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COMPARATIVE EFFECTS OF INTRANEURAL FACILITATION THERAPY AND NERVE FLOSSING TECHNIQUE ON PAIN, BALANCE, GAIT, AND QUALITY OF LIFE IN PATIENTS WITH DIABETIC PERIPHERAL NEUROPATHY: A RANDOMIZED CLINICAL TRIAL

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ABSTRACT

Background: *Diabetic peripheral neuropathy (DPN) impacts >50% of type 2 diabetes patients, leading to microvascular ischemia, neuropathic pain, and functional impairments in balance and gait. Intraneural Facilitation (INF) therapy is a manual technique that reduces endoneurial hypoxia, while the Nerve Flossing (NF) technique enhances neurodynamics through mechanical mobilization. This study compared the effects of INF therapy and NF techniques on pain, balance, gait, and quality of life in patients with diabetic peripheral neuropathy.* ***Methods:*** *This randomized clinical trial employed a non-probability, convenience sampling technique, in which 44 patients with diabetic peripheral neuropathy were randomly allocated to Group A (INF = 22) and Group B (NFT = 22) using a computer-generated method. Interventions were performed in both groups for 50-60 minutes, three times a week, over 8 weeks, and a follow-up was conducted after 2 months. Pain was measured using the Numeric Pain Rating Scale, Balance using the Berg Balance Scale, Gait with the Dynamic Gait Index, and Quality of life was assessed using the QOL-DN Questionnaire. For the between-group comparison, the Mann-Whitney U test was used, and for the within-group comparison, the Friedman test was used.* ***Results:*** *The trial reported that INF significantly improved pain scores ($p = 0.01$), quality of life ($p = 0.018$), and balance ($p = 0.02$) at 16 weeks compared to NFT. Gait also showed significant enhancement ($p=0.001$), with INF demonstrating superior efficacy.* ***Conclusion:*** *The study reported that both INF and NFT improve pain, balance, gait, and quality of life in patients with diabetic peripheral neuropathy. However, INF demonstrated superior results, particularly in reducing neuropathic pain, enhancing balance and gait, and improving quality of life.*
Keywords: *diabetic peripheral neuropathy; gait; intraneural facilitation therapy; pain; type 2 diabetes; quality of life.*

INTRODUCTION

Diabetic peripheral neuropathy is the most common microvascular sequela of diabetes, and 50% of patients with diabetes eventually develop neuropathy during their illness. (1) Pain, diminished endurance, numbness, paresthesia, decreased coordination, muscle weakness, and impaired balance are among the many symptoms that many of the patients with diabetes mellitus are currently experiencing when they visit the physical therapy clinic. (2-4) Worldwide healthcare spending in 2017 for individuals aged 20-79 was approximately 727 billion dollars. (5)

Diabetes is reaching epidemic proportions, as evidenced by the 2021 IDF Diabetes Atlas, which reported that one in ten adults has the condition, necessitating concerted efforts toward prevention and management. (6) According to the IDF 2021, Pakistan has the highest prevalence of diabetes worldwide (26.3%). The country has the third-greatest number of diabetic patients worldwide, after China (140 million) and India (74 million), with one in four people living with the disease. (6) In Pakistan, peripheral neuropathy is primarily caused by diabetes. The total prevalence of DPN was found to be 43.16%. The subgroup meta-analysis revealed that Khyber Pakhtunkhwa had the greatest prevalence of DPN (55.29%), followed by Sindh (40.04%), and Punjab had the lowest (34.90%). (7) The estimated monthly overall cost of diabetes management in Pakistan is Rs 36,577,200,000, with the potential to increase if hospitalization expenses are included. The estimated average cost is approximately 5542 rupees. (8)

Peripheral nerves are encased in perineurium, which permits only a few transperineurial arterioles to infiltrate the endoneurium. (9) Peripheral nerves typically have a restricted circulatory supply, making them more susceptible to ischemia. (9) Endoneurial microangiopathy, demyelination, and axonal degeneration of myelinated fibers in the nerve, and degeneration with regeneration of unmyelinated fibers are physical manifestations of diabetic neuropathy. (9, 10) Currently, the pathogenesis of DPN remains controversial, particularly regarding the role of microvascular changes. Blood and oxygen deficiency resulting from microvascular changes are believed to contribute to the progression of DPN. The sciatic nerve has also been shown to exhibit endothelial cell dysfunction brought by reduced neural blood flow and intraneural oxygen tension. (11, 12) Degeneration of pericytes, thickening of the microvascular basement membrane within the nerve, proliferation and swelling of the vascular endothelium, and a decrease in vascular tight junction-associated proteins were among the other aberrant vasculature alterations seen in the peroneal nerve of DPN patients. The peripheral nerve tissue will subsequently experience ischemia and hypoxia as a result of these aberrant alterations, which will also narrow the arteries and reduce blood flow. (13, 14) The neural microenvironment's hypoxia will worsen the inflammation and oxidative stress, harming Schwann cells and neurons and resulting in nerve damage. (15)

