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A Randomized Sham-controlled Trial of Sciatic Nerve Neurodynamic Mobilization in Painful Diabetic Peripheral Neuropathy

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Abstract

Objective: To study the efficacy of sciatic nerve neurodynamic mobilization as compared to control intervention on vibration thresholds, neuropathic pain severity, sciatic nerve neurodynamic test range of motion and neuropathy specific quality of life (NeuroQoL) in painful diabetic peripheral neuropathy patients.

Design: Observer-blinded randomized sham-controlled trial.

Methods: The study conduct was approved by Institutional Ethics Committee and was registered at Clinical Trials Registry- India. Thirty two patients of age (60.12 ± 11.41years), both gender (13 male, 19 female) were selected on convenient sampling. Subjects were selected based on following: Physician diagnosed type-II DM of atleast eight years duration; complaint of neuropathic pain (screened using neuropathic pain questionnaire NPQ) in the legs and feet; mechanical behavior of neuropathic pain (aggravated and/or relieved by movements); ability to understand and co-operate for instructions of tester. The twenty one excluded subjects had either of the following: progressive worsening neurological deficit, irritable pain, allodynia/ hyperalgesia, musculoskeletal problems, cognitive maladaptation syndrome. The independent blinded observer then recorded neuropathic pain intensity on NPQ, sciatic nerve neurodynamic test range of motion at initial resistance R1, vibration thresholds by Biothesiometry and NeuroQoL. The subjects then were randomized to receive either of two interventions-control and experimental. The control group received sham treatment, drugs for glycemic control, Gabapentin for neuropathic pain, diet-lifestyle modification and walking exercise prescription. The experimental group received in addition, sciatic nerve neurodynamic mobilization consisting of nerve massage and nerve sliders. The treatment session was of 45 min duration on five sessions (one session per week) for total study duration of five weeks. Patients were instructed to perform self-mobilization once daily and were given patient log to ensure compliance. Data was collected twice- pre and post intervention.

Results: The groups were comparable in age, gender, chronicity and severity of neuropathic pain. Both groups showed significant improvements. The experimental group showed significant improvements post treatment in all the four study outcomes. The between-group mean differences were NPQ (18.89 ± 2.46), neurodynamic range of motion (4.00 ± 3.85 degrees), vibration threshold (5.94 ± 1.12 volts) and NeuroQoL (15.93 ± 2.85) in favour of experimental group. All differences were statistically significant at $p<.05$ when analyzed using students' t-test at 95% confidence interval using SPSS 12.0.1 for Windows.

Conclusion: Sciatic nerve neurodynamic mobilization comprising of nerve massage and nerve sliders was shown to be an effective treatment adjunct for painful diabetic peripheral neuropathy.

Implications for practice: Neurodynamic assessment and intervention should be considered as an effective therapeutic option for painful diabetic peripheral neuropathy patients who complain of pain in the sciatic nerve distribution.

Implications for research: Studies on other nerves, other neuropathic pain syndromes, other outcomes (electrophysiologic studies) are warranted.

Keywords: Neuropathic pain; Neurodynamics; Diabetes mellitus.

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Introduction

The term diabetes mellitus describes a metabolic disorder of multiple aetiology characterized by chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both.[1] The prevalence of diabetes for all age-groups worldwide was estimated to be 2.8% in 2000 and 4.4% in 2030. The total number of people with diabetes is projected to rise from 171 million in 2000 to 366 million in 2030. The prevalence of diabetes is higher in men than women, but there are more women with diabetes than men. The urban population in developing countries is projected to double between 2000 and 2030.[2] The microvascular complications of diabetes are termed collectively as "triopathy" which includes retinopathy, neuropathy and nephropathy and the macrovascular complications include peripheral vascular disease, cerebrovascular disease and cardiovascular disease.[3,4]

