The efficacy of physiotherapy interventions in mitigating the symptoms and complications of diabetic peripheral neuropathy: A systematic review

Narges Jahantigh Akbari¹ · Mohammad Hosseinifar² · Sedigheh Sadat Naimi³ · Saeed Mikaili⁴ · Soulmaz Rahbar⁵

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Abstract

Purpose Diabetic peripheral neuropathy (DPN) leads to decreased sole sensation and balance disorder, all of which increase the risk of falls and socioeconomic costs. Since the physiotherapists do not use the same manner to lessen the complications of this problem. Therefore, this review study was directed to appraise physiotherapy intervention efficiencies in diminishing DPN's symptoms and complications.

Method A database search of Pubmed, Elsevier, Google Scholar, and Embase was performed to determine DPN's published documents. Finally, studies of DPN and treatments available in this field, particularly physiotherapy that included electrotherapy, exercise therapy, and other therapies, were identified.

Result According to a database search on August 1, 2019, from 1989 to 2019, in the last 30 years, about 968 articles were found, 345 of which were free full text available, and finally, 19 articles were approved. These articles examined the effects of physiotherapy interventions, including exercise therapy, electrotherapy, and other treatment techniques on DPN patients.

Conclusions The results showed that most diabetic peripheral neuropathy patients suffer from muscle weakness, pain, loss of balance, and lower limb dysfunction. As a result, their daily activity and Life satisfaction are gradually impaired. Exercise therapy, electrotherapy, and other physiotherapy methods have been used to reduce the mentioned cases. Among these interventions, exercise therapy has been the most effective. Although there was little evidence of aerobic exercise in these patients, further studies should be done on other therapies' effects.

Keywords Diabetic neuropathies · Physiotherapy techniques · Exercise therapy

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✉ Sedigheh Sadat Naimi
naimi.se@gmail.com; naimi.se@sbmu.ac.ir

- ¹ Department of Physical Therapy, School of Rehabilitation, Shahid Beheshti University of Medical Sciences, Tehran, Iran
- ² Health Promotion Research Center, Zahedan University of Medical Sciences, Zahedan, Iran
- ³ Department of Physiotherapy, School of Rehabilitation, Shahid Beheshti University of Medical Sciences, Tehran, Iran
- ⁴ Department of Physical Therapy, School of Rehabilitation, Shahid Beheshti University of Medical Sciences, Tehran, Iran
- ⁵ Department of Physiotherapy, School of Rehabilitation, Hamadan University of Medical Sciences, Hamadan, Iran

Introduction

One of the prevalent diseases in the universe is diabetes. According to a report in 2018, about 350 million people are affected by this disease. Among patients, 9 out of 10 people have diabetes mellitus (type 2 diabetes[1]. Diabetes mellitus is a public health problem in two forms of diabetes, and 95% of people worldwide have this type of diabetes [2]. Diabetes is a disease mainly associated with microvascular and macrovascular complaints, including retinopathy, nephropathy and neuropathy, and ischemic heart disease, leading to organ and tissue damage in approximately one-third of the people with diabetes [2]. About half of people with diabetes have peripheral neuropathy, which is polyneuropathy and mononeuropathy [2]. The prevalence of peripheral neuropathy was 54% in type 1 diabetes and 45% in another type of diabetes[3].

Risk factors for diabetes-related peripheral neuropathy include age, obesity, smoking, poor glycemic control, and hypertension [4]. Among the risk factors for diabetic foot ulcers in more than 80% of cases is peripheral neuropathy [4]. In the study of Tabatabai and her colleagues (2010), age over 50 years, diabetes duration over ten years, and fasting blood sugar above 200 were among the risk factors for neuropathy [4]. One study found that the rate of neuropathy increased with age, with people under the age of 50 making up about 300 cases per 100,000 people a year, and people over the age of 75 making up 32% of the total [5]. 0.75% of diabetic patients with body mass index (BMI) above 25 had neuropathy [6]. High BMI and obesity can lead to low metabolic status, insulin resistance, and a higher prevalence of its complications [6]. A link between insulin resistance and microvascular complications such as neuropathy and endothelial dysfunction has been reported [6]. Higher neuropathy incidence in diabetes mellitus patients is likely to be secondary to several factors, including differences in the age of diabetics and differences in pathophysiology [5]. The duration of diabetes and hemoglobin A1c levels are essential predictors of diabetic neuropathy [5]. These two predictors are commonly associated with other metabolic factors for diabetic neuropathy, particularly those associated with type 2 diabetes, such as insulin resistance and hypertension [5].

