VPT and temperature by infrared thermal imaging. All the subjects completed laser treatment without any adverse reaction. Data was analyzed using SPSS package version 16. Descriptive statistics and paired 't' test was performed to analyze the pre-post changes within the group. Level of significance was set at $p<0.05$.

Figure 1: Scanning method of Laser application

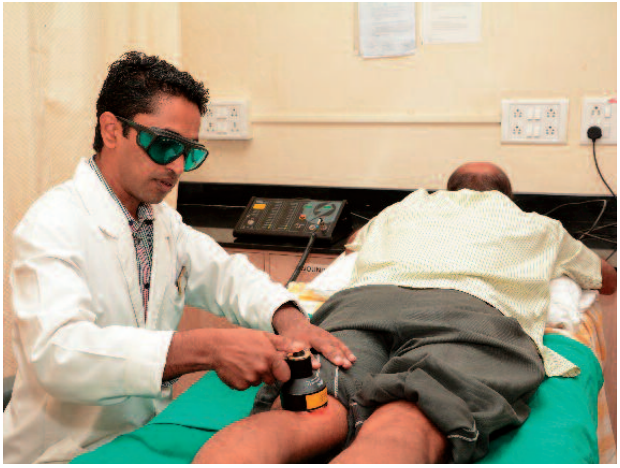

Figure 2: Laser with Probe method application

Result analysis

Nineteen T2DM subjects with mean age of 49.58 ± 6.89 years and DPN with mean duration of 7.84 ± 3.77 years. **Table 1** shows the demographic characteristics of the T2DM subjects.

The result analysis showed significant reduction in Pain using VAS scale (6.47 ± 0.84 to 1.21 ± 0.78 ($p<0.001$), MNSI (5.52 ± 1.26 to 2.71 ± 0.97 (<0.001). In addition we observed significant reduction in Vibration perception threshold (32.68 ± 6.08 to 24.84 ± 4.29 (<0.001) and a significant increase in the temperature from baseline to post intervention (30.01 ± 2.11 to 31.75 ± 1.03 ($p<0.001$). **(Table 2)**

Discussion

Painful DPN is one of the common complications in subjects with T2DM. From a pathophysiological standpoint, DPN is derived not only from injury to peripheral nerves but most commonly of micro vascular origin. [18), 19)] So the treatment of DPN pain could be directed to improve microcirculation, enhance regeneration of nerve injury and reduce pain.

In the present study, we used low level laser therapy to determine its effect on painful Diabetic Peripheral Neuropathy (DPN). The results showed significant reduction in the pain **(Table 2)**. The possible explanatory factor for reduction in pain could be due to increased microcirculation to the periphery. [20)] The possible mechanism is that low-level laser therapy stimulates the release of cytokines and growth factors into the circulation which are responsible for the vasodilatation of the vessels and formation of new capillaries. A study conducted by Funk et al. documented that exposure to He-Ne laser stimulates the release of cytokines such as IL-1α, IL-2, IFN-γ and TNF- α which plays a major role in cell signalling. [21)]

Other possible reason for reduction in pain can also be due to increased ATP production by mitochondria and increased cellular oxygen consumption by nerve regeneration. Low-level laser therapy increases microcirculation to the periphery and to understand this mechanism, in the present study we used Infrared thermal camera to record the foot temperature, as temperature represents the state of blood circulation where reduced temperature is considered as diminished blood supply to the periphery and increased temperature represents increased blood circulation to the periphery. In the present study, with laser irradiation, we found an increase in temperature following laser therapy. Our result were supported by the previous finding on improvement of microcirculation at the irradiation site. [22), 23)]

Table 1: Demographic characteristics of the subjects

Parameters	Mean±SD
Age (years)	49.58±6.89
Gender	Male-12 & Female-07
BMI (Kg/m^2)	24.94±2.03
Fasting Blood Sugar (mg/dl).	184.47±30.08
Post Prandial Blood Sugar (mg/dl)	242.74±60.06
HbAc (%)	9.08±1.09
Duration of T2 DM (years)	13.58±5.08
Duration of Peripheral Neuropathy (years)	7.84±3.77

Table 2: Pre-Post Mean changes in outcome measures after low level laser therapy in T2DM with peripheral Neuropathy