Diabetic peripheral neuropathy (DPN) is a common complication estimated to affect 30% to 50% of individuals with diabetes. Chronic sensorimotor distal symmetric polyneuropathy is the most common form of DPN. The prevalence of neuropathy in type 2 diabetes ranges from 27% to 63% and from 14% to 70% in diabetes mellitus in general.[4] The higher prevalence of neuropathy in type 2 diabetes patients is related to greater age, male gender, longer diabetes duration, higher levels of glycosylated hemoglobin, lower HDL cholesterol, smoking; peripheral vascular disease and insulin use.[5]

Diabetic neuropathy has been defined as Peripheral somatic or autonomic nerve damage attributable solely to diabetes mellitus. It may be of two types symmetrical and asymmetrical. The symmetrical type was the commonest and it affects the sensory and autonomic functions of mostly peripheral nerves whereas the asymmetrical type affects the cranial nerves in their sensory and motor functions.[6] The first description of "diabetic neuropathy as a presence of pain and paresthesiae in lower limbs" was done by Rollo in 1798.[7] The consensus of opinion at the San Antonio conference on diabetic neuropathy was that diabetic neuropathy was "a descriptive term meaning a demonstrable disorder, either clinically evident or subclinical that occurs in a setting of diabetes mellitus without other causes of neuropathy. The neuropathic disorder includes manifestations in both somatic and/or autonomic parts of the nervous system."

Diabetic peripheral neuropathic pain (DPNP) or painful diabetic peripheral neuropathy (PDPN) affects approximately 11% of patients with diabetic peripheral neuropathy (DPN). The most common type of neuropathy in DM is DPN, with up to 50% of patients experiencing some degree of painful symptoms and 10% to 20% having symptoms severe enough to warrant treatment. A classic population-based study found some degree of neuropathy in 66% of patients with DM. Among those with type 1 and type 2 DM, 54% and 45%, respectively, had DPN and 15% and 13%, respectively, were symptomatic.[8]

The peripheral neuropathic pain can rise from musculoskeletal causes due to entrapment syndromes and also from movement induced mechanosensitivity.[6,9] Identification of musculoske letal peripheral neuropathic pain is made based on mechanical behavior of symptoms which alter with postures and/or movements.[7,10] Symptoms arising from peripheral nerves have been categorized into positive symptoms (dysesthetic pain such as hyperalgesia, allodynia, tingling, numbness, paresthesia and/or shooting pain) and negative symptoms (with neurological deficits such as sensory loss, motor loss and reflex loss)[8,11] and appropriate management was indicated to suit individual patient presentations with shrewd clinical reasoning.[9, 12]

Evaluation and treatment of this type of pain was proposed to be done utilizing neurodynamic testing that aims at checking neural mobility both intra and extraneural.[10,13] Intraneural mobility involves mobility between the nerve and its connective tissue sheaths, and extraneural mobility for between nerve and its surrounding structures.[11,14]

Neurodynamic mobilization involves nerve-specific movement testing (nerve slider and tensioner) and graded mobilization, nerve massage (longitudinal and transverse) applied to the affected nerve on thorough understanding of its neuroanatomy and neurophysiology.[7,12,13,14,10,15-17] Studies on neurodynamic treatment effects were done as nerve gliding exercises for carpal tunnel syndrome,[15,16,18,19] cubital tunnel syndrome,[17, 20] radial tunnel syndrome,[18,21] thoracic outlet syndrome,[19,22] and as neural mobilization for cervical cord compression,[20,23] cervical radiculopathy,[21,24] non radicular low back pain,[22,25] lower extremity symptoms[23, 26] and lumbar spine surgery.[24,27]

Two types of neurodynamic dysfunction were identified to be slider and tensioner dysfunction[28] (Shacklock, 2005a) based on the underlying biomechanical basis of convergence and divergence

in response to joint motion (Topp and Boyd, 2006).[29] Correspondingly two neurodynamic mobilization techniques were categorized to be sliders and tensioner techniques (Shacklock, 2005a).[28] Typically the nerve slider technique produces greater longitudinal excursion of the nerve along its bed compared to tensioner technique (Coppieters and Butler, 2008).[30]