Peripheral neuropathy is the most common diabetes mellitus complaint that occurs mainly in the lower extremities and affects the sensory, motor, and autonomic systems in particular. Symptoms of diabetic peripheral neuropathy (DPN) include paresthesia, hyperesthesia, and dysesthesia [7]. DPN is associated with complications such as depression, anxiety, sleep disorders, and social costs [8]. After DPN, small foot muscle and joint problems reduce individuals' willingness to participate in daily physical activity. In the end, this process can create fertile ground for ulcers in the leg [9]. The etiology of DPN is not entirely understood [10]. The most common diabetes-related factors that caused DPN are a sedentary lifestyle or low physical activity, and being overweight [11]. Reduced physical activity, functional deficits, and increased risk of falls lead to increased healthcare costs and economics [11]. Among the risk factors, the sedentary lifestyle was reported as the most critical agent in the progress of diabetes. [12]. In diabetic patients, regular physical activity reduces body weight and improves blood glucose control and insulin sensitivity, reducing neuropathy risk [13]. A diet and increased physical activity are typical in treating obesity and treating diabetes mellitus [14]. There is some evidence that adults with type 1 diabetes are more likely to exercise than people with another type of diabetes [14]. The evidence supports the ability of practice interventions to improve diabetes control [14]. Most studies have reported that in diabetic patients with a risk factor for diabetic foot ulcers for peripheral neuropathy, it is best to perform training interventions

between 8 weeks and 12 months. These studies have seen significant improvements in physical activity without increased risk of injury [14]. If health care is incomplete, foot ulcers may develop, which is the most common cause of hospitalization and amputation [15]. Usually, the combination of various treatments, including pharmacotherapy, physiotherapy, and orthotic devices, are used to maintain biomechanical parameters, physiological patterns, and at last for wound healing. [10].

Insulin therapy, including pharmacotherapy and lifestyle interventions, is considered conventional treatments for preventing diabetes complaints [16]. In a study carried out by Lee et al. (2013), the effect of electro-acupuncture and routine physiotherapy treatments was compared on patients with DPN, and it was concluded that electro-acupuncture is an effective and safe method in DPN patients [17]. Furthermore, Sartor et al. (2012) reported that exercise therapy interventions include strengthening, stretching, functional exercises, improved gait biomechanics, and foot function in patients with DPN [10]. The study of Najafi et al. (2017) found that plantar electrical stimulation improved postural balance and plantar sensation in patients with DPN. It also suggested that daily use of plantar electrical stimulation was a suitable tool for enhancing motor performance plantar sensation [11]. Ahn et al. (2012) Tai Chi exercises had many benefits on glucose control, balance, peripheral nerve involvement complications, and ameliorating life in patients with diabetes mellitus and neuropathy [18]. Monteiro et al. (2018) examined the effect of foot-ankle flexibility and strength exercises on DPN patients and found that exercises positively affected musculoskeletal, biomechanical, and clinical variables and increased activity levels [19]. Although exercise therapy is recognized as an effective intervention in patients with DPN, there are still insufficient guidelines in these patients, and further researches should be done with well-designed studies in them [20]. Therefore, we needed to review the effect of physiotherapy interventions on patients with DPN in this study.

Polyneuropathy is a common problem in diabetic patients that is very challenging for physicians [10]. Many lower extremities and foot disorders such as deformity, decreased range of motion, impaired balance incoordination, and muscle weakness can be caused by diabetes [19]. Diabetes causes high public health costs and significantly reduces the satisfaction of individuals' lives in the community [21]. Preventive interventions are still an essential intervention in preventing diabetes complications [10]. Some therapeutic interventions improve life satisfaction and diabetes [22], but there is still insufficient evidence to determine the effective physiotherapy intervention in patients with diabetes; thus, further studies are required. So far, no study has reviewed the effect of physiotherapy interventions on patients with DPN. Therefore, this study aims to determine the effect of physiotherapy interventions on DPN patients. Unlike other studies, we have divided

physiotherapy interventions into three subsets of exercise therapy, electrotherapy, and other treatments.

