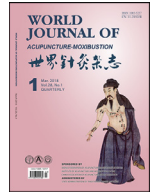




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Electroacupuncture combined with intermittent pneumatic compression therapeutic apparatus for diabetic peripheral neuropathy and the effect on HIF-1 α and VEGF levels

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ABSTRACT

Objective: To observe the clinical efficacy of electroacupuncture combined with intermittent pneumatic compression therapeutic apparatus for treatment of diabetic peripheral neuropathy, and the effect on serum VEGF and HIF-1 α levels of patients.

Methods: Ninety-six patients were randomly divided into electroacupuncture treatment group (EA group), intermittent pneumatic compression treatment group (IPC group), electroacupuncture combined with intermittent pneumatic compression treatment group (EA+IPC group) and cobamamide group (CM group), with 24 cases in each group. Electroacupuncture treatment (once a day), intermittent pneumatic compression treatment (twice a day) and intramuscular injection with cobamamide (1 mg, once a day) were carried out in EA group, IPC group and CM group, respectively, and intermittent pneumatic compression treatment (twice a day) was conducted on the basis of electroacupuncture treatment (once a day) in EA+IPC group. After treatment for 2 consecutive weeks, the differences in subjective symptoms, motor nerve conduction velocity, sensory nerve conduction velocity and serum HIF-1 α and VEGF levels of patients in the four groups before and after treatment were observed and compared.

Results: After treatment for 2 weeks, the differences in total effective rate between EA group and CM group, IPC group and CM group, as well as EA+IPC group and CM group were all significant (all $P < 0.05$), and the total effective rate in EA+IPC group was significantly higher than that in EA group and IPC group (both $P < 0.05$). After treatment for 2 weeks, the motor nerve conduction velocity and sensory nerve conduction velocity of median nerve and common peroneal nerve of patients in EA group, IPC group and EA+IPC group were all higher than that before treatment (all $P < 0.05$); the motor nerve conduction velocity of median nerve and the sensory nerve conduction velocity of common peroneal nerve in EA group were all higher than that in CM group (both $P < 0.05$); the motor nerve conduction velocity and sensory nerve conduction velocity of median nerve in IPC group were also all higher than that in CM group (both $P < 0.05$); the motor nerve conduction velocity and sensory nerve conduction velocity of median nerve and common peroneal nerve in EA+IPC group were all higher than that in CM group (both $P < 0.05$); the sensory nerve conduction velocity of common peroneal nerve in EA+IPC group was higher than that in EA group and IPC group (both $P < 0.05$), and the motor nerve conduction velocity of median nerve in EA+IPC group was higher than that in IPC group ($P < 0.05$). The serum HIF-1 α and VEGF levels of patients in EA group, IPC group and EA+IPC group after treatment significantly reduced (all $P < 0.05$), and were lower than that in CM group after treatment (all $P < 0.05$); the serum HIF-1 α and VEGF levels of patients in EA+IPC group after treatment were lower than that in EA group and IPC group, and the difference in serum HIF-1 α level was statistically significant (both $P < 0.05$).

Conclusion: Electroacupuncture combined with intermittent pneumatic compression therapeutic apparatus can effectively improve the clinical symptoms of patients with diabetic peripheral neuropathy, the efficacy were better than electroacupuncture, intermittent pneumatic compression treatment and cobamamide.

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As one of the most common chronic complications in diabetic patients [1], diabetic peripheral neuropathy (DPN) has such clinical manifestations as symmetric limb numbness and pain, and glove-like or sock-like hyperaesthesia. According to electrophysiological examination, the patient with DPN manifests as the reduction of motor and sensory nerves conduction velocity. Due to the hidden onset and various clinical manifestations, DPN is hard to be discovered in early time. Once being diagnosed with DPN, the diabetic patients' survival rate in 3 years is about only 53% [2], which seriously affect the patients' quality of life. About 50% of the diabetic patients suffer from DPN [3]. The worldwide incidence of diabetes mellitus is increasing year by year with an increased proportion of about 5% per year [4]. It is estimated that the number of diabetic patients in the world will exceed 640 million by 2040. Further study of the effective treatment methods for DPN is of positive significance for the prevention and treatment of DPN. The pathogenesis of DPN is complicated, which may be related to many factors such as metabolic disorder, vascular injury, neurotrophic disorder, oxidative stress, and heredity and autoimmunity caused by hyperglycemia [5,6]. Metabolic disorder and vascular injury are the main causes of tissue hypoxia. To improve the microcirculation and tissue oxygen supply in DPN patients will be one of the important measures to prevent DPN.

Electroacupuncture (EA), as a mature therapy at meridian acupoints developed on the basis of traditional acupuncture therapy, can relieve pain, adjust muscular tension, accelerate nerve regeneration and improve the neurological function recovery through regulating physiological function of human body [7]. In addition, it can also promote blood circulation, and better improve the adhesion molecule level [8]. As a new physical therapy, intermittent pneumatic compression (IPC) therapy can produce a kind of circulating pressure that acts on the limbs and tissues through repeated air inflation and deflation to the air bag in an ordered and regular manner, which can promote the flow of blood and lymph, and improve the microcirculation. IPC therapy is mainly used for the prevention of deep vein thrombosis of the lower limbs [9]. EA therapy can regulate the neurological function and blood circulation, and EA therapy combined with IPC treatment can further improve the microcirculation, which may have a positive therapeutic effect on DPN patients.

