

CLINICAL RESEARCH

Efficacy of traditional Chinese medicine combined with warm acupuncture on diabetic foot and its effect on inflammatory status

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Abstract

Objective To investigate the clinical efficacy of traditional Chinese medicine (TCM) combined with warm acupuncture in the treatment of diabetic foot patients and its effect on inflammatory status, with a view to providing a reference for clinical treatment of diabetic foot. **Methods:** 136 diabetic foot patients admitted to our hospital from Mar. 2018 to Mar. 2020 were selected and divided into the observation group and control group according to the random number table method, with 68 cases in each group. Patients in the control group were given conventional treatment and foot debridement, and the observation group was given TCM decoction and warm acupuncture treatment on the basis of the control group. The clinical efficacy, clinical symptoms before and after treatment, foot condition, serum index and safety of treatment were compared between the two groups. **Results:** The total effective rate in the observation group was significantly higher than that in the control group ($P<0.05$). After treatment, the clinical symptoms in the observation group were significantly better than those in the control group ($P<0.05$). The blood flow velocity, motor nerve conduction velocity and sensory nerve conduction velocity in the observation group were significantly higher than those in the control group; and the serum levels of interleukin-6 (IL-6) and tumor necrosis factor- α (TNF- α) in the observation group were significantly lower than those in the control group, and the level of vascular endothelial growth factor (VEGF) in the observation group was significantly higher than that in the control group ($P<0.05$); there were 57 patients with safety grade 1 and 11 patients with grade 2 in the observation group and 55 patients with safety grade 1 and 13 patients with grade 2 in the control group, but there was no significant difference in safety grade between the two groups ($Z=-0.448$, $P=0.654$). **Conclusion:** The

combination of TCM and warm acupuncture can effectively improve the clinical symptoms of patients with diabetic foot, promote foot wound healing, relieve disease progression, and have a safe and reliable efficacy.

Introduction

Diabetic foot belongs to the severe complications of diabetes mellitus, which refers to the disease state in which diabetic patients have combined neuropathy and peripheral vasculopathy leading to lower limb protective function decline, arterial hypoperfusion, microcirculation disturbance, and then ulceration and gangrene, and is also one of the important causes of disability and lethality of diabetes [1]. The clinical manifestations of diabetic foot patients are mainly characterized by redness and swelling on the surface of foot skin, infection, ulceration, pain, and as the disease aggravates, skin surface damage will gradually form deep penetrating ulcers, leading to osteomyelitis, and eventually whole foot gangrene, severely affecting patient's life health and quality of life, therefore, how to prevent and treat the diabetic foot has become a focus of attention in the clinical treatment of diabetic complications [2]. At present, symptomatic interventions such as blood flow reconstruction, anti infection, blood glucose control and wound cleaning are mainly used in the treatment of diabetic foot in clinic, but the overall efficacy is not good; traditional Chinese medicine (TCM) has a long history and has accumulated extensive experience in the treatment of diabetic foot, with unique insights and advantages for the treatment of this disease [3]. In

recent years, a large number of studies have confirmed that TCM treatment is able to effectively improve the efficacy of clinical treatment for the diabetic foot [4,5]. Based on this, in this study, a self-made TCM decoction combined with warm acupuncture was used to treat diabetic foot, to explore the efficacy of this therapy for diabetic foot and the effect on its inflammatory status, with a view to providing a reference for clinical treatment of diabetic foot in Chinese and Western medicine, and the results are reported below.

Materials and methods

General data

A total of 136 diabetic foot patients who were admitted to our hospital from March 2018 to March 2020 were selected as study subjects and divided into the observation group and control group according to the random number table method, with 68 cases in each group. There were no significant difference in the general data such as gender, age, disease duration, and Wagner grade between the two groups ($P>0.05$), which were comparable and shown in Table 1. This study was approved by the ethics committee of our hospital, and all patients voluntarily participated and signed informed consent.

