

Research Progress of Buyang Huanwu Decoction in the Treatment of Diabetic Peripheral Neuropathy

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Abstract: Diabetes peripheral neuropathy is a complication aused by diabetes, involving peripheral nerves. The onset of DPN is occult and the process is slow, and the late stage of the disease will lead to severe nerve damage. With the change of modern people's lifestyle, the number of obese people is increasing, which leads to the increasing number of DPN patients. Common hypoglycemic drugs can not control blood sugar well and can not interfere with the process of DPN. Opioid analgesics and antiepileptic drugs are often used to relieve neuropathic pain and other symptoms in clinic. However, these drugs can only relieve the pain at that time, treat the symptoms but not the root cause, and have great toxic and side effects on human body. Therefore, the research and development of DPN specialty drugs has attracted wide attention around the world. Unfortunately, most of the drugs under research have failed due to safety problems. Therefore, there is an urgent need for safe and effective drugs to treat DPN. Therefore, it is necessary to treat this disease by means of traditional Chinese medicine. The Buyang Huanwu Decoction recorded in the medical forest correcting mistakes is a famous prescription for supplementing qi and activating blood circulation, which has the pathogenesis of DN. The research shows that the effect of Buyang Huanwu Decoction on DPN is accurate, but the effective substances and the mechanism of action in Buyang Huanwu Decoction are not clear. This subject takes Buyang Huanwu decoction as the research object to explore its mechanism of action and the research progress of clinical application, so as to lay a solid foundation for the treatment of diabetes peripheral neuropathy by traditional Chinese medicine. The Buyang Huanwu Decoction recorded in the medical forest correcting mistakes is a famous prescription for supplementing qi and activating blood circulation, which has the pathogenesis of DN. The research shows that the effect of Buyang Huanwu Decoction on DPN is accurate, but the effective substances and the mechanism of action in Buyang Huanwu Decoction are not clear. This subject takes Buyang Huanwu decoction as the research object to explore its mechanism of action and the research progress of clinical application, so as to lay a solid foundation for the treatment of diabetes peripheral neuropathy by traditional Chinese medicine.

1. Introduction

A series of symptoms of diabetes peripheral neuropathy are mainly due to the disorder of metabolic function, blood vessels, nerves and other cytokines in diabetes patients. The above disorder symptoms will induce glycosylation reaction, hinder protein synthesis of nerve cells, and finally form a series of nerve cell structures and dysfunction^[1]. However, from the perspective of traditional Chinese medicine, the symptoms of diabetes involve many functions, and the pathogenesis of the disease is similar to that of Qi Yin deficiency and phlegm obstruction in traditional Chinese medicine, which are caused by blood stasis. Therefore, in addition to repairing the function of nerve cells, improving the overall blood circulation is also of positive significance for the recovery of the overall function of patients with diabetes peripheral neuropathy^[2]. Many drugs in the prescription of Buyang Huanwu Decoction can play the role of removing blood stasis and generating body fluid, and become the research object of many doctors.

2. Understanding of diabetes peripheral neuropathy by traditional Chinese and Western Medicine

2.1. Understanding of diabetes peripheral neuropathy by traditional Chinese

DPN belongs to the category of "arthralgia syndrome" in traditional Chinese medicine. Its pathogenesis is long-term thirst, long-term disease entering the collaterals, blood stasis caused by damage to blood vessels, loss of kidney essence and blood, blood stasis caused by veins, poor blood circulation, and loss of nourishment of limbs and meridians. Vein stasis, qi stagnation and blood stasis are the main pathogenesis of DPN, it belongs to the syndrome of deficiency and standard solid, which is deficiency of qi and standard for blood stasis.

