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A clinical study on the treatment of postherpetic neuralgia with pulsed radiofrequency of the dorsal root ganglion with pain management

*[1]Zhi-Hong Xiong *BS*, *[1]Xue-Fang Tang *BS*, [1]Le-Tian Huang *BS*, [2]Li-Rong Yue *BS*
*ZH Xiong and XF Tang contribute equally to the work and are co-first authors

[1]Department of Pain & [2]Department of Radiology, The Second People's Hospital of Yunnan Province, Kunming, China

Abstract

This study aimed to investigate the clinical efficacy of pulsed radiofrequency (PRF) of the dorsal root ganglion (DRG) with pain management as treatment of post-herpetic neuralgia (PHN). A total of 78 patients with PHN in the thoracolumbar region were randomly divided into two groups (n = 39 for each group): Group A, oral drug treatment only; Group B, DRG PRF of the thoracic spinal nerve combined with oral drug treatment. The numerical rating scale (NRS) scores of both groups were observed before treatment and at 1, 4, 8, and 12 weeks after treatment. The results showed that the NRS scores of both groups were significantly decreased after treatment ($P < 0.05$). In addition, the NRS score in Group B decreased significantly more than in Group A ($P < 0.05$). In conclusion, DRG PRF with pain management is a safe and effective treatment for elderly PHN patients, and it can quickly alleviate pain symptoms.

Keywords: Dorsal root ganglion, pulsed radio frequency, post-herpetic neuralgia, pain management

INTRODUCTION

Post-herpetic neuralgia (PHN) commonly manifests as a spontaneous burning and sharp pain that persists after clinical recovery from herpes zoster (shingles) infection. The incidence of pain sequelae in shingles patients who are >60 years old can be as high as 50%–75%.[1,2] The course of PHN can last from several months to several years, and it is often complicated with insomnia, restlessness, depression, and other mental symptoms. It can seriously affect patients' quality of lives and sleep, resulting in great discomfort. Therefore, it is a significant clinical problem calling for better medical treatment.[3,4]

This study aimed to investigate the clinical efficacy of pulsed radiofrequency (PRF) of the dorsal root ganglion (DRG) with pain management as treatment of PHN.

METHODS

A total of 78 patients with PHN in the thoracolumbar region were randomly divided into two groups. Group A received oral drug treatment only, while group B received DRG PRF of the thoracic spinal nerve in addition to oral drug treatment. The study fulfilled the requirements of the World Medical Association's Declaration of Helsinki and was approved by Ethics Committee of the Second People's Hospital of Yunnan Province. All participating patients provided a signed informed consent.

Inclusion and exclusion criteria

The inclusion criteria were as follows: (1) patients diagnosed with PHN; (2) patients were >18 years old; and (3) patients were willing to provide a signed informed consent. The following were exclusion criteria: (1) patients with severe vertebral hyperosteogeny; (2) patients with compression fracture; (3) patients with human immunodeficiency virus infection; (4) patients with malignant tumors; and (5) patients with severe heart, liver, or kidney dysfunction.

Instruments and medicines

The following were used for the study: radiofrequency puncture needle and radio-frequency therapeutic apparatus (Baylis, Canada);

Address Correspondence to: Li-Rong Yue, Department of Radiology, The Second People's Hospital of Yunnan Province, No. 176 of Qingnian Street, Wuhua District, Kunming 650021, China. Tel:+8615368066132, Email: lrydrmn_666@163.com

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ketorolac tromethamine injection (Shandong New Era Pharmaceutical Co., Ltd., China), oral sustained-release tramadol hydrochloride (Guizhou Yikang Pharmaceutical Co., Ltd., China), oral gabapentin (Jiangsu Enhua Pharmaceutical Co., Ltd., China), and oral mecobalamin (Eisai [China] Pharmaceutical Co., Ltd.).

DRG pulsed radiofrequency therapy

Patients in Group A were given a daily injection of 30 mg of ketorolac tromethamine, *q8h*, *iv* for five days. After discontinuation of intravenous infusion, the tramadol hydrochloride sustained-release capsule (100 mg, *q12h*) was taken orally. Then, oral gabapentin capsules were used in addition, starting at 300 mg per dose. The dose was increased daily until it reached 900 mg on the third day (300 mg per dose, three times a day), and then the dose was maintained. After three months, the dose was gradually reduced until the drug was discontinued. The patients also took an estazolam tablet every night before bed to improve sleep. In addition, they took mecobalamin tablets orally 0.5 mg per dose, three times a day for three months.