Table 1 Comparison of general data between the two groups

Group	Cases	Gender (cases)		Age (years)	Disease duration (years)	Wagner grade (cases)		
		Male	Female			I	II	III
Observation group	68	38	30	54.26±9.27	6.57±2.12	14	33	21
Control group	68	36	32	55.35±8.68	6.84±2.20	16	35	17
$\chi^2/t/Z$			0.119	-0.708	-0.729		-0.735	
P			0.731	0.480	0.467		0.462	

Diagnostic criteria

The Western medicine diagnosis conformed to the

diagnostic criteria of diabetic foot according to the *Chinese guidelines for the diagnosis and treatment of*

diabetic foot [6] and the *International guidelines on diabetes mellitus* [7]: clear history of diabetes mellitus, rest pain, lower limb vasculopathy, attenuation or disappearance of the dorsalis pedis artery, abnormal temperature sensation and vibration sense, ulceration and swelling of skin surface, and arteriosclerotic occlusion of lower limbs was confirmed by color ultrasound.

The TCM diagnosis met the diagnostic criteria for diabetic foot in the *Guidelines for prevention and treatment of diabetes in traditional Chinese medicine* formulated by the Chinese Association of Chinese Medicine [8]: limb cold, puffiness, erosion, ulcer, walking inconvenience, foot pumping pain, diminished pulsation, dark tongue with ecchymosis, thin and white fur, and deep uneven pulse.

Inclusion criteria

Fulfilled the diagnostic criteria for diabetic foot in Chinese and Western medicine; aged 20~65 years; disease duration greater than 2 years; consistent with the Wagner classification of foot gangrene grade I to III [9]; clinical data were complete and patients gave informed consent.

Exclusion criteria

Those with severe impairment of heart, brain, liver, kidney, and other organ function; those with severe systemic infectious diseases; those allergic to the drugs of this study; those with a history of mental illness and cognitive impairment, and were difficult to complete the experiment; non-diabetic arteriosclerosis of lower limbs; those with Wagner grade IV to V of foot gangrene; lactating or pregnant women.

Methods

Treatment measures

The control group was given conventional basic treatment and foot debridement, the basic treatment included hypoglycemic drug treatment, insulin subcutaneous injection, patients were instructed to have a reasonable diet, work and rest regularly, and were guided to elevate the affected limbs to improve lower extremity blood circulation, and were given anti

infective treatment to correct water, electrolytes, acid-base balance disturbance and hypoalbuminemia; foot debridement included removing necrotic tissue, placement and drainage, routine disinfection and dressing changes, and the treatment lasted for 2 months. The observation group was treated with Chinese herbal decoction combined with warm acupuncture on the basis of the control group, and the specific methods were as follows: (1) oral administration of TCM decoction was given, and the prescription was: Radix astragali 30 g, prepared rehmannia root 15 g, Achyranthes bidentata 10 g, Salvia miltiorrhiza 10 g, safflower 15 g, earthworm 15 g, Rhizoma Chuanxiong 10 g, dendrobium 10 g, suberect spatholobus stem 15 g, peony root 10 g, and added mealy fangji 10 g and common clubmoss herb 10 g when the limbs were numb, added myrrh 10 g and frankincense 10 g when the pain was obvious, added Chinese angelica 10 g and cassia bark 10 g when the limbs were cold; one dose a day, 200 mL was decocted and divided into two warm parts and taken in the morning and evening. (2) Warm acupuncture treatment was given, Yangling, Qihai, Zusanli, Taixi and Sanyinjiao acupoints were selected as main acupoints, 1-2 acupoints were selected as the matching acupoints at the adjacent non-damaged skin according to the different gangrene sites. After routine disinfection of acupoints, No.28 2-3 inch acupuncture needle (Huatuo brand) was taken and quickly entered the acupoint, twisted to get Qi, then inserted a 2 cm long moxa stick segment into the needle handle and ignited the segment. After the moxa stick segment was burned out, replaced it with a next one, 2 columns for each acupoint, and continuously treated with acupuncture for 6 days a week, rest for 1 day, for a total of 2 months.

