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Original Article

Clinical efficacy of Chinese herbal footbath plus traditional Chinese medicine decoction in diabetic peripheral neuropathy

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Abstract: Objective: To evaluate the clinical efficacy of Chinese herbal footbath plus traditional Chinese medicine (TCM) decoction in diabetic peripheral neuropathy. Methods: This retrospective study enrolled 120 patients with diabetic peripheral neuropathy treated in Shanghai Jinshan TCM-Integrated Hospital from January 2019 to January 2021. The eligible patients received either routine treatment (control group) or Chinese herbal GuBu Decoction footbath plus oral Yiqi Huoxue Decoction (experimental group), with 60 patients in each group. The duration of treatment was one month. Outcome measures included motor nerve conduction velocity (MNCV) and sensory nerve conduction velocity (SNCV) of the common peroneal nerve, blood glucose, TCM symptom scores and clinical efficacy. Results: TCM interventions resulted in significantly faster MNCV and SNCV versus routine treatment ($P<0.05$). Patients with TCM treatment exhibited lower fasting blood glucose, 2 h postprandial glucose and glycosylated hemoglobin than those with routine treatment ($P<0.05$). Remarkably lower TCM symptom scores were observed in the experimental group than in the control group ($P<0.05$). Chinese herbal GuBu Decoction footbath plus oral Yiqi Huoxue Decoction regimen was associated with a significantly higher clinical efficacy when comparing with routine treatment ($P<0.05$). The incidence of adverse events was not significantly different between the two groups ($P>0.05$). Conclusion: Chinese herbal GuBu Decoction footbath plus oral Yiqi Huoxue Decoction can provide promising blood glucose control, alleviate clinical symptoms, accelerate nerve conduction speed and enhance clinical efficacy.

Keywords: Chinese herbal footbath, traditional Chinese medicine decoction, diabetic peripheral neuropathy

Introduction

The prevalence of diabetes mellitus is gradually increasing, and it is the third most common disease after tumors and cardiovascular diseases [1, 2]. Diabetes mellitus is a metabolic disease characterized by chronic hyperglycemia as a result of multiple etiologies. Ineffective glycemic control and aggravation of diabetes will result in multiple complications, in which diabetic peripheral neuropathy (DPN) is a common complication with manifestations such as pain, numbness, weakness and abnormal sensation in the limbs [3]. The aggravation of the disease will involve the motor nerves of the limbs and weaken the muscle tone, leading to motor impairment or even muscle atrophy, severely compromising the physiological functions of patients [4, 5]. The etiology and pathogenesis of DPN remain poorly understood. The clinical management of DPN in modern medicine includes regulation of blood glucose, blood lipid and blood pressure levels, and improvement of blood circulation, followed by supplementation of neurotrophic factors. However, the clinical efficacy leaves much to be desired [6, 7].

In traditional Chinese medicine (TCM), DPN belongs to the category of “paralysis”, “blood paralysis” and “pain”, and TCM treatment such as acupuncture, herbal medication and external compression can provide favorable therapeutic benefits for DPN patients [8]. GuBu Decoction is a TCM formula, in which Astragalus benefits the spleen and lung meridians, and has the effect of invigorating qi and protecting

the exterior barriers, as well as detoxifying and draining pus. Years of clinical experience with TCM have found that GuBu Decoction footbath significantly reduces foot gangrene, but related studies have been marginally reported [9]. The current study was performed to evaluate the clinical efficacy of Chinese herbal footbath plus TCM decoction in DPN.

Materials and methods

Participants

The data of 120 patients with DPN treated in Shanghai Jinshan TCM-Integrated Hospital from January 2019 to January 2021 were analyzed retrospectively, among them, 60 patients received routine treatment (control group), and another 60 patients received Chinese herbal footbath plus TCM decoction treatment (experimental group). This study was approved by the Ethics Committee of Shanghai Jinshan TCM-Integrated Hospital.

Inclusion and exclusion criteria

Inclusion criteria: (1) patients who met the diagnostic criteria of DPN in Chinese and Western medicine; (2) patients who voluntarily signed the informed consent; (3) patients with good compliance and cooperation with treatment; (4) patients who were 18-73 years; (5) patients with glycated hemoglobin (HbAlc) ≤7.5% and fasting blood glucose (FPG) within 7.0 mmol/L; (6) patients with no treatment history of Chinese herbal footbath combined with TCM decoction.