Patients in group B were treated with the same oral medication as those in Group A, but they also received DRG PRF. In Group B, the injections of lidocaine, mecobalamin, and betamethasone were given at the same time as the PRF treatment. The oral medications were as stated for Group A. For the PRF treatment, one or two segments of the area where the patient was feeling the most severe pain were selected. One segment above and one segment below were also included; therefore, each time, three to four segments of the DRG were treated with PRF. The patient was lying in the prone position, and a pillow was placed under the chest to flatten the thoracic spine. Positioning was performed under C-arm fluoroscopy. A vertical line was drawn at 4–5 cm outside the line parallel to the spinous process on the affected side, a horizontal line was drawn at the root of the inferior articular process of the affected side to be punctured, and the intersection of these two lines was considered as the puncture point. After application of local anesthesia, a 20-G radiofrequency trocar was inserted at an angle of 45°–60° to the sagittal plane of the body. Under the guidance of X-ray lateral projection fluoroscopy, the needle point was located at the back and upper 1/2 quadrant of the posterior intervertebral foramen behind the facet joint, and the anteroposterior projection was under the lateral margin of the pedicle of the vertebral arch. The test resistance was 350–450 Ω, and the sense test was performed at 50 Hz until the patients still had the pain of the radiation anesthesia in the nerve distribution area when the threshold of electrical stimulation was below 0.3 V. After the test was determined to be correct, the PRF treatment parameters were adjusted as follows: treatment temperature = 42°C; frequency = 2 Hz; pulse width = 20 ms; voltage = 26–56 V; duration = 180 seconds; and interval = 15 seconds. The spinal nerves of the upper and lower segments were modulated by PRF in the same manner. After the completion of PRF treatment, the radiofrequency puncture needle should not be pulled out in a hurry. When it was confirmed that the position was correct and that no blood or cerebrospinal fluid was drawn back, 3 ml of the prepared compound betamethasone solution was injected in to dorsal root ganglion, comprising 3 mL of 2% lidocaine, 1 mg of mecobalamin, and 1 mL of compound betamethasone. The solution was diluted to 9 mL with normal saline, and the dorsal root ganglion of the adjacent upper and lower segments were blocked simultaneously. The PRF was carried out twice, with an interval of 12 h between the two treatments.

Pain management regime

(1) The drug treatment plan was determined, and the precautions for pain management were observed. For patients with a numerical rating scale (NRS) score ≥7 and/or a sleep disturbance score ≥4, sedatives and analgesics were given temporarily. (2) Pain assessment. Pain was evaluated by numerical scoring as follows: for patients with NRS scores ≥7 points, 4 times/day (06:00H, 14:00H, 18:00H, and 22:00H); for patients with NRS scores of 4–6, 3 times/day (06:00H, 14:00H, and 22:00H). The highest daily NRS scores of the patients were compared. If the patient fell asleep during the evaluation, it was recorded as "fall asleep" in the "pain level" column, and the score was not connected with the front and back scores. If the NRS scores during a consecutive 24 h period were ≤2 points, the assessment was stopped on the same day. At 14:00H every day, the degree of sleep disturbance by pain within the previous 24 h was recorded, and the condition of any patient with NRS score ≥4 was reported to the physician in charge at the time. (3) Improving the compliance of patients. Analgesics were regularly used, and patients' pain levels were monitored and proactively reported to physicians, rather than waiting until the pain became unbearable.

Observation indexes

The NRS scores of the two groups were observed before treatment and at 1, 4, 8, and 12 weeks after treatment. (1) The NRS score was used to evaluate the degree of pain. A score of 0 represented 'painless', an increased score represented an increased degree of pain, and 10 points represented the most severe, intolerable pain. The patients' NRS scores were estimated four times each day for 12 weeks. (2) The degree of sleep disturbance by pain[2] was presented on an 11-point scale, from 0 to 10. The patient was instructed to mark a number to represent the extent to which their sleep had been affected by pain in the past 24 hours, with 0 meaning not affected, an increased number representing an increased degree of disturbance, and 10 representing complete disturbance.

Statistical analysis

The data were analyzed using statistical software SPSS 14.0. The measurement data were expressed as mean ± standard deviation, and count data were expressed as percentages (%). The normality of variables was tested using a *W*-test, and the homogeneity of variance was tested using an *F*-test. Multi-group comparison of the measurement data was conducted using univariate analysis of variance, and post-hoc testing was conducted using the measure of least significant difference (LSD). Inter-group comparison was conducted using a *t*-test. Non-normally distributed mean or normally distributed mean with a heterogeneity of multiple samples were evaluated using non-parametric testing, and count data were assessed using a chi-squared test. A P value of <0.05 was considered statistically significant.

RESULTS

The lesions were located in the T3-12 spinal nerve distribution area. The differences in gender