Efficacy evaluation

The clinical efficacy of diabetic foot was evaluated according to the relevant diagnostic criteria for the treatment of diabetic foot complications and the evaluation criteria for the curative effect of gangrene [10]: well-healed: the foot wound was completely healed, the symptoms of inflammation and swelling

disappeared, there was no obvious pain, the lower limb blood circulation was significantly improved, and patients could walk normally; markedly effective: more than 2/3 of the original ulcer area was healed, the inflammation and swelling basically subsided, the pain was significantly reduced, and the lower limb blood circulation was improved; effective: more than 1/3 of the original ulcer area was healed, patients still had swelling and inflammation and pain symptoms, lower limbs blood circulation was slightly improved; ineffective: the wound did not heal, swelling and inflammation did not subside, blood circulation did not improve, clinical symptoms were not controlled or even aggravated, the total effective rate = (well-healed + markedly effective + effective) cases/total cases × 100%.

Outcome measures

The wound depth, carrion coverage, swelling range, granulation, secretion, and pain degree before and after treatment in the two groups were observed and recorded, and each index was scored from 0 to 6 points, with higher scores indicating more severe symptoms. (2) Blood flow velocity of the dorsalis pedis artery, motor nerve conduction velocity, and sensory nerve conduction velocity were measured before and after treatment in both groups using ultrasonic Doppler blood flow detector (DPL-02, Bestman). (3) Fasting peripheral venous blood was drawn from patients before and after treatment, supernatant was collected after centrifugation, and serum levels of interleukin-6 (IL-6), tumor necrosis

factor- α (TNF- α) and vascular endothelial growth factor (VEGF) were measured by enzyme-linked immunosorbent assay (ELISA), the kits were purchased from Shanghai Weitong Biological Co., Ltd. and the operation was strictly performed according to the instructions. (4) The safety was evaluated according to the occurrence of adverse reactions during the treatment. Grade 1: no adverse reactions, safe; grade 2: adverse reactions occurred but could be relieved by itself, and could continue to be treated, relatively safe; grade 3: obvious adverse reactions occurred, and could continue to be treated after treatment can, there were safety problems; grade 4: the trial was stopped due to adverse reactions, and the safety problem was serious.

Statistical analysis

Statistical analysis was performed using SPSS 20.0, and the count data were compared using χ^2 test, the rank data were compared using the rank sum test, the measurement data were expressed by the mean \pm standard deviation ($\bar{x} \pm s$) and compared by t test, and $P < 0.05$ was taken as statistically significant.

Results

Comparison of clinical efficacy between the two groups

Table 2 shows that the total effective rate in the observation group was significantly higher than that in the control group, and the difference was statistically significant ($P < 0.05$).

Table 2 Comparison of clinical efficacy between the two groups [cases (%)]

Group	Cases	Well-healed	Markedly effective	Effective	Ineffective	Total effective rate
Observation group	68	14 (20.58)	34 (50.00)	16 (23.53)	4 (5.88)	64 (94.12)
Control group	68	8 (11.76)	25 (36.76)	22 (32.35)	13 (19.12)	55 (80.88)
χ^2						5.445
P						0.020

Comparison of clinical symptoms before and after treatment between the two groups

Table 3 shows that before treatment, there was no significant difference in the wound depth, carrion coverage, swelling range, granulation, secretion and pain degree between the two groups ($P>0.05$). After treatment, the scores of wound depth, carrion coverage, swelling range in the two groups were significantly lower than those before treatment, and the scores in the observation group were significantly lower than those in the control group, the difference was statistically significant ($P<0.05$).

Comparison of foot condition before and after treatment between the two groups

Table 4 shows that before treatment, there was no significant difference in the dorsalis pedis artery blood flow velocity, motor nerve conduction velocity and sensory nerve conduction velocity between the two groups ($P>0.05$). After treatment, the dorsalis pedis artery blood flow velocity, motor nerve conduction velocity and sensory nerve conduction velocity in the two groups were significantly greater than those

before treatment, and these velocity in the observation group were significantly greater than those in the control group, the difference was statistically significant ($P<0.05$).

