

# Physical Therapy for Diabetic Peripheral Neuropathy: A Narrative Review

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## ABSTRACT

*Diabetic peripheral neuropathy (DPN) is the most common complication of diabetes mellitus in both developed and developing countries. It is found in about 10% of diabetic clients at diagnosis, and in the majority of clients 25 years down the line. Clients with pre-diabetes may also develop neuropathies that are similar to diabetic neuropathies. Long-term hyperglycemia can cause peripheral nerve damage, resulting in distal-predominant nerve fibre degeneration. Loss of feeling in the lower limbs is a high risk for limb amputation. Despite efforts to make an early diagnosis and to halt the progression of diabetic neuropathy, currently there is no effective treatment available at a global level, except for strict control of blood glucose.*

*Physical therapy can improve the overall quality of life of diabetes mellitus clients with peripheral neuropathy and can alleviate the symptoms of neuropathy. This paper assesses the effectiveness of interventions used by physical therapists to minimise dysfunctions in people with DPN. It reviews the different treatment strategies and presents evidence and conditions for its applications.*

**Key words:** *diabetic neuropathy, physical therapy, pain, aerobic exercise, balance*

## INTRODUCTION

Diabetes has become one of the largest global healthcare problems of the 21<sup>st</sup> century. In 2017, International Diabetes Federation estimates showed that approximately 425 million adults (20-79 years of age) were living with diabetes; by 2045 this number will rise to 629 million (Cho et al, 2018).

Diabetic neuropathy is the most common complication associated with diabetes

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mellitus. Diabetes causes a broad spectrum of neuropathic complications, including acute and chronic forms affecting each level of the peripheral nerve, from the root to the distal axon. The lifetime prevalence of diabetic neuropathy in Type 2 DM may be up to 50%. Diabetic peripheral neuropathy (DPN) is a common chronic complication of diabetes mellitus that has, for a long time, been very challenging for clinicians. DPN is a leading cause of disability due to foot ulceration and amputation, gait disturbance, and fall-related injury. Diabetic peripheral neuropathy significantly lowers quality of life and substantially increases health costs associated with diabetes (Asif, 2014). Those with DPN experience a twofold increase in healthcare costs, and those with severe painful peripheral neuropathy experience a fourfold increase. On a larger scale, it has been estimated that about 27% of healthcare costs of diabetes can be attributed to DPN.

Diabetes causes a wide variety of acute, chronic, focal, and diffuse neuropathy syndromes. By far the most common is DPN, which accounts for 75% of diabetic neuropathy. DPN has been defined by the Toronto Consensus Panel on Diabetic Neuropathy as a “symmetrical, length-dependent sensorimotor polyneuropathy attributable to metabolic and micro-vessel alterations as a result of chronic hyperglycemia exposure and cardiovascular risk covariates” (Juster-Switlyk and Smith, 2016). Sensory symptoms start in the toes and over time affect the upper limbs in a distribution classically described as a “stocking and glove” pattern. Motor involvement is not typically seen in the early stages of DPN.

## **AIM**

The aim of this narrative review is to introduce literature on physical therapy for diabetic peripheral neuropathy to deepen the understanding of exercise therapy, and then describe how to prescribe physical therapy for clients with diabetic peripheral neuropathy.

## **METHOD**

A literature search was performed using Google Scholar, PubMed and Cochrane databases. A total of 66 items showed up on PubMed and 20 on Cochrane with the term “balance training in DPN”. The search terms used were ‘Diabetes mellitus’, ‘physical therapy’, ‘neuropathic pain’, ‘diabetic peripheral neuropathy’, ‘glycemic control’, ‘balance’, ‘gait’, ‘falls risk’, ‘proprioception’ and

'postural control'. Research articles published in English, between the years 2000 and 2018, were included. All study designs were eligible for review, with the exception of case reports. A broad research approach was chosen to minimise the chances of missing relevant articles. Articles that assessed variables reflecting diabetic peripheral neuropathy and the effect of physical therapy provided to DPN clients independently or in combination with other exercise, were included. Exercise interventions other than physical therapy were excluded. The studies were double checked and only full text articles were used for the review. Totally, 21 studies were selected to emphasise the effect of physical therapy among DPN clients. These studies were reviewed in a narrative way, and the main findings are summarised.

