Observation on Therapeutic Effect of Lotus Needle Cupping Therapy for Removing Blood Stasis in Zhuang Medicine on PHN and Its Influence on Inflammatory Mediators

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Abstract [**Objectives**] To observe the clinical effect of the lotus needle cupping therapy for removing blood stasis in Zhuang medicine in treating PHN and its influence on inflammatory factors. [**Methods**] 96 patients with PHN were randomly divided into three groups: lotus needle cupping therapy group, TCM surrounding acupuncture group and gabapentin group. Venous blood and acupoint blood were collected at 0, 21 and 42 d of treatment, and the expression levels of 5-HT, SP and CGRP inflammatory mediators were detected before and after treatment. The changes of VAS scores before, during and after treatment and the clinical efficacy were observed. [**Results**] The total effective rate of the lotus needle cupping group was 87.50%, which was better than that of the TCM acupuncture group (81.25%) and the gabapentin group (62.50%); after treatment, the VAS scores and the expression of inflammatory mediators in the three groups of patients were lower than those before treatment, and the decrease was more significant in the treatment group ($P<0.05$). [**Conclusions**] The lotus needle cupping therapy for removing blood stasis in Zhuang medicine is effective in treating PHN, and its mechanism is to reduce the release of inflammatory mediators, reduce hyperalgesia, relieve pain and improve the quality of life of patients.

Key words Lotus needle cupping therapy for removing blood stasis in Zhuang medicine, Postherpetic neuralgia, Inflammatory mediator

1 Introduction

Postherpetic neuralgia (PHN) is a common complication of herpes zoster[1]. The prevalence rate of herpes zoster in China is 7.7%, and 29.8% of herpes zoster patients develop PHN[2]. PHN is difficult to treat, and less than half of patients can reduce pain by 50%. Clinical studies have confirmed the exact efficacy of lotus needle cupping therapy for removing blood stasis in Zhuang medicine in treating PHN[3], and found the influence of serum neurotransmitter substance P and receptor neurokinin-1 on PHN[4]. Some studies have found that inhibiting the expression of pro-inflammatory factors IL-18 and TNF-α can alleviate inflammatory reaction, thus achieving the purpose of PHN analgesia[5]. In this study, the lotus needle cupping therapy for removing blood stasis in Zhuang medicine was adopted to treat PHN, to explore the mechanism of inflammatory mediators in the occurrence and development of PHN pain, and to provide a new target for the treatment of PHN in the future.

2 Data and methods

2.1 Clinical data From March 2019 to October 2021, 96 PHN patients who met the inclusion criteria were included in the inpatient department and outpatient department of the First Hospital Affiliated to Guangxi University of Chinese Medicine and Guangxi International Zhuang Medicine Hospital. They were randomly divided into treatment group (lotus needle cupping therapy for removing blood stasis in Zhuang medicine), control group 1 (TCM acupuncture treatment group) and control group 2 (gabapentin treatment group), with 32 cases in each group. Compared with the general data, the difference was not statistically significant ($P>0.05$). See Table 1 for details.

Table 1 Comparison of gender, age and course of disease among the three groups of patients ($n=32$)

Group	Gender		Average age $\bar{x}\pm s$, years	Average course of disease $\bar{x}\pm s$, months
	Male	Female		
Treatment	15	17	53.78±7.74	3.47±0.95
Control 1	16	16	54.41±7.45	3.19±1.12
Control 2	17	15	54.75±7.30	3.13±0.91
$\chi^2(F)$ value	0.250	0.271	2.563	
P value	0.966	0.873	0.278	

2.2 Inclusion criteria The diagnosis refers to the criteria of PHN in *Dermatology and Venereology of Integrated Traditional Chinese and Western Medicine* edited by Wang Genhui[6]; age ≥ 20 years, ≤70 years; VAS score > 5; those who did not take any treatment measures against PHN within 1 week before the trial; those who voluntarily sign informed consent; those who have not participated in any drug clinical trials within 3 months before this trial.

2.3 Exclusion criteria Patients with PHN in the face and perineum; skin condition is not suitable for treatment; compli-

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cated with severe systemic diseases or systemic failure; patients with pain caused by other diseases; pregnant or lactating woman.