Outcome measures	Base Line	10th day	95% confidence Interval		p
	Mean ±SD	Mean ±SD	Lower	Upper	
Pain	6.47±0.84	1.21±0.78	-4.75	5.76	<0.0001
MNSI	5.52±1.26	2.71±0,97	-1.90	3.72	<0.0001
VPT	32.68±6.08	24.84±4.29	-6.05	9.62	<0.0001
Temperature	30.01±2.11	31.75±1.03	-0.84	4.11	<0.0001

In addition to decrease in pain and improved micro circulation, we observed that there is mean decrease in Michigan Neuropathy Screening Instrument (MNSI) and vibration threshold in all subjects. **(Table 2)** However, study conducted by Arnall et al [24] evaluated the vibration perception threshold (VPT) and found no improvement after laser irradiation, but in the present study we found decrease in the vibration perception threshold following laser irradiation. The possible reason could be due to increased microcirculation and release of cell signaling proteins like cytokines.

Conclusion

In the present study, we found that low-level laser therapy is effective in reducing pain in T2DM with peripheral neuropathy.

Limitation of the study

Present study is a pre-post experimental study with no control group.

Table 3: Demographic & Clinical characteristics of Participants

Case	Gender	Age (Years)	BMI (kg/m2)	Glycated Hb (%)	Duration of Diabetes (Years)	Peripheral Neuropathy (Years)
Case 1	Male	45	24.5	11.2	13	7
Case 2	Female	57	24.7	9.3	8	4
Case 3	Male	42	26	7.1	5	2
Case 4	Female	53	22.8	12.3	15	9
Case 5	Male	42	22.7	10.4	14	10
Case 6	Male	55	27.6	11.5	15	7
Case 7	Female	58	26.8	10.2	18	12
Case 8	Male	44	25.8	9.4	19	14
Case 9	Male	55	27.5	7.4	9	5
Case 10	Male	49	24.5	10.6	15	9
Case 11	Female	41	27.6	8.3	18	13
Case 12	Male	57	26.8	11.2	26	15
Case 13	Male	44	25.8	9.5	13	9
Case 14	Female	61	20.1	8.6	15	6
Case 15	Female	57	24.7	9.3	8	4
Case 16	Male	42	26	7.1	5	2
Case 17	Female	53	22.8	12.3	15	7
Case 18	Male	45	24.5	11.2	13	6
Case 19	Male	42	22.7	10.4	14	8

Table 4: Pre and post changes in outcome measures after low level laser therapy T2DM with Peripheral neuropathy

Case	FBS pre (mg/dl)	FBS post (mg/dl)	PPBS pre (mg/dl)	PPBS post (mg/dl)	VAS pre	VAS post	MNSI pre	MNSI post	VPT pre	VPT post	Temperature pre	Temperature post
Case 1	147	128	155	158	7	2	7	4	45	26	28.1	31.4
Case 2	260	191	197	152	6	1	7.5	3	38	29	31.2	31.3
Case 3	131	136	215	196	6	0	5	4	28	22	32.1	31.2
Case 4	185	136	153	162	7	1	6	2	31	21	26.3	30.5
Case 5	191	152	241	198	5	2	4	2.5	33	30	27.3	31.5
Case 6	261	179	284	219	8	2	3.5	3.5	32	24	30.2	31.8
Case 7	155	121	238	198	7	2	6.5	3	35	26	31.4	32.2
Case 8	321	141	368	198	6	1	7	2	43	32	31.12	33.2
Case 9	138	109	120	141	8	2	6	2.5	26	19	28.3	33.2
Case 10	198	138	210	191	6	1	5.5	2	42	33	30.2	31.7
Case 11	203	198	314	262	7	2	4	4	26	21	33.4	32.5
Case 12	141	256	214	312	6	0	7	0	35	23	31.21	32.8
ase 13	210	198	300	231	7	1	5	2	32	24	26.3	29.4
Case 14	252	291	529	324	6	2	6	2.5	29	25	31.34	33.2
Case 15	109	139	213	242	7	0	5	2.5	25	18	33.2	31.2
Case 16	103	98	173	169	6	1	5	3.5	24	21	30.2	32.4
Case 17	226	218	332	242	5	2	6	2	33	25	28.3	31.3
Case 18	112	109	193	157	7	1	6	3	35	30	31.1	32.2
Case 19	162	125	163	155	6	0	3	3.5	29	23	29.1	30.3

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