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Efficacy of Acupuncture in Treatment of Parkinson's Disease with Orthostatic Hypotension: A Randomized Controlled Clinical Trial

Yue Liu[1], Yun Dang[3], Peng Tang[1Corresponding author], Jiaxin Zhao[1], Peipei Li[2], Hong Wang[1], Dongliang Wang[2]

1. The third department of Neurology, the Shaanxi Provincial People's Hospital, Xian 710068, China.

2. The department of Acupuncture, the Shaanxi Provincial People's Hospital, Xian 710068, China.

3. The First Affiliated Hospital of Xi'an Medical University, Xian 710077, China.

Abstract: **Objective:** To evaluate the therapeutic effect and safety of acupuncture on Parkinson's disease (PD) with orthostatic hypotension (OH) patients. **Methods:** A randomized controlled clinical trial was used to observe the efficacy of acupuncture in the treatment of 51 PD with OH patients. The observation time was 1 week. **Results:** After 1 week of acupuncture treatment, the blood pressure and blood flow velocity of left middle cerebral artery of the treatment group increased compared with the control group, and the difference was statistically significant (P<0.05); the visual vertigo analog scale (VVAS) of the treatment group decreased compared with the control group, and the difference was also statistically significant (P<0.05). After 1 week of acupuncture treatment, the heart rate of the treatment group increased compared with the control group, and the modified Rankin score (mRS) of the treatment group decreased compared with the control group, but there was no statistical difference (P>0.05). There were no serious adverse events and adverse reactions during the observation period. **Conclusion:** Acupuncture is effective and safe in the treatment of PD with OH.

Keywords: Parkinson's Disease; Orthostatic Hypotension; Acupuncture; Randomized Controlled Clinical Trial

Introduction

Parkinson's disease (PD) is one of the most common neurodegenerative diseases in elderly people. Statistics in 2005 showed that about 1.7 million people in China suffered from PD[1]. About 30%-50% of PD patients have orthostatic hypotension (OH), which is one of the most common non-motor symptoms[2-4]. The treatment of PD with OH patients is difficult, and they are prone to falls in daily life, which often leads to clinical malignant events such as intracranial hemorrhage, pelvic and lower extremity large joint fractures and so on[5]. This study investigated the therapeutic effect of acupuncture on PD with OH patients through a randomized controlled trial.

1. Materials and Methods

1.1 Materials

A total of 60 PD with OH patients who were treated in Shaanxi Provincial People's Hospital from January 2021 to June 2021 were collected and randomly divided into a treatment group of 30 cases and a control group of 30 cases according to the random number table. At the end of the follow-up, the treatment group dropped out 6 cases and the control group dropped out 3 cases, so the final treatment group included 24 cases and the control group included 27 cases. The age of the treatment group was 57~79 years old, with an average age of (74.17±7.42) years, including 16 males and 8 females. The age of the control group was 55 to 80 years old, with an average age of (71.37±10.48) years, including 17 males and 10 females. The study has been registered in the China Clinical Trials Registry with the registration number of ChiCTR2000041486.

1.2 Inclusion criteria

① Age 18-80 years old; ② Meet the PD diagnostic criteria issued by MDS in 2015[6]; ③ Meet the diagnostic criteria for OH[7]: a drop in systolic blood pressure of at least 20 mmHg or a drop in diastolic blood pressure of at least 10 mmHg within

3 minutes of the patient changing from a supine position to standing position; ④ Informed consent was written and this study was approved by the medical ethics committee of the Shaanxi Provincial People's Hospital.

1.3 Exclusion criteria

① Severe PD patients who cannot cooperate; ② Patients with severe renal insufficiency; ③ Patients with severe heart disease, infection, etc.

1.4 Study design

A randomized controlled trial in PD with OH patients.

1.5 Interventions

The treatment group was given acupuncture on the basis of basic medication, and we selected Neiguan, Zusanli and Baihui as the main points. After routine disinfection of the local acupoints, acupuncture with 0.25×25 or 0.25×50 filigree needles was performed. After arrival of qi, the Zusanli acupoint was needled with the twisting and rejuvenation method, and Baihui and Neiguan acupoints were needled with the flattening and reducing method. Each treatment time was 30 mins. The intensity should be within the tolerance of the patients. The treatment was given once a day, for 7 days. The control group was only given basic medication. Basic medication was the anti-Parkinson's disease drugs according to the patient's condition, and the use of drugs which may affect blood pressure was avoided when not necessary. Full treatment regimen including baseline, treatment period and 1 week follow-up.