Professor Zhou Guoying believes that the deficiency of DPN is mainly Qi deficiency and yin deficiency, which can eventually affect the kidney and cause deficiency of yin and "Yang. Lingshu five changes", says: "all the five viscera are weak, and they are good at disease and itching". It shows that the weakness of the viscera is the root of thirst^[3]; According to Wang Xugao's medical case, "the hands and feet are numb and the limbs are as cold as ice"^[4], which reveals that the long-term diabetes can cause the appearance of related symptoms of arthralgia syndrome. Professor Zhou Guoying also believed that the main blame for the standard is blood stasis, or combined with phlegm turbidity, which can be summarized as the vein obstruction^[5]. "Five Changes of Spiritual Pivot", says, "blood can not... Therefore, it is miasma", indicating that diabetes is inseparable from blood obstruction^[6]. The so-called "blood without honor is wood", so Professor Zhou Guoying pointed out that the syndrome of Xiaoke Bi is a syndrome of deficiency and excess. The etiology of blood stasis according to Professor Zhou Guoying, the etiology of blood stasis is as follows: First, the patient is usually Yin deficiency, and the deficiency does not support the blood vessels, and the lack of blood leads to blood stasis, or yin deficiency leads to endogenous dryness and heat, which leads to fluid deficiency and blood accumulation into blood stasis; Second, due to eating out of control, excessive eating of fat taste and spicy products, the brand is not transported to the valley, and the water dampness accumulates into phlegm, phlegm Yang blood vessels, phlegm and blood stasis, or phlegm dampness turns into heat, and dampness and heat stagnates, resulting in dampness, heat and blood stasis; Third, due to long-term illness, yin and yang deficiency or damage to the card, kidney and liver, yin and blood deficiency to nourish blood vessels and become blood stasis. Second, due to eating out of control, excessive eating of fat taste and spicy products, the The spleen does not transport water and food, and the water dampness accumulates into phlegm, phlegm Clog blood vessels, phlegm and blood stasis, or phlegm dampness turns into heat, and dampness and heat stagnates, resulting in dampness, heat and blood stasis; Third, due to long-term illness, yin and yang

deficiency or damage to the card, kidney and liver, yin and blood deficiency to nourish blood vessels and become blood stasis. In short, there are various causes of blood stasis. Clinically, blood stasis does not exist alone, and it is mostly mixed with temperature, fever, heat and deficiency.

2.2. Understanding of diabetes peripheral neuropathy by Western Medicine

The pathogenesis of DPN has not been fully elucidated at present, but it is generally believed that impaired immune function, oxidative stress, vascular endothelial damage, decreased levels of neurotrophic factors and metabolic disorders are closely related to the pathogenesis of DPN [7]. In the past, most studies only focused on the metabolism of DPN. In recent years, with the increasing understanding of DPN by a large number of doctors, studies have found that the pathogenesis of DPN is closely related to immune mechanism, genetic mechanism and the influence of hypoglycemic drugs.

2.2.1. Metabolic factor

In recent years, it has been found that the metabolic pathogenesis factors of diabetes peripheral neuropathy are mainly related to oxidative stress, glycosylation end product pathway, vascular endothelial dysfunction, etc. Pericytes play a very important role in the pathogenesis of DPN and may be related to blood nerve barrier dysfunction [8]. Diabetes patients accumulate glycosylation end products through oxidation and glycosylation of non sugar substances, further activate NADPH oxidase, promote oxidative stress, and activate NF through signal transduction pathway and transcriptional regulation pathway- κ B. It affects the blood supply and structural integrity of the nerve and aggravates the peripheral nerve injury [8]. Inhibition of glycosylation end product receptors also plays an important role in nerve growth and nutrition. Saleh et al. [9] activated NF by in vitro- κ B. JAK-STAT pathway and ERK signal transducer and activator of transcription extracellular signal regulated kinase pathway promote the generation of a large amount of rage in mouse nerves and timely eliminate the oxidative stress products of injured nerves. Therefore, the relationship between nerve repair, regeneration and ligand RAGE axis deserves further study. Long term hyperglycemia not only affects the vascular structure, but also affects the vascular endothelial function. In a hyperglycemic environment, glucose mediated genes such as transforming growth factor β 1 and plasminogen activator inhibitor can accelerate the proliferation of fibers and the mitosis of smooth muscle cells in blood vessels, cause structural changes such as tube wall thickening, lumen narrowing and endothelial cell swelling of microvessels, significantly increase the vascular resistance, and lead to changes and necrosis of corresponding nerves due to ischemia and hypoxia [10].

2.2.2. Immune related factors

In the pathogenesis of DPN, the immune mechanism can not be ignored. Among them, the cellular immune mechanism dominated by the changes of regulatory T lymphocyte subpopulations is the most important. Dong Rongfang et al [11] confirmed through nerve biopsy and immunohistochemical study on DPN pathology that moderate and severe DPN is mainly caused by axonal degeneration, and on this basis, demyelination changes gradually appear. Meanwhile, long-term hyperglycemia environment directly causes Schwann cell damage. Myelin protein can be used as a specific immune indicator after peripheral nerve damage, and is secreted by Schwann cells. Therefore, demyelination indicates the aggravation of nerve damage, it is convenient to judge the curative effect and prognosis after DPN treatment.

2.2.3. Gastrointestinal biological factors

With the continuous in-depth study of various systemic diseases, DPN lesions have been found to be related to gastrointestinal microorganisms. The intestinal flora can obtain energy through the host, produce monosaccharides and short chain fatty acids, promote the expression of endocrine cells in gastrointestinal mucosa through G protein coupled receptor pathway, and play the role of anti-inflammatory, wound healing and mucosal protection ^[12]. When the gastrointestinal flora is dysregulated, the permeability of the intestinal wall is increased, and it is easy to be infected by bacteria, resulting in inflammation and oxidative stress, which promotes the body to produce obesity related metabolic syndrome, and the peripheral nerve damage is also spared.