Method

Eligibility criteria

The eligibility criteria were as follows: (1) Articles with Randomized controlled trial (RCT), Quasi-randomized controlled trials, or Quasi-experimental designs. (2) Patients with DPN. (3) Examining physiotherapy interventions but not pharmacotherapy or other therapies. (4) Control group. (5) These studies were not restricted by age. (6) All outcomes were included in this study. (7) Inclusion of both males and females. (8) Investigating a population with DPN. (9) Human studies. (10) Studies were incorporated with conclusions. (11) Studies with tools for measuring fatigue variables. (12) the English language. (13) Studies with quantitative but not qualitative results.

Information sources

The electronic databases (Pubmed, Elsevier, Google Scholar, and Embase) were searched on August 1, 2019, to find relevant articles on Do physiotherapy interventions affect diabetic peripheral patients neuropathy?

Search

The authors searched all the electronic databases using a combination of MeSH (Medical Subject Headings) terms, including (physiotherapy or physical therapy) and (diabetic peripheral neuropathy, DPN).

Study selection

Two independent reviewers screened the study title and abstract of retrieved articles. They reviewed full-text articles and included for analysis based on the eligibility criteria. Another author confirmed these eligibility criteria.

Data items

Shreds of evidence were extracted from apiece essays, containing contributors data (such as genus, lifetime, assessment of DPN), the particularity of the intervention, and inhabitants, the evaluation methods used for variables, and follow up period.

Research conducted on August 1, 2019, in this study, 968 articles were found, But 345 of them were free full text, and finally, 20 articles were related and accepted. Studies in this article included: (1) examining physiotherapy interventions

but not pharmacotherapy or other therapies (2) studies of individuals with DPN (3) Studies with human samples (4) These studies were not restricted by age or gender (5) Studies with quantitative but not qualitative results (6) Studies in English. (7) The researchers searched for related articles using some keywords (physiotherapy or physical therapy) and (DPN).

The authors found 19 articles on physiotherapy interventions in DPN from the mentioned databases, in the electrotherapy field (five articles in electrical stimulation, one article in low-level laser therapy). Authors reviewed in [Exercise therapy](#) section (11 articles in the effects of strengthening, stretching, functional training, foot-ankle training program, weight-bearing, Tai chi, aerobic and resistance exercises) and in other treatments section (one article with whole-body vibration, one article with electro-acupuncture, one article with Thai foot massage).

Exercise therapy

Exercise and medication, and diet are considered three significant interventions in diabetic patients [16]. The positive effects of exercise therapy on glucose control, cardiovascular risk factors, and lipid metabolism in diabetic patients are well known. However, there is still no consensus among researchers about the best exercise regimen [23]. On the other hand, people with diabetes are less likely to participate in exercise than healthy people are. Therefore, safe and active training needs to be applied and motivational strategies to stimulate to take part in more extended training programs [24]. Several studies have investigated the positive effects of aerobic, Tai Chi, weight-bearing, non-weight-bearing, functional, strengthening, and stretching exercises in patients with diabetes [18, 19].

One of these exercises is Tai Chi, which is an increasingly popular multimodal mind-body exercise that incorporates physical, cognitive, social, and meditative components in the same activity [25]. Tai Chi exercises have been shown to influence on glucose control and lipid metabolism and micro-circulation in the lower extremities positively [23]. Recovery following Tai Chi exercises can be attributed to glucose metabolism improvements, resulting in HbA1c lower levels and insulin resistance [25]. However, a systematic review study found controversial results regarding the effects of Tai Chi exercises on glucose control, which may be due to differences in the type of Tai Chi exercises, duration, and intensity of these exercises in different studies [26]. Wang et al. (2011). showed that Tai Chi exercises had a positive effect on peripheral sensory function. They reported increased blood volume in the skin of diabetic patients following Tai Chi exercises [27]. Antecedent research has demonstrated that Tai Chi workouts have an affirmative outcome. People with diabetes

who have somatic restrictions can follow and confidently perform those practices [23].