The American Diabetes Association suggests using medications to manage pain from DPN. However, despite ongoing research, these medications only provide limited relief and haven't shown significant success in slowing the progression of the disease itself. Numerous non-pharmaceutical techniques, such as infrared therapy, shoe magnets, Reiki therapy, exercise, acupuncture, transcutaneous electrical nerve stimulation, spinal cord stimulation, and biofeedback behavioral therapy, have been employed to enhance neural circulation and mitigate the impairing effects on nerve axons in type 2 diabetes mellitus (T2DM). Although both pharmacologic and non-pharmacologic therapies may occasionally improve functions and relieve symptoms, there is still no definitive cure. (16)

INF Therapy represents an innovative manual intervention that originated in South Carolina and was introduced to Loma Linda University in 2011. The three simultaneous goals of this therapeutic approach are to restore perfusion to the ischemic nerve through a sequence of manual holds performed by a practitioner(17). This strategy seeks to enhance endoneurial capillary circulation, bias blood flow into the neural fascicle, and reverse intrafascicular ischemia. To redirect blood to the ischemic nerves, this passive approach involves skin traction, visceral tissue distention, muscle stretching, joint mobilization, and stretching blood vessels. (18)

The Nerve Flossing Technique, as proposed by Shacklock. M is an active treatment approach that offers conservative benefits through physiological and mechanical means. This evidence-based treatment approach aims to enhance neurodynamics, improve the range of motion, and enhance the quality of life. (19) Shacklock outlined two primary NM approaches: neuromobilization gliding (NG), characterized by mobilizing the nerve through alternating sliding movements across at least two joints, thereby tensioning the peripheral nervous system while simultaneously reducing nervous system tension through movement at another joint; and neuromobilization stretching (NS), which entails the coordinated movement of two joints, with one joint loading the nervous system while the other increases tension on it. (20) Neuromobilization exercises involve the movement of peripheral nerves along their respective paths. One or both ends of the nerve pathway may initiate these movements. Studies have shown that nerve flossing exercises, which begin with a single joint movement at one end of the nerve pathway, produce much less nerve excursion than exercises that begin at both ends of the nerve and involve multiple joints. (20)

Microvascular ischemia, which causes small-fiber degeneration and subsequent perineural fibrosis, which limits axonal glide, are the two interdependent pathways by which diabetic peripheral neuropathy (DPN) advances. Nerve Flossing (NFT) technique reduces secondary mechanical dysfunction caused by adhesions, whereas Intraneural Facilitation (INF) therapy directly addresses endoneurial hypoperfusion, the main insult in DPN. This randomized controlled trial explores a key challenge in treating advanced DPN, determining whether restoring blood flow (through intraneural facilitation therapy) or improving nerve mobility (via neural flossing techniques) plays a bigger role in functional recovery. The study findings provide a pathology-stratified framework by quantifying differential effects on pain, balance, gait, and QOL in patients with fibrotic restrictions who may respond better to NFT, than those with predominant microvascular compromise may benefit more from INF. Clinical judgment in DPN management may be improved by this paradigm shift from generic to mechanism-targeted rehabilitation. This study aims to compare the impacts of INF therapy and NFT on key parameters, including pain, balance, gait, and overall QOL in DPN patients. This research might provide valuable insights for physical therapists, ultimately offering a non-pharmacological intervention that can significantly improve the lives of individuals living with DPN.

2. Materials and Methods:

2.1. Study Design and Setting:

This study followed a non-probability convenience sampling technique, a randomized clinical trial design conducted at the Siddique Family Hospital and Jinnah Hospital, Gujranwala, Pakistan, between September 2024 and July 2025. The trial adhered to the CONSORT 2010 guidelines of a randomized clinical trial. Ethical approval was obtained from the Research and Ethical Review of Riphah College of Rehabilitation and Allied Health Sciences, and the study was registered on ClinicalTrials.gov (NCT06663670) prior to enrollment. The full study protocol is publicly available on ClinicalTrials.gov.