2.2.4. Hereditary factor

However, studies have shown that metabolic disorders in diabetes may be related to the expression of corresponding genetic genes. Zhang Chunxue et al ^[13] explored the effect of metformin on the expression of cholesterol metabolism related genes through animal experiments and found that the lipid level in DM group was significantly increased, and the liver lipid deposition and fat vacuoles under HE staining were significantly increased; However, after metformin treatment, the fat accumulation and lipid level were significantly reduced, which further confirmed that abnormal lipid metabolism played an important role in DM, and also confirmed that SREBP-2 gene was up-regulated and low density lipoprotein receptor (LDLR) mRNA expression was up-regulated, which could promote cholesterol synthesis and metabolism and significantly reduce the risk of DM complications.

3. Study on the treatment of diabetes peripheral neuropathy with traditional Chinese and Western Medicine

3.1. TCM treatment

Traditional Chinese medicine has made many researches on DPN and put forward many schemes, such as oral decoction, foot bath, acupuncture and moxibustion, which can play multiple roles, inhibit nerve damage, improve neuropathy, stabilize blood sugar during treatment, prevent other complications, maintain the safety of DPN treatment and improve the life of DPN patients ^[14].

3.1.1. Chinese herbal medicine treatment

In the application of Chinese herbal medicine to treat DPN, various doctors have their own different opinions and experiences. Han Baorui ^[15] applied Danggui Sini decoction combined with Chinese herbal fumigation to treat 82 patients with diabetes peripheral neuropathy. The results showed that the total effective rate of the observation group was higher than that of the control group. Zou Xiaoxia ^[16] treated 70 patients with diabetes peripheral neuropathy with Yiqi Huoxue Tongbi Decoction. It was found that Yiqi Huoxue Tongbi Decoction plays a very important role in improving the nerve conduction velocity and quality of life of patients in the treatment of diabetes peripheral neuropathy. Shen Yuting ^[17] applied Huangqi Guizhi Wuwu Decoction to Treat 60 cases of DPN. The results showed that the total effective rate of the study group was significantly higher than that of the control group, and the difference was statistically significant.

3.1.2. Foot bath treatment

Foot bath has a long history in the treatment of traditional Chinese medicine. Keeping the feet soaked after decocting various drugs can give full play to the thermal and stimulating effects,

improve the penetration of drugs, correct the blood circulation, maintain the neurotrophic state, and reduce the nerve function damage. The effects of *Caulis Spatholobi* mainly include dredging meridians and activating collaterals, relieving pain and activating blood circulation; In addition to this effect, Tougu grass can also promote blood circulation and remove blood stasis; Wormwood Leaves and *Zanthoxylum bungeanum* can relax meridians and collaterals, promote blood circulation and remove blood stasis, regulate qi and relieve pain. Studies have shown that after decoction, the drug can play the role of relieving pain and activating blood circulation, unblocking meridians and activating collaterals, improving the nutritional status of the body, restoring the blood oxygen supply of nerves, reducing nerve damage, inhibiting the progress of DPN, and stabilizing blood sugar [18].

3.1.3. Acupuncture treatment

Acupuncture and moxibustion also has unique value for DPN. Xia Zheng et al [19] believe that selecting Sanyinjiao point can activate blood circulation and remove stasis after acupuncture and moxibustion at this position, and can also play the role of nourishing yin and supplementing qi. At the same time, selecting Kunlun point and other points for acupuncture and moxibustion can strengthen the waist and legs, activate blood circulation and relieve pain, and reduce the degree of neuropathy. Fang wenhuang et al [20] proposed that whether to perform acupuncture on Ashi point should also be selected. Ashi point is an important reaction point outside the body disease. Acupuncture on it can unblock Qi and blood, dredge meridians, and improve and eliminate the pain and numbness of patients. Sun Yali [21] used acupuncture combined with moxibustion to treat 48 patients with DPN as the treatment group. The acupuncture points and methods were as follows: the twisting, lifting, inserting and purging method was used to directly stab Quchi point; Use the laxative method to directly stab Hegu, Zusanli and Taichong; Use the tonic method to directly stab Taixi point and Yinling spring; Use the method of tonifying first and then purging, and directly stab Sanyinjiao. 46 cases in the control group took Mecobalamin tablets orally. After treatment, it was shown that the treatment group was significantly better than the control group in the treatment effective rate and blood sugar improvement at the same time period ($P < 0.05$).

