

Research Progress on Mechanism of Acupuncture in Treating Diabetic Peripheral Neuropathy

Yuanyuan Li¹, Ximei Xie^{2,*}

¹Shaanxi University of Chinese Medicine, Xianyang 712046, Shaanxi, China

²Xi'an Hospital of Traditional Chinese Medicine, Xi'an 710021, Shaanxi, China

*Correspondence Author

Abstract: *Diabetic peripheral neuropathy (DPN) is one of the neurological diseases with high morbidity, and its course is migratory and progressive. Currently, the effectiveness of acupuncture therapy in the prevention and treatment of diabetes and its complications has been confirmed by clinical and basic research. Acupuncture treatment modality has the advantages of low cost, high safety, no toxic side effects, and good efficacy, and is easily accepted by patients in treatment. The authors have documented the inflammatory response, glycolipid metabolism disorders, oxidative stress, blood rheology and nerve conduction in function. The authors have documented the inflammatory response, glycolipid metabolism disorders, oxidative stress, blood rheology and nerve conduction function in patients with DPN treated with acupuncture to summarize the mechanism of action of acupuncture in treating DPN and to provide a reference basis for clinical and scientific research.*

Keywords: Acupuncture, Diabetic peripheral neuropathy, Mechanism of action, Review.

1. Introduction

Diabetes mellitus is a metabolic disorder characterized by elevated blood glucose, with the extension of diabetes mellitus, blood glucose metabolism continues to be disturbed, patients show symptoms related to neurological dysfunction, the incidence of DPN is obviously on the rise [1]! The main clinical manifestations of DPN are numbness and insensitivity of the limbs, or like ants, sensory loss, pain, and limb weakness, muscle atrophy and even amputation if the disease does not recover [2]. DPN is considered to be one of the most common forms of DPN in Chinese medicine. Chinese medicine believes that DPN belongs to the category of "thirst, paralysis" and other diseases, and in 2010, the State Administration of Traditional Chinese Medicine (TCM) named DPN as "thirst paralysis" [3]. In 2010, the State Administration of Traditional Chinese Medicine named DPN as "paralysis of thirst". DPN is a migratory disease with symptoms of pain, numbness and sensory impairment, which seriously reduces the quality of life of patients and has a certain impact on the economy of the country. Therefore, improving effective preventive and therapeutic measures for DPN to avoid aggravation of the disease and improve the quality of patients' survival is the purpose of our continuous exploration of optimal treatment. In the choice of treatment, Western medicine drugs are mainly used to improve the neural microcirculation, anti-oxidative stress and nutritive nerve treatment thereby controlling blood sugar and alleviating the patients' condition [4]. The main purpose of western medicine is to improve nerve microcirculation, anti-oxidative stress and nutritional therapy to control blood glucose and alleviate patients' condition. Acupuncture in Chinese medicine is a relatively ideal treatment method to improve the therapeutic effect and improve the nerve conduction speed of patients by warming the meridians and tonifying the deficiency, warming the meridians and activating the blood circulation, and removing blood stasis [5]. It is a relatively ideal treatment method. Some related studies have shown that [6] that acupuncture can improve the clinical signs of DPN patients and is better than the western medicine group in terms of efficacy. Acupuncture treatment is to

stimulate the acupoints to regulate the function of internal organs, so that the balance of qi, blood, yin and yang in the body, in the treatment of DPN patients can play a role in tonifying the qi, blood and collaterals. However, there are fewer studies on the mechanism of acupuncture in treating DPN, and more scholars are still needed to conduct in-depth studies and research. The author has analyzed the literature on acupuncture treatment of DPN patients in the past ten years, and summarized the mechanism of acupuncture treatment of DPN, which is now summarized as follows:

2. Acupuncture Reduces the Inflammatory Response

The divine inflammatory response is an autonomous immune defense mechanism that activates inflammatory cells and releases multiple pro/anti-inflammatory mediators. Inflammation is able to clear damaged tissues in a timely manner, while a dysregulated inflammatory response impairs the function and structure of tissues [7]. Under sustained hyperglycemic conditions, the NF- κ B signaling pathway can be activated by a variety of substances, initiating the inflammatory signaling mechanism, producing a large number of pro-inflammatory factors, causing the body's axonal edema, myelin sheath detachment, and aggravating the symptoms of DPN. Acupuncture has an anti-inflammatory effect. Some scholars [8] Studies have shown that electroacupuncture can improve blood glucose levels, serum hs-CRP levels are significantly reduced, CRP synthesis is reduced, insulin function is improved, acupuncture can also reduce the level of IL-1 β , IL-6 gene expression, and increase the level of gene expression of IL-2 and IL-10. This indicates that acupuncture can achieve the regulation of inflammatory factors by reducing the level of pro-inflammatory factors and increasing the level of anti-inflammatory factors. Clinical studies [9] demonstrated that the use of acupoint acupuncture therapy for DPN patients can produce a relaxing and analgesic effect on muscles, induce the body to release more analgesic substances, inhibit the release of various pro-inflammatory factors and promote the metabolism of inflammatory mediators. This may be related to the inhibition of the release

and expression of inflammatory mediators by acupuncture, thus reducing the effects of inflammatory factors on nerve structure and function. Zhou Xinyu [10] A study on the mechanism of action of electroacupuncture (EA) on the spine to inhibit the inflammatory response showed that EA on the spine could inhibit the inflammatory response by down-regulating the expression of inflammatory factor COX-2 through the NF- κ B signaling pathway. In summary, acupuncture reduces the inflammatory response by inhibiting the NF- κ B signaling pathway and inhibiting the expression and activity of NF- κ B, which reduces the synthesis and release of pro-inflammatory factors and increases the level of anti-inflammatory factors, improves the inflammatory response, and exerts anti-inflammatory effects.

3. Acupuncture Improves Disorders of Glucose-fat Metabolism

Disorders of glucose metabolism are abnormalities in hormones or enzymes, tissues, and organs that regulate the metabolism of glucose, fructose, galactose, and so on, and disorders of lipid metabolism are quantitative and qualitative abnormalities of lipids and their metabolites in the body. [11] Lipid metabolism disorder refers to quantitative and qualitative abnormalities of lipids and their metabolites in the body. Disorders of glucose metabolism and lipid metabolism interact with each other, causing neuroendocrine, intestinal flora disorders, oxidative stress and chronic inflammatory response [12]. The disorders of glucose metabolism and lipid metabolism interact to cause neuroendocrine, intestinal flora dysregulation, oxidative stress and chronic inflammation. Under persistent hyperglycemia, the interaction of glucose metabolism disorder and lipid metabolism disorder leads to various pathological changes in neuronal cells, Schwann cells and glial cells, thus affecting the progression of DPN. Clinical studies [13] showed that electroacupuncture combined with lipoic acid could reduce serum triglyceride (TG), total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C), promote metabolite absorption and improve lipid metabolism. This may be related to the fact that electroacupuncture promotes the metabolism and redistribution of lipids in the body, thus enabling the patients to lose weight and reduce lipids, and alleviating the state of metabolic disorders. Ye Xin [14] et al. treated patients with DPN by combining acupuncture with methylcobalamin, which showed that patients' fasting glucose (FPG), triglyceride (TG), total cholesterol (TC), and glycosylated hemoglobin (HbA_{1c}) decreased, and the disorders of glucose and lipid metabolism were effectively improved. Duan Haoru [15] Duan Haoru et al. used high-fat dietary feeding to construct a spontaneous T2DM obese rat model, Zucker diabetic obese (ZDF) rats fasting blood glucose and lipid levels increased, and serum adiponectin (APN) levels decreased, and the experimental results proved that electroacupuncture can improve serum APN levels and skeletal muscle adenylate-activated protein kinase (AMPK)/peroxisome proliferator-activated receptor (PPAR α) signaling pathway transduction, which in turn improves the glucose-lipid metabolism disorders. signaling pathway transduction, which in turn promotes glycolipid metabolism. In conclusion, the improvement of glycolipid metabolism disorders by acupuncture may improve insulin resistance and regulate insulin secretion, reduce lipid deposition and