Comparison of serum indicators before and after treatment between the two groups

Table 5 shows that before treatment, there was no significant difference in the serum levels of IL-6, TNF- α and VEGF between the two groups ($P>0.05$). After treatment, serum IL-6 and TNF- α levels in the two groups were significantly lower than those in the control group, and the levels in the observation group were significantly lower than the control group, the difference was statistically significant ($P<0.05$), and serum VEGF level in the two groups was significantly higher than that before treatment, and the level in the observation group was significantly higher than that in the control group, the difference was statistically significant ($P<0.05$).

Table 3 Comparison of clinical symptoms before and after treatment between the two groups (points)

Group	Cases	Wound depth		Carrion coverage		Swelling range	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	68	4.28±0.75	2.85±0.57*	3.67±0.85	2.13±0.55*	4.66±0.61	2.26±0.48*
Control group	68	4.33±0.82	3.32±0.65*	3.60±0.77	2.68±0.67*	4.60±0.72	2.73±0.67*
<i>t</i>		-0.371	-4.483	0.503	-5.232	0.524	-4.702
<i>P</i>		0.711	0.000	0.616	0.000	0.601	0.000

Group	Cases	Granulation		Secretion		Pain degree	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	68	3.84±0.92	1.85±0.52*	3.56±0.77	1.65±0.47*	3.12±0.70	1.68±0.42*
Control group	68	3.92±0.85	2.13±0.63*	3.61±0.82	2.02±0.54*	3.22±0.85	2.18±0.50*
<i>t</i>		-0.527	-2.827	-0.367	-4.262	-0.749	-6.314
<i>P</i>		0.599	0.005	0.715	0.000	0.455	0.000

Note: compared with before treatment: * $P<0.05$.

Table 4 Comparison of foot condition before and after treatment between the two groups (points)

Group	Cases	Dorsalis pedis artery blood flow velocity (cm/s)		Motor nerve conduction velocity (m/s)		Sensory nerve conduction velocity (m/s)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
		Observation group	68	28.65±5.37	44.56±6.72*	30.56±5.12	42.74±4.54*
Control group	68	29.24±6.68	36.38±5.85*	31.34±4.38	38.38±3.69*	31.46±3.75	38.62±3.76*
	<i>t</i>	-0.568	7.571	-0.955	6.145	0.928	2.973
	<i>P</i>	0.571	0.000	0.341	0.000	0.355	0.003

Note: compared with before treatment: * $P < 0.05$.

Table 5 Comparison of serum indicators before and after treatment between the two groups (ng/L)

Group	Cases	IL-6		TNF- α		VEGF	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	68	16.54±3.74	7.36±2.12*	18.41±4.20	9.56±2.75*	82.46±12.34	112.38±15.37*
Control group	68	17.05±3.85	10.38±2.75*	17.95±3.82	12.20±3.05*	84.36±10.52	104.35±11.46*
	<i>t</i>	-0.784	-7.172	0.668	-5.301	-0.966	3.454
	<i>P</i>	0.435	0.000	0.505	0.000	0.336	0.001

Note: compared with before treatment: * $P < 0.05$.

Safety evaluation of treatment in the two groups

There were 57 cases of safety grade 1 and 11 cases of grade 2 in the observation group, and 55 cases of safety grade 1 and 13 cases of grade 2 in the control group. There was no significant difference in safety grade between the two groups ($Z = -0.448$, $P = 0.654$).