3.1.4. Massage

Massage therapy has the effects of dredging meridians, promoting blood circulation and strengthening nerve function. Jiang Yong et al [22] treated 40 patients with DM in the control group with insulin injection, and 40 patients in the observation group were treated with massage and massage on this basis, so as to achieve the function of dispersing meridians and unblocking collaterals, promoting qi and activating blood circulation. After the treatment, the incidence of DPN in the observation group (5%) was much lower than that in the control group (20%), and the difference between the two groups was statistically significant ($P < 0.05$), indicating that massage therapy can reduce the incidence of DPN and has an obvious effect in the prevention and treatment of DPN. Chen Lu et al [23] 119 randomly divided 60 patients with DPN into two groups, 30 patients in each group. On the basis of routine treatment, the control group was given routine acupoint massage, and the observation group used the diabetes therapeutic instrument to place Chinese medicine sticks at relevant acupoints (main acupoints; Zusanli, Yongquan, Taixi, Zhongyuan, etc.) for massage treatment. The total effective rate of the observation group was significantly higher than that of the control group; Moreover, in improving the skin color, temperature, tendon reflex and nerve conduction velocity at the extremities of the patients, the observation group was better than the control group ($P < 0.01$). Xu Xiuying et al [24] (201) 200 patients with DPN were randomly divided into 2 groups, with 100 patients in each group. The control group adopted the routine

treatment scheme, and the experimental group applied the massage along the meridians on this basis. The specific scheme was to massage Sanyinjiao, Yongquan, Zusanli, Chengshan and other acupoints with finger massage. After one month of treatment, the results showed that the total effective rate of the experimental group was 98%, higher than that of the control group (78%), and the neuropathy score of the experimental group was lower than that of the control group, The difference was statistically significant ($P < 0.05$). Fan Wuhua et al ^[25] (211) 30 cases in the control group were treated with conventional regimen and 30 cases in the treatment group were treated with conventional regimen+Weiliang traumatology oil point massage therapy. The results showed that the total effective rate of the treatment group (96.7%) was significantly better than that of the control group (66.7%); In terms of improving EMG performance, the treatment group had more advantages, and the difference was statistically significant ($P < 0.05$).

3.2. Western medicine treatment

The pathogenesis of DPN is complex and changeable, and it has not been fully understood in modern medicine. Its treatment is mainly based on strict control of blood sugar, and measures to relieve clinical symptoms. At present, western medicine mainly uses aldose reductase inhibitors, anti-oxidation stress treatment drugs, neurotrophic and repair drugs, drugs to improve microcirculation, vitamins and so on.

4. Research progress of Buyang Huanwu Decoction in treating diabetes peripheral neuropathy

4.1. Analysis on prescription of Buyang Huanwu Decoction

Buyang Huanwu decoction is selected from Wang Qingren's medical "Yi lin gai cuo" in the Qing Dynasty: "200g Astragalus membranaceus, 3G Angelica tail, 3G red spoon medicine, 3G earthworm, 3G chuanxiong, 3G peach kernel, 3G safflower, decoction". Astragalus membranaceus is mainly used in this prescription. It is said in the "Yi xue zhong zhong can xi lv": "Astragalus membranaceus 200g is mainly used in this prescription, mainly to replenish qi". Qi can move blood, and Qi is abundant and blood moves; Angelica sinensis is the holy medicine for nourishing blood. The tail of Angelica sinensis is the root of Angelica sinensis, and breaking blood does not hurt Zheng Zheng; Chuanxiong is the Qi medicine in blood. "Together with Paeonia lactiflora, peach kernel and safflower, it is an auxiliary medicine. The earthworm is good at walking and moving around, searching for and removing various evils, breaking blood and removing blood stasis. When used in combination, the above medicines have the effect of Invigorating Qi, activating blood circulation and unblocking collaterals. In Buyang Huanwu Decoction, large-dose Astragalus membranaceus is mainly used, and its functions of Nourishing Qi, nourishing fluid and blood, and removing stagnation and arthralgia are taken; White peony can strengthen the spleen and replenish qi, promote fluid production and nourish blood; Rehmannia glutinosa, Paeonia lactiflora, Angelica sinensis and Ligusticum chuanxiong cooperate to nourish and activate blood, harmonize blood, replenish blood without stagnation, and harmonize blood without hurting blood; Red peony, safflower and peach kernel can promote blood circulation, remove blood stasis and relieve pain; The Earth Dragon is good at walking and passing through the meridians. The combination of the above drugs can strengthen the spleen and Qi, consolidate the foundation of the day after tomorrow, make the blood biochemical active, have sufficient blood and blood, and have a smooth vein, so that the muscles and veins can be nurtured, blood can be invigorated, blood stasis can be removed, the vein can be dredged, and there is no pain when it is unblocked; So that various symptoms can be alleviated.