### **Clinical Presentation**

The presentation of diabetic neuropathy is variable, although the clinical picture is most frequently dominated by pain. Of note, pain is reported by approximately one-third of clients with diabetes, regardless of associated neurological deficits (Bril et al, 2011). The classic description is that of an unremitting burning pain that is characteristically worse at night, with a gradual distal-to-proximal progression of symptoms in a glove-and-stocking distribution (Javed et al, 2014). A number of other features have been associated with the pain of diabetic neuropathy (Table 1). Motor symptoms occur less frequently, and typically appear as the disease progresses. Deficits in deep-tendon reflexes are similarly associated with advanced disease. It has been suggested that damage to small nerve fibres (carriers of nociceptive and thermal signals) may precede damage to large nerve fibres (Breiner et al, 2014). Additionally, autonomic neuropathy can occur concurrently or independently of the somatic and motor dysfunction.

**Table 1: Symptoms associated with Painful Diabetic Neuropathy**

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| <ul style="list-style-type: none"><li>• Pain</li><li>• Paresthesia</li><li>• Allodynia</li><li>• Impairment of vibration sense</li><li>• Reduced thermal sensation</li><li>• Loss of pinprick sensation</li><li>• Bed sheet or sock intolerance</li><li>• Restless legs syndrome</li></ul> |
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## DPN in Early Adulthood

The longstanding notion that DPN occurs only after longstanding hyperglycemia has been replaced by the observation that even those with good glycemic control are at risk (Dobretsov et al, 2007).

The increasing prevalence of Type 1 (T1D) and Type 2 diabetes (T2D) in children and adolescents is likely to result in increased numbers of individuals with diabetes-related complications in their early adulthood. Diabetic peripheral neuropathy is a debilitating complication and prevalence of DPN increases approximately twofold with an increase in duration of diabetes from 5–10 years to >10 years. The pathophysiological pathways driving the neural damage in these two groups could be divergent. Glycotoxicity and its downstream pathways could be a key player in T1D, while lipotoxicity and insulin resistance could be the major drivers among those with T2D (Jaiswal, 2013). Moreover, youth with T1D and T2D are known to have different cardiovascular risk profiles, which could in part explain the difference in rates of DPN in this population at such a young age. Associations between diabetic dyslipidemia (higher triglycerides and lower HDL) and neuropathy have been reported in several landmark studies (Singleton et al, 2008; Smith and Singleton, 2013).

Counselling clients and early detection in primary care settings are necessary to initiate the appropriate interventions in order to decrease disability and limb loss, and improve the quality of life by addressing the risk factors (Table 2).

**Table 2: Risk Factors for DPN**

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| <ul style="list-style-type: none"> <li>• Older age</li> <li>• Smoking</li> <li>• Heavy alcohol intake</li> <li>• Change in Hb A1c</li> <li>• Longer duration of diabetes</li> <li>• Long-term poor glycemic control: Perturbation of insulin signalling, secondary to insulin resistance, results in neuronal damage and contributes to the pathogenesis of DPN</li> <li>• Cardiovascular risk factors: obesity, dyslipidemia, and hypertension</li> <li>• Long-term poor glycemic control and dyslipidemia emerge as the major modifiable risk factors</li> </ul> |
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## Treatment of Diabetic Peripheral Neuropathy

Despite the significant individual and social burden associated with diabetic neuropathy, its treatment remains unsatisfactory. This is in part due to the

innately unpredictable and complex nature of the disease, combined with limited systematic diagnostic testing, which differs from diabetic retinopathy and nephropathy where the disease is more predictable and the diagnostic testing is widespread and systematically applied. Although the American Diabetes Association (ADA) recommends neuropathy testing annually after 5 years of Type 1 diabetes and from the diagnosis of Type 2 diabetes onwards, the testing advocated (monofilament/clinical examination) detects only advanced disease and is rarely implemented (Boulton et al, 2005). Painful diabetic neuropathy should be evaluated against a combination of typical symptoms of painful neuropathy, associated with neurological deficits. A number of tools have evolved to aid the clinician in the diagnosis of diabetic neuropathy (Table 3).