2.4 Treatment methods

2.4.1 Treatment group (lotus needle cupping therapy for removing blood stasis in Zhuang medicine). (i) Acupoint selection. Longji acupoint, bilateral Xiangling acupoint, bilateral Zhuangyi Jiaji acupoint and Lianhua acupoint were selected[7]. Longji acupoint: There is one point under the spinous process of each vertebra. Xiangling acupoint: 1.5-inch acupoint was opened on both sides of Jinglongji acupoint, with 7 acupoints on each side, totaling 14 acupoints. Zhuangyi Jiaji acupoint: 1.5-inch and 3-inch acupoints were opened on both sides of Xionglongji acupoint, which are called Zhuangyi Jinjiaji acupoint and Zhuangyi Yuanjiaji acupoint respectively. Lianhua acupoint: A group of acupoints located in and around a lump or skin lesion, shaped like the lotus flower. (ii) Operation. After routine disinfection with iodophor, the selected acupoints were tapped with seven star dermal needle. It is better to make blood seep slightly locally, and then cups were applied quickly using a suction device on the tapped acupoints. Cupping was kept for 10 – 15 min and then cups were removed, and it was treated once every 3 d. (iii) Course of treatment. 3 weeks as a course of treatment, with a total of 2 courses of treatment.

2.4.2 Control group 1 (TCM acupuncture treatment group). (i) Acupoint selection. Same as the treatment group. (ii) Operation. After iodophor disinfection, Lianhua acupoint, Longji acupoint, Xiangling acupoint and Jiaji acupoint were selected for acupuncture using filiform needles with a specification of 0.35 mm × 45 mm, and Lianhua acupoint was pricked obliquely. Peripheral needling was performed around the initial position of the disease, and the needle penetration depth was about half an inch. Xiangling acupoint, Jiaji acupoint and Longji acupoint were pricked 0.5 – 1.0 inch. All patients were given the method of mild reinforcing and attenuating, without lifting, inserting and twisting, and the needle was slowly released after 15 min.

2.4.3 Control group 2 (gabapentin capsule group). (i) Drug. Gabapentin capsules (300 mg/capsule, produced by Jiangsu Enhua Pharmaceutical Co., Ltd., SFDA approval number 20051068). (ii) Method. Baseline period: take it once on the first day, 300 mg each time, and take it orally before going to bed; take it twice on the second day, 300 mg each time; from the third day, the single dosage remained unchanged, but the times of administration increased to 3 for one week. Incremental period: the daily total dose gradually increased to 1 800 mg on the 8^{th} to 14^{th}, that is, the target dose (dose recommended by FDA for treating PHN). Maintenance period: from the third week, the total daily amount was maintained at 1 800 mg (600 mg/time, three times a day) until the end of the observation period. (iii) Course of treatment. 3 weeks as a course of treatment, with a total of 2 courses of treatment.

2.4.4 Sample collection. Blood samples (3 mL) were collected from fasting vein at 0, 21 and 42 d before treatment.

For the patients in each group, "acupoint blood" samples were collected 0, 21 and 42 d before treatment. Blood collection site. Selected Lianhua acupoint where the pain was most serious. "Acupoint blood" specimen collection method. Cupping was rapidly performed after acupuncture with plum-blossom needle, and after blood outflow before coagulation, a pipette was used to suck 3 mL of blood to be placed in the test tube containing EDTANa2 and mixed evenly for anticoagulation.

2.4.5 Experimental methods. Serum 5-HT, SP and CGRP levels were detected by enzyme-linked immunosorbent assay.

The experimental operation steps were followed according to the kit instructions, and the standard curves were drawn to calculate the content of 5-HT, SP and CGRP.

2.5 Observation index (i) Visual analogue scale (VAS) was used to assess the pain degree of the patients, and VAS pain scores were given at 3 observation points 0, 21 and 42 d before treatment. (ii) The levels of pro-inflammatory mediators 5-HT, SP and CGRP in venous blood and acupoint blood of the three groups of patients before and after treatment were compared.

2.6 Efficacy evaluation standard It was based on the methods recommended in *Clinical Diagnosis and Treatment Guidelines—Pain Branch*. VAS score was used as the curative effect index. Cured: curative effect index ≥ 95%; marked: 75% ≤ curative effect index < 95%; ineffective: curative effect index < 30%. Effective rate = (cured cases + markedly effective cases + effective cases)/total cases × 100%.