4.2. Experimental study on Buyang Huanwu Decoction

4.2.1. Study on the components of Buyang Huanwu Decoction

(1) Flavonoid ^[26]: it mainly includes isoflavones, flavonoids, pterostane and chalcone, among which isoflavones are most abundant in *Astragalus membranaceus*, and isoflavones in *Astragalus membranaceus* include, pistil isoflavones, anthocyanins, etc; Flavonoids include kaempferol, quercetin, rutin, etc. Pterostane includes: 9, 10-dimethoxypterostane-3-o-b-d-glucoside, (6aR,11ar) - 10-hydroxy-3, 9-dimethoxypterostane; Char is mainly derived from safflower. Almost all the yellow and red pigments in safflower belong to the carboglycosides of awake chalcone, mainly including hydroxysafflower yellow A and hydroxysafflower yellow B.

(2) Saponins ^[27]: at present, more than 40 saponins have been identified in *Astragalus membranaceus*, including astragaloside, soybean saponin, acetyl astragaloside, isoastragaloside, etc.

(3) Volatile oil ^[28]: volatile oil is the active ingredient of the tail of *Angelica sinensis* and *Ligusticum chuanxiong*. About 1% of the volatile oil in *Angelica sinensis* contains phenolic volatile oil represented by ligustilide; Volatile oil of phthalide dimer represented by 7.3'- diglycolide: other volatile oils such as a-ene, butenylphenol, etc.

(4) Others ^[29]: mainly including amino acids, caffeic acid, chlorogenic acid, palmitic acid, folic acid, ferulic acid, isoferulic acid, linoleic acid, linolenic acid, trace elements, vanillic acid, p-hydroxyphenylacrylic acid, lupinol, b-sitosterol, n-hexadecanol, hypoxanthine, xanthine, guanine, uracil and other nucleotides, tannins and other ingredients.

4.2.2. Pharmacological study on Buyang Huanwu Decoction

(1) Neuroprotective effect: Benying ^[30] and others found that *Astragalus membranaceus* in Buyang Huanwu decoction has a significant effect on diabetes peripheral neuropathy rats. Increase the conduction velocity of sciatic nerve by reducing oxidative stress response; Di Shi et al. Observed the growth of Schwann cells cultured in vitro in Buyang Huanwu Decoction and found that the cell state of the administration group was better than that of the control group. Zhao Mengdi^[31] and others found that it has a protective effect on the model by constructing an oxygen glucose deprivation model of neuronal cells and intervening with Buyang Huanwu Decoction, and may interfere with TLR4/NF- κ B signaling pathway.

(2) Anti inflammatory effect: Bao Peng et al ^[32] found that after the intervention of Buyang Huanwu Decoction in diabetes peripheral neuropathy mice, compared with the model group, the levels of IL-1B and TNF-a in the treated mice were significantly down regulated, suggesting that Buyang Huanwu Decoction can significantly inhibit the expression of IL-1B and TNF-a and improve diabetes peripheral neuropathy to a certain extent.

(3) Antioxidant effect: Buyang Huanwu Decoction can reduce the damage of hydrogen peroxide to PC12 cells, reduce the level of reactive oxygen species in cells by increasing the level of GSH, thus protecting PC12 cells. Mou Jian ^[33] Found that the Buyang Huanwu Decoction administration group increased the antioxidant activity of heart and kidney compared with the model group by measuring the SOD activity and MDA content in serum and tissues of diabetes rats, and found that paeoniflorin and pistil Isoflavone Glycoside might be the main active substances through the drug time curve, which provided a basis for Buyang Huanwu Decoction to prevent and treat diabetes and its complications.

4.3. Clinical application of Buyang Huanwu Decoction in the treatment of DPN

Wang Wen et al. ^[34] Patients with DPN were randomly divided into control group and treatment