Progressive resistive protocols are especially suitable for enhancing muscle strength. They can also help increase muscle mass, reduce pain, and disability [28]. Previous studies have reported some benefits of foot and ankle exercises [19]. One study has shown that protocol for one month reduced plantar pressure during gait in patients with DPN [29]. A physiotherapy protocol that includes strengthening exercises and flexibility of the foot and ankle can improve lower extremity function, complications, and levels of daily living activities [19]. Improvements following strength training can be attributed to the benefits of these exercises in reducing pain and disability. Whole-body strengthening exercises positively affect foot structure and function; however, these exercises neglect foot intrinsic muscles and ankle. [19].

A home-based exercise therapy program was defined as structured walking advice supplemented with an observation part (e.g., exercise logbooks, pedometers) [30]. Concerning active and passive stretching exercises, it can be said that these exercises improved the mobility of the ankle joints while reducing the peak pressure in diabetic patients [10]. These exercises lasted 10 seconds per joint position and were performed three times a day for one month [10]. General exercises to improve balance are practical and useful in DPN patients [10]. In the RCT article, Allet et al. (2010). showed that a specific training program that includes balance exercises and circuit exercises leads to improvements in time-space gait parameters [31]. Improvement following balance training can be attributed to improvement in neuromuscular control and plantar sensation in these patients. In their study, Richardson et al. (2001). reported an improved balance in DPN patients, while one group received foot and ankle strengthening exercises in a closed kinetic chain, and the other received balance exercises in single and double support positions [29]. Studies have shown that home exercise enhances the foot joints' mobility and distributes plantar pressure during gait [32].

Weight-bearing exercise activities are defined as units per week that include 15 minutes for intense weight-bearing activities and 30 minutes for moderate-weight-bearing activities [33]. Weight-bearing exercises are often crucial in patients with DPN because they maintain mobility, bone health, and general fitness, and are generally done in the form of walking and do not require special equipment [34]. One study found that participating in a low-intensity walking program in patients with DPN resulted in daily walking activity improvements without increased wounds [34]. People who do not have open ulcers or severe foot deformities should participate in a weight-bearing and non-weight-bearing program that should be individualized and adaptable to personal goals [35]. The exercise guidelines in diabetic patients have recently

changed to weight-bearing exercises. Furthermore, those few studies conducted so far have positive effects on these patients [34].

Aerobic exercises, defined as exercises that include large muscle groups and repetitive movements, also increase heart rate for a sudden duration while reducing chronic illness [36]. Increased shear stress during aerobic exercise is beneficial and may facilitate adaptive structural changes in the arterial wall [1]. Studies suggest that moderate-intensity aerobic exercise reduces cardiovascular risk by improving overall vascular health [36]. DPN disrupts nerve degeneration, which can affect vascular measurements, such as flow-mediated dilation [37]. One study reported that aerobic exercise for 16 weeks resulted in improved maximal arterial diameter and faster response to maximal dilatation [36].

One study has shown that exercise therapy reduces diabetes-related neuropathic pain, including increased thermal sensitivity and mechanical allodynia [38]. Although animal models have reported the feasibility, safety, and efficacy of exercise therapy in reducing pain, rare human-based model studies have been conducted on the benefits of exercise in reducing diabetes-related pain. Further research needs to be done [39]. One study showed that neuropathic pain was assessed with a visual analog scale after a 6-month balance training exercise and showed a moderate effect size; however, it did not show significant changes than the education group [40]. Objective measurements of brain function and self-report pain measures will better understand physiological changes that need further study [41]. One study reported that aerobic exercise led to improved aerobic fitness in patients with DPN, while no improvement in BMI, HBA1C, and blood pressure was recorded [41]. Aerobic exercise improves vascular endothelial function, but little information is available on DPN patients [36].

Electrotherapy

Interventions in electrotherapy include plantar electrical stimulation, percutaneous electrical nerve stimulation (PENS), and low-level laser therapy. This section describes each of these interventions and their effects.

