Effectiveness of physiotherapy interventions in alleviating symptoms and complications of diabetic peripheral neuropathy: A review of evidence

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This review presents a comprehensive analysis of physiotherapy interventions for Diabetic Peripheral Neuropathy (DPN), summarizing key findings derived from an examination of approximately 654 studies, including randomized controlled trials, systematic reviews, meta-analyses, conducted up to September 2021. Ultimately, 19 studies met the inclusion and exclusion criteria. The findings affirm the effectiveness of physiotherapy interventions in enhancing the quality of life for individuals with DPN. Notable discoveries encompass the positive impact of various interventions, such as aerobic and resistance exercises, electrical stimulation modalities (e.g., transcutaneous electrical nerve stimulation, percutaneous electrical nerve stimulation, and functional electrical stimulation), as well as manual therapies (e.g., massage and joint mobilization). These interventions have demonstrated their ability to reduce pain, enhance balance, and improve sensory function. While acknowledging certain limitations, this review underscores the potential of evidence-based physiotherapy interventions to optimize DPN management and enhance patient outcomes.

Keywords: Diabetes mellitus, diabetic neuropathy, aerobic exercise, percutaneous electrical nerve stimulation, transcutaneous electrical nerve stimulation.

INTRODUCTION

Diabetes mellitus affects approximately 422 million people worldwide.1 One of the most common and debilitating complications of diabetes is diabetic peripheral neuropathy (DPN), which can result in reduced mobility, pain, and poor quality of life.2 It is estimated that total annual cost of DPN and its complications in the U.S. is between $4.6 and $13.7 billion.3 The prevalence and the risk factors of DPN on a global scale, especially in low and middle-income countries, remain unclear. Lu et al reported that more than a quarter of individuals (26.71%) with type 2 diabetes develop DPN and the risk factors independently associated with DPN include the duration of diabetes, history of cardiovascular disease, depressive symptoms, hypertension, and poor glycemic control (higher HbA1c levels).4

Managing DPN involves considering multiple treatment avenues, including pharmacological approaches, surgical procedures, and non-surgical therapies like physiotherapy. Most DPN patients suffer from muscle weakness, pain, loss of balance, and lower limb dysfunction.5-11 As a result, their daily activity and life satisfaction are gradually impaired.12 Exercise therapy, electrotherapy, and other physiotherapy methods have been used to reduce the complications, disease progression and improving the quality of life of the patients suffering from DPN. Therefore, this review aims to explore the efficacy of physiotherapy interventions in mitigating the symptoms and complications of DPN.

METHODOLOGY

A comprehensive literature search was conducted using the Web of Science and Scopus databases. The search included keywords such as “diabetic peripheral neuropathy,” “physiotherapy,” “exercise,” “electrical stimulation,” and “manual therapy.” Inclusion criteria included randomized controlled trials (RCT), systematic reviews, and meta-analyses that evaluated physiotherapy interventions for DPN. The search was conducted from...
Table 1: Inclusion and exclusion criteria.

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<th>Inclusion Criteria</th>
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<tr>
<td>Studies published in peer-reviewed journals.</td>
<td>Studies published in non-peer-reviewed sources, such as</td>
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<tr>
<td>Studies conducted on human subjects.</td>
<td>conference abstracts.</td>
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<tr>
<td>Studies focusing on diabetic peripheral neuropathy (DPN) as the primary condition.</td>
<td>Studies conducted on animals or in vitro experiments.</td>
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<tr>
<td>Studies that investigate the efficacy of physiotherapy interventions in managing DPN.</td>
<td>Studies not primarily focused on DPN, or where DPN is not</td>
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<td>Studies that include interventions related to exercise, electrical stimulation, or manual therapy in the context of DPN.</td>
<td>the main condition under investigation.</td>
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<tr>
<td>Randomized controlled trials (RCTs), systematic reviews, and meta-analyses.</td>
<td>Studies that do not assess the effectiveness of physiotherapy interventions for DPN.</td>
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<td>Studies that do not involve interventions related to exercise, electrical stimulation, or manual therapy in the context of DPN.</td>
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<td>Studies with insufficient data or incomplete information to evaluate the intervention's efficacy.</td>
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<td>Studies published in languages other than English.</td>
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the inception of the databases until September 2021. A total of 654 articles were identified. After removing duplicates and screening titles and abstracts, 38 articles were selected for full-text review. Of these, 19 articles met the inclusion criteria and were included in the review. The quality of the included studies was assessed using the Cochrane Risk of Bias Tool for randomized controlled trials and the AMSTAR 2 tool for systematic reviews and meta-analyses.