group. The control group was given vitamin B1 and intramuscular injection of mecobal. The treatment group was treated with this prescription on the basis of the control group. Observe for 30 days. The experimental results show that the effective rate of the treatment group is significantly higher than that of the control group, which shows that Buyang Huanwu Decoction can improve the microcirculation of nerve tissue to a certain extent. Liu Caijin et al. [35] used Buyang Huanwu Decoction to treat sciatica in 38 patients. The effective rate of treatment was 94.7%, and the effect was significant. Chu Lisheng et al. [36] Rats were randomly divided into Buyang Huanwu Decoction group, model group and sham operation group. The middle dynamic Yang plug model of rats was prepared by thread plug method, and the behavior was detected by limb placement experiment, staggered step experiment and viscose removal experiment; Immunohistochemistry was used to detect the expression of vascular endothelial growth factor and microvessel density in ischemic area. It is concluded that Buyang Huanwu Decoction can effectively improve the limb placement disorder of rats and shorten the mucus latency. The results confirmed that Buyang Huanwu Decoction can promote the recovery of neural function after cerebral ischemia. Mei Xiaoyun et al. [37] prepared a rat model of common peroneal nerve pinch injury and measured the action potential of composite muscles, regenerated myelinated nerve fibers and shoe pin thickness in each group. Suggesting that Buyang Huanwu decoction is conducive to promoting the regeneration of rat pinched nerves. Yang Wenyan [38] randomly divided 60 DPN patients into control group (30 cases) and treatment group (30 cases). Both groups were given insulin detemir, cobalamine adenosine and lipoic acid, on this basis, the patients in the treatment group were treated with Buyang Huanwu Decoction, and the nerve conduction velocity was better than that in the control group. Sun Boxin et al. [39] divided 94 patients with diabetes peripheral neuropathy into two groups with a random number table. The observation group was treated with basic treatment plus Buyang Huanwu Decoction, and the control group was treated with basic treatment plus Mecobalamin. The curative effects of the two groups and the changes in the levels of FBG, 2hPG, HBA1C, total MNCV, total SNCV, median MNCV and median SNCV of patients before and after treatment were observed. The results show that Buyang Huanwu Decoction can repair the damaged nerves, improve the blood sugar level of the body, and is an effective drug for the treatment of diabetes peripheral neuropathy. Zu Lihua et al. [40] divided 104 patients with diabetes peripheral neuropathy into control group and observation group according to random number table method. The control group was treated with basic treatment combined with lipoic acid, and the observation group was treated with Buyang Huanwu Decoction based on the treatment scheme of the control group. Nerve conduction velocity, oxidative stress index, C-peptide and glycosylated hemoglobin (HbA1c) levels were measured in the two groups, and the incidence of adverse reactions and clinical efficacy were counted. The results showed that Buyang Huanwu Decoction Combined with lipoic acid was effective in the treatment of diabetes peripheral neuropathy. It could regulate the levels of serum C-peptide and glycosylated hemoglobin 2h after meal, improve the total antioxidant capacity of the body, reduce oxidative stress damage, repair damaged nerves, and have high safety.

5. Conclusion

With the improvement of people's living standards, the complications caused by diabetes are becoming more and more common, which is a major hazard to people's health. Nowadays, many doctors have their own unique opinions on the use of Buyang Huanwu Decoction to treat DPN, and the clinical effect is remarkable. It is pointed out that the essence of the disease is deficiency of Qi and blood stasis. Xiaoke arthralgia syndrome is based on the deficiency of Qi and Yin caused by Xiaoke disease for a long time, which can eventually lead to the deficiency of yin and Yang, pain and blood stasis blocking the meridians and collaterals. Therefore, the pathogenesis of Xiaoke

arthralgia syndrome is based on the deficiency of Qi and blood, with blood stasis, phlegm dampness, qi stagnation and occlusion as the standard, and the deficiency and excess are mixed, of which the pathogenesis of blood stasis runs through the whole process of the disease. Therefore, more and more doctors believe that Buyang Huanwu decoction is a good prescription for eliminating thirst and arthralgia. This prescription can replenish qi, activate blood and unblock collaterals. The whole recipe can make Qi prosperous, blood flow and collaterals smooth. In clinical use, the effect is excellent, and its experience is worth learning from.