2.7 Statistical analysis SPSS 22.0 software was used for statistical analysis. Mean ± standard deviation was used for measurement data, and analysis of variance was used for comparison of data conforming to normal distribution. The counting data were expressed by frequency, X^2 test was used to compare the differences between groups, and repeated measurement data were compared by repeated analysis of measurement variance. $P < 0.05$ indicated that the difference was statistically significant.

3 Results and analysis

3.1 Comparison of VAS scores among the three groups of patients before and after treatment As can be seen from Table 2, there was no significant difference in VAS scores among the three groups before treatment ($P > 0.05$), with comparability. There were statistically significant differences in treatment at 42 d and 0 d in the three groups of patients ($P < 0.05$); after treatment for 21 and 42 d, there were significant differences among the three groups of patients ($P < 0.05$); after 42 d of treatment, the treatment group was compared with control group 1 and control group 2, $P < 0.05$, indicating that it had more advantages in reducing the pain degree of VAS than control group 1 and control group 2.

Table 2 Comparison of VAS scores among the three groups of patients ($\bar{x} \pm s$, $n = 32$)

Group	Treatment for 0 d//ng/mL	Treatment for 21 d//ng/mL	Treatment for 42 d//ng/mL	P_{12}	P_{13}	P_{23}
Treatment	7.19 ± 1.28	4.50 ± 1.70	2.00 ± 2.08	<0.001	<0.001	<0.001
Control 1	7.13 ± 1.18	4.97 ± 1.93	3.22 ± 2.50	<0.001	<0.001	<0.001
Control 2	7.19 ± 1.20	5.75 ± 1.97	4.56 ± 2.63	<0.001	<0.001	<0.001
Treatment/Control 1	0.893	0.318	0.046			
Treatment/Control 2	1.000	0.009	<0.001			
Control 1/Control 2	0.893	0.098	0.028			

Note: *P* treatment group/control group 1, the significance between treatment group and control group 1 at the same time; P_{12}, the significance between 0 and 21 d after treatment in the same group; P_{13}, the significance between 0 and 42 d after treatment in the same group; P_{23}, the significance between 21 and 42 d after treatment in the same group. The same below.

3.2 Comparison of clinical efficacy among the three groups of patients It can be seen from Table 3 that after treatment, the total effective rate of the treatment group was 87.50%; the total effective rate of control group 1 was 81.25%, and the total effective rate of control group 2 was 62.50%.

Table 3 Comparison of clinical efficacy among the three groups of patients ($n = 32$)

Group	Cured	Markedly effective	Effective	Ineffective	Total effective rate//%	*Z*	Significance
Treatment	9	13	6	4	87.50■●	15.391	0.000
Control 1	5	9	12	6	81.25		
Control 2	2	5	13	12	62.50		

Note: Compared with control group 1, ■$P < 0.05$; compared with control group 2, ●$P < 0.05$.

3.3 Comparison of 5-HT values in venous blood of three groups of patients As shown in Table 4, before treatment, there was no significant difference in venous blood 5-HT among the three groups of patients ($P > 0.05$), with comparability. There were statistically significant differences between 42 and 0 d after treatment in the three groups of patients ($P < 0.05$); after treatment for 21 and 42 d, there were significant differences among the three groups of patients ($P < 0.05$); after 42 d of treatment, the treatment group was compared with control group 1 and control group 2, $P < 0.05$, indicating that it had more advantages in reducing venous blood 5-HT value than control group 1 and control group 2.

Table 4 Comparison of 5-HT values of venous blood before and after treatment among the three groups of patients ($\bar{x} \pm s$, $n = 32$)

Group	Treatment for 0 d//ng/mL	Treatment for 21 d//ng/mL	Treatment for 42 d//ng/mL	P_{12}	P_{13}	P_{23}
Treatment	740.30 ± 78.27	460.27 ± 61.56	300.81 ± 51.16	<0.001	<0.001	<0.001
Control 1	739.73 ± 74.31	629.56 ± 79.90	515.84 ± 79.34	<0.001	<0.001	<0.001
Control 2	744.27 ± 91.80	729.97 ± 67.60	643.69 ± 96.60	0.268	<0.001	<0.001
Treatment/Control 1	0.865	<0.001	<0.001			
Treatment/Control 2	0.743	<0.001	<0.001			
Control 1/Control 2	0.618	<0.001	<0.001			

3.4 Comparison of 5-HT values in acupoint blood of three groups of patients It can be seen from Table 5 that there was no significant difference in 5-HT values of acupoint blood among the three groups of patients before treatment ($P > 0.05$), with comparability. The difference was statistically significant ($P < 0.05$) in the three groups of patients after treatment for 42 and 0 d; after treatment for 21 and 42 d, the difference was statistically significant among the three groups of patients ($P < 0.05$); after 42 d of treatment, the treatment group was compared with control group 1 and control group 2, $P < 0.05$, indicating that it had more advantages in reducing the value of 5-HT in acupoint blood than control group 1 and control group 2.