Plantar electrical stimulation is defined as the use of an electrotherapy device to stimulate the plantar surface. An RCT study has shown that daily use of plantar electrical stimulation is a secure and clinical method that improves motor performance in patients with DPN without any side effects [11]. Improvement of plantar sensation in patients with DPN following daily electrical stimulation can be attributed to improved plantar skin perfusion [11]. Decreased local blood flow in patients with DPN may lead to oxidative stress and release of factors that inhibit the passage of nerve signals, as previously described by Malik et al. (1989) [42]. In a systematic

review study involving 21 RCT papers, the researchers used electrical stimulation to heal wounds and showed that they have many benefits and that this results in increased perfusion of the skin through the release of vascular endothelial growth factor [43]. Recovery following plantar electrical stimulation may be attributed to increased blood flow using these stimuli and eventually healing the foot ulcers [11]. In one study, the improvement in balance was more considerable in the daily use of electric stimulation for six weeks than the balance exercise group in patients with DPN [44]. Numerous studies have shown that electrical noise sent directly to sensory neurons can significantly increase their ability to detect weak signals, increase skin perfusion, and heal damaged neurons in DPN patients [45].

Electro-acupuncture involves inserting needles into different body parts to correct energy imbalances in the body [46]. In addition to stimulating the spinal cord, transcutaneous, or percutaneous electrical nerve stimulation (TENS or PENS) has been used to relieve pain and relief associated with peripheral neuropathy [47]. PENS is a new electro analgesic treatment that combines TENS and electro-acupuncture with acupuncture-like needles placed on the skin that stimulate peripheral sensory nerves located in the neuropathic pain area [47]. PENS' cumulative benefits over time indicate that this treatment has long-term effects, consistent with the study results by Mo et al. (1996), who used the combination therapy of TENS and electro-acupuncture in animal models of DPN [48]. PENS use's precise analgesia mechanism is not fully understood but may be attributed to two factors: neural modulation and an increase in opioid-like substances such as dynorphin, endorphin, and enkephalin in the central nervous system [49]. Both Cameron et al. (1993), and Mo et al. (1996), in their studies, showed that the use of electrical stimulation played a significant role in normalizing neural conduction velocity in the animal samples studied [50] (Fig. 1).

Various studies have reported that electrotherapy may reduce the mechanical pain threshold, local vasodilator effect, and wound healing in diabetic neuropathy [51]. One study examined the potential effect of low-level neurologic electrical stimulation in patients with neuropathic diabetes who suffered from loss of sensation and showed that it improves the efficiency of a variety of mechanoreceptor cells that provide a protective sense in the foot [52]. One of the theories that may explain the benefits of using electrical stimulation is background noise or synaptic noise [53]. Studies show that tactile and proprioceptive sensory thresholds during the electrical stimulation are lower in patients with diabetic neuropathy, and that gait distribution pathways in these patients include small and large nerve fibers [45]. Schwann cells are reduced in diabetic patients, which can disrupt nerve cells' normal conduction and, consequently, lead to decreased nerve conduction velocity so that nerve function can be affected by

Fig. 1 Electroanalgesia with PENS for neuropathic pain .The needle locations for each pair of positive and negative [40]

hyperglycemic, hypoxia, and other conditions [53]. Electrical stimulation can be used for Schwann cell regeneration and a suitable tool for altering nerve conduction pathways in diabetic neuropathy [54]. Due to medication's unintended side effects, pharmacotherapy alone is not enough to counteract DPN's progression. In contrast, studies have shown that electrical stimulation around the medulla can reduce pain and improve life satisfaction [55].

Low-level laser therapy can also be used to treat diabetes problems, including foot ulcers [56]. This kind of laser's potential benefits has been attributed to its anti-inflammatory effect, inhibition of pain activity, and improved circulation [57]. Various studies have reported that low-level laser therapy is an effective treatment for nerve regeneration, and the effect of low-level laser therapy on painful DPN has also been reported in patients with diabetes mellitus [58]. One study used low-level laser therapy to reduce pain in patients with DPN, whose reduction in pain may be attributed to increased microcirculation; a possible mechanism may be the release of cytokines and circulating growth factors responsible for

vasodilation and the formation of new capillaries [59]. Among the electrotherapy modalities, laser therapy can be used in diabetic neuropathy patients because it affects the nervous system and can treat nerve damage and other neurological pathologies [53].