2.2. Participants:

Adults aged 50-75 years were eligible for inclusion. Inclusion criteria were: (1) Patient with type 2 diabetes mellitus (diagnosed by the physician) (21, 22); (2) Patient score >3 on Michigan Neuropathy Screening Instrument-Questionnaire and score >2 on MNSI-Physical Examination (23); and (3) Patient with diabetic peripheral neuropathy symptoms below the ankle (numbness, tingling, burning, sharp pain, increased sensitivity, etc.) (10). Exclusion criteria included: (1) Patient with the presence of any other systemic disease other than diabetes, such as end-stage renal failure, uncontrolled hypertension, severe dyslipidemia, chronic liver disease, autoimmune disease, advanced chronic obstructive pulmonary disease, etc. (10, 22); (2) Patient with a diabetic ulcer in either foot. (24); (3) Patient with total or partial amputation of lower extremities. (21, 22); (4) Patient who has active inflammations or other inflammatory neuropathies, such as autonomic neuropathies, proximal diabetic neuropathy, chemotherapy-induced peripheral neuropathy, chronic inflammatory demyelinating polyneuropathy, or other neuropathies unrelated to diabetes mellitus, like B12 deficiency. (10); and (5) Patient has a history of nerve injuries from fractures, strains, or trauma within the past 12 months. (24) All participants who qualified provided their informed consent, and then they were briefed about the intervention. A total of 44 participants met the eligibility criteria and enrolled in the study (55% female; 45% male).

2.3. Randomization and Blinding:

Participants were randomly assigned to either the INF therapy group or NF technique group using an online research randomizer tool, accessible at (https://www.randomizer.org/), after baseline assessment. Information was input, including the total number of participants, the number of groups, and the number of participants in each group. Due to the nature of the intervention, the therapist could not be blinded; however, the outcome assessor administering the NPRS, BBS, DGI, and the Quality of Life DPN questionnaire, and the data analysts remained blinded to treatment assignment throughout data collection and analysis.

2.4. Intervention:

2.4.1. Intraneural Facilitation (INF) Therapy along with Home care plan:

Participants in the INF therapy group received 24 sessions delivered three times per week over eight weeks, with each session lasting 60 minutes. Intraneural facilitation therapy represents a groundbreaking manual physical therapy method supported by anecdotal data indicating a reduction in symptoms associated with peripheral neuropathy. (25) INF aims to enhance the connection between macrocirculation and microcirculation, leading to a rise in neurovascular pressure that effectively counteracts the resistance of neural capillaries induced by diabetes. (22) INF postulates that this goal can be accomplished through a system consisting of three holds.

- The initial hold, known as **the facilitation hold**, entails positioning the contralateral joint in the most comfortable loose-pack position. Placing the ankle joint on the opposite side in full plantar flexion and inversion serves as an example of this. A stretch strap was used to maintain this position during the entire session. It is crucial to emphasize that there is only a slight stretch in the joint where the facilitation occurs and no muscle engagement. (25) It is hypothesized that this widens the opening of the arterial connection, allowing more blood flow into the epineurium, due to the increased neural excursion relative to which artery elongates the coiled nourishing vessel connecting the artery and the nerve. Theoretically, this causes the epifascial vascular pressure to rise. (10, 25, 26)
- Once the pressure elevation occurs, the subsequent phase, known as the **secondary hold,** is initiated to direct the augmented flow of epineurial blood toward the transperineurial vessels connecting the epineurial capillaries and the endoneurial capillaries of the target area. (25)
- The final maneuver, the **sub hold**, leverages Bernoulli's principle to augment blood flow through the ischemic endoneurial capillaries experiencing heightened transmural pressure. The third hold, which uses bolsters and pressure points away from the secondary hold, creates a kind of microvascular vacuum and promotes distant circulatory flow. (22, 25)

2.4.2. Nerve flossing Technique along with Home care plan:

The participants received the nerve flossing technique, administered in three sets of 30 repetitions, with a 5-minute interval between sets. A total of 24 sessions were conducted over eight weeks (three sessions per week), with each session lasting between 50 and 60 minutes.

