Journal of Regional Anesthesia & Pain Medicine

Research Article

doi: 10.39127/2022/JRAPM:1000112
Fei Y, et al. J Reg Anes Pain Med: JRAPM-112

Efficacy of Internal Heat Acupuncture Combined with High-Voltage Long-Duration Pulsed Radiofrequency on Subacute Postherpetic Neuralgia

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Citation: Fei Y, Yao M, Huang B, Xu L, Liu B (2022) Efficacy of Internal Heat Acupuncture Combined with High-Voltage Long-Duration Pulsed Radiofrequency on Subacute Postherpetic Neuralgia. J Reg Anes Pain Med: JRAPM-112.

Received Date: 11th February, 2022; **Accepted Date:** 16th February, 2022; **Published Date:** 23rd February, 2022

Abstract

Objectives: *The aim of this study was to investigate the therapeutic effect of internal heat acupuncture (IHA) combined with high-voltage long-duration pulsed radiofrequency (PRF) on subacute postherpetic neuralgia (PHN).*
Methods: *This retrospective study was conducted 81 cases with PHN. They were divided into three groups: the internal heat acupuncture combined with high-voltage long-duration PRF group (group IHA-PRF), the intradermal injection combined with high-voltage long-duration PRF group (group II-PRF) and the high-voltage long-duration PRF group (group PRF). The pain numerical rating score (NRS), Gal-3, IL-6 and blood glucose levels were recorded before and after treatment.*
Results: *Compared with before treatment, the NRS score of three groups were all decreased at each time point. Compared with group PRF, the NRS scores of patients in group IHA-PRF decreased significantly at 1, 4, 8 and 12 weeks after treatment, while those in group II-PRF only decreased significantly at 1 week after treatment. Compared with group II-PRF and group PRF respectively, the levels of Gal-3 and IL-6 in serum of patients in group IHA-PRF were significantly decreased at 4 and 12 weeks after treatment. The effective rate of group IHA-PRF was 88.9%, which was significantly higher than that of group II-PRF (63.0%) and group PRF (63.0%). Compared with group II-PRF, the blood glucose levels of patients in group IHA-PRF and group PRF significantly decreased at 3 days and 1 week after treatment.*
Conclusion: *Internal heat acupuncture combined with high-voltage long-duration pulsed radiofrequency has a satisfactory therapeutic effect on subacute PHN and has no obvious adverse reactions, which is especially suitable for patients with poor blood glucose control.*

Keywords: *Internal heat acupuncture; PRF; subacute stage; PHN.*

Introduction

Herpes zoster is caused by varicella-zoster virus infecting dorsal root ganglion or cranial nerve, which is more common in middle-aged and elderly people with reduced immunity [1]. Neuralgia is one of the most common and serious symptoms of herpes zoster, which seriously affects the life quality of patients and increases the medical burden [2,3.] Nerve regulation technology is one of the effective methods for clinical treatment of PHN [4]. PRF technology is widely used in the treatment of PHN because of its simple operation, low cost and high patient acceptance [5,6]. However, the standard PRF therapy for PHN is often difficult to achieve lasting therapeutic effect [7]. It was reported that high-voltage long-duration PRF is more effective than standard PRF in the treatment of herpes zoster trigeminal neuralgia in acute and subacute stage.(8) However, most patients still have residual pain on the skin surface after operation. It was reported that the internal heat acupuncture therapy is effective, safe and reliable in the treatment of post-stroke shoulder pain [9].

Due to the complexity of pathological changes of PHN, some patients need to be combined with other treatment methods to relieve pain [10]. PHN is not only related to acute nerve injury, but also closely related to local ischemia, neurotrophic disorder and scar formation caused by arteriosclerosis of the supporting nerve [11]. Therefore, alleviating the local blood circulation in the lesion area is also one of the effective methods for the treatment of PHN. Therefore, this study proposes silver needle heating combined with radiofrequency therapy for the treatment of PHN.

In this study, internal heat acupuncture combined with high-voltage long-duration PRF were used to treat subacute stage PHN and observe the efficacy.

