MINI REVIEW

Effect of acupuncture on diabetic neuropathy: A mini review

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ABSTRACT

Diabetic neuropathy, a prominent consequence of diabetes mellitus, refers to a group of clinically varied nerve system abnormalities that can cause discomfort. Despite the fact that the number of individuals suffering from severe neuropathy is growing, no optimum therapeutic technique has yet been identified. Acupuncture is widely known for its capacity to alleviate many types of pain, and some studies have indicated its benefit on diabetes mellitus; nevertheless, its efficacy and underlying mechanism against diabetic neuropathy are still unclear. This study examined 10 and five research conducted in people and animals, respectively, and found that acupuncture effectively alleviated diabetic neuropathy. The most often utilised acupoints were ST36, BL13, BL20, SP6, and SP9.

Key Words: *Acupuncture; Electro-acupuncture; Diabetic neuropathy; Pain*

INTRODUCTION

According to the International Diabetes Federation, 463 million individuals had diabetes in 2019, with the number anticipated to climb to 578 million by 2030 [1]. Diabetes can lead to a variety of significant consequences, including ischemic heart disease, stroke, and renal disease. Diabetic neuropathy, caused by damage to the peripheral and autonomic nerve systems, is by far the most common diabetes complication, affecting up to half of all diabetics [2]. Diabetic neuropathy is a clinically varied group of illnesses that affect the nerve system as a result of hyperglycemia and microangiopathy .

According to the International Diabetes Federation, one-third of the population will develop diabetes by 2050, and half of them will have neuropathy if no viable intervention is implemented [3]. Distal symmetric polyneuropathy, small-fiber predominance neuropathy, radiculoplexopathy, and mononeuropathy are the most common nerve damage types in diabetic neuropathy . In afflicted individuals, these disorders produce significant morbidity, increased mortality, and discomfort. Neuropathic pain, in particular, produces spontaneous pain, allodynia, hyperalgesia, hyperpathia, reduced physical activity, increased tiredness, and sleep issues, all of which have a detrimental impact on quality of life.

Diabetic neuropathy is now managed by glycemic control, lifestyle changes (such as diet and exercise), and drug-based pain management. However, comprehensive meta-analyses have found that glycemic control has little effect on neuropathy patients, particularly those with type 2 diabetes, indicating that concentrating just on glycemic control may not be enough to prevent diabetic neuropathy. Various therapies for neuropathy have been proposed, including aldose reductase inhibitors, -lipoic acid, and benfotiamine. However, their effectiveness is still being debated [4]. Additionally, calcium channel 2 ligands, serotonin and noradrenaline reuptake inhibitors (SNRI), and Tri Cyclic Antidepressants (TCAs) have been employed, although comparative efficacy studies to establish the optimum pharmaceutical option are sparse [5].

Acupuncture has long been used to treat a variety of ailments. Several investigations on asthma, rheumatoid arthritis, epicondylitis, complicated regional pain syndrome type 1, and vasculitis have found it to be anti-inflammatory. Acupuncture is also known to cure several nervous system illnesses, such as Parkinson's disease, by lowering dopaminergic drug dosage and relieving nerve dysfunction in the motor, non-motor, pre-motor, and autonomic nerves .Furthermore, acupuncture has been shown to be useful and effective for pain reduction in a variety of settings, including lower back pain , chronic tension-type headaches, and migraine prevention. Acupuncture has also been shown in trials to successfully control hyperglycemia in people with diabetes mellitus.

Studies conducted in rodents

Three of the five *in vivo* experiments focused on the DRG, while the other two focused on the spinal cord studied Electro-Acupuncture (EA) on Strep To Zotocin (STZ)-induced diabetic neuropathy in rats [6]. A single intraperitoneal injection of STZ was used to induce diabetes, and animals with fasting blood glucose levels of 16.65 mM or above were employed in the tests. For one week, EA treatments were given for 30 minutes, once a day. Acupuncture was stimulated using alternate frequencies of 2 Hz and 100 Hz. The rats were split into three groups for the studies.

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EA was applied to ST36 and BL42 in the first and second groups, respectively. The needles were placed into ST36 without any electrical stimulation in the third group. When compared to the control, a single EA treatment on bilateral ST36 substantially enhanced the Paw Withdrawal Thresholds (PWT) at 2 hours and 4 hours. Furthermore, numerous EA treatments improved PWT considerably. In comparison to the control, this impact began 30 minutes after EA treatment and remained until day 5.

However, when EA was administered to BL43, there was no significant change as compared to the control. They concentrated on Nuclear Factor kappa-B (NF-B) and cystathionine synthase to understand the mechanism of action of EA on diabetic neuropathy (CBS). When compared to the control, numerous EA treatments inhibited both p65 and CBS expression in the L4-6 DRG. Sensitization of the DRG is thought to be a crucial element in the development of abnormal pain. Furthermore, in animals with neuropathic pain caused by sciatic nerve damage, NF-B was dramatically enhanced in the DRG [7], indicating that NF-B is implicated in the development of neuropathy.

Researcher also found that EA had an impact on STZ-induced diabetic neuropathy in rats with fasting blood glucose levels of 16.7 mM or above. EA was given for 20 minutes, once a day, six days a week for a total of 12 weeks. Acupoints BL13, BL20, BL23, LI4, LR3, ST36, and SP6 were employed. The frequency was set at three hertz (Hz). The control group received only STZ injections and no EA therapy. Thermal sensitivity, Motor Conduction Velocity (MCV), and sensory conduction velocity were all enhanced by EA. Furthermore, nerve fibres were shown to be injured in the STZ-only group, as the myelin sheaths were loose with irregular membranous masses, whereas EA therapy alleviated these abnormalities.