1.6 Curative effect evaluation index

Blood pressure and heart rate of patients in the sitting position were monitored by using Mindray ECG monitor iMEC5. Transcranial Doppler examination also was performed. The TC-2020 type transcranial color Doppler diagnostic instrument produced by German EME Company was used, and a 2MHz pulse wave probe was used to detect the left middle cerebral artery of the patient in the sitting state through the temporal window, and to observe the direction and speed of its blood flow. The visual vertigo analogue scale (VVAS) was used to assess the presence and the degree of dizziness in patients (0 indicates no dizziness, 10 indicates extreme dizziness). The modified Rankin scale (mRS) was used to assess the level of daily functional disability in patients.

1.7 Safety evaluation

Acupuncture and drug-related adverse reactions were mainly monitored and recorded.

1.8 Statistical method

Efficacy analyses were based on the population of patients who underwent randomization. Student’s t-test was performed to analyze the differences between the two groups in continuous variables such as age, blood pressure and disease duration. Chi-square tests were carried out to examine the gender differences between the two groups. Statistical analyses were performed using SPSS version 19.0 for Windows (SPSS Inc., Chicago, IL, USA).

2. Results

2.1 Basic Clinical Information (Table 1)

The disease duration of PD patients in the treatment group was (6.08±1.20) years, and the HY grade was (3.87±0.64); the disease duration of the PD patients in the control group was (6.12±1.09) years, and the HY grade was (3.96±0.58) grade. There was no significant difference in the gender ratio, age, disease duration and HY grade of PD patients between the two groups（$P>0.05$）.

Table 1 Comparison of basic data of patients in two groups

	Treatment group（n=24）	Control group（n=27）	P
Gender (male/female)	16/8	17/10	＞0.05
Age（ $\bar{\chi}$±s，year）	74.17±7.42	71.37±10.48	＞0.05
Disease duration（ $\bar{\chi}$±s，year）	6.08±1.20	6.12±1.09	＞0.05
HY grade（ $\bar{\chi}$±s）	3.87±0.64	3.96±0.58	＞0.05

2.2 Efficacy analysis (Table 2)

Table 2 Comparison of main curative effect parameters at baseline and after 1 week of acupuncture treatment between two groups of patients（ $\bar{\chi}$±s）[a]$P < 0.05$, compared with the two groups.

		treatment group（n=24）	control group（n=27）	t	P
Systolic blood pressure(mmHg)	Baseline	126.13±17.59	124.04±16.68	0.435	0.666
	After 1 week	134.67±14.98	122.93±17.17	2.587	0.013[a]
Diastolic blood pressure(mmHg)	Baseline	64.79±10.63	64.52±10.39	0.093	0.927
	After 1 week	70.54±10.86	64.07±10.06	2.208	0.032[a]
Blood flow velocity of left middle cerebral artery(cm/s)	Baseline	65.58±5.56	64.74±4.86	0.578	0.566
	After 1 week	69.17±6.06	64.37±4.74	3.167	0.003[a]
VVAS	Baseline	5.67±0.87	5.63±0.88	0.151	0.881
	After 1 week	4.38±1.06	4.93±0.68	2.245	0.029[a]
Heart rate(times/min)	Baseline	72.21±7.56	72.56±7.32	0.167	0.868
	After 1 week	73.04±7.83	72.26±6.90	0.380	0.706
mRS	Baseline	3.46±0.51	3.37±0.57	0.581	0.564
	After 1 week	3.29±0.46	3.41±0.57	0.796	0.430

Baseline data showed that there were no significant differences in blood pressure (systolic blood pressure, diastolic blood pressure), heart rate, blood flow velocity of left middle cerebral artery, VVAS, and mRS between the two groups（P＞0.05）. After 1 week of acupuncture treatment, the systolic blood pressure, diastolic blood pressure and blood flow velocity of left middle cerebral artery of the treatment group were increased compared with those of the control group, and the difference was statistically significant between the two groups (P< 0.05)； The VVAS of the treatment group was also decreased compared with the control group, and the difference was statistically significant between the two groups (P< 0.05). After 1 week of acupuncture treatment, the heart rate of the treatment group increased and the mRS decreased compared with the control group, but there was no statistical difference（P＞0.05）.