Discussion

Microangiopathy and microcirculatory disturbance are the main pathological manifestations in diabetic patients and are the pathological basis for the development of complications such as diabetic foot in the later stage [11]. Clinical studies have shown [12,13] that diabetic foot vasculopathy can lead to functional and organic damage of related blood vessels of nutritional nerve, trigger neurotrophic disorders and ischemic neuritis, and successively produce neuronal microdamage, resulting in dysfunction of body defense mechanism mobilization and aggravation of ulcer formation. In addition, the

high glucose blood of diabetic foot patients also provides a survival environment for pathogenic bacteria, causing the body to have an increased risk of infection and decreased immune function. Moreover, due to the foot wound is chronically in a state of microbial invasion, a large number of inflammatory factors released with the disease, further damaging the wound repair mechanism, triggering a vicious cycle. Therefore, how to effectively alleviate the clinical symptoms and avoid the deterioration of condition in diabetic foot patients is the focus of clinical research. Modern Western medicine has achieved certain results in the treatment of diabetic foot, but the efficacy is limited, and based on the occurrence and development of the disease is a multifactorial and multifaceted comprehensive process, the combination application of a variety of treatment methods is advocated in clinic, in order to improve the treatment efficiency. TCM therapy has the characteristics of syndrome differentiation and holistic regulation, which make it

play an irreplaceable role in the prevention and treatment of diabetic complications.

According to the clinical manifestations of diabetic foot, TCM classified it into the categories of "gangrene", "arthralgia" and "wasting from thirst". TCM holds that wasting from thirst with gangrene is a disease of deficiency in origin and excess in superficiality and deficiency-excess mixing, with Qi and Yin damage as the root, endogenous blood stasis and heat toxin burning fluid as the symptoms; suffering from wasting from thirst for a long time will damage Qi and Yin, Qi deficiency will lead to weakness of blood circulation, blood stasis, vein obstruction, Yang Qi can not be transmitted and warm the four limbs, resulting in numbness and pain of the affected area; after that, the blood becomes blood stasis, the skin loses its nourishment, and the toxic pathogens invade to damage the meridians and collaterals, and rot the skin, muscles and bones, causing redness and swelling, ulceration, blackening and necrosis of the extremities [14]. Therefore, TCM treatment for diabetic foot should pay attention to both the symptoms and the root causes, with tonifying Qi and nourishing blood, warming Yang and dispersing cold, clearing heat and detoxifying as the main treatment principles. There have been studies on the treatment of diabetic foot with Wenyang decoction, Simiao Huoxue decoction, Buyang Huanwu decoction and other decoction, and have achieved good results [4,5]. In this study, combined with the above TCM formulas, following the principle of removing gangrene, an oral decoction was prepared by ourselves, which composed of Radix astragali, prepared rehmannia root, Achyranthes bidentata, Salvia miltiorrhiza, safflower, earthworm, Rhizoma Chuanxiong, dendrobium, suberect spatholobus stem, and peony root, Radix astragali in the formula has the effect of tonifying blood flow and promoting blood circulation, removing blood stasis and dredging collaterals; Salvia miltiorrhiza, safflower, earthworm and suberect spatholobus stem can improve blood circulation and disperse stasis, activate meridians to stop pain; prepared rehmannia root and Achyranthes bidentata can disperse blood stasis and dredge

meridians, strengthen and relaxing tendons; Rhizoma Chuanxiong and peony root can dispel wind and relieve pain; dendrobium can clear away deficient heat, strong muscles and bones; the combination of all kinds of drugs can play the role of tonifying Qi, nourishing Yin, promoting blood circulation and removing blood stasis. Warm acupuncture is a TCM external treatment that uses acupuncture with heat conduction to excite Qi of meridians to achieve the purposes of pain and spasm relief, warming and invigorating meridians, and activating blood circulation and eliminating stasis, which can be clinically used to improve the body's local blood circulation and promote nerve terminal injury repair [15]. In this study, the main acupoints, including Yangling, Qihai, Zusanli, Taixi, and Sanyinjiao acupoints, were selected, of which Yangling acupoint is located outside the knee and belongs to Yang, which can regulate Shaoyang, clearing away heat and promote gallbladder; Qihai is a acupoint of Yin intersection uploaded along the Ren pulse, which has the effect of reinforcing the primordial Qi, tonifying and restoring Yang; Zusanli belongs to the stomach meridian, which has the effect of ascending and descending Qi, clearing and activating the channels and collaterals; Taixi acupoint belongs to foot Shaoyin kidney meridian, which is located in the ankle region and can benefit the kidney to tonify deficiency, nourish Yin to lower fire, regulate meridian to remove dampness; Sanyinjiao acupoint belongs to the spleen meridian, which is often used to treat meridian Qi stagnation. The cooperation of all acupoints can warm meridians and relieve pain, regulate Qi, clear heat and remove dampness [16,17]. The above therapy is a combination of internal and external treatment of TCM, which takes into account the whole body, can nourish the whole body, regulate the balance of Yin and Yang, and dredge Qi and blood. In the results of this study, the total effective rate and the improvement effect of clinical symptoms after treatment in the observation group were significantly better than those in the control group, indicating that the curative effect of TCM decoction combined with warm acupuncture in the treatment of diabetes is clear and better than the