promote lipid clearance, thus lowering the indexes of blood glucose, blood lipids and glycated proteins in patients with DPN, and improving the metabolic disorders of the body, decreasing the damage to the neural structure, and improving the function of peripheral nerves.

4. Acupuncture Inhibits Oxidative Stress

Oxidative stress, also known as reactive oxygen-antioxidant imbalance, is an imbalance between the oxidative and antioxidant systems when the organism is subjected to a variety of harmful stimuli that produce excessive amounts of highly reactive molecules such as reactive oxygen species (ROS) and reactive nitrogen species (RNS). [16]. Sustained hyperglycemic conditions that produce excess oxidants damage neurons and axons, leading to cellular dysfunction, immune activation, and inflammatory responses that promote oxidative damage to DPN. Cui Yan [17] et al. used the fixed-base and channeling electroacupuncture combined with eight-vein rendezvous point acupuncture for patients with DPN, and the results showed that serum superoxide dismutase (SOD) levels increased significantly, malondialdehyde (MDA) and ultrasensitive C-reactive protein (hs-CRP) levels decreased, and the patients' symptoms improved, and the fixed-base and channeling electroacupuncture had the effects of fixing the root and cultivating the vital energy and eliminating blood stasis and channeling the blood. This may promote the absorption of localized metabolites of damaged nerves. Clinical studies [18] showed that the combination of Yiqi, Qi, turbid and water-relieving formula and acupuncture in the treatment of DPN, patients' serum superoxide dismutase (SOD) and TAOC increased, suggesting that the combination of acupuncture and medicine and acupuncture treatment can reduce oxidative stress injury, promote the recovery of nerve function, and improve the clinical symptoms. This may be related to the fact that acupuncture can promote the recovery of oxidative stress balance, enhance the function of pancreatic β -cells, and improve the blood supply and oxygenation of the nerves. There are also scholars [19] studies have shown that treating DPN patients with warm acupuncture combined with acupoint burrowing can significantly improve patients' clinical symptoms, promote nerve repair, and reduce the degree of oxidative stress in the organism. This suggests that acupuncture can significantly improve the body's immune function and regulate the body's oxidation/antioxidant balance. In summary, the study analyzed that acupuncture inhibits oxidative stress response may eliminate harmful substances produced by the organism during metabolism by increasing the levels of serum SOD and TAOC, inhibiting the oxygen radical chain reaction, reducing the free radicals of the organism, bringing the oxidative stress response into balance, protecting the structure and function of the nerve cells, and then improving the symptoms of DPN patients.

5. Acupuncture Improves Abnormal Blood Rheology

Blood rheology is the study of the deformability and fluidity patterns of blood and its components in blood flow and their effects on the blood circulation and the body as a whole [20]. The study of blood rheology is the study of the deformation and flow patterns of blood and its components and their effects on blood circulation and the whole organism. Under