Straight Leg Raising (SLR) test is a common neurodynamic test used for years to aid in the diagnosis of lumbar disc lesions and nerve root compression since its initial documented description by J. J. Frost in 1881 (cited in Urban, 1981).[31] The neuromechanical responses to SLR test were studied during structural differentiation manoeuvres like ankle dorsiflexion (Gajdosik et al, 1985; Hall et al, 1998; Boland and Adams, 2000; Herrington et al, 2008; Boyd et al, 2009),[32-36] cervical flexion (Hall et al, 1998),[33] pelvic rotation (Bohannon et al, 1985),[37] or hip movements (Cameron et al, 1994; Coppieters et al, 2005).[38, 39] SLR mobilization was also studied as a treatment technique in spinal surgery patients by authors earlier (Kitteringham, 1996; 27. Scrimshaw and Maher, 2001).[27, 40]

Neurophysiological effects of SLR test was studied by Ridehalgh et al[41] (2005) who examined the effects of superficial peroneal nerve tensioner technique a modified straight leg raise with plantar flexion and inversion on vibration perception thresholds (VPT) and the findings showed that the tensioner technique increased the VPT compared to sham technique but the effects were reversible within ten minutes among both runners and non-runners. Earlier study by Humphreys et al[42] (1998) on ten healthy subjects, demonstrated longer tibial nerve F-wave latencies when measured in straight leg raise position, proposedly indicating the neurophysiological effect of the SLR position and the author recommended neurophysiologic testing in nerve lengthened positions so as to elicit subtle neural involvement signs.

Earlier study by Coppieters and Butler[30] (2008) suggested that the nerve slider and tensioner techniques prove to be a valuable treatment tool in patients with neuropathies. Coppieters et al[43] (2009) also stressed the importance and safety of use of slider techniques in increasing nerve mobility and excursion without compromising neural circulation when in-vivo ultrasound imaging for median nerve was used to compare the slider and tensioner techniques. The evidence is continuously growing in favor of neurodynamic mobilization for patients with neural dysfunctions[44] (Ellis and Hing, 2008) and for patients with peripheral neuropathic pain (Nee and Butler, 2006).[45]

Bilateral leg symptoms in painful diabetic peripheral neuropathy patients are characteristically distributed in the sciatic nerve distribution. Involvement of sciatic nerve is common in PDPN which could be due to its large size and cross-sectional diameter; it is the autonomic supply for the lower limb; and it is the longest peripheral nerve in the body. Though straight leg raise tests evolved primarily as clinical diagnostic test for reproduction of patient symptoms from sciatic nerve, the SLR techniques was not studied as a treatment technique until straight leg raise mobilization has been shown to have influence on the vibration thresholds[25, 41] of the feet thus establishing evidence for neuromechanics and neurophysiology.

Studies on effects of sciatic nerve neurodynamic mobilization could not be retrieved from the existing literature. The purpose of our study was to observe the efficacy of sciatic nerve neurodynamic mobilization comprising of nerve massage and nerve sliders when added to control intervention of standard care on vibration perception thresholds, neuropathic pain severity, sciatic nerve neurodynamic test range of motion and neuropathy specific quality of life (NeuroQoL) in PDPN patients.

Materials and Methods

This Observer blinded Randomized Controlled Trial was approved by Institution Ethics committee and registered at Clinical Trials Registry- India and then conducted at Shri Rama Shakti Mission Charitable Trust and Hospital, Shakti Nagar, Mangalore in the period of four months, from January to April 2008. Thirty two patients were recruited on incidental sampling of either sex (15 male, 17 female), with mean age 60.12 ± 11. 41 years, who volunteered to participate after giving written informed consent. Subjects were deemed eligible if they were known physician diagnosed cases of Diabetes Mellitus for atleast six years; had neuropathic symptoms in both legs and feet (in sciatic nerve distribution- back of thigh and leg) for atleast 6 months; had mechanical behavior of neuropathic symptoms altered by positions and/or movements; had positive response to tibial nerve neurodynamic testing using SLR.[1] Excluded subjects (16 in number) consisted of inability of subjects to understand and/or co-operate during quantitative sensory testing and/or manual nerve mobility testing and/or treatment; Progressive worsening neurological deficit, irritable pain, allodynia/ hyperalgesia, musculoskeletal problems, cognitive maladaptation syndrome. Please refer to CONSORT

2010 flow diagram in figure-1.