Materials and Methods

Participant

In this study, the inclusion criteria were: patients were on oral medication before presentation and the degree of pain was still moderate to severe (NRS > 3). There were 39 males and 42 females in the age range 44-86 years old, course of disease range 1-3 months. Nerve distribution area of all patients with PHN is spinal segment including 59 cases in thoracic segment and 22 cases in lumbar segment. This study was conducted 115 cases with PHN from the Department of Pain, Affiliated Hospital of Jiaxing University. Exclusion criteria were: patients with infection or tumor at puncture site, allergic to lidocaine hydrochloride, compound betamethasone and other drugs, severe cardiovascular and cerebrovascular diseases, liver and kidney dysfunction, abnormal bleeding and coagulation function, diabetic patients with poor blood sugar control, long-duration use of immunosuppressant or systemic failure, severe mental illness and inability to cooperate with surgery. After excluding these patients who do not meet the inclusion criteria, the medical records of 81 patients were analyzed. According to the random number table method, they were divided into three groups: the internal heat acupuncture combined with high-voltage long-time PRF group (group IHA-PRF, n=27), and the intradermal injection combined with high-voltage long-duration PRF group (group II-PRF, n=27) and the high-voltage long-duration PRF group (group PRF, n=27). Summary of patient progression through the study is displayed in Figure 1.

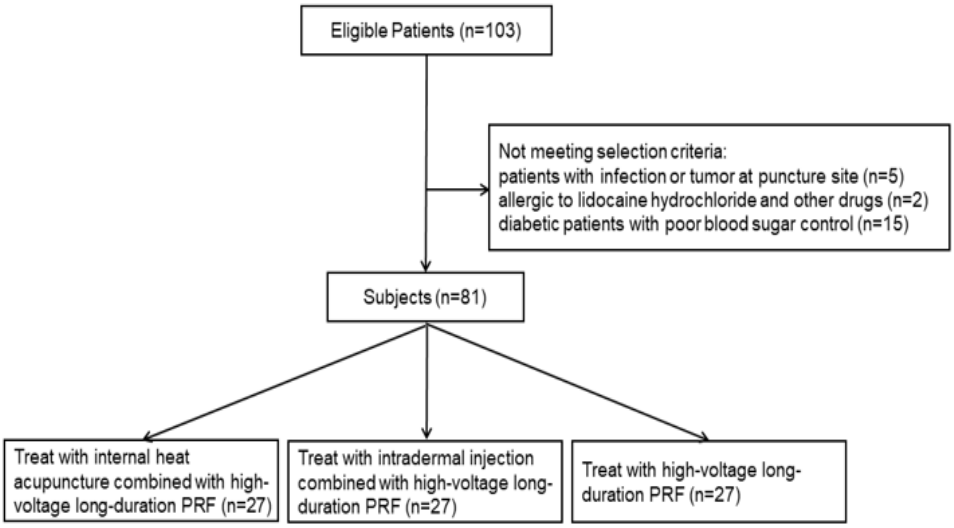

Figure 1: Flow diagram of the study participants.

All treatments were performed by the same senior pain doctor. The research was approved by the hospital ethics committee (approval number: LS2019-288), and all the subjects had informed consent to the research contents.

Therapeutic methods

PRF therapeutic steps

Patients lied prone on the CT treatment bed, centering on the most painful segment, and extending one segment up and down respectively, with 3 segments each time to perform PRF therapy of dorsal root ganglion. The upper edge of the ventral intervertebral foramen was selected as the puncture point for CT positioning and the puncture path was designed. 1.0% lidocaine hydrochloride was used for local infiltration anesthesia and radiofrequency trocar (20 G, length 150 mm, length of movable end 10 mm) was slowly pushed for puncture under CT. Finally, the needle point is located in the upper quadrant of the ventral side of the intervertebral foramen and root pain may occur from the puncture point to the chest wall. The radiofrequency test (Baylis medical Inc., Montreal, Canada) is a sensory test with setting parameters including voltage: 0.1-0.5 V and frequency: 50 Hz. It can induce discomfort such as acid, swelling, numbness or tingling in the original pain area. In the exercise test, low frequency current was used and parameters were set voltage: 0.1-0.5V, frequency: 2 Hz. The corresponding segments had corresponding trunk muscle fibrillation and pulsation. The three-position reconstruction diagram is shown in Figure 2.

