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Treatment of Diabetic Peripheral Neuropathy Using the "Xinrun Tongluo" Method Based on the Theory of Meridian Pathology

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Abstract: ***This paper elucidates the pathogenesis of diabetic peripheral neuropathy (DPN) and the theoretical framework of the Theory of Meridian Diseases in the Huangdi Neijing. It analyzes the essence and mechanism of action of the Pungent-Moistening and Meridian-Unblocking Method, and, through case studies, demonstrates its significant efficacy in improving symptoms and neurological function in DPN patients, thereby expanding new perspectives for the treatment of DPN in Traditional Chinese Medicine.***

Keywords: The Yellow Emperor's Inner Canon, Theory of Meridian Diseases, Pungent-Moistening and Meridian-Unblocking Method, Diabetic Peripheral Neuropathy.

1. Introduction

In Traditional Chinese Medicine, diabetic peripheral neuropathy (DPN) can be classified under categories such as "Bi Syndrome" and "Pain Syndrome." Its occurrence is typically associated with long-term diabetes, leading to the depletion of qi and yin, deficiency of yin-yang and qi-blood, impaired blood circulation, and obstruction of the meridians [1]. Research indicates that when the body's vital energy (zhengqi) is deficient, it triggers qi deficiency, making it difficult to maintain robust defensive functions and causing the pores of the skin to become porous. Under these conditions, pathogenic wind takes advantage of the situation to invade the body, traveling along the meridians to penetrate deeply, thereby causing the meridians to become obstructed by pathogenic factors and ultimately leading to the onset of disease.In modern medicine, this refers to symptoms and/or signs in diabetic patients associated with peripheral nerve dysfunction, with numbness, pain, burning sensations, or other sensory abnormalities being common symptoms [3].The theory of Luo disease in Traditional Chinese Medicine (TCM) offers a unique perspective for understanding and treating DPN. Ye Tianshi of the Qing Dynasty, building upon the theories of the *Huangdi Neijing* and inspired by Zhang Zhongjing's *Treatise on Cold Damage* regarding the treatment of malaria, proposed the concept of "chronic disease invading the Luo channels." This theory posits that in certain chronic diseases, after a prolonged course of illness, pathogenic factors penetrate deep into the body, leading to damage to the blood vessels and collaterals. The "Pungent-Moistening Method for Unblocking the Collaterals" proposed by Ye Tianshi shows great promise for clinical application and warrants further research [4].

2. Pathogenesis of Diabetic Peripheral Neuropathy

2.1 Direct Toxic Effects of Hyperglycemia

Under conditions of prolonged hyperglycemia, glucose can enter nerve cells directly without insulin mediation, causing an increase in intracellular osmotic pressure and resulting in nerve cell edema and degeneration. Concurrently, hyperglycemia can reduce inositol levels within nerve cells, thereby affecting nerve conduction velocity [5].

2.2 Mechanisms Related to Metabolic Abnormalities

Under hyperglycemic conditions, a series of changes occur in the body's internal environment, abnormally activating the polyol pathway. As a result, the activity of aldose reductase significantly increases, promoting the conversion of large amounts of glucose into sorbitol. As this conversion process continues, sorbitol accumulates and becomes trapped within nerve cells, causing intracellular osmotic pressure to rise gradually. This increase in osmotic pressure acts like a "heavy blow," further exacerbating the extent of damage to nerve cells and exerting numerous negative effects on the maintenance of their normal structure and function. Simultaneously, it reduces inositol levels within the nerves, impairing nerve conduction. Hyperglycemia can activate PKC; the activation of PKC alters blood flow within the neural membrane, affecting nerve conduction, and is involved in abnormal processes such as increased vascular permeability, cell proliferation, and angiogenesis, thereby causing damage to the neural microvasculature.