Outcome measurement

Vibration thresholds VibrothermTM Biothesiometer (Diabetic Foot Kare India, Chennai): The transducer probe of the biothesiometer was placed at one of the three sites in the sole of the foot (in a randomly selected order) and then instructed to report when he/she started feeling the onset of sensation of vibration.[46] Biothesiometer assessment of quantitative sensory testing was validated highly and studied extensively for its high reliability and responsiveness.[47]

Tibial Nerve Neurodynamic Test Straight Leg Raise Test (SLR) 1: Originally proposed by Butler9, the test was done as follows; The patient lay supine on the plinth, the tester stands at the tested side lower extremity. With his distal hand performed dorsiflexion and eversion of the foot while the proximal hand performed the straight leg raise fixing the knee in extension simultaneously. The leg was lifted till the tester felt the onset of first initial resistance R1. Patient's symptom reproduction is considered to be a positive test which should again be confirmed for neural tissue involvement by structural differentiation.48 The tester once the symptom provocation was felt at the tibial nerve distribution, performed ankle plantarflexion or eversion and noted change in symptoms. Change in symptoms with structural differentiation is essential before considering neural tissue as the cause of the limitation of range of SLR. The range of SLR2 was then measured using a standard universal goniometer in degrees.

Neuropathic Pain Questionnaire: NPQ49: It was a 12-item self report questionnaire which has high sensitivity and specificity and test retest reliability for use in neuropathic pain trials. Each item has a visual analogue scale of 0 to 10 where 0 indicates no "pain" and 10 indicates "maximum or worst pain" possible for 10 different perceptions of neuropathic pain. Refer appendix-1 (reproduced with permission from authors). Score ranges from 0 to 100 where 0 denotes no neuropathic pain and 100 denotes worst neuropathic pain when scored.

Neuropathy-Specific Quality of Life Neuro QoL50: It was a 18 item self report questionnaire for measuring the quality of life in neuropathy subjects due to their foot problems. Each item had five responses ranging from "always" to "never". Another set of 3 responses which denote the importance of each item was also taken. Total score is thus obtained between 0 and 100 where 0 indicates poor quality of life and maximum score indicates good quality of life.

Interventions

After the outcome assessment by the blinded observer, the subjects were then randomized to receive either of the two interventions- control or experimental group by block randomization. The allocation was concealed from the primary investigator who administered the neurodynamic intervention.

Control group

Standard care was given by physician for patients in this group comprising of glycemic control, diet advice and palliative care for neuropathic pain. Another blinded physiotherapist prescribed group exercise of gentle active movements, 25 min walking exercise prescription to be done 5 times a week, The treatment lasted for 45 min duration.

Experimental group:

This group received in addition to standard care, neurodynamic intervention which consisted of, in the same order: Active movements of hip, knee, ankle and foot 5 reps, lasting 2 mins. Passive stretching for hip, knee, ankle and foot, each stretch held for 30 secs for plantar fascia, Gastrosoleus, hamstrings, piriformis and rectus femoris muscles, lasting 5 mins.

Sciatic nerve massage beginning with tibial nerve palpation along its course, transverse massage was given from proximal to distal. Longitudinal massage was then performed proximally and the progressing distally, lasting 3 mins. See fig 2.

Sciatic nerve Sliders: Sciatic nerve sliders were administered by simultaneous offloading of knee during hip loading and vice-versa. Subject was positioned in side lying and treating therapist performed straight leg raise upto onset of symptom. Combination of hip flexion with knee flexion and hip extension with knee extension was performed as two ended slider technique for 3 mins duration. The hip position is taken before the painful position and knee extension oscillations were performed as distal tensioner and hip flexion oscillations with knee in pre-loaded position as proximal tensioner for another 3 mins; and the session completed with active movements again for 2 mins.