**Table 3: Screening and Diagnosis**

<ul style="list-style-type: none"> <li>• HbA1c (reflective of how well diabetes is controlled)</li> <li>• Biochemistry: Triglycerides, HDL, LDL</li> <li>• Renal Function Tests</li> <li>• Blood Pressure</li> <li>• MRI</li> <li>• Nerve Conduction Testing</li> <li>• The Michigan Neuropathy Screening Instrument (MNSI)</li> <li>• Brief Pain Inventory short form for Diabetic Peripheral Neuropathy (BPI-DPN).</li> <li>• Neuropathy Disability Score (NDS)</li> <li>• Neuropathy Symptom Score (NSS)</li> <li>• Visual Analog Scale</li> <li>• Semmes Weinstein Monofilament (SWM)</li> <li>• BMI</li> <li>• Reflexes</li> </ul>
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Treatment of diabetic peripheral neuropathy primarily involves treatment of the diabetes. Anti-diabetic therapy with insulin or oral agents is used, depending on the type of diabetes. Management of DPN is generally multifaceted. Avoidance of complications through excellent blood glucose control appears to be the most effective strategy for prevention. Pharmacological interventions for symptom management are available. Some medications have been found to be effective but side effects often limit their use.

## Physical Therapy for Diabetic Peripheral Neuropathy

Despite the identification of numerous molecular pathways involved in DPN pathogenesis, clinical trials targeting specific molecules have demonstrated only modest benefits in slowing disease progression and have been largely ineffective in reducing pain; these results suggest that pharmacological therapies may not be sufficient to reverse or slow DPN (Finnerup et al, 2010).

Exercise is known to improve multiple metabolic factors that may affect nerve health and microvascular function, which may indirectly protect against peripheral nerve damage. Exercise training is a unique therapeutic strategy for improving metabolic dysregulation and, in parallel, may directly promote nerve regeneration and function (Singleton et al, 2015). Emerging evidence from human and animal research is expanding knowledge about the molecular transducers that promote positive nerve adaptations (morphological and physiological) in response to exercise (Nimmo et al, 2013). Physical activity will influence some of the underlying mechanisms of DPN in the form of microvascular dilatation, attenuation of oxidative stress and release of neurotrophic mediators, in addition to its well-established role as inflammatory modulator and insulin sensitiser. Type 2 DM is inseparably linked to the obesity epidemic; about 90% of diabetic risk is attributable to excess bodyweight. Exercise has an important role in improving the condition of the client, quality of life, glycemic control, and control of fat mass. Physical therapy can improve the overall quality of life of DM clients with peripheral neuropathy, and can alleviate the symptoms of diabetic neuropathy. It can also improve muscle strength, joint mobility, balance, coordination and physical function. In addition, exercises to help peripheral neuropathy, when done regularly, may reduce neuropathic pain and can help control blood sugar levels. Physiotherapists use a variety of electro-physical agents and other inexpensive, safe and non-pharmacological therapies to treat pain associated with DPN (Table 4).

**Table 4: Physical therapy in pain management of DPN**

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| <ul style="list-style-type: none"> <li>• Transcutaneous Electrical Nerve Stimulation (TENS)</li> <li>• Low Level Laser Therapy (LLLT)</li> <li>• Transcranial Magnetic Stimulation (TMS)</li> <li>• Visual mental exercises</li> <li>• Mirror therapy</li> <li>• Low frequency currents</li> <li>• Monochromatic Infrared Photo Energy (MIPE)</li> </ul> |
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## **Aerobic Training**