Furthermore, as compared to the control, EA reduced the fraction of apoptotic cells. Most crucially, EA reduced the levels of G-Protein Coupled Receptor 78 (GPR78) and caspase-12, both of which are essential players in the Endoplasmic Reticulum Stress (ERS) apoptotic pathway [7]. Under high-glucose circumstances, ERS apoptosis is thought to be the most significant mechanism. Protein folding mistakes occur in the endoplasmic reticulum when cells are exposed to hyperglycemia, resulting in the buildup of unfolded proteins and the disturbance of calcium homeostasis [8]. ERS apoptosis is induced in these situations. Furthermore, endoplasmic reticulum chaperones, including as the glucose-regulated protein, are increased in response to ERS to stabilise protein folding and prevent apoptosis [9].

Studies conducted in humans

A study on 44 diabetic neuropathy patients was done to study the impact of acupuncture on diabetic neuropathy. 29 of them were already getting standard therapies such anticonvulsants and tricyclic medications. LI3, SP6, SP9, and ST36 were all treated with acupuncture. The primary and secondary symptoms were considerably reduced in 34 of the 44 patients (77%) after six sessions of acupuncture treatment over ten weeks. They classified main symptoms as the most bothersome and secondary symptoms as insignificant. Furthermore, seven patients (21%) experienced total symptom alleviation.

The 34 patients who improved after acupuncture were monitored for 18-52 weeks, and 67% were able to discontinue or reduce their drugs. During the therapy, however, there were no significant improvements in the Neuropathy Disability Score (NDS), Vibration Perception Threshold (VPT), or HbA1c levels. The NDS has been demonstrated to be a sensitive measure of neuropathy impairment, whereas the VPT can help detect neurological dysfunctions. Only one person in this research felt uneasy and left after two sessions treated 45 diabetic neuropathy patients with genuine or sham acupuncture in their trial [8]. Ten sessions of acupuncture therapy were administered to the LR3, KI3, SP6, SP10, and ST36 acupoints during a 10-week period. Sham acupuncture was also conducted in the same acupoints as a control, but the needles did not enter the skin.

Both treatments lasted 30 minutes, followed by 15 minutes of manipulation. Patients in the acupuncture group improved better than those in the sham group in terms of LANSS score, Visual Analogue Scale (VAS), pain intensity, Measure Yourself Medical Outcome Profile (MYMOP) score, Sleep Problem Scale (SPS), and the physical component of the Short Form 36 (SF-36).

Doctor treated diabetic neuropathy with needle acupuncture, laser acupuncture, and placebo laser acupuncture [9]. Acupoints Ex-LE10, Ex-LE12, and ST34 were chosen. In the laser acupuncture group, a 685 nm wavelength, 35 mW optical power, 2.3 kJ/cm^2 power density, and 500 m spot diameter laser was delivered directly to the skin at 90 for 20 minutes on the same acupoints. In the placebo group, laser acupuncture was performed without the use of a laser. For ten weeks, all individuals gotten identical therapy sessions every week. After the therapy, sural Sensory Nerve Action Potential (SNAP) was raised in all three groups. However, only the manual and laser acupuncture groups had increased Sensory Nerve Conduction Velocity (SNCV). Only the manual acupuncture group's mean tibial MNCV improved, and no significant change in Motor Nerve Action Potential (MNAP) was seen across all groups. In terms of the mean changes in diabetic neuropathy-related symptoms from baseline to after 15 weeks of treatment, patient-related outcome measures (assessed using 11-point NRS questionnaires) revealed that acupuncture administration resulted in significant changes in all 12 items (neuropathic pain, hyperesthesia, cold sensation, heat sensation, burning pain, tingling, muscle cramps, numbness, unsteadiness of gait, impact on daily activities, impact on quality of life).

DISCUSSION

Diabetic neuropathy is a severe concern to diabetic patients, and while there are several therapeutic options available, an ideal medicine or treatment strategy has yet to be established. This review contained 15 publications on the impact of acupuncture for diabetic neuropathy, with 10 and five investigations conducted in people and rats, respectively. To the best of our knowledge, this is the first study that summarized and analyzed the efficacy of acupuncture on diabetic neuropathy using data from both humans and rats. There has been no previous research on the subject. The subjects of similar articles were slightly different.

One previous research looked at the connection between acupuncture and neuropathy, but it didn't explicitly look at diabetic neuropathy [9]. Another research examined diabetic neuropathy, although only acupuncture at ST36 was investigated. Another research concentrated solely on manual acupuncture and diabetic neuropathy [10]. The other looked on the effectiveness of manual acupuncture in the treatment of diabetic neuropathy. However, in this study, we attempted to clarify the impact of acupuncture, including manual, electro acupuncture, and laser acupuncture, as well as examine the underlying mechanisms of action using animal experiments.

Four of the five *in vivo* trials employed EA, while one employed manual acupuncture. Among the clinical studies, eight employed manual acupuncture, one utilized EA, and one used combined manual and laser acupuncture. ST36 was the most often utilized acupoint, appearing in four in vivo research and six clinical trials . BL13 and BL20 were the most often utilized acupoints after ST36 in rodent investigations. SP6 (seven times), ST36 (six times), and SP9 were chosen more than four times in clinical studies (four).

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