Therefore, EA combined with IPC was adopted in this study, and the clinical efficacy and its effect on serum VEGF and HIF-1 α levels of patients were observed, thus providing evidence for its clinical effectiveness.

1. Materials and methods

1.1. General information

The 96 patients were selected from the inpatients who visited to the Department of Endocrinology and Department of Rehabilitation Medicine of the First Affiliated Hospital of Chengdu Medical College from June 2016 to June 2017. According to the random number table, the patients were divided into cobamamide group (CM group, $n=24$), electroacupuncture treatment group (EA group, $n=24$), intermittent pneumatic compression treatment group (IPC

group, $n=24$) and electroacupuncture combined with intermittent pneumatic compression treatment group (EA + IPC group, $n=24$). According to statistical analysis of the general information (age, gender, DM and DPN course of disease, HbA1c level) on patients in the four groups, the differences were not significant (all $P > 0.05$), and the results were comparable (Table 1). This study has been reviewed and approved by Ethics Committee of the First Affiliated Hospital of Chengdu Medical College with the approval No. of CY-YFEC2015027.

1.2. Inclusion criteria

(1) The patients with type 2 diabetes mellitus conformed to the diagnostic criteria of diabetes mellitus formulated by the Expert Committee of Diabetes Mellitus of World Health Organization in 1999 and the diagnostic criteria of diabetic peripheral neuropathy (DPN) [10]: the patients ①with obviously spontaneous neuralgia, numbness and other neuropathy symptoms with the more obvious abnormality in the lower limbs; ②neural EMG indicated that nerve conduction velocity had declined in terms of two or more items as follows: motor nerve conduction velocity and sensory nerve conduction velocity of median nerve and common peroneal nerve; (2) the plasma glucose level was controlled within stable range for more than 4 weeks after hypoglycemic therapy with glycosylated hemoglobin A1C (HbA1c) $< 9.0\%$; (3) the patients who had signed the informed consent form and voluntarily accepted observation, subsequent visit and follow-up visit regularly.

1.3. Exclusion and elimination criteria

The patients (1)with type 1 diabetes mellitus or other special types of diabetes mellitus; (2)with other nervous system diseases or peripheral neuropathy caused by other reasons; (3)with severe dysfunction of the heart, liver or kidney; (4)with diseases which were contraindicated to intermittent pneumatic compression therapy, including the patients with ①severe infection in the limbs which was not effectively controlled; ②deep venous thrombosis in the lower limbs recently; ③a large area of ulcerative rash; ④bleeding tendency; ⑤ the patients who had permanent cardiac pacemaker.

1.4. Methods

All the included patients accepted education for knowledge about diabetes mellitus after admission to the hospital, and were given insulin or orally hypoglycemic agents on the basis of moderate activities and diet control. During treatment, all the patients' plasma glucose level was controlled within stable range with the fasting plasma glucose level < 10 mmol/L, and postprandial plasma glucose < 15 mmol/L. The conventional treatment and hypoglycemic treatment for the included patients before and after treatment remained unchanged.

In CM group, intramuscular injection with 2 mL of water for injection and 1 mg of cobamamide was performed for once a day.

In EA group, electroacupuncture was mainly performed at Jiānyú (肩髃LI 15), Qūchí (曲池LI 11), Nèiguān (内关PC 6), Hégū

Table 1
Comparison of general information on patients in the four groups ($\bar{x} \pm s$).

| Groups | Patients | Gender (cases) | | Age(years) | | | DM course of disease (year) | | | DPN course of disease (year) | | | HbA1c (%) |
|----------|----------|----------------|--------|--------------|------------|----------------|-----------------------------|-------------|----------------|------------------------------|-------------|---------------|---------------|
| | | Male | Female | The youngest | The oldest | Average | The shortest | The longest | Average | The shortest | The longest | Average | |
| CM | 24 | 10 | 14 | 54 | 74 | 64.6 \pm 5.7 | 4 | 16 | 11.5 \pm 3.9 | 1 | 7 | 3.9 \pm 1.8 | 7.8 \pm 0.4 |
| EA | 24 | 11 | 13 | 58 | 75 | 65.4 \pm 5.0 | 4 | 17 | 10.9 \pm 3.8 | 1 | 8 | 3.8 \pm 2.2 | 7.7 \pm 0.4 |
| IPC | 24 | 13 | 11 | 56 | 73 | 63.7 \pm 4.9 | 4 | 16 | 10.5 \pm 3.4 | 1 | 8 | 3.6 \pm 1.8 | 7.8 \pm 0.5 |
| EA + IPC | 24 | 12 | 12 | 57 | 75 | 65.4 \pm 5.4 | 5 | 18 | 11.1 \pm 3.4 | 1 | 8 | 4.4 \pm 2.0 | 7.9 \pm 0.5 |

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