Exclusion criteria: (1) patients with stroke, nephropathy or peripheral neuropathy caused by other factors; (2) patients who received major surgery during treatment; (3) patients with contraindications to the drug used in this study; (4) patients with ketoacidosis caused by metabolic disorders due to poor glycemic control; (5) patients with lower limb edema or skin disease which was contraindicated to the decoction and footbath; (6) patients with mental retardation or psychiatric disorders.

Treatment methods

The control group received standardized treatment conforming to the current routine diagnosis and treatment guidelines, including blood glucose monitoring and control, specific medications and drug adjustment.

The experimental group received Chinese herbal footbath plus TCM decoction. Oral administration of Yiqi Huoxue Decoction: 30 g of Astragalus mongholicus, 10 g of Angelica sinensis, 10 g of chuanxiong rhizome, 10 g of Persicae Semen, 10 g of Flos Carthami, 12 g of Paeonia veitchii Lynch, 15 g of earthworm, 10 g of centipede, 12 g of papaya, 10 g of Cyathulae Radix, 12 g of Dendrobii Caulis, 15 g of Radix Scrophulariae, 10 g of Rice-grain Sprout, and 6 g Fructus Amomi were decocted with water to obtain the filtrate, which was administered twice a day in the morning and in the evening. Chinese herbal footbath: 20 g of Angelica sinensis, 10 g of Flos Carthami, 15 g of Radix Scrophulariae, 15 g of Cyathulae Radix, 20 g of Suberect Spatholobus Stem, 20 g of fructus liquidambaris, and 20 g of retinervus luffae fructus were decocted with water to obtain the filtrate, which was used for 20-min footbath at a temperature within 39°C, twice daily. The duration of treatment was one month.

Outcome measures and evaluation criteria

The nerve conduction velocity: The motor nerve conduction velocity (MNCV) and sensory nerve conduction velocity (SNCV) of the common peroneal nerve were measured in both groups by electromyography on the day of enrollment (before treatment) and after one month of treatment (after treatment), and the changes in the nerve conduction velocity in both groups were compared.

Blood indicators: Before and after treatment, 3 ml of venous blood was collected from the patients to determine the serum FBG, 2 h postprandial blood glucose (2hPG) and HbAlc.

TCM symptom score: A total of 5 TCM symptoms were evaluated including limb numbness, limb pain, local burning, local cold sensation and tendon reflexes, with a total score of 6 points for each item. To be specific, 0 points were for normal symptoms, 2 for mild symptoms, 4 for moderate symptoms and 6 for severe symptoms. Higher scores indicate more serious TCM symptoms.

Efficacy evaluation criteria: After the treatment, the efficacy was determined according to the

Table 1. Baseline clinical profiles

Group	n	Sex [n, (Male/Female)]	Age (year)	Duration of disease (year)	FPG (mmol/L)	2hPG (mmol/L)	HbAlc (%)
Experimental group	60	34/26	56.18±7.65	15.55±3.84	6.92±0.57	8.89±0.84	7.23±0.46
Control group	60	35/25	56.42±8.17	14.92±4.33	6.94±0.54	8.86±0.76	7.24±0.48
X^2/t			0.166	0.843	0.197	0.205	0.117
P			0.868	0.408	0.844	0.838	0.907

FPG: fasting blood glucose; 2hPG: 2 h postprandial blood glucose; HbAlc: glycated hemoglobin.

Table 2. Nerve conduction velocity ($\bar{x}$±s)

Group	n	MNCV (m/s)		SNCV (m/s)	
		Before treatment	After treatment	Before treatment	After treatment
Experimental group	60	41.38±4.96	48.05±3.54	31.79±4.56	38.11±4.24
Control group	60	41.06±5.03	43.20±4.13	31.27±4.35	34.27±4.15
t		0.351	6.906	0.639	5.013
P		0.726	0.001	0.524	0.001

MNCV: motor nerve conduction velocity; SNCV: sensory nerve conduction velocity.

mitigation of clinical symptoms and pain and the improvement of electromyography (EMG) nerve conduction velocity. Markedly effective: clinical symptoms such as numbness and constriction of limbs disappeared, with significantly reduced pain and increased EMG nerve conduction velocity by more than 5.0 m/s; Effective: clinical symptoms such as numbness and constriction of the limbs were reduced, with slightly alleviated pain, and EMG nerve conduction velocity increased by 4.9 m/s or less than before; Ineffective: patients were still showing clinical symptoms such as numbness and constriction of limbs, with no improvement or even aggravation of pain, and no change in EMG conduction velocity compared with that before treatment. Total response rate = number of (markedly effective + effective) cases/total number of cases × 100%.