The fact that diabetes and its associated complications can be prevented by strictly regulating blood glucose through diet, exercise, or medication has been well established. More recently, several large randomised controlled trials established that aerobic exercise improves physical fitness, glycemic control, and insulin sensitivity in people with diabetes. The aim is to complete 150 minutes of aerobic exercise per week, spread over 3 days, with no more than 2 consecutive days between exercise bouts. The physical therapist should assess the baseline activity level with a quantitative device to achieve this aim. Therefore, exercise is recommended as a way for people with diabetes to improve glycemic control and minimise diabetic complications. However, people with DPN have been advised to be cautious about increasing their activity level. Aerobic training including cycle ergometers, treadmills, recumbent steppers, and elliptical trainers can be used. Exercise sessions should start with brief stretching and/or a 5-minute warm-up period, and finish with a 5–10 minute cool-down period. A recent single-group trial with an aerobic exercise intervention demonstrated decreased pain interference as well as decreased general and physical fatigue (Yoo et al, 2015). In a randomised controlled trial, Dixit et al (2014) also found that aerobic exercise had a positive effect on nerve conduction velocity.

## **Weight-bearing Exercises: Are they Safe?**

Previous guidelines primarily focussed on protecting the insensitive foot from physical stress. Unloading was recommended to heal wounds, protective footwear was prescribed to help prevent skin breakdown of insensitive feet, and people with neuropathy were advised to avoid weight-bearing exercise (Sigal et al, 2006). Although unloading injured tissues clearly can help them heal, according to the PST (Physical Stress Theory) prolonged levels of low stress will lead to subsequent decreased tolerance of the tissues for stress and an even lower threshold for injury. Before 2009, the Standards of Medical Care in Diabetes position statement published by the American Diabetes Association (ADA) included the recommendation that “in the presence of severe peripheral neuropathy, it may be best to encourage non-weight-bearing activities such as swimming, bicycling, or arm exercises” because of the increased risk of skin breakdown, and Charcot joint destruction. However, the findings of a study published in *Physical Therapy* were instrumental in leading to a substantial change in these guidelines. The authors concluded that increased weight-bearing activity in participants with diabetes and a prior history of foot ulcer did not

increase the risk of foot re-ulceration (LeMaster, 2008). It is demonstrated that collagen fibrils have increased diameter after exposure to compressive and shear stresses, and are organised and packed into structures that appear to adapt to their mechanical environment (Flynn et al, 2010). This paradigm shift represents a true change from traditional thinking, with the new perspective that people with DPN should be encouraged to maintain and even increase weight-bearing activities, rather than avoid them. It appears that with appropriate monitoring, weight-bearing exercise is safe and feasible for this population, and leads to positive outcomes. Modest improvements in gait speed and habitual physical activity can be expected. During weight-bearing exercises, additional care is taken to maintain proper foot support: the toes should always touch the floor, avoiding hammering or clawing when possible, and the ankle should not be laterally tilted (with lateral deviations). Thus, self-perception of the foot and ankle position is stimulated even during the most challenging tasks.

### **Balance and Gait Training Strategies**

Previous studies reviewed the gait characteristics in DPN (Allet et al, 2008) and the effect of various modalities to improve balance in DPN clients (Ites et al, 2011). However, they did not take into account balance exercises as an intervention. Weakness in the distal parts of the body happens late in the natural history of DPN. With increased severity of DPN, a positive Romberg's sign and ataxia may be found due to the weakness in the ankle plantar flexors and dorsiflexors (Andreassen et al, 2006). This instability in the muscles leads to difficulty in maintaining balance and ultimately affects the gait. Static as well as dynamic balance both are affected in DPN. Various factors that affect the balance in this population are a result of significantly impaired sensation, proprioception impairment, movement strategy impairment, biomechanical structural disorders, and disorientation.