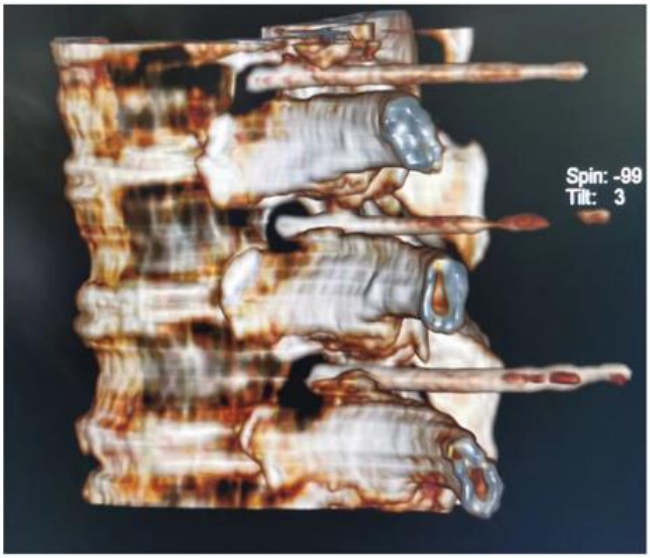

Figure 2: Three position reconstruction of corresponding segments.

There is no blood, gas or liquid in the withdrawal puncture needle and 2 ml of 1.0% lidocaine hydrochloride is injected into each target for 3 min. Adjusting the radiofrequency generator to manual pulsed mode and set the temperature, time, pulse duration, pulse rate and voltage as 42 ℃, 900 s, 20 ms, 2 Hz and 90 V respectively. After the radiofrequency was finished, the electrode needle core was pulled out, the puncture needle was withdrawn without blood, gas or liquid and 5ml of mixed solution is injected into each segment. The formula of the mixed solution was 2% lidocaine injection 100 mg (batch number H20133209, Tianjin Jinyao Pharmaceutical Co., Ltd.), 500g of mecobalamin injection (batch number 190707A, Japan Eisai Co., Ltd.) and compound betamethasone injection (batch number J20140160, Hangzhou Merck pharmaceutical co., ltd.) 1 ml and recombinant human interferon-2b injection (batch number S20040010, Anhui anke biotechnology Engineering Co., Ltd.) 1,000,000 U and 30% iodohyanol injection (batch number H20000591, Shanghai General Electric Pharmaceutical Co., Ltd.) 3 ml. The mixed solution was diluted to 15 ml with 0.9% normal saline. The puncture point was compressed after the needle was pulled out. After observation for 15 min, the patient was sent back to the ward when the vital signs were stable.

Internal heat acupuncture treatment steps

Mark the skin lesion area and design the needle distance to be 2 cm, and the internal heat-type acupuncture needle with a model of 0.70 mm*110 mm in the rear row enters the middle of the two needles in the front row with a needle distance of 1 cm. The needle entry method: after penetrating the subcutaneous tissue vertically, keep the angle between the needle and the skin within 5°, push forward slowly until the internal heat acupuncture enters the subcutaneous tissue 5 cm. According to this puncture method and design until the whole skin lesion area was covered, generally 10-20 needles were injected. A K-type internal heat acupuncture therapeutic apparatus (Shandong Jining Jiake Medical Technology Co., Ltd.) was connected and the temperature was set at 42℃ and heated for 20 min. Patients in group IHA-PRF were treated with internal heat acupuncture 1, 2, and 3 weeks after high-voltage long-duration PRF operation.

Intradermal injection treatment steps

Make circular punctate puncture around the painful part with the needle tip penetrating at an angle of 30-45 with the skin, slowly push the drug into the subcutaneous tissue, with a spacing of 5 cm at each point and finally cover the whole skin lesion area with the injection and generally puncture 10-20 needles. Drug formula for intradermal injection: 2% lidocaine hydrochloride injection 5 ml, mecobalamin injection 0.5 mg, compound betamethasone injection 1 ml, diluted to 20 ml by 0.9% sodium chloride injection. Patients in group II-PRF were treated with intradermal injection at 1, 2, and 3 weeks after high-voltage long-duration PRF operation.