Adverse effects: The adverse effects during the treatment were observed and recorded, including skin allergies, digestive tract symptoms, dizziness and headache.

Statistical analysis

SPSS 22.0 software was used to statistically analyze the data. Measurement data were expressed as ($\bar{x}$±s). Pairwise t test was adopted for the intragroup before-after comparisons, and independent t test was adopted for between-group comparisons. Count data were expressed as number of cases (%) and analyzed using the Chi-square test. Statistical significance was indicated by P<0.05.

Results

Baseline clinical profiles

The two groups were well-balanced in terms of sex, age and duration of disease (P>0.05), and the differences in FPG, 2hPG and HbAlc levels between the two groups before treatment were not statistically different (P>0.05). See **Table 1.**

Nerve conduction velocity

TCM interventions resulted in significantly faster MNCV and SNCV versus routine treatment (P<0.05). See **Table 2.**

Blood glucose and HbAlc levels

Patients with TCM treatment exhibited lower FPG, 2hPG and HbAlc levels than those with routine treatment (P<0.05). See **Table 3.**

TCM symptom scores

Remarkably lower TCM symptom scores were observed in patients with TCM treatment than in those with routine treatment (P<0.05). See **Table 4.**

Table 3. Blood glucose and HbAlc levels

Group	n	FPG (mmol/L)		2hPG (mmol/L)		HbAlc (%)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Experimental group	60	6.92±0.57	5.37±0.43	8.89±0.84	7.53±1.15	7.23±0.46	5.78±0.55
Control group	60	6.94±0.54	6.08±0.54	8.86±0.76	8.13±1.04	7.24±0.48	6.09±0.61
T		0.197	7.967	0.205	2.997	0.117	2.923
P		0.844	0.001	0.838	0.001	0.907	0.001

FPG: fasting blood glucose; 2hPG: 2 h postprandial blood glucose; HbAlc: glycated hemoglobin.

Table 4. TCM symptom scores

Group	n	Limb numbness		Limb pain	
		Before treatment	After treatment	Before treatment	After treatment
Experimental group	60	3.41±0.93	1.13±0.26	3.58±0.82	1.27±0.18
Control group	60	3.38±0.96	1.85±0.43	3.57±0.77	2.34±0.37
t		0.174	11.098	0.069	20.146
P		0.862	0.001	0.945	0.001

Group	n	Localized burning		Localized cold sensation		Tendon reflex	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Experimental group	60	1.53±0.45	0.46±0.22	2.45±0.65	0.90±0.34	0.81±0.23	0.25±0.21
Control group	60	1.48±0.42	0.77±0.23	2.53±0.74	1.41±0.46	0.84±0.22	0.46±0.13
T		0.629	7.544	0.629	6.906	0.730	6.586
P		0.531	0.001	0.524	0.001	0.446	0.001

TCM: traditional Chinese medicine.

Clinical efficacy

Chinese herbal footbath plus TCM decoction regimen was associated with a significantly higher clinical efficacy versus routine treatment ($P<0.05$). See **Table 5.**

Adverse effects

The adverse effects rate was 95% (3/60) in the experimental group and 91.67% (5/60) in the control group. Chinese herbal GuBu Decoction footbath plus oral Yiqi Huoxue Decoction did not increase adverse events in the patients when compared with routine interventions ($P>0.05$). See **Table 6.**

Discussion

There are two current theories for DPN. One is the increased level of glycated hemoglobin due to abnormal glucose metabolism [10], and alternatively, vascular lumen narrowing leads to tissue hypoxia-ischemia and increased oxygen radical synthesis, producing peripheral neuropathogenesis [11, 12]. Previous experimental studies have mostly targeted specific dysregulated pathways (e.g., increased fluxes of polyol pathways, PKc pathways, increased AGEs, vascular damage and oxidative stress). Currently, the mechanisms under study are mainly hyperglycemia, oxidative stress, lipid metabolism disorders and related factors that lead to Schwann cell lesions, damage to glial-axonal communication and imbalance of neurohomeostasis, which eventually causes fiber loss, neurodegeneration and pain [13, 14]. Clinically, neurotrophic agents, antioxidants and aldose reductase inhibitors are usually recommended. Nevertheless, these drugs feature obvious side effects and high prices, resulting in limited clinical use. According to TCM, the pathological mechanism of this disease is long-term thirst, deficiency of both qi and blood, insufficient blood flow, and blood stagnation in the veins, resulting in damage to the veins and ligaments [15]. The disease is located in the skin, tendons and veins, as well as the liver, kidney, spleen, stomach, and other internal organs