For the Tibial nerve

- **Remote Sliders:** The therapist began by positioning the patient's ankle into dorsiflexion and eversion, then gently guided the hip into flexion while attentively monitoring for any reproduction of symptoms or discomfort. Upon identifying the point at which symptoms emerged, the therapist slightly lowered the hip just enough to reach a symptom-free position and allowed the patient to remain comfortable. From this adjusted position, the knee was moved into flexion to offload tension on the tibial nerve, while maintaining ankle dorsiflexion and eversion to continue neural engagement. To complete the sequence, the therapist returned the knee to extension, thereby reapplying neural tension, while simultaneously shifting the ankle into plantarflexion to reduce tibial nerve stress.
- **Local Sliders:** The therapist initially positioned the patient's ankle into dorsiflexion and eversion, then passively moved the hip into flexion while maintaining the knee in extension. Throughout this movement, careful attention was given to detect any onset of symptoms or pain. Once symptoms were elicited, the hip was slightly lowered to achieve a symptom-free position. From this adjusted position, the therapist proceeded to move the hip further into flexion, unloading the tibial nerve while maintaining ankle dorsiflexion and eversion to sustain neural loading. To complete the sequence, the hip was returned to extension, reintroducing neural tension, while the ankle was moved into plantarflexion to reduce tibial nerve stress.
- **Tensioners:** The therapist gently lifted the patient's leg off the table, maintaining the hip in flexion and the knee in extension to position all non-moving joints in a sustained stretch. Once this posture was established, the ankle was carefully moved into dorsiflexion and eversion to apply neural loading, then gradually released into plantarflexion to unload the neural structures. (24, 27)

For the Common peroneal nerve

• **Remote sliders:** The therapist began by positioning the patient's ankle into plantarflexion and inversion, then passively moved the hip into flexion while closely monitoring for any onset of symptoms or pain. Upon eliciting symptoms, the hip was gently lowered by a few degrees to reach a symptom-free position. From this adjusted posture, the therapist flexed the knee, offloading the peroneal nerve while maintaining ankle plantarflexion and inversion to continue neural loading. To complete the sequence, the knee was extended, thereby reapplying neural tension, while the ankle was moved into dorsiflexion to unload the peroneal nerve.

• **Local Sliders:** The therapist began by positioning the patient's ankle into plantarflexion and inversion, followed by a passive movement of the hip into flexion while keeping the knee fully extended. Throughout this process, the therapist closely observed for the emergence of any symptoms or discomfort. Upon identifying a symptom-free position, the hip and knee were held steady. From this position, the therapist then moved the hip further into flexion to unload the peroneal nerve, while simultaneously maintaining ankle plantarflexion and inversion to apply neural tension. To complete the sequence, the hip was returned to extension, thereby reloading the nerve, as the ankle was moved into dorsiflexion to relieve the neural stress.

• **Tensioners:** The therapist gently lifted the patient's leg off the table, maintaining the hip in flexion and the knee in extension to create a stretch position across all non-moving joints. With the limb stabilized, the ankle was then guided into plantarflexion and inversion to apply a neural load, followed by a controlled transition into dorsiflexion to release the tension and facilitate unloading. (24, 27)

2.5. Outcome Measures:

The Michigan Neuropathy Screening Instrument was used as a screening tool to determine the severity of Diabetic peripheral neuropathy. (28) The assessment tool's first section consists of a self-administered questionnaire with 15 yes-or-no questions about foot sensation, covering topics like discomfort, numbness, and temperature sensitivity. The next section involves a brief physical examination, which includes visually inspecting the feet, testing ankle reflexes with a tendon hammer, measuring vibration perception with a 128 Hz tuning fork, and assessing tactile sensation with a 10 g Semmes-Weinstein Monofilament (SWM). A score greater than 3 on the MNSI-Q and greater than 2 on the MNSI-PE suggests diabetic peripheral neuropathy. (29)

The primary outcome measure was pain assessed by the **Numeric Pain Rating Scale**. According to the NPRS, 0 denotes no pain, 1–3 mild pain, 4–6 moderate pain, and 7–10 severe pain. NPRS was administered at baseline (Visit 1), 8 weeks (Visit 24), and follow-up after 2 months. (30)

The secondary outcome measures were balance, gait, and quality of life. Balance was assessed using the **Berg Balance Scale**, which includes tasks such as reaching forward, standing, and sitting unsupported, as well as putting the alternating foot on a stool. The maximum possible score is 56 points, with each of the 14 items being scored on a 5-level ordinal scale ranging from 0 ("unable to perform or requiring help") to 4 ("normal performance"). (31) BBS was administered at baseline (Visit 1), 8 weeks (Visit 24), and follow-up after 2 months.

The **Dynamic Gait Index,** an ordinal scale ranging from 0 to 3, is used to score each item; a higher score denotes superior performance of the given task. A total score of 12 is assigned to the test. (32, 33) DGI was administered at baseline (Visit 1), 8 weeks (Visit 24), and follow-up after 2 months.