conventional treatment of Western medicine. Studies suggested [18] that the vascular pathology of diabetic foot patients is mainly characterized by thickening and elasticity loss of the foot vascular wall, which leads to luminal narrowing and blood flow slowing; moreover, with the expansion of microcirculation disturbance and skin damage, peripheral nerve function damage is aggravated, which will affect nerve conduction velocity; meanwhile skin damage can lead to the immune barrier being destroyed, exacerbating the body inflammatory response. VEGF is an angiogenic factor that, after binding to its receptors on vascular endothelium, can promote endothelial cell division and proliferation to form a new blood vessel lumen, which has a positive significance in delaying the progression of diabetic foot disease. In our results, the dorsalis pedis artery blood flow velocity, motor nerve conduction velocity, sensory nerve conduction velocity and VEGF level after treatment in the observation group were significantly increased compared with those in the control group, whereas serum IL-6 and TNF- α levels in the observation group were significantly lower than those in the control group, which indicated that the TCM decoction combined with warm acupuncture effectively improved blood circulation and nerve conduction velocity in the foot of patients with diabetic foot, contributing to promoting the formation of new vessel lumen and alleviating the inflammatory response in the affected limb. The reasons may be that: the prescription in this study can be modified according to the specific situation of the patient and the change of the patient's condition, which was applied flexibly, conformed to the principle of holistic concept and syndrome differentiation, based on the main effect of invigorating blood circulation and eliminating stasis, plus and minus herbs such as mealy fangji, common clubmoss herb, myrrh, frankincense and Chinese angelica, so that people with diabetic foot got their own benefit, and fully exerted the effects of relieving pain and spasm, warming and nourishing meridians. And modern pharmacological studies have shown that the total alkaloid and ligustrazine in *Rhizoma*

Chuanxiong can reduce vascular resistance, dilate blood vessels, increase limb blood flow, meanwhile inhibit platelet aggregation, inhibit pathogenic bacteria infection, and have the function of antibacterial, anti-inflammatory and free radical elimination; lumbrokinase and urokinase in earthworm can inhibit thrombosis and anticoagulate, reduce whole blood viscosity and plasma viscosity, and improve blood flow velocity; the components of safflower, such as red pigment, alkaloids and flavone, have analgesic, sedative, anticoagulant and immunomodulatory effects, and are commonly used in the treatment of skin surface injury and swelling [19,20]. In addition, warm acupuncture can warm meridians and dredge meridians, activate Qi and blood circulation, improve and regulate microcirculation metabolism, effectively relieve vasospasm, reduce vascular resistance, promote neovascularization, further alleviate neuropathy and improve nerve conduction velocity. In this study, there was no significant difference in the safety of the two groups, suggesting that the addition of TCM therapy can improve the clinical efficacy of diabetic foot without obvious side effects, and the effect is safe and reliable. In conclusion, the combination of TCM and warm acupuncture in the treatment of diabetic foot can effectively improve the clinical symptoms of patients, promote foot blood circulation and wound healing, and improve nerve conduction velocity, which can help alleviate disease progression and have safe and reliable efficacy.

Declaration of conflict-of-interest

The authors declare no conflict-of-interest.

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