Table 5. Clinical efficacy

Group	n	Markedly effective	Effective	Ineffective	Total response (%)
Experimental group	60	39	20	2	58 (96.67)
Control group	60	23	24	13	47 (78.33)
χ^2					9.219
P					0.002

Table 6. Adverse effects

Group	n	skin allergies	digestive symptoms	Others	adverse effects rate (%)
Experimental group	60	2	1	0	3
Control group	60	1	2	2	5
χ^2					0.536
P					0.464

[16, 17]. In clinical practice, it has been found that the physiological and pathological characteristics of prolonged diabetes, high blood viscosity and microvascular and nerve damage in DPN are highly compatible with the pathogenesis in the Chinese medical theory of "continuously evil qi resides, poorly nourished qi and blood, blocked veins and blood, and injured qi and blood". In addition, the obstruction of the choroid veins can also obstruct the distribution of qi, blood and fluid, with the patient's vasculature losing nourishment, thereby exacerbating the injury and necrosis [18].

In the present study, patients in the experiment group were given TCM decoction and footbath. The oral administration of Yiqi Huoxue Decoction included Astragalus mongholicus, Angelica sinensis, chuanxiong rhizome, Persicae Semen, Flos Carthami, Paeonia veitchii Lynch, earthworm, centipede, papaya, Cyathulae Radix, Dendrobii Caulis, Radix Scrophulariae, Rice-grain Sprout and Fructus Amomi [19]. In the formula, Astragalus mongholicus inhibits hyperglycemia and avoids microvascular damage, Paeonia veitchii Lynch inhibits thrombosis, Paeonia veitchii Lynch, Flos Carthami, Persicae Semen and chuanxiong rhizome activate blood circulation and resolve blood stasis, and Earthworm soothes the tendons and activates the blood [20]. Herbal footbath is an external treatment method in Chinese medicine that improves blood circulation and peripheral nerve function by stimulating the skin, blood vessels and nerves at the site of action through the warming effect of bath water and medication [21]. In the footbath formula, Angelica sinensis, Radix Scrophulariaeand Angelica sinensis activate blood stasis and relieve pain, improving hemodynamics and microvascular circulation and achieving anti-blood thrombosis and antiplatelet aggregation. Peony phenol has antipyretic and anti-inflammatory, hypoglycemic and pharmacological activities of protecting vascular endothelial cells and immune regulation, and curcumin has the effect of antioxidant thereby reducing plasma viscosity [22]. Moreover, Angelica sinensis and Flos Carthami inhibit platelet aggregation, and Radix Scrophulariae, Cyathulae Radix, Suberect Spatholobus Stem, fructus liquidambaris and retinervus luffae fructus resolve blood stasis, open the ligaments, nourish blood and replenish deficiency [23, 24].

In the present study, Chinese herbal footbath plus TCM decoction regimen was associated with a significantly higher clinical efficacy versus routine treatment ($P<0.05$), and patients with TCM treatment exhibited lower FPG, 2hPG and HbAlc levels than those with routine treatment ($P<0.05$), suggesting TCM decoction plus Chinese herbal footbath provides marked clinical efficacy, significant alleviates clinical symptoms, and significantly controls and stabilizes blood glucose levels. In addition, TCM interventions resulted in significantly faster MNCV and SNCV versus routine treatment ($P<0.05$), indicating that TCM oral administration combined with Chinese herbal footbath may promote the repair of neurological impairment in patients. Nerve conduction velocity is clinically available to assess the degree of peripheral nerve injury and to detect changes in peripheral nerves so as to indicate therapeutic status [25]. Modern pharmacological studies have confirmed that the use of Chinese herbal medicine can improve the microcirculation of the body, reduce platelet viscosity, increase vascular permeability to improve blood supply to organs and nerves, and subsequently increase nerve conduction velocity [26].

Conclusion

Chinese herbal GuBu Decoction footbath plus oral Yiqi Huoxue Decoction can provide promising blood glucose control, alleviate clinical symptoms, accelerate nerve conduction speed and enhance clinical efficacy.

Disclosure of conflict of interest

None.

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