Table 5 Comparison of 5-HT values of acupoint blood before and after treatment among the three groups of patients ($\bar{x} \pm s$, $n = 32$)

Group	Treatment for 0 d//ng/mL	Treatment for 21 d//ng/mL	Treatment for 42 d//ng/mL	P_{12}	P_{13}	P_{23}
Treatment	784.79 ± 78.02	493.78 ± 68.91	349.96 ± 55.07	<0.001	<0.001	<0.001
Control 1	739.97 ± 82.32	610.84 ± 79.08	503.65 ± 63.54	<0.001	<0.001	<0.001
Control 2	774.32 ± 95.27	761.22 ± 90.85	676.97 ± 102.60	0.044	<0.001	<0.001
Treatment/Control 1	0.557	<0.001	<0.001			
Treatment/Control 2	0.490	<0.001	<0.001			
Control 1/Control 2	0.203	<0.001	<0.001			

3.5 Comparison of venous blood SP among the three groups of patients From Table 6, we can see that there was no significant difference in venous blood SP among the three groups of patients before treatment ($P > 0.05$), with comparability. The

difference was statistically significant ($P < 0.05$) in the three groups of patients after treatment for 42 d and 0 d; after treatment for 21 and 42 d, the difference was statistically significant among the three groups of patients ($P < 0.05$); after 42 d of treatment, the treatment group was compared with control group 1 and control group 2, $P < 0.05$, indicating that it had more advantages in reducing venous blood SP than control group 1 and control group 2.

Table 6 Comparison of venous blood SP before and after treatment among the three groups of patients ($\bar{x} \pm s$, $n = 32$)

Group	Treatment for 0 d//ng/mL	Treatment for 21 d//ng/mL	Treatment for 42 d//ng/mL	P_{12}	P_{13}	P_{23}
Treatment	1 524.46 ± 222.01	920.18 ± 193.95	581.80 ± 78.84	<0.001	<0.001	<0.001
Control 1	1 544.78 ± 243.94	1 208.87 ± 235.11	895.52 ± 181.88	<0.001	<0.001	<0.001
Control 2	1 511.32 ± 185.52	1 508.76 ± 182.89	1 300.95 ± 149.07	0.452	<0.001	0.001
Treatment/Control 1	0.651	0.001	<0.001			
Treatment/Control 2	0.836	<0.001	<0.001			
Control 1/Control 2	0.510	<0.001	<0.001			

3.6 Comparison of acupoint blood SP among the three groups of patients It can be seen from Table 7 that before treatment, there was no significant difference in acupoint blood SP among the three groups of patients ($P > 0.05$), with comparability. The difference was statistically significant ($P < 0.05$) in the three groups of patients after treatment for 42 and 0 d; after treatment for 21 and 42 d, the difference was statistically significant among the three groups of patients ($P < 0.05$); after 42 d of treatment, the treatment group was compared with control group 1 and control group 2, $P < 0.05$, indicating that it had more advantages in reducing acupoint blood SP than control group 1 and control group 2.

Table 7 Comparison of acupoint SP before and after treatment among the three groups of patients ($n = 32$)

Group	Treatment for 0 d//ng/mL	Treatment for 21 d//ng/mL	Treatment for 42 d//ng/mL	P_{12}	P_{13}	P_{23}
Treatment	1.02 ± 0.21	0.63 ± 0.09	0.52 ± 0.08	<0.001	<0.001	<0.001
Control 1	1.01 ± 0.18	0.82 ± 0.12	0.71 ± 0.09	<0.001	<0.001	0.001
Control 2	1.02 ± 0.15	1.01 ± 0.19	0.84 ± 0.09	0.804	<0.001	<0.001
Treatment/Control 1	0.847	<0.001	<0.001			
Treatment/Control 2	0.979	<0.001	<0.001			
Control 1/Control 2	0.826	<0.001	<0.001			

3.7 Comparison of venous blood CGRP among the three groups of patients It can be seen from Table 8 that there was no significant difference in venous blood CGRP among the three groups of patients before treatment ($P > 0.05$), with comparability. The difference was statistically significant ($P < 0.05$) in the three groups of patients after treatment for 42 and 0 d; after treatment for 21 and 42 d, the difference was statistically significant among the three groups of patients ($P < 0.05$); after 42 d of treatment, the treatment group was compared with control group 1 and control group 2, $P < 0.05$, indicating that it had more advantages in reducing venous blood CGRP than control group 1 and control group 2.