General exercises for balance improvement have already been shown to be efficient in DPN clients. A good body of studies reported that there was improvement in static balance such as one-leg stance (Song et al, 2011), tandem stance (Richardson et al, 2001), as well as in the dynamic balance such as forward reached test, walk over beam and five times sit to stand (Lee et al, 2013). A marked progress in the gait parameters such as gait speed, stride length and cadence (Raghav et al, 2013) was also recorded following balance training. It was reported that 12 weeks of Tai Chi has resulted in improved median and tibial nerve conduction velocities (Hung et al, 2009) and improved quality of life,

balance, and neuropathic symptoms (Ahn & Song, 2012). The findings of a recent RCT conducted among DPN clients reported significant improvement in balance and gait speed following multisensory training (Majeed & Majida, 2013). Current data suggests that balance exercises are feasible and safe, and have the potential to improve balance and gait.

### **Flexibility Exercises**

Flexibility exercises should also be included because they address joint range-of-motion limitations, particularly in the ankle, hip and shoulder. Finally, a thorough musculoskeletal examination by a physical therapist can identify individual needs that should be addressed to maximise joint alignment and minimise movement-related injuries. Flexibility exercises, also called stretching, help keep joints flexible. Gentle stretching for 5 to 10 minutes helps the body to warm up and get ready for aerobic activities such as walking or swimming. Hamstring stretch, calf stretch, knee to chest stretch, toe curls and bipedal ankle inversion and eversion can be safely utilised as flexibility exercises.

Specific ROM restrictions have already been shown to contribute to increased mechanical stress over the plantar surface. It is stated that the smaller the first metatarsal and lateral forefoot sagittal motion and calcaneus eversion/inversion, the higher the magnitude of plantar loading under the respective segment (Rao et al, 2010). Physical therapy procedures, such as stretching, pushing them to their limits, induce mechanical stress. Although it is not known if the remodelling of these structures is preserved in clients with diabetes mellitus, home exercise therapy has been suggested to improve distal joint mobility and plantar pressure distribution during gait in a randomised, controlled trial with DPN clients (Goldsmith et al, 2002).

### **Strength Training Exercises**

In addition to aerobic conditioning, the joint statement of the American College of Sports Medicine and the ADA recommends 2 or 3 days of large-muscle-group resistance training per week. This training should include a minimum of 1 set of 5 or more resistance exercises (Colberg et al, 2010). DM2 has a major effect on maximal muscle strength with reductions of approximately 30–50% in both the upper and lower leg. The findings of a good body of studies highlighted that leg muscle weakness was particularly observed in clients with severe, symptomatic neuropathy and not in clients with less severe DPN (Andersen, 2004; Andreassen et al, 2006). These data suggest that additional loss of muscle strength is a relatively

late phenomenon in the course of DPN and occurs at a severe stage of the disease. Diminished ankle strength and rate of force production may lead to balance impairments, as normal recovery from perturbation involves rapid production of adequate muscle force to maintain the body's centre of mass over its base of support. Exercise may delay or even prevent the onset of DPN in diabetic clients. Randomised controlled trials provide preliminary evidence to support the efficacy of strength and balance training for neuropathy (Richardson et al, 2001; Allet et al, 2010). It was also reported that there was significantly improved balance and strength, increased walking speed, and decreased fear of falling in participants after a 60-minute twice-weekly for 12 weeks strength, balance and functional training programme. The results were sustained for a period of 6 months. Furthermore, the training programme was feasible and safe for persons with peripheral neuropathy (Allet et al, 2010). Strengthening exercise programmes can include a variety of exercises designed to target specific groups or individual muscles.

## CONCLUSION

The literature review shows that individuals with DPN can improve their confidence and balance with aerobic exercise, balance and gait training strategies, flexibility exercise, and strength training exercise. The successful engagement of the previously inactive and chronically debilitated population in routine exercise programmes poses a huge challenge for physical therapists. Weight-bearing exercises can be safely administered in clients with DPN. Regardless of the type of exercise chosen, a slow, progressive programme will allow the time required to assess the tissue response after exercise and to modify the prescription to ensure that the exercise programme is safe and beneficial. A well-designed therapeutic exercise protocol, including interventions aimed at joint, muscle, and locomotor task recovery, should be part of a physical therapy routine prescription for clients with DPN.

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