References

- [1] Dong Yanyan. Research progress in the treatment of diabetes peripheral neuropathy with traditional Chinese medicine [J]. *Journal of Jiangxi University of traditional Chinese medicine*, 2020, 32 (3): 118-120.
- [2] Jin Zhe, Yang Xiao, Jiang Hong, et al. Clinical study of Buyang Huanwu Decoction Combined with α -lipoic acid in the treatment of diabetes peripheral neuropathy [J]. *Shaanxi traditional Chinese medicine*, 2020,41 (9) 1266-1268.
- [3] Zhao Hua. Modified Buyang Huanwu Decoction Combined with α -lipoic acid in the treatment of diabetes peripheral neuropathy of qi deficiency and blood stasis type [J]. *Journal of transportation medicine*, 2019, 33 (2): 152-154.
- [4] Liu Mingsheng. Consensus on diagnosis and treatment of diabetes peripheral neuropathy [J]. *Chinese Journal of Neurology*, 2013, 46 (11): 787-789.
- [5] Liu Jinling. Clinical observation of Buyang Huanwu Decoction Combined with acupuncture and moxibustion in treating diabetes peripheral neuropathy of qi deficiency and blood stasis type [D]. *Heilongjiang University of traditional Chinese medicine*, 2020. Doi: 10.27127/d.cnki.ghlzu.2020.000334.
- [6] Pei Qiang, Wu Yang, Wang Tao. Effect of modified Buyang Huanwu Decoction on serum pntigf-1 in patients with diabetes peripheral neuropathy [J]. *Chinese Journal of experimental formulary*, 2019, 25 (16): 67-72.
- [7] Ke Wenjin. Clinical observation on the treatment of 55 cases of diabetes peripheral neuropathy with Buyang Huanwu Decoction plus Western Medicine [J]. *Gansu science and technology*, 2021, 37 (08):165-167+170.
- [8] Huang Hailun, Wu Shan. Research progress on the pathogenesis of diabetes peripheral neuropathy [J]. *Chinese Journal of brain disease and rehabilitation (Electronic Edition)*, 2019,9 (03): 176-180.
- [9] Ali Saleh et al. Receptor for advanced glycation end-products (RAGE) activates divergent signaling pathways to augment neurite outgrowth of adult sensory neurons [J]. *Experimental Neurology*, 2013, 249: 149-159.
- [10] Shi Lili, Ren Mingshan, Wu Yuanjie. Research status of diabetes peripheral neuropathy and oxidative stress [J]. *Journal of Anhui Medical University*, 2012, 47 (1): 94-96.
- [11] Dong Rongfang, Zhang Ming, Zheng Danfeng, et al. Pathological study of diabetes peripheral neuropathy [J]. *Journal of diagnostic pathology*, 2015, 22 (3): 133-138.
- [12] Sohail MU, Asmaa A, Haseeb Aet al. Role of the gastrointestinal tract microbiome in the pathophysiology of diabetes mellitus [J]. *J Dlabetes Res*, 2017, 2017: 9631435.
- [13] Zhang Chunxue, Wang Yan, Zheng Xiaoyan, Xu yeqiu, Yun Shuguang. Effect of metformin on cholesterol metabolic pathway in type 2 diabetes rats [J]. *Chinese Journal of Gerontology*, 2017, 37(21): 5238-5240.
- [14] Zeng Lisheng, Ouyang Chunxi. Effect of Integrated Chinese and Western Medicine on peripheral neuropathy of diabetes and its influence on serum homocysteine and cystatin C levels [J]. *Chinese contemporary medicine*, 2019, 26 (17): 151-153 + 156.
- [15] Han Baorui. Clinical observation on the treatment of diabetes peripheral neuropathy with Danggui Sini decoction combined with traditional Chinese medicine fumigation [J]. *Modern distance education of Chinese traditional medicine*, 2021, 19 (24): 77-78 + 111.
- [16] Zou Xiaoxia. Clinical observation on the treatment of diabetes peripheral neuropathy with Yiqi Huoxue Tongbi Decoction [J]. *Modern distance education of Chinese traditional medicine*, 2021, 19 (24): 84-85.
- [17] Shen Yuting. Effect and safety of Huangqi Guizhi Wuwu Decoction in the treatment of diabetes peripheral neuropathy [J]. *Inner Mongolia traditional Chinese medicine*, 2021, 40(11): 36-37. Doi: 10.16040/j.cnki.cn15-1101.2021.11.021.
- [18] Li Peirong, Lin Yuehua, Wang Guochen. Effect of temperature and immersion time of Chinese traditional medicine Muzu Decoction on clinical efficacy of patients with diabetes peripheral neuropathy [J]. *Chinese patent medicine*, 2020, 42 (12): 3361-3363.
- [19] Xia Zheng, Tong Baiyang. Effect of Integrated Chinese and Western Medicine on improving the quality of life of patients with diabetes peripheral neuropathy [J]. *Diabetes new world*, 2021, 24 (18): 10-13.
- [20] Fang wenhuang, Chen Xueying, Qiu Yingming. Clinical effect of acupuncture and moxibustion combined with western medicine on peripheral neuropathy in diabetes [J]. *Diabetes new world*, 2021, 24 (14): 21-24 + 44. Doi:

10.16658/j.cnki.1672-4062.2021.14.021.