Data collection

The pain degree of patients was evaluated by Numerical Rating Scale (NRS): 0 means painless, and 10 means unbearable pain. The NRS scores of patients before and after treatment were evaluated 3 days, 1, 4, 8 and 12 weeks respectively. Serum galectin-3 (Gal-3) and interleukin-6 (IL-6) levels were measured before treatment and 3 days, 1, 4 and 12 weeks after treatment. To evaluate the curative effect, it was effective to reduce NRS score by 25% or more compared with that before treatment. Among them, the reduction of 80% or more is excellent, 40-80% is good, 25-40% is acceptable, and less than 25% is poor. The effective rate was recorded 12 weeks after treatment. The effective rate was the ratio of the number of cases whose NRS score decreased by 25% or more to the total number of cases.

Statistical analysis

All the data were analyzed by SPSS 21.0 statistical software, and the measurement data conforming to normal distribution were expressed by mean standard deviation, the repeated measurement data were analyzed by multivariate analysis, the pairwise comparison was conducted by LSD test, and the counting data were compared by Chi-square test. $P < 0.05$ was statistically considered significant.

Results

General data of patients in each group was no significant difference

All patients were on oral medication before presentation and the degree of pain was still moderate to severe. There was no significant difference in age, gender, course of disease, nerve distribution area among the three groups (P > 0.05) as shown in Table 1.

	Number of cases	Age (years)	Gender (male/female)	Course of disease (months)	Chest/waist segment (example)
Group IHA-PRF	27	66.19±10.792	13/14	1.74±0.656	21/6
Group II-PRF	27	64.70±10.894	12/15	1.74±0.526	18/9
Group PRF	27	66.15±11.055	14/13	1.78±0.801	20/7
t/χ^2 value		0.161	0.297[a]	0.027	0.847[a]
P value		0.852	0.862	0.973	0.646
Note: [a] is the value of χ^2.					

Table 1: General data of patients.

The NRS scores decreased after treatment in each group

Compared with before treatment, the NRS scores of the three groups were all decreased at each time point after treatment. Compared with group II-PRF, NRS scores of patients in group IHA-PRF decreased at 4, 8 and 12 weeks after the treatment course and the differences were statistically significant (P < 0.05). Compared with group PRF, the NRS scores of patients in group IHA-PRF decreased at 1, 4, 8 and 12 weeks after the treatment course. The NRS scores of patients in group II-PRF decreased 1 week after the treatment course and the differences were statistically significant (P < 0.05) as shown in Figure 3.

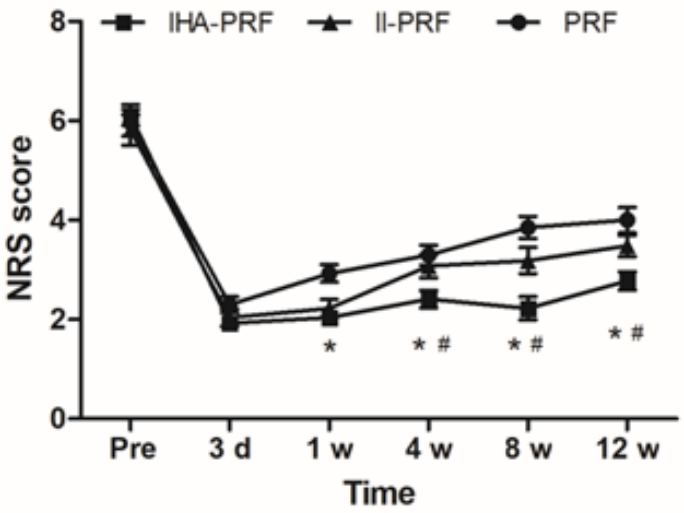

Figure 3: The NRS scores decreased after treatment in each group. Compared with before treatment, the NRS scores of the three groups were all decreased at each time point after treatment. The NRS scores of patients in group IHA-PRF significantly decreased at 4, 8 and 12 weeks after the treatment course. the NRS scores of patients in group IHA-PRF decreased at 1, 4, 8 and 12 weeks after the treatment course. The NRS scores of patients in group II-PRF decreased 1 week after the treatment course. *P < 0.05 compared with group II-PRF. #P <0.05 compared with group PRF.