Other treatment

Acupuncture is a conventional treatment used by traditional Chinese medicine practitioners [46]. Acupuncture in West Asia has been used to relieve pain based on Qi theory in patients with DPN, and acupuncture can alleviate pain in these patients by adjusting the Qi imbalance [17]. The following mechanisms may explain the analgesic effect of acupuncture: local effect induced by adenosine A1 receptors, Segmental analgesic effect established by the theory of pain gate control theory, special segmental analgesic effect including the release of opioid peptides, and the other mechanism is central regulation of the limbic system [60]. Acupuncture has been widely used to treat DPN in clinical trials [17], and some studies have shown that acupuncture has positive results in these patients.

These exercises are defined as standing and maintaining a swinging position on a vibrating plate form while the individual has to squat on one leg [61]. Lee et al. (2011). examined the effects of whole-body vibration plus balance training on strength and balance in elderly patients with diabetic neuropathy, who were at risk of falling due to reduced physical function and problems following diseases. This study showed the beneficial effects of whole-body vibration [55]. These interventions also led to a significant reduction in HbA1c levels in patients with diabetes [55]. Studies have shown that whole-body vibration has many benefits in these people.

A Thai foot massage is a form of deep massage with the thumb presses along the foot's midline and toe distraction [62]. Some studies have used this massage to improve balance in patients with DPN [18]. Thai massage is an alternative treatment for patients with DPN to improve balance efficiency based on the increased range of motion and foot sensation [18]. Thai massage stimulates the nervous system to help the myelin sheath of the nerves [63]. Some studies have shown that western foot massage, combined with mobilization, can improve cutaneous and joint sensation, increasing standing balance in patients with DPN [64]. According to these studies, this type of massage has many benefits in patients with diabetic neuropathy. Therefore, further studies are recommended to determine its effects in different conditions of this complication (Fig. 2).

Fig. 2 Thai foot and leg massage points and lines. At the sole of foot: 4-massage lines from the heel to the base of metatarsophalangeal joints (MTP) (A), 5-massage points; one point at the base of 3rd MTP (B) and four points at the head of MTP (C). At the dorsum of the foot: 4-massage lines from the ankle to the base of MTP (D), 5-massage points at the head of MTP (E), and distraction of all joints of toes (F). Massage lines at the anterior leg, posterior leg, and knee (G, H) [56]

Discussion

In recent decades, the incidence of diabetes mellitus has been rising. Together with diabetes, overweight and sedentary lifestyle that can be caused by changes in the diet regimen and low somatic mobility can lead to DPN. Like other metabolic syndromes, a higher-than-normal body mass index (at the level overweight or obesity) can contribute to DPN [11]. Patients with diabetes experience problems such as peripheral neuropathy, visual impairments, kidney failure, and hypoglycemia, several mental and physical limitations, and problems [11]. We did this systematic review to reveal the efficacy of common physiotherapy interventions in eliminating or reducing DPN complications and symptoms. They were assuming that

physiotherapy interventions will improve symptoms in patients with DPN. The results showed that physiotherapy interventions, especially exercise therapy, recovered patients' status with diabetes mellitus.

In this review, we divided physiotherapy interventions in DPN patients into three categories: exercise therapy, electrotherapy, and other therapies. The effects of strengthening, stretching, functional, aerobic, Tai Chi, weight-bearing versus non-weight-bearing exercises were assessed in exercise therapy. In the [Electrotherapy](#) section, the effects of spinal cord electrical stimulation, plantar electrical stimulation, Percutaneous Electrical Nerve Stimulation (PENS), and low-level laser therapy were examined. Finally, in other treatments, the effects of acupuncture, whole-body vibration, and Thai foot massage were assessed.

Dallemole et al. (2012) examined the effects of a combination program of strength, stretching, and functional exercises on gait parameters in patients with DPN. In their study, patients were studied for 12 weeks (24 sessions). Their results showed that these treatments had beneficial effects on reducing abnormal pressure on the foot while walking. Therefore, the use of these treatments may indirectly affect wound healing [10]. The physiological changes following exercise therapy have not been cleared yet, but increased levels of glycation and production (AGE) and protein kinase C (PKC) can be responsible for peripheral nerve injury in DPN patients [41].