- [21] Sun Yali. Observation on the therapeutic effect of acupuncture and moxibustion on peripheral neuropathy in diabetes [J]. *Beijing Traditional Chinese medicine*, 2014,33 (10): 759-761. Doi: 10.16025/j.1674-1307.2014.10.018.
- [22] Jiang Yong, Liu Lijun. Clinical study on the prevention and treatment of diabetes peripheral neuropathy with massage therapy [J]. *Diabetes new world*, 2017,14 (7): 181-182.
- [23] Chen Lu, Zhang Chunling, Chen Qiuyuan, et al. Observation on the curative effect of 30 cases of diabetes peripheral neuropathy improved by point massage with medicine stick [J]. *Journal of Guiyang University of traditional Chinese medicine*, 2015,37 (6): 69-72.
- [24] Xu Xiuying, Xu jingling, Zhuo Fangying. Application of massage along meridians in peripheral neuropathy of diabetes [J]. *Diabetes new world*, 2018,14 (23): 176-177.
- [25] Fan Shunhua, Chen Fasheng, Xiao Xueyun. Clinical observation on the auxiliary treatment of diabetes peripheral neuropathy with oil point massage in Qingliang Department of Traumatology [J]. *Chinese medical guide*, 2014,12 (11): 269-270.
- [26] Fu J, Wang Z, Huang L, et al. Review of the botanical characteristics, phytochemistry, and pharmacology of *Astragalus membranaceus* (Huangqi)[J]. *Phytotherapy Research*, 2014, 28(9): 1275-1283.
- [27] Ma Yuanyuan, Wang Jing, Luo Qiong, et al. Research progress on pharmacological action of total saponins of *Astragalus* [J]. *Journal of Liaoning University of traditional Chinese medicine*, 2020. 22 (7) 153-157.
- [28] Li Xi, Zhang Lihong, Wang Xiaoxiao, et al. Research progress on chemical constituents and pharmacological effects of *Angelica sinensis* [J]. *Chinese herbal medicine* 2013, 36 (6) 1023-1028.
- [29] Huang Guangxiao. Study on the pharmacodynamic substances and mechanism of Buyang Huanwu Decoction in intervention of diabetes peripheral neuropathy [D]. *Guangdong Pharmaceutical University*, 2021. Doi: 10.27690/d.2021.000042.
- [30] Ben Ying, Zhang Fenghua, Liang Wenjie, Zhang Dong, Fang Qian. Effects of Buyang Huanwu Decoction with different *Astragalus* doses on peripheral nerve function and oxidative stress in diabetes rats [J]. *Chinese patent medicine*, 2015, 37 (01): 199-202.
- [31] Zhao Mengdi, Yang Jiehong, Zhou Huifen, et al. Study on the in vitro protective effect and mechanism of Buyang Huanwu Decoction on hippocampal neuronal cells after oxygen glucose deprivation and reoxygenation [J]. *Chinese Journal of pharmacy*, 2020, 55 (9): 728-736.
- [32] Bao Peng, Li Xue, Sun Lisa, et al. Buyang Huanwu Decoction alleviates inflammation of peripheral neuropathy in dB/DB diabetes mice by inhibiting TLR4 signaling [J]. *Journal of Shanxi Medical University*, 2020, 51(2): 153-157.
- [33] Mou Jian, Zhuang Guihua, Shang Hongli. Effect of Jiawei Buyang Huanwu Decoction on blood glucose and its antioxidant activity in diabetes rats [J]. *Chinese patent medicine*. 2017, 39 (08): 1561-1566.
- [34] Wang Wenhui, Yang Jin, Xia Jin'e. Treatment of diabetes peripheral neuropathy with integrated Chinese and Western Medicine [J]. *Journal of Liaoning University of traditional Chinese medicine*, 2010, 12 (4): 191-192.
- [35] Liu Caijin, Yuan Liuxian, he Xiaofeng. Observation on the efficacy of Buyang Huanwu Decoction in treating 38 cases of sciatica [J]. *Chinese and foreign medical research*, 2011, 9(7): 36-36.
- [36] Chu Lisheng, Jiang Yanyan, Ke Qing, et al. Buyang Huanwu Decoction promotes angiogenesis and functional repair after focal cerebral ischemia in rats [J]. *Chinese Journal of traditional Chinese medicine*, 2011, 29 (2): 335-338.
- [37] Mei Xiaoyun, Zhou Lan, Wu Haoxin, et al. Experimental study on Buyang Huanwu Decoction promoting regeneration of rat common peroneal nerve [J]. *Chinese Journal of experimental formulary* 2010, 16(5): 114-117.
- [38] Wenyuan. Observation on the efficacy of Buyang Huanwu Decoction in the treatment of peripheral neuropathy in type 2 diabetes [J]. *Journal of practical Chinese medicine*, 2018, 34(11): 1338-1339.
- [39] Sun Boxin, Li Lingqing. Clinical observation of Buyang Huanwu Decoction in the treatment of diabetes peripheral neuropathy [J]. *Genomics and applied biology*, 2017, 36 (7): 3398-3402.
- [40] Zu Lihua, Wang Xindong, Qin Jiugang. Clinical study of Buyang Huanwu Decoction Combined with lipoic acid in the treatment of diabetes peripheral neuropathy [J]. *New Chinese medicine*, 2020, 52 (12): 37-41.