2.3 Vascular Factors

In diabetic patients, metabolic disorders lead to a series of pathological changes triggered by prolonged hyperglycemia. The microvascular system is particularly affected, with thickening of the basement membrane and abnormal proliferation of endothelial cells. The synergistic effect of these two factors causes the original lumen of microvessels to gradually narrow, obstructing blood circulation and consequently impairing normal perfusion and metabolic function of tissues and organs. Concurrently, abnormalities in blood rheology—such as increased whole-blood viscosity , reduced red blood cell deformability, and enhanced platelet aggregation—reduce microvascular perfusion to the nerve endothelium, leading to neural ischemia and hypoxia. In the

diabetic state, the neurovascular barrier is compromised, vascular permeability increases, and plasma proteins leak out, further exacerbating edema and ischemia in neural tissues and impairing normal nerve function.

2.4 Deficiency of Nerve Growth Factor

Nerve growth factor (NGF) is crucial for maintaining the survival, growth, and differentiation of nerve cells. In diabetic patients, impaired synthesis, transport, and axonal transport of NGF lead to reduced NGF levels in neural tissue. As a result, nerve cells do not receive adequate nutritional support, thereby promoting the development of neuropathy.

3. Theoretical Basis of the Theory of Internal Meridian Pathology

3.1 Origins of the Meridian Theory

The theory of meridians and collaterals originates from the *Huangdi Neijing* (The Yellow Emperor's Inner Canon). The *Lingshu: Pulse Measurements* first mentions: "The meridians are the main channels; those that branch off and run horizontally are the collaterals; and the branches of the collaterals are the sub-collaterals." This introduced the concept of collaterals [6]. The meridians and collaterals connect the internal organs internally and the limbs and joints externally, serving as channels for the circulation of qi and blood. Qi and blood circulate throughout the body via the meridians and collaterals, maintaining normal physiological functions. When the meridians and collaterals are unobstructed and the circulation of qi and blood is normal, the body is healthy; conversely, when the meridians and collaterals are obstructed and the circulation of qi and blood is impaired, various diseases arise.

3.2 The Essence of Luo Disease

Luo disease refers to conditions caused by the disruption of qi and blood circulation in the meridians due to dysfunction of the zang-fu organs, deficiency of qi and blood, or the influence of endogenous pathogenic factors (such as phlegm, stasis, and dampness). Its onset is insidious, it interacts with pathological changes in the zang-fu organs, and it typically has a prolonged course. When diabetes insipidus occurs, pathogenic heat easily damages qi and yin; if the condition persists, it penetrates into the collaterals. In states of both qi and yin deficiency, as well as both yin and yang deficiency, internal heat, phlegm-dampness, qi stagnation, and blood stasis intertwine and congeal, thereby giving rise to the pathological changes of "micro-masses" in the collaterals [7]. Given that the collaterals are widely distributed throughout the body, this may trigger complications in various systems. When stasis and congealing occur in the collaterals of the limbs, it can lead to blood-obstruction-induced paralysis and syncope, or result in pathological conditions such as gangrene [8].

4. Theoretical Basis and Implications of the "Pungent-Moistening to Unblock the Collaterals" Method

4.1 The Theory of "Moistening Through Pungency"

The concept of the "Pungent-Moistening Method" originated in the *Huangdi Neijing* (The Yellow Emperor's Inner Canon), where the mechanism of "moistening" is manifested in the ability of pungent herbs to open the "mysterious orifices," thereby facilitating the distribution of body fluids throughout the body and ensuring the smooth flow of qi and blood. In cases where meridian blockages and impaired circulation of qi and blood prevent body fluids from moistening the meridians, pungent herbs can effectively nourish and moisten the meridians. During the Qing Dynasty, Ye Tianshi built upon the theories of the *Inner Canon* and, inspired by Zhang Zhongjing's (Eastern Han Dynasty) approaches to treating malaria, proposed the concept of "chronic diseases penetrating the collaterals." This theory posits that in certain chronic conditions, prolonged illness allows pathogenic factors to penetrate deeply into the body, resulting in damage to the blood collaterals. His treatment principles for meridian disorders include "moistening and unblocking the meridians with pungent herbs," "regulating yang to unblock and tonify," and "combining dispersion and tonification, with a preference for gentle methods." He frequently employed methods such as moistening and unblocking the meridians, utilizing vine-like herbs—whose morphology resembles the meridians—to harness their ability to guide and convey therapeutic effects through methods of analogy and correspondence, thereby promoting the circulation of qi and blood and the unimpeded flow of the meridians.