Patients in the three groups were followed up for 12 weeks after treatment. The effective rate in group IHA-PRF (88.9%) was significantly higher than that in group II-PRF (63.0%) and group PRF (63.0%) with statistical difference (P < 0.05) as shown in Figure 4.

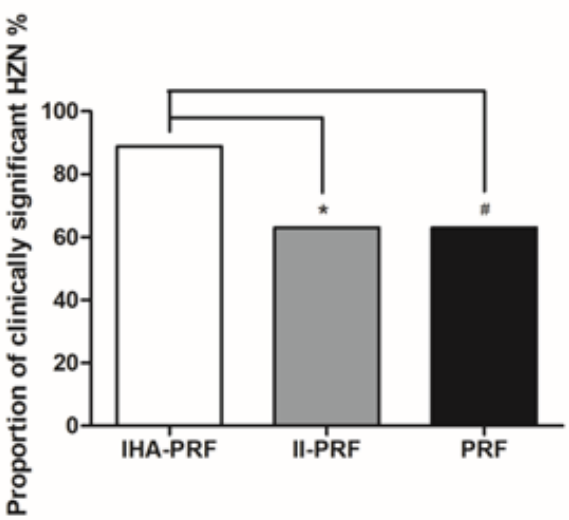

Figure 4: The effective rate of group IHA-PRF was significantly higher than that of the other two groups. Patients in the three groups were followed up for 12 weeks after treatment. The effective rate in group IHA-PRF (88.9%) was significantly higher than that in group II-PRF (63.0%) and group PRF (63.0%). *P < 0.05 compared with group II-PRF. #P <0.05 compared with group PRF.

Complications such as local anesthetic poisoning, nausea and vomiting and infection at the treatment site were not found in all three groups.

The levels of Gal-3 and IL-6 in serum decreased after treatment in group IHA-PRF

Compared with before treatment, the levels of Gal-3 and IL-6 in blood of the three groups decreased at each time point after treatment. Compared with group II-PRF and group PRF respectively, the levels of Gal-3 and IL-6 in serum of patients in group IHA-PRF decreased 4 and 12 weeks after treatment and the differences were statistically significant (P < 0.05) as shown in Figure 5.