The **Norfolk QOL-DN** instrument is an extensive and validated 47-item questionnaire that covers the full range of DN symptoms associated with small fibers, large fibers, and autonomic neuropathy. It is divided into two sections, one of which focuses on the symptoms that diabetic patients face, and the other on how the patient's neuropathy impacts their ADLs. Overall QOL, symptoms, ADLs, physical functioning (large fibers and small fibers), and autonomic neuropathy are the six domains into which the items are categorized. In most domains, intra-class correlation coefficients for the Norfolk QOL-DN reach 0.9, indicating a comparatively strong reliability profile. Evaluation of internal consistency for the fiber-specific domains revealed a Cronbach's alpha of 0.60-0.80. (34, 35) QOL-DN was administered at baseline (Visit 1), 8 weeks (Visit 24), and follow-up after 2 months.

2.6. Sample Size and Power Analysis:
Power analysis (G*Power v3.1.9.7) indicated that 36 participants would be required to detect a significant difference in the Berg Balance Scores between groups, with an α level of 0.05 and a study power of 0.95. To account for an anticipated 20% attrition rate, the target sample size was increased to 44 participants, with approximately 22 patients with diabetic peripheral neuropathy allocated to each group.

2.7. Statistical Analysis:
The data was analysed using IBM SPSS Statistics version 27 for Windows software. The normality of the data was assessed through the Shapiro–Wilk test. Within-group differences were analysed with repeated measures ANOVA for parametric data, and the Friedman test for non-parametric data. Between-group comparisons were assessed with an independent samples t-test for parametric data, and the Mann–Whitney U test for non-parametric data. Effect sizes were calculated using Cohen's d. Statistical significance was set at $p \leq 0.05$.

3. Results:
The planned sample size was 44 participants aged 50-75 years with diabetic peripheral neuropathy. Recruitment occurred from September 2024, and all follow-up assessments were completed by July 2025. A total of 36 participants were enrolled and completed the study (INF therapy group, n = 18; NF technique group, n = 18). (Figure 1)

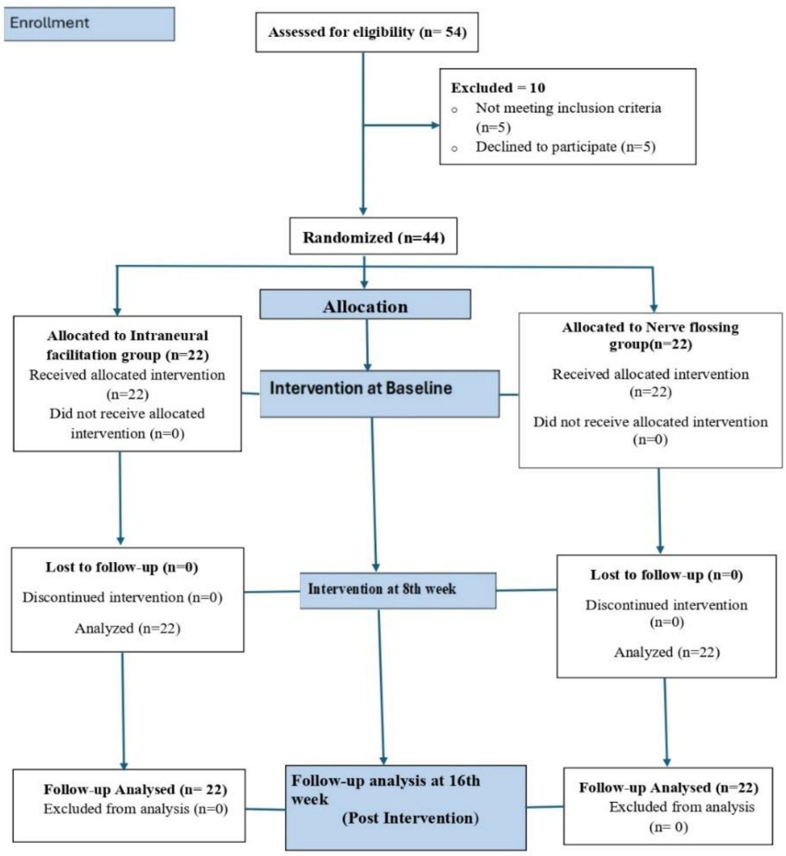

Figure 1. CONSORT flow diagram of participant recruitment, allocation, and follow-up.

Baseline demographics and clinical characteristics were comparable between groups (Table 1).