4.2 The Significance of Meridian Unblocking

The goal of unblocking the meridians is to restore their unimpeded flow. In DPN, pathological products such as phlegm and blood stasis obstruct the meridians, hindering the circulation of qi and blood. Unblocking the meridians allows qi and blood to flow normally to the limbs, nourishing neural tissues and improving symptoms of neuropathy.

4.3 Principles of Formula Composition for the Pungent-Moistening Method to Unblock Meridians

Formulas for the Pungent-Moistening Method of Meridian Unblocking typically center on pungent herbs, such as Asarum (Xixin) and Cinnamomum (Guizhi). Asarum is pungent and warm, with a penetrating action, capable of dispelling cold and unblocking meridians; Cinnamomum is pungent, sweet, and warm, and can warm and unblock the meridians. At the same time, herbs that activate blood circulation and resolve stasis, such as Ligusticum (Chuanxiong) and Paeonia rubra (Chishao), are combined to disperse blood stasis; combined with herbs that resolve phlegm and dispel dampness, such as Pinellia and Poria, to eliminate phlegm-dampness. Depending on the patient's deficiencies in qi, blood, yin, and yang, appropriate herbs that tonify qi and nourish blood or nourish yin and warm yang—such as Astragalus, Angelica sinensis, Rehmannia glutinosa, and Cistanche—are added to strengthen the body's vital energy and facilitate meridian unblocking.

5. Mechanism of Action of the Pungent - Moistening and Meridian - Unblocking Method in Diabetic Peripheral Neuropathy

5.1 Improving Neurovascular Microcirculation

The active components in pungent-moistening and meridian-unblocking herbs act on vascular smooth muscle to induce vasodilation. For example, active components in Cinnamomum cassia, such as cinnamyl alcohol and cinnamaldehyde, promote vasodilation and improve blood circulation [10]. Some herbs can also reduce blood viscosity, inhibit platelet aggregation, and enhance the deformability of red blood cells. For instance, Danshenketone IIA, a compound found in Danshen, possesses the ability to inhibit platelet aggregation and repair damaged vascular endothelium, thereby promoting blood circulation, reducing thrombus formation, and improving blood flow in neural microvessels [11].

5.2 Regulation of Metabolic Disorders

Inhibition of the Polyol Pathway

Components in Astragalus, such as Astragalus polysaccharides, may improve abnormal metabolism in the polyol pathway by regulating the activity of relevant enzymes, thereby reducing the accumulation of sorbitol in nerve cells and alleviating nerve cell edema and damage.

Regulating the PKC Pathway

The Xinrun Tongluo formula may regulate intracellular signal transduction, inhibit the excessive activation of PKC, and restore normal blood flow and nerve conduction function in the neural membrane.

5.3 Antioxidant and Anti-stress Effects

Most of the herbs in the Xinrun Tongluo formula possess antioxidant activity. They can scavenge free radicals, such as superoxide anions and hydroxyl radicals, while simultaneously enhancing the activity of the body's antioxidant enzymes. For example, ferulic acid in Angelica sinensis has antioxidant effects, which can reduce lipid peroxidation damage to neuronal cell membranes caused by free radicals, thereby protecting the structure and function of neurons.