Total treatment duration 45 mins. All patients were seen at same time of the day, 10 am to 12 noon, to avoid influence from any diurnal variations

on the outcome measures or on the responses to testing and interventions. The patients were then instructed to comply with home programme which was indicated by giving patient log. The independent observer collected the data twice- pre and post intervention for all the subjects.

Data analysis

All outcomes were analysed for their pre and post differences in within-subject comparisons using students' t-test at 95% confidence interval using SPSS 16.0 for Windows.

Results

Descriptive statistics

Comparison of patient characteristics between control and experimental groups.

	Control group	Experimental group	P- Value
Number of subjects	16	16	1.000
Age (years)	57.43 12.04	62.81 10.43	.187
Gender Male (female)	7 (9)	6 (10)	.723
Duration of Neuropathic pain (years)	3.75 ± 2.23	3.00 ± 1.75	.299
NPQ pre	61.53 ± 12.76	59.99 ± 12.06	.729
NeuroQoL pre	64.06 ± 13.79	61.50 ± 13.51	.599
Vibration Thresholds pre (volts)	34.75 ± 2.38	34.21 ± 2.38	.533
SLR1 ROM pre	17.5 ± 11.83	19.37 ± 10.14	.634

All comparisons between the two groups were not statistically significant at p <.05. The two groups were comparable before intervention.

Inferential statistics

Mean Differences	Control group	Experime-ntal group	Between group Difference	P- Value
NPQ (pre- post)	9.61 ± 4.69	28.5 ± 7.15	18.89 ± 2.46	.000*
NeuroQoL (pre- post)	12.7 ± 3.99	28.63 ± 6.84	15.93 ± 2.85	.000*
Vibration Thresholds (pre- post) volts	10.56 ± 2.22	16.5 ± 3.14	5.94 ± 1.12	.000*
SLR1 ROM (pre- post) degrees	-4.62 ± 2.94	-8.62 ± 5.79	4.00 ± 3.85	.020*

*- Statistically significant at p<.05

Neuropathic Pain Questionnaire

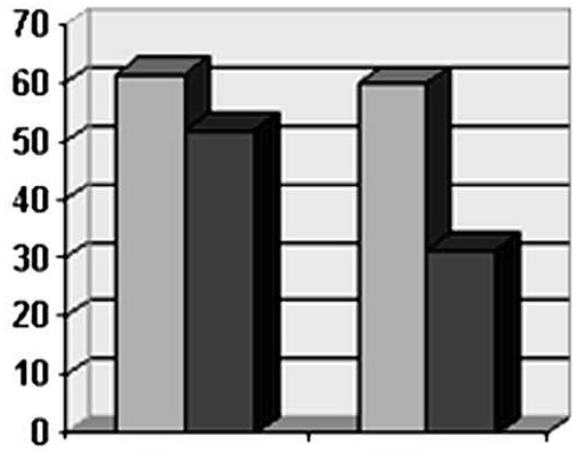

Fig. 1: Control Group Experimental Group.

Neuropathy Specific Quality of Life

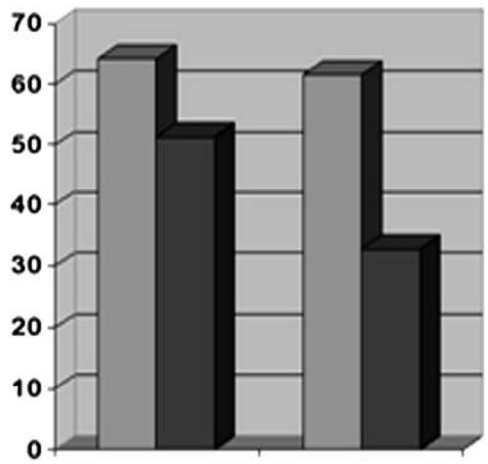

Fig. 2: Control Group Experimental Group.