persistent hyperglycemia, the abnormalities of lipid metabolism and activation of coagulation-fibrinolytic system make the blood rheology indexes in an abnormal state, and the dysfunction of microcirculation of tissues and organs and the change of microvascular structure cause ischemia and hypoxia of neural cells, which ultimately progress to DPN. Acupuncture is able to promote the blood circulation. Some scholars [21] Studies have shown that combining acupuncture with Jiezhi Xiepao Tang in treating DPN patients can improve blood viscosity, lower blood glucose and blood rheology indexes, and improve the therapeutic effect. This may be due to the effect of acupuncture in dilating microvessels, increasing tissue perfusion and local blood flow, and reducing blood viscosity. Clinical studies [22] showed that improving hemodynamics and peripheral nerve perfusion in patients with DPN is better than Western medicine. Warm acupuncture can activate blood circulation and remove blood stasis, warm menstruation and relieve pain through acupuncture meridian points, and promote the repair of damaged nerves. There are also studies [23] have shown that electroacupuncture can improve the sensory and motor functions of DPN patients, promote the regeneration of damaged nerves, regulate the local blood flow, and improve the blood lipids and blood rheology indexes of patients. To summarize the analysis of the above studies, acupuncture may increase blood perfusion, improve local blood flow, reduce blood viscosity, delay vascular sclerosis, improve the relevant indicators of blood rheology, and then improve the structure and dysfunction of nerve tissue.

6. Acupuncture Improves Nerve Conduction Velocity

Nerve conduction velocity is a technique used to assess the conduction function of peripheral nerves [24]. Diabetic peripheral neuropathy presents with motor and sensory nerve abnormalities; motor nerve conduction velocity (MNCV) basically reflects the tendency of pathological changes in myelin sheaths in the DPN, and sensory nerve conduction velocity (SNCV) reflects the extent of axonal damage. Under persistent hyperglycemia, axon degeneration occurs and segmental demyelination or myelin hyperplasia occurs in nerve fibers. a large number of experiments have shown that acupuncture can improve SNCV and MNCV in DPN patients. acupuncture has the ability to improve local microcirculation, promote the repair of nerve endings, alleviate the patient's clinical manifestations, and improve nerve conduction velocity. Some scholars [25] study showed that acupuncture combined with herbal fumigation in treating patients with sugar DPN of the damp-heat and blood stasis type reduced symptoms such as numbness and pain and promoted faster nerve conduction velocity. This may be due to the ability of acupuncture to stimulate motor and sensory nerves and enhance muscle excitation and contraction. Liu Yadong [26] et al. showed that needling Xing and Lung and Xihe points in treating patients with DPN, and the study showed that needling could increase neuromuscular excitability, improve nerve conduction velocity, and reduce patients' pain symptoms. Acupuncture at Xingxing, Transfusion and Xiahe points can regulate the qi of the organs and meridians in the patient's body, promote the repair of nerve tissues and accelerate the conduction speed. Clinical studies [27] showed that acupuncture can repair neurotrophic dysfunction, inhibit

myelin loss, promote axonal structure recovery, and then improve nerve conduction velocity. Ding Yaqin [28] et al. treated DPN patients with acupuncture combined with Zhiguo Tongxin granules, and showed that the combined use of acupuncture and medicine could promote axonal regeneration and nerve fiber repair, and improve the function of nerve conduction velocity in patients. In summary, the study analyzed that acupuncture may stimulate muscles, increase muscle excitability, inhibit myelin sheath loss and axonal damage, repair neurotrophic factors, improve nerve structure and function, and alleviate patients' symptoms.

7. Summary

The pathogenesis of DPN acts in a complex way, by a variety of factors acting together in the peripheral nervous system, neurons, Sherwan's cell apoptosis. Acupuncture is safe and effective in treating DPN, and its mechanism of action is multifaceted, mainly from the improvement of inflammatory response, glycolipid metabolism disorders, oxidative stress, blood rheology, and nerve conduction function, to alleviate the symptoms of patients. Exploring the mechanism of action of acupuncture on DPN patients provides more theoretical basis for acupuncture treatment of DPN. However, most of the studies on the mechanism of action of acupuncture in treating DPN are based on the observation of relevant indicators of clinically treated DPN patients, and there are fewer experimental studies on the use of animals. Therefore, in order to make the experimental results more authentic and reliable, more multi-center, large-sample, standardized randomized controlled trials are needed, and the mechanism of acupuncture in treating DPN should be gradually improved by using modern advanced technology and means.

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