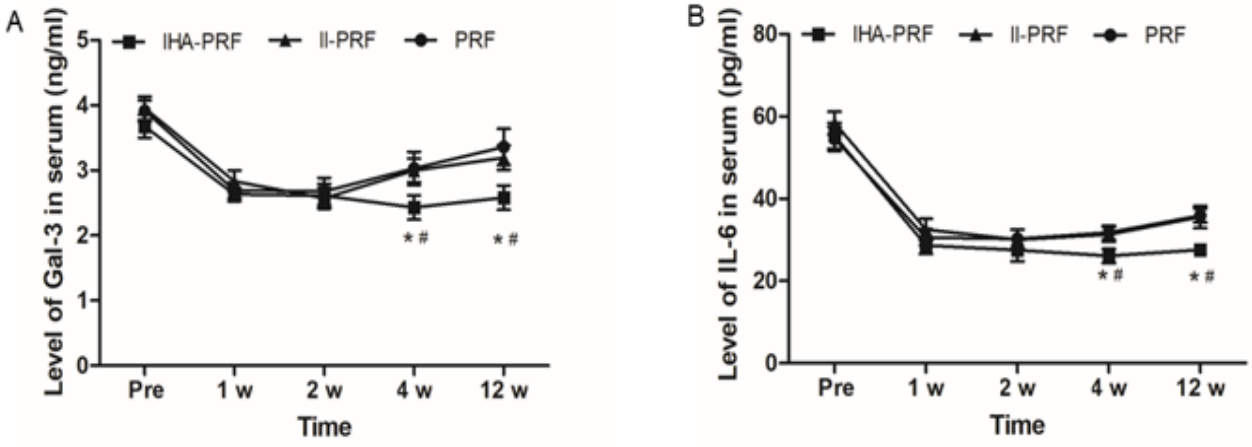

Figure 5: The levels of Gal-3 and IL-6 in serum decreased after treatment in group IHA-PRF. The levels of Gal-3 (A) and IL-6 (B) in blood of the three groups decreased at each time point after treatment. Compared with group II-PRF and group PRF respectively, the levels of Gal-3 and IL-6 in serum of patients in group IHA-PRF significantly decreased 4 and 12 weeks after treatment. *P < 0.05 compared with group II-PRF. #P <0.05 compared with group PRF.

The blood glucose levels of patients in group IHA-PRF and group PRF decreased 3 days and 1 week after treatment

Compared with before treatment, the blood glucose of patients in group IHA-PRF and group PRF increased 3 days after the treatment course and that of patients in group II-PRF increased 3 days and 1 week after the treatment course with significant differences (P < 0.05). Compared with group II-PRF, the blood glucose levels of patients in group IHA-PRF and group PRF decreased 3 days and 1 week after treatment and the differences were statistically significant (P < 0.05) as shown in Figure 6.

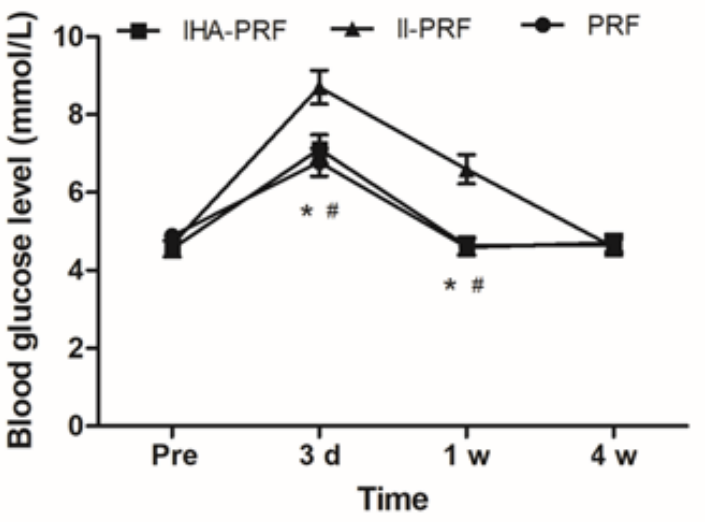

Figure 6: The blood glucose levels of patients in group IHA-PRF and group PRF decreased 3 days and 1 week after treatment. Compared with before treatment, the blood glucose of patients in group IHA-PRF and group PRF increased 3 days after the treatment course and that of patients in group II-PRF increased 3 days and 1 week after the treatment course with significant differences. The blood glucose levels of patients in group IHA-PRF and group PRF decreased 3 days and 1 week after treatment. *P < 0.05 compared with group II-PRF. #P <0.05 compared with group PRF.

Discussion

PHN is difficult to be treated clinically because of its complicated pathogenesis [12]. At present, all clinical treatments are aimed at reducing the occurrence of PHN (PHN). Due to the lack of understanding of pain department, as a disease 1-3 months) or even complicated with PHN. The pathological features of PHN in subacute stage are that the skin lesions have scabbed with severe neuralgia [13]. These patients are extremely prone to complicated with PHN and need timely treatment. PRF of dorsal root ganglion is an intermittent pulsed current emitted by a radio generator, which acts around the diseased dorsal root ganglion and nerve fibers [14]. It plays an analgesic role by recuperating the disordered electrical signals and reducing the substance P level of dorsal root ganglion [15]. Since the temperature at the tip of the electrode does not exceed 42 ℃. Therefore, this kind of energy transmission does not destroy the anatomical basis of pain impulse transmission, let alone the motor nerve function. Compared with the traditional continuous radiofrequency, it has no thermal damage to nerve and will not aggravate the original neuropathic pain. However, due to the low field strength (40 V) and short duration (180-300 s) of standard voltage PRF treatment, its action intensity is limited. It can't make patients get a lasting treatment effect and can't significantly reduce the incidence of PHN. Teixeira et al. found that the PRF field strength was positively correlated with the therapeutic effect [16]. Wan C et al. reported that high-voltage long-duration PRF was used to treat PHN [8]. The field strength was manually adjusted and gradually increased according to the patient's tolerance (maximum 90 V). The treatment duration was 900 s. The NRS of patients with PHN decreased at 1, 4, 8, 12 weeks after operation and the quality of life improved. However, most patients still have the residual pain on the skin surface after operation [17]. Some scholars have reported that internal heat acupuncture can solve the pain of nerve endings on the skin surface of herpes zoster and improve the quality of life and satisfaction of patients [18].