Table 1: Demographic information of study participants

		Intraneural Facilitation Therapy		Nerve Flossing Technique		Total	
Variables	Levels	N	%	n	%	N	%
Gender	Male	11	50	9	40	20	45
	Female	11	50	13	60	24	55
Age years *M±SD*		63.55±4.06		60.95±4.26		62.25±4.31	
	55-59	3	14	10	45	13	30
	60-64	10	45	8	36	18	40
	65-69	9	41	4	18	13	30
Height cm *M±SD*		166.95±10.75		171.6±11.61		169.28±11.29	
	150-159	7	32	3	14	10	23
	160-169	7	32	4	18	11	25
	170-179	6	27	10	45	16	36
	180-189	2	9	5	23	7	16
Weight kg *M±SD*		69.35±20.24		72.35±20.8		70.85±20.3	
	40-59	8	36	8	36	16	36
	60-79	3	14	0	0	3	7
	80-89	7	32	10	45	17	39
	90-109	4	18	4	18	8	18
BMI							
	Underweight <18.5	3	14	7	32	10	23
	Normal weight 18.5–24.9	9	41	4	18	13	30
	Overweight 25.0–29.9	5	23	4	18	9	20
	Obesity Class I 30.0–34.9	5	23	7	32	12	27
HbA1c Level							
	7.1%-8.0%	11	50	11	50	22	50
	Above 8.0%	11	50	11	50	22	50

Table 1 describes the demographics of the 44 participants who participated in this study, of whom 36 completed the study. Out of 44 participants in both groups of INF and NFT, 20 were males, and 24 were females. 13 participants were in the age group 55-59 years in both groups, 18 participants were in the age group 60-64 in both groups, and 13 were in the age group 65-69 in both groups. 10 participants were underweight, 13 were normal weight, 9 were overweight, and 12 were in the category of obese. 22 had HbA1c levels of 7.1 – 8.0, and 22 had HbA1c levels of more than 8.0

Table 2: Between-Group Comparison of Michigan Neuropathy Screening Instrument Scores

Time	INF (Mean ± S.D)	NFT (Mean ± S.D)	P-value
Baseline	9.15 ± 1.31	10.00 ± 1.45	0.051
8th week	3.65 ± 0.81	3.95 ± 1.00	0.445
16th week	1.70 ± 1.13	2.80 ± 0.83	0.002*

Table 2 describes the between-group comparison of MNSI scores, which indicates a significant difference at the 16th week with a P value of 0.002

Table 3. Between-Group Comparison of Quality of Life in Diabetic Neuropathy Scores

Time Point	INF (Mean ± SD)	NFT (Mean ± SD)	P-value
Baseline	74.45 ± 7.98	75.10 ± 8.46	0.804
8th week	36.05 ± 9.13	43.65 ± 10.64	0.200
16th week	31.00 ± 9.92	39.55 ± 11.86	0.018*

Table 3 describes between-group comparisons of Quality of Life in Diabetic Neuropathy Scores, which shows a significant difference between the two groups at week 16 with a P value of 0.018

Table 4. Combined Between-Group Comparison of Pain, Balance, and Gait Outcomes at Baseline, 8th Week, and 16th Week.

Outcome Measure	Time Point	INF (Mean ± SD)	NFT (Mean ± SD)	P-value	Effect Size
NPRS	Baseline	7.75 ± 0.97	7.35 ± 0.75	0.152	–
	8th week	2.05 ± 1.10	2.50 ± 1.24	0.236	–
	16th week	1.25 ± 1.02	2.20 ± 1.01	**0.010***	Moderate
BBS	Baseline	27.95 ± 5.52	27.00 ± 4.77	0.152	–
	8th week	42.55 ± 2.86	41.65 ± 5.20	0.502	–
	16th week	46.35 ± 2.81	43.70 ± 3.95	0.020*	Moderate
DGI	Baseline	4.00 ± 0.86	3.95 ± 1.00	0.776	–
	8th week	8.35 ± 1.42	8.20 ± 1.11	1.000	–
	16th week	10.65 ± 1.37	9.50 ± 0.95	0.001*	Large

Table 4 presents the between-group comparison of pain intensity, balance, and gait performance measured using the Numeric Pain Rating Scale (NPRS), Berg Balance Scale (BBS), and Dynamic Gait Index (DGI), respectively, at baseline, 8 weeks, and 16 weeks. At baseline, no statistically significant differences were observed between the Intraneural Facilitation (INF) therapy group and the Nerve Flossing Technique (NFT) group for any outcome measure ($p > 0.05$), indicating baseline comparability between groups.