Exercise Interventions
Exercise interventions have been widely studied in the context of DPN, with aerobic and resistance exercise programs being the most common forms investigated. The primary goal of these interventions is to improve glycemic control, increase peripheral blood flow, enhance muscle strength, and improve balance and proprioception.

Aerobic Exercise: Aerobic exercise has been shown to improve glycemic control, reduce inflammation, and increase nerve function in individuals with DPN. A systematic review and meta-analysis by Allet et al, included seven RCTs, involving 358 participants with DPN. They found that aerobic exercise led to significant improvements in pain, balance, and quality of life for individuals with DPN. Aerobic exercise programs, consisting of walking, cycling, or treadmill exercises performed 3 to 5 times per week for 30 to 60 minutes per session.14

Resistance Exercise: This has been reported to improve muscle strength, proprioception, and functional capacity in individuals with DPN. This study involving 29 participants with DPN found that a 10-week progressive resistance exercise program led to significant improvements in muscle strength, balance, and functional performance.15

Combined Aerobic and Resistance Exercise: A meta-analysis by Allet et al, found that combined exercise programs led to improvements in pain, balance, and quality of life for individuals with DPN. The authors concluded that combined exercise programs are more effective than either aerobic or resistance exercise alone in improving these outcomes.14

Electrical Stimulation
Electrical stimulation has been proposed as a potential treatment for DPN, with transcutaneous electrical nerve stimulation (TENS) being the most widely studied modality. TENS involves the application of electrical currents to the skin surface to stimulate the underlying nerves and modulate pain perception.

Transcutaneous Electrical Nerve Stimulation (TENS): TENS has been shown to reduce pain and improve sensory function in individuals with DPN. A systematic review by Gibson et al included nine RCTs involving 568 participants with DPN. They concluded that TENS led to significant reductions in pain intensity and improvements in sensory function compared to sham or control interventions.16

Other Electrical Stimulation Modalities: Other electrical stimulation modalities, such as percutaneous electrical nerve stimulation (PENS) and functional electrical stimulation (FES), have also been investigated in the context of DPN. A RCT by Ahmed et al involving 60 participants with DPN found that FES led to significant improvements in pain, balance, and functional capacity compared to a control group.17

Manual Therapies
Massage and joint mobilization, have been proposed as a
potential treatment option for individuals with DPN. These aim to improve joint range of motion, reduce pain, and improve function.

**Massage Therapy:** It has been shown to improve joint range of motion, reduce pain, and improve function in individuals with DPN. A RCT by Ferreira et al involving 40 participants found that a 12-week program of massage therapy led to significant improvements in pain, joint range of motion, and functional capacity.18

**Joint Mobilization:** A systematic review by Gordon et al included five studies involving 267 participants with DPN. The authors found that joint mobilization was effective in reducing pain, improving balance, and increasing muscle strength in individuals with DPN.19

**Exercise Adherence**
Most patients with diabetes or at highest risk for developing type 2 diabetes do not engage in regular physical activity. The adherence to exercise plays a vital role in the management of DPN by addressing both its symptoms and underlying causes, improving balance and mobility, controlling blood glucose levels, enhancing muscle function, prevent complications, and ultimately enhance the quality of life. Allet et al, reported that in a 12-week physiotherapy program, showed significant improvements in walking speed, balance, mobility, and muscle strength.14 Moreover, the exercise adherence was notably high, with participants attending a median of 21 sessions. Despite two cases of Achilles tendon pain, the intervention group maintained improved performance even at the 6-month follow-up, highlighting the importance of exercise adherence in achieving positive outcomes.

Monteiro et al, conducted a RCT involving individuals and a 12-week foot-ankle exercise program was found to be both feasible and effective.20 The intervention group showed an impressive 80% adherence rate and high satisfaction levels. Significant improvements were observed in areas like toe strength, gait parameters, and DPN symptoms, demonstrating the positive impact of the exercise program compared to usual care.

Van Sloten et al, have reported that the daily walking activity significantly decreased with higher BMI, waist circumference, the presence of peripheral neuropathy, peripheral arterial disease, and reduced muscle strength.21 The final regression model after adjusting for age and sex, it was demonstrated that peripheral neuropathy was associated with a reduction of 167 steps per day, decreased muscle strength, and each 1 kg/m² increase in BMI corresponds to 210 fewer steps per day. These results indicate how factors like neuropathy, muscle weakness, and obesity act as strong determinants of reduced physical activity, highlighting the challenges individuals with DPN may encounter when adhering to exercise programs.

**DISCUSSION**
This review demonstrates the potential of physiotherapy interventions to mitigate the symptoms and complications of diabetic peripheral neuropathy. The evidence supports the use of exercise interventions, electrical stimulation, and manual therapies in improving pain, balance, and function in individuals with DPN. However, more research is needed to determine the optimal frequency, duration, and intensity of these interventions and to investigate the potential synergistic effects of combining different physiotherapy approaches.13

Exercise interventions, including aerobic and resistance exercise, have been shown to be effective in reducing pain, improving balance, and enhancing functional capacity in individuals with DPN.4,5 The inclusion of both aerobic and resistance exercises in a comprehensive exercise program may offer the greatest benefits for patients with DPN, as these modalities can target different aspects of the condition, such as cardiovascular health and muscle strength.13 Electrical stimulation, particularly TENS, has been found to be effective in reducing pain and improving sensory function in individuals with DPN.16 Other electrical stimulation modalities, such as PENS and FES, have also shown promise in the management of DPN.17 However, further research is needed to compare the effectiveness of different electrical stimulation modalities and to optimize treatment protocols.

Manual therapies, such as massage and joint mobilization, aim to improve joint range of motion, reduce pain, and improve function.18,19 While the available evidence supports the use of manual therapies, more research is needed to identify the most effective techniques and to determine the optimal frequency and duration of treatment.

Individuals with DPN face several challenges and limitations related to their neuropathy, muscle strength, obesity, and the complex interactions among these factors. Addressing these challenges and providing tailored exercise programs that consider these limitations is crucial to improving exercise adherence in this population. Van Sloten et al, reported that factors such as higher BMI, increased waist circumference, the presence of peripheral neuropathy, peripheral arterial disease (PAD), and reduced muscle strength are associated with decreased daily walking activity.21 Peripheral neuropathy significantly reduces daily walking activity but may not impact performance in standardized functional capacity tests. This suggests that
its influence on mobility is more pronounced in challenging everyday environments than in controlled settings.\textsuperscript{14,22} While some studies have found associations under ideal conditions, further research is needed to understand the full extent of peripheral neuropathy's impact on mobility.

Despite the promising findings presented in this review, several limitations should be noted. Many of the included studies had small sample size, which may limit the generalizability of the results. Additionally, the heterogeneity of the study populations, interventions, and outcome measures makes it difficult to draw firm conclusions about the efficacy of specific physiotherapy interventions for DPN. Lastly, most of the included studies were conducted in high-income countries, which may limit the applicability of the findings to low-resource settings.

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