5.4 Promotion of Nerve Growth Factor Expression

The "Pungent-Moistening and Meridian-Unblocking Method" can improve the internal environment of nerve cells, regulate the expression of relevant genes, and promote the synthesis and secretion of nerve growth factors. This helps maintain nerve cell survival and promote nerve fiber regeneration, thereby improving neurological function in patients with DPN.

5.5 Resolving Phlegm and Removing Stasis to Unblock the Meridians

The phlegm-resolving herbs in the formula reduce the accumulation of phlegm-dampness in the meridians, while the blood-stasis-removing herbs disperse blood stasis and eliminate meridian obstruction. Phlegm-resolving herbs such as Pinellia and Tangerine Peel dry dampness and resolve phlegm, ensuring the unobstructed flow of meridians; blood-stasis-removing herbs such as Chuanxiong and Salvia miltiorrhiza invigorate blood circulation and resolve stasis, improving the circulation of qi and blood. Once phlegm and blood stasis are resolved, the normal flow of qi and blood in the meridians is restored, alleviating DPN symptoms.

6. Clinical Case

Case Details

Patient Li, a 62-year-old man, has had diabetes for 12 years. Over the past 3 years, he has experienced numbness and prickling pain in both lower limbs, which worsen at night, accompanied by cold feet and fatigue. Examination revealed diminished superficial sensation in both lower limbs and slowed nerve conduction velocity, leading to a diagnosis of diabetic peripheral neuropathy. The patient also presented with symptoms such as dry mouth, fatigue, and soreness in the lower back and knees. His tongue was pale with a dark hue, coated with a white, greasy coating, and his pulse was deep, fine, and thready.

Differential Diagnosis and Treatment

Deficiency of the Spleen and Kidney, with phlegm and blood stasis obstructing the meridians. Treatment was administered using the method of dispersing and moistening to unblock the meridians. The formula is as follows: Asarum (Xixin) 3g, Cinnamomum (Guizhi) 10g, Astragalus (Huangqi) 30g, Angelica (Danggui) 15g, Ligusticum (Chuanxiong) 12g, Salvia (Danshen) 15g, Pinellia (Banxia) 10g, Poria (Fuling) 15g, Rehmannia (Shudidi) 20g, Epimedium (Xianlingpi) 15g.One dose daily, decocted in water and taken orally.

Treatment Outcomes

After 3 months of treatment, the patient's symptoms of numbness and tingling in both lower limbs were significantly alleviated, cold feet improved, and fatigue subsided. Follow-up tests showed an increase in nerve conduction velocity, and the patient's quality of life improved significantly. After 2 months of continued consolidation therapy, the symptoms remained largely stable.

7. Discussion and Outlook

7.1 Discussion

The "Pungent-Moistening and Meridian-Unblocking Method," based on the theory of meridian pathology in the Huangdi Neijing, has demonstrated significant advantages in the treatment of diabetic peripheral neuropathy (DPN). Theoretically, this approach closely aligns with the pathogenesis of DPN and the characteristics of meridian pathology, improving patients' symptoms and nerve function through multiple mechanisms. Clinical studies and case reports have also fully validated its efficacy. However, several issues remain. First is the standardization of formulas: the

herbal compositions and dosages of the "Pungent-Moistening Meridian-Unblocking" formulas used by different practitioners vary, necessitating further standardization. Second is the need for in-depth research into the mechanism of action; although some understanding currently exists, more advanced technologies are required to further elucidate its molecular-level targets.

7.2 Outlook

Future research should focus on conducting large-scale, multicenter clinical trials to optimize the formulae of the Xinrun Tongluo Method and establish standardized treatment protocols and efficacy evaluation criteria. Concurrently, modern techniques such as molecular biology and metabolomics should be utilized to thoroughly investigate the mechanism of action, identifying key drug targets and signaling pathways. Furthermore, the combined application of the Xinhun Tongluo method with modern medical treatments (such as blood glucose-lowering drugs and microcirculation-improving agents) could be explored to enhance the therapeutic efficacy of DPN and provide patients with better treatment options.

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