2.3 Safety analysis

There were no serious adverse events and no adverse reactions in the two groups of patients.

3. Discussion

In this study, through the design method of a randomized controlled clinical trial, a comprehensive observation was made from objective indicators such as blood pressure (systolic blood pressure, diastolic blood pressure), heart rate, blood flow velocity of left middle cerebral artery, and subjective indicators such as VVAS and mRS to explore the clinical effect of acupuncture on PD with OH patients. The results showed that the blood pressure (whether systolic or diastolic) in sitting position increased significantly and the cerebral blood velocity of left middle cerebral artery by Transcranial Doppler examination increased simultaneously in PD with OH patients after 1 week of acupuncture treatment. At the same time, the dizziness sensation (VVAS) of the patients was also significantly relieved. Therefore, this study confirmed the clinical efficacy of acupuncture in the treatment of PD with OH patients.

Acupuncture belongs to traditional Chinese medicine, which is broad and profound. It is the treasure of the Chinese nation with a long history of thousands of years. Numerous evidence show that acupuncture has an obvious regulatory effect on blood pressure[8]. Yin et al[9] used electroacupuncture to stimulate Neiguan and Gongsun points to treat patients with primary hypotension and achieved obvious clinical effects. It has also been reported that acupuncture at Baihui, Neiguan and Zusanli points can improve the basal blood pressure level in patients with orthostatic hypotension[10]. More studies have found that acupuncture has a unique blood pressure boosting effect for diabetic patients with OH[11]. In this study acupuncture was used to improve PD with OH patients' hypotension and result showed that it can relieve their clinical symptoms when Neiguan, Zusanli and Baihui were selected as the main points.

Clinically, OH can be caused by a variety of abnormal physiological states and common factors include hypovolemia, excessive blood loss and drugs (including various common antihypertensive drugs, antidepressant drugs and antiparkinsonian drugs such as levodopa, dopamine receptor agonists, etc). The causes of OH associated with PD may be related to the impairment of sympathetic nerve function and the lack of norepinephrine secretion. This OH commonly saw in neurodegenerative diseases such as PD and multiple system atrophy is also called neurogenic OH[12]. PD with OH patients may have various symptoms such as dizziness, fatigue, cognitive decline, syncope, etc. In addition, PD patients have severe motor symptoms such as bradykinesia, rigidity, and postural gait disturbance which can easily lead to falling in daily life[13], which eventually leads to clinical malignant events such as intracranial hemorrhage, pelvic and lower extremity large joint fractures, etc. It not only increases the PD patient's economic burden and family care burden[14] , but also greatly shortens the patient's life expectancy and seriously reduces the patient's quality of life[5].

However, the frustrating reality says there are currently no effective treatment for PD with OH[15]. Currently the most frequently used clinical treatment options include non-drug therapy and drug therapy[16]. Commonly used non-drug treatment measures include the use of elastic stockings, etc., but there are various limitations such as too long and complicated wearing time, severe discomfort, and poor compliance. However, there are just a handful of drugs that can improve the symptoms of PD with OH. At present, they are not generally available on the market in China, and even large hospitals cannot purchase them normally, and there are some limitations such as short maintenance time, weakened long-term efficacy, and high costs. At the same time, about half of PD with OH patients also have supine hypertension, that is, the blood pressure is higher than the normal range when the patient is lying down, and obvious nocturnal hypertension can occur[17]. However, all the current drugs for the treatment of OH, although they can partially improve the symptoms of OH, will inevitably aggravate the patient's supine hypertension, and in the long-term will aggravate the patient's arteriosclerosis process and ultimately lead to a significantly increased risk of cardiovascular and cerebrovascular diseases in patients. Acupuncture treatment can not only boost blood pressure, but also has many advantages such as convenience, economy and safety.

The main disadvantage of this study is that the number of study samples is small, and its long-term efficacy and safety need to be further verified by extended clinical trials. Despite this, the results of this study still suggest that acupuncture in Neiguan, Zusanli and Baihui is clinically effective and safe for PD with OH patients, and the mechanism remains to be further studied.

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Conflict of Interest: The authors declare that they do not have a conflict of interest.

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