Both groups demonstrated improvements in pain, balance, and gait over time. However, at the 16-week follow-up, the INF group showed significantly greater reductions in pain compared to the NFT group, with mean NPRS scores of 1.25 ± 1.02 and 2.20 ± 1.01, respectively ($p = 0.010$). Similarly, balance outcomes measured using the BBS revealed a statistically significant between-group difference at 16 weeks, favouring the INF group (46.35 ± 2.81) over the NFT group (43.70 ± 3.95; $p = 0.020$).

Gait performance, assessed using the Dynamic Gait Index, improved in both groups across the intervention period. While no significant between-group differences were observed at baseline or at 8 weeks ($p > 0.05$), the INF group demonstrated significantly superior gait performance at 16 weeks, with a mean DGI score of 10.65 ± 1.37 compared to 9.50 ± 0.95 in the NFT group (p = 0.001).

4. Discussion:

Recent research advancements have demonstrated the unique mechanism of Intraneural Facilitation therapy in patients of diabetic peripheral neuropathy, which seeks to enhance endoneurial capillary circulation, bias blood flow in the neural fascicle, and reverse intrafascicular ischemia. To redirect blood to the ischemic nerves, this passive approach involves skin traction, distention of visceral tissues, muscle stretch, joint mobilization, and stretching of blood vessels. (18) The observed clinical benefits of the nerve flossing technique have been explained through several theories, including central effects like improving the motor's functional outputs and physiological effects like removing intraneural edema. (36) Enhancing neurodynamics, range of motion, and quality of life are the aims of this treatment strategy. (37) In recent years, increasing cases of diabetic peripheral neuropathy have led to increased research in its management. To the best of the authors' knowledge, no study has yet examined the comparative effects of intraneural facilitation therapy and nerve flossing technique on diabetic peripheral neuropathy. A well-designed protocol was used based on the clinical manifestations of diabetic peripheral neuropathy. The current study, the first of its kind, was conducted to compare the effects of intraneural facilitation therapy and the Nerve flossing technique on pain, balance, gait, and quality of life in Diabetic peripheral neuropathy.

The analysis showed no significant difference in baseline demographic characteristics of either group, confirming the random assignment of study participants in the INF or NFT groups. The baseline pain intensity measured using a Numeric Pain Rating Scale (NPRS) was almost comparable before the intervention. The findings of the current study reported a significant decrease in pain intensity in both the INF and NFT groups over time. But the decrease was greater in the INF group, with a p-value of 0.01 by the 16th week. The result of this study was statistically better in pain reduction in the INF group (p=0.01), while Kyan et al. (2022) reported comparable baseline scores (INF: mean3.76; Sham: mean4.27) with greater but non-significant reduction in the INF group (p>0.05). Both studies observed INF's particular effectiveness for severe pain (>7 NPRS), with the Kyan INF group showing complete resolution of severe pain. The improved outcome in the study was due to greater treatment sessions (24 sessions over 8 weeks versus 9 sessions over 3 weeks). (22)

The present study demonstrated a significant enhancement in balance, as assessed using the Berg Balance Score (BBS), among diabetic peripheral neuropathy patients undergoing INF therapy by week 16, compared to those in the NFT group, with a p-value of 0.02. The current study findings are in line with earlier investigations, supporting the therapeutic advantage of INF in improving balance in patients with diabetic peripheral neuropathy. Analogous research has indicated a notable enhancement in balance for individuals receiving INF therapy. For instance, using computerized dynamic posturography, Alshahrani et al. (2016) demonstrated that INF was more effective than conventional therapy, improving balance scores by 28% (p=0.01). (25) While standard neural mobilization primarily affects nerve mobility alone, INF's proposed dual mechanism of action may be responsible for the different results. It simultaneously addresses neural microcirculation and improves proprioceptive feedback. (17)

In the current study, the INF and NFT groups showed significant improvement in balance and gait, but the INF group demonstrated superior gains by week 16, with higher BBS and DGI scores (p<0.001). These results align with Sharma and Kalia (2023), who reported significant improvements in BBS (from 40.5 to 47.5, p<0.001) and DGI (from 13.35 to 18.60, p<0.001) following tibial nerve mobilization combined with gait training. (38) While they also assessed mobility with TUG and sensory function using VPT, the consistent improvements in BBS and DGI across both studies support the role of neural mobilization in enhancing postural stability and gait. Their finding further suggest that combining nerve technique with functional training can yield broader sensory and motor benefits, paralleling the more pronounced outcomes seen in our INF group. A significant study by Kyan Zahra-Shahba et al. (2021) shows that INF significantly improves gait parameters (p<0.05) in patients with moderate-to-severe diabetic peripheral neuropathy, compared to sham treatment. Their results showed that after a 3-week intervention period, INF improved dynamic gait index scores by 32%, suggesting INF's potential to treat neuropathic gait abnormalities. (10) These findings are strongly supported and extended by the current study results (p=0.001). The current study found that, for a 16-week intervention protocol, INF therapy improved gait more than NFT, especially in dynamic stability measures.