Vibration Thresholds

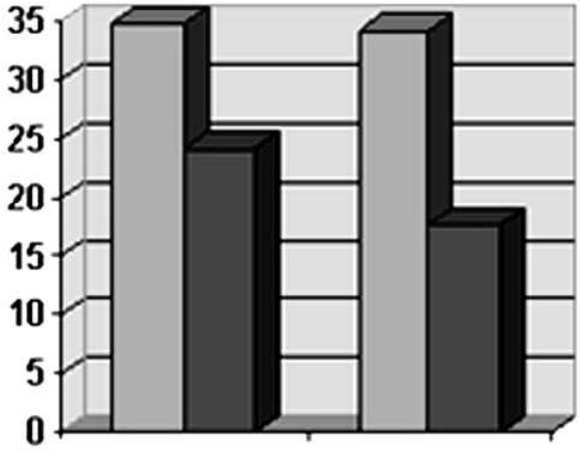

Fig. 3: Control Group Experimental Group.

Sciatic Nerve Neurodynamic Test Range of Motion

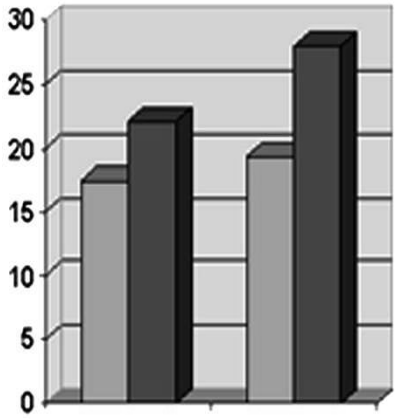

Fig. 4: Control Group Experimental Group.

Discussion

The study had important observations; Both the groups showed statistically significant improvements in all the four variables studied, which may be attributable to the standard care (glycemic control, palliative care, diet and exercise prescription) that subjects received might have influenced the recovery of the peripheral neuropathic pain in these subjects, as it was found in other studies.[51,52] The experimental group however had a statistically significant large treatment effect when compared the control group which can only be attributable to the neurodynamic mobilization the subjects received, thus rejecting the null hypothesis. TENS Transcutaneous Electrical Nerve Stimulation was another physical therapy modality of choices which had been studied earlier[53,54,55] was not given in this study due to community setting, and weekly follow-up which conflicted with the prescription dosage of TENS. The study had its own limitations; The confounding effect of placebo could not be ruled out in experimental group, due to the direct touch and its effects on patient perception as a manually applied technique of neurodynamic mobilization. However, use of placebo56 in neuropathic pain trials was more indicated for drug trials[57] than for others.

The following are the significance of this study; the first of its kind in neurodynamic mobilization and its clinical reasoning based application in so called presumably contra-indicated in regular settings. The neurophysiological effects were studied using vibration thresholds, and adoption of quality of life measure showed it had an impact on their way of life.

The combination of nerve massage, nerve sliders and nerve tensioners was never before been applied in clinical trials of neurodynamics. This opens up a new research scope for the effects of nerve sliders and tensioners in various other pathologies as well as claimed by other researchers58. Clinically, the sliders were well tolerated by the subjects and they showed within session improvements both qualitatively and quantitatively. The straight leg raise test 2 or tibial nerve neurodynamic test mobilization involved the component of SLR[59] added, which again might have mobilized the proximal trunks of sciatic nerve to exert an indirect influence on the tibial nerve. Future studies are warranted in other neuropathic pain syndromes, other peripheral nerves, measuring outcomes such as longitudinal nerve motion[60] using ultrasonography, nerve conduction studies.

Conclusion

Sciatic nerve neurodynamic mobilization in addition to standard care was better than standard care alone in type II diabetes mellitus subjects with peripheral neuropathic pain. Sciatic nerve neurodynamic mobilization should be considered as an effective treatment adjunct to standard care in treatment of neuropathic pain symptoms in type II diabetes mellitus patients.

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