In this study, compared with before treatment, the NRS score of patients treated with high-voltage long-duration PRF of dorsal root ganglion combined with internal heat acupuncture decreased significantly after treatment, which indicated that the curative effect of internal heat acupuncture was more lasting than that of intradermal injection. The mechanism may be to eliminate inflammation of skin nerve endings and release local muscles.

Some scholars have studied that after varicella-zoster virus infection, the expression of mRNA and protein level of Gal-3 in the dorsal horn of spinal cord of mice increased significantly and the intrathecal injection of Gal-3 antibody in mice with Gal-3 gene deletion significantly reduced the touch-induced pain, which indicated that Gal-3 was involved in the production of PHN [19]. In addition, Gal-3 may mediate PHN through macrophages and microglia. Serum Gal-3 level was positively correlated with the severity of neuropathic pain [20,21]. The function of IL-6 is to regulate cell growth and differentiation and to regulate immune response and acute reaction. IL-6 plays a very important role in anti-infection immune response. Serum IL-6 level was positively correlated with nerve injury. High level of IL-6 is the key factor leading to nerve injury and chronic pain development and may play an important role in the formation of neuropathic pain [22]. Our team's previous research results also showed that the serum levels of Gal-3 and IL-6 in patients with PHN were significantly higher than those in normal people [23]. It can be used as an early diagnosis of PHN and a predictor of PHN [24]. In this study, it was found that the levels of Gal-3 and IL-6 in the serum of patients in the group of internal heat acupuncture combined with high-voltage long-duration PRF decreased significantly at 4 and 12 weeks after treatment, which indicated that the

effect of internal heat acupuncture on eliminating skin nerve endings inflammation was more lasting.

Complications such as local anesthetic poisoning, nausea, vomiting and infection at the treatment site were not found in all three groups. On the 3rd day after treatment, the blood glucose of patients in the three groups increased. This study found that the blood glucose level of patients in group IHA-PRF and group PRF decreased more significantly than group II-PRF at 3 days and 1 week after treatment, which indicates that the internal heat acupuncture combined with high-voltage long-duration PRF treatment is more suitable for patients with poor blood glucose control.

The limitations of this study are as follows: there may be differences between the actual pain score and the expressed value; the sample size is relatively small and the follow-up time is short. Further long-duration observation is needed to determine the duration of the effect of internal heat acupuncture combined with high-voltage long-duration PRF on subacute PHN. To verify our results in a larger population, a larger sample size and an appropriate control group will be needed to overcome the limitation of small sample size.

Conclusion

In summary, the treatment of subacute PHN with internal heat acupuncture combined with high-voltage long-duration PRF of dorsal root ganglion has a satisfactory therapeutic effect and has no obvious adverse reactions, which is especially suitable for patients with poor blood glucose control.

Acknowledgment

This study was supported by Key Discipline Established by Zhejiang Province and Jiaxing City Jointly-Pain Medicine (2019-ss-ttyx); Science and Technology Project of Jiaxing City (2019AD32150); Medical and Health Science and Technology Research Program of Zhejiang Province (2021KY352) and Jiaxing Key Laboratory of Neurology and Pain Medicine.

Author Contributions

B Liu contributed to design of research, edited and revised manuscript; L Xu performed acquisition of data or analysis and interpretation of data; Y Fei drafted manuscript and performed research; B Huang revising manuscript critically for important intellectual content; M Yao performed research and prepared figures. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published; and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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