The results of this investigation showed that INF therapy produced significantly greater improvement in QOL with DPN compared to NFT, with the differences becoming statistically significant by the 16 weeks ($p = 0.018$). The findings of the current study are supported by Kyan Zahra-Shahba et al. (2022), who similarly found INF significantly improved QOL-DN scores ($p<0.05$) in patients with diabetic peripheral neuropathy. (22) A study reported by Ashoori et al. confirmed that neurodynamics techniques (similar to NFT) improved neuropathy-related QOL, though their study lacked direct comparison with INF therapy. (39) Our current study results imply that although NFT offers significant advantages, INF's dual mode of action, combining vascular and neuromuscular effects, produces better long-term results. Bussell et al. (2025) provided additional support for this, demonstrating that INF can restore endoneurial microcirculation ($p = 0.000$), which probably adds to its increased effectiveness. (17)

Up to the researcher's knowledge, this is the first randomized clinical trial to systematically demonstrate that intraneural facilitation therapy (INF) produces better pain reduction and quality-of-life improvements in diabetic peripheral neuropathy (DPN) when compared to standard nerve flossing technique (NFT). This confirms that ischemia-targeting mechanisms are clinically significant. This study also fills a significant gap in the literature by offering new evidence that NFT, although effective in compressive neuropathies, is ineffective in metabolic neuropathies like DPN. Neuropathic pain characteristics in adults with DPN were significantly reduced in the short term by both INF therapy and NFT. When exercise participation is low, INF therapy may be useful as a passive adjunct or substitute, as evidenced by the wider within-group improvements. These results lay the groundwork for more extensive mechanistic experiments integrating microvascular and clinical results.

Limitations:

This study has several limitations. A comparatively small sample size was used in the study, which could limit generalizability to larger diabetic populations and lower statistical power. The absence of long-term follow-up to evaluate the sustainability of treatment effects, and the intervention period was restricted to 16 weeks. Convenience sampling from two centers limits generalizability to diverse diabetic populations (e.g., HbA1c levels). Lack of nerve conduction studies or microvascular imaging to objectively verify INF's proposed mechanism (endoneurial perfusion). Despite blinding of assessors, therapist bias could not be eliminated, given that treatment providers are aware of the group allocation.

5. Conclusion:

Intraneural Facilitation (INF) therapy and the Nerve Flossing technique are both efficacious interventions for alleviating pain, as well as enhancing balance, gait, and overall quality of life in patients with diabetic peripheral neuropathy. NF technique remains an important part of rehabilitation because it offers numerous functional benefits. On the other hand, INF therapy is a promising passive treatment that may more directly address problems with the neural and microvascular systems. In particular, INF therapy produced more substantial and sustainable improvements in neuropathic pain reduction, dynamic balance, gait performance, and improved quality of life, indicating increased efficacy in symptom modulation and functional recovery, according to comparative analysis. This study emphasizes the potential benefit of focused interventions that address both systemic and localized causes of neuropathic impairment by combining the results of the current trial with the body of knowledge regarding INF therapy and NFT. For the long-term management of diabetic peripheral neuropathy, additional research using objective assessment methods such as near-infrared spectroscopy is necessary to clarify mechanistic pathways, investigate potential synergistic effects, and optimize integrative treatment strategies.

Author Contributions:

The authors confirm their contribution to the paper as follows: **Dr. Amina Nazir,** Study conception, data collection, statistical analysis, manuscript writing, and editing; **Dr. Hira Jabeen,** data interpretation, and critical revision of the manuscript. All authors reviewed and approved the publishing version of the manuscript.

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Conflict of Interests:
The author declares no conflicts of interest in the publication of the paper.

Abbreviations:
The following abbreviations are used in this manuscript:

DPN	Diabetic Peripheral Neuropathy
T2D	Type 2 Diabetes
INF therapy	Intraneural Facilitation Therapy
NFT	Nerve Flossing Technique
NPRS	Numeric Pain Rating Scale
MNSI	Michigan Neuropathic Screening Instrument
BMI	Body Mass Index
DGI	Dynamic Gait Index
BBS	Berg Balance Scale
QOL	Quality of Life

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