Table 8 Comparison of venous blood CGRP before and after treatment among the three groups of patients ($\bar{x} \pm s$, $n = 32$)

Group	Treatment for 0 d//ng/mL	Treatment for 21 d//ng/mL	Treatment for 42 d//ng/mL	P_{12}	P_{13}	P_{23}
Treatment	725.41 ± 80.34	307.30 ± 62.84	201.04 ± 37.14	<0.001	<0.001	<0.001
Control 1	722.75 ± 121.00	598.91 ± 82.90	496.61 ± 56.34	<0.001	<0.001	<0.001
Control 2	724.62 ± 84.95	708.47 ± 88.04	624.77 ± 90.35	0.452	<0.001	0.001
Treatment/Control 1	0.651	0.001	<0.001			
Treatment/Control 2	0.836	<0.001	<0.001			
Control 1/Control 2	0.510	<0.001	<0.001			

3.8 Comparison of acupoint blood CGRP among the three groups of patients As can be seen from Table 9, before treatment, there was no significant difference in the acupoint CGRP among the three groups of patients ($P > 0.05$), with comparability. The difference was statistically significant ($P < 0.05$) in the three groups of patients after treatment for 42 and 0 d; after treatment for 21 and 42 d, the difference was statistically significant among the three groups of patients ($P < 0.05$); after 42 d of treatment, the treatment group was compared with control group 1 and control group 2, $P < 0.05$, indicating that it had more advantages in reducing acupoint blood CGRP than control group 1 and control group 2.

Table 9 Comparison of acupoint CGRP before and after treatment among the three groups of patients (n = 32)

Group	Treatment for 0 d // ng/mL	Treatment for 21 d // ng/mL	Treatment for 42 d // ng/mL	P_{12}	P_{13}	P_{23}
Treatment	1.02 ± 0.21	0.63 ± 0.09	0.52 ± 0.08	< 0.001	< 0.001	< 0.001
Control 1	1.01 ± 0.18	0.82 ± 0.12	0.71 ± 0.09	< 0.001	< 0.001	0.001
Control 2	1.02 ± 0.15	1.01 ± 0.19	0.84 ± 0.09	0.804	< 0.001	< 0.001
Treatment/Control 1	0.847	< 0.001	< 0.001			
Treatment/Control 2	0.979	< 0.001	< 0.001			
Control 1/Control 2	0.826	< 0.001	< 0.001			

4 Discussion

In this study, the PHN treatment group was treated with lotus needle cupping therapy for removing blood stasis in Zhuang medicine. The VAS and clinical curative effect of treatment group (lotus needle cupping therapy for removing blood stasis in Zhuang medicine) were better than those of control group 1 (TCM acupuncture treatment group) and control group 2 (gabapentin treatment group) (P < 0.05). The content of 5-HT, SP and CGRP in venous blood and acupoint blood at 0 d before treatment decreased compared with those at 21 and 42 d before treatment, and the treatment group had more advantages than the other two groups (P < 0.05). According to Zhuang medicine, the inflammatory mediators (5-HT, SP, CGRP, *etc.*) of PHN inflammation are equivalent to the categories of "blood stasis" and "toxin" in Zhuang medicine theory. Treatment of PHN by lotus needle cupping therapy for removing blood stasis in Zhuang medicine[8] refers to acupuncture at specific surface acupoints, and then sucking out the pathogenic toxin in the body with an air pump. This therapy combines the effects of acupoint tapping, bloodletting and negative pressure cupping, and can stimulate the special acupoints on muscle surface, so as to exert the effects of "detoxification" and "removing blood stasis". On the one hand, it can drive PHN's "static blood" and "toxin" out to dredge the two channels; on the other hand, it adjusts the functions of the two channels, harmonizes qi and blood, and makes the heaven, earth and human run synchronously, so as to realize the balance of qi and blood, reduce the inflammatory reaction and achieve the purpose of analgesia.

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