On the other hand, recovery after exercise could be assigned to improve glycemic control by reducing HbA1C levels [41]. Najafi et al. (2017) showed that plantar electrical stimulation improves postural balance and plantar sensation in patients with DPN. This study was performed for six weeks daily, and ankle and COM sway significantly improved in the intervention group while no difference was reported in the control group. Besides, all gait parameters were improved in the intervention group [11]. In their survey, the cause of improvement in ankle stability can be accredited to an increase in somatosensory feedback, which is confirmed by the increased vibrating sensation [11]. Najafi et al. (2013) introduced a new method for plantar electrical stimulating. Based on their results, the presented technology was suitable for enhancing protective sensation. A possible effective mechanism was to raise the mechanoreceptors' performance [53]. Schwann cells, on the other hand, are damaged in these patients so that electrical stimulation can boost Schwann cell function because of nerve conduction and improved foot sensation. Another electrical stimulation mechanism can be attributed to increased circulation of the skin so that reduced blood flow can lead to oxidative stress, the release of factors that impedes the passage of neurological signals. Electrical stimulation will increase dermal flow by releasing vascular endothelial growth factor (VEGF).

VEGF has been shown to increase Schwann cell proliferation and stimulate axonal growth and promote Schwann cell nerve and cell regeneration. Thus electrical stimulation increases VEGF secretion while it enhances mRNA activity in skeletal muscle [53].

Lee et al. (2013) examined the effects of whole-body vibration combined with balance exercises on muscle strength, balance, and hemoglobin levels in elderly patients with DPN. Their results showed that applying the two methods mentioned together resulted in a significant improvement of static and dynamic balance, muscle strength, and hemoglobin level [65]. Recovery from whole-body vibration may be ascribed to several operations, including short duration of intervention, and ease of use, preventing falls in patients with DPN [65]. Lee and colleagues (2013) examined the effect of electro-acupuncture compared with placebo and usual care on pain in DPN patients, and showed that electro-acupuncture is an effective and safe treatment in these patients. The active mechanism is that electroporation leads to increased pain threshold, and blood flow changes significantly on central endorphins, including beta-endorphin and dynorphin [17]. The mechanisms of recovery following electro-acupuncture increased flux through the polyol pathway, glycation and advanced glycation end products, oxidative stress, protein kinase C activity, and inflammatory processes. On the other hand, recovery following electro acupuncture includes cutaneous reinnervation, decreased pain, and peripheral nerve receptors. It has also been reported that electro-acupuncture can alter blood flow by affecting central endorphins, such as beta-endorphin or dynorphin [17].

Ahn et al. (2012) examined the effects of Tai Chi exercises on neuropathy scores, balance, glucose control, and life quality in DPN patients. Their intervention lasted three months, and the results showed that Tai Chi exercises led to a significant improvement in glucose control, balance, some dimensions of life satisfaction, and neuropathy scores. Improvement following Tai Chi exercises can be attributed to increased glucose metabolism leading to lower HbA1c levels and insulin resistance [18].

According to previous studies, physiotherapy interventions, including exercise therapy, electrotherapy, and other therapies, effectively improve DPN patients. However, there was no consensus among the researchers' results, and in some cases, the method of intervention or the characteristics of the samples were not comparable. Previous researchers suggested further studies should be undertaken due to the small sample size, high excluding sample rate from research, and lack of follow-up. It is recommended that future studies in clinical trials compare the effects of exercise therapy with electrotherapy or other therapies that are more effective.

Conclusions

The results showed that in the **Electrotherapy** section, improvement in the variables of motor efficiency, pain, postural stability, plantar sensation, physical activity, sleep quality, and life satisfaction was reported following interventions. Improvement in the foot and ankle function, range of motion, gait speed, daily physical activity level, standards of life, foot muscle strength, glucose levels, balance, neuropathic symptoms were also reported in the **Exercise therapy** section. Other treatments also reported improved static balance, dynamic balance, HbA1 levels, muscle strength, pain, range of motion, and foot sensation following treatment.

Compliance with ethical standards

Conflict of interest On behalf of all authors, the responsible author declares that there is no conflict of interest. This research has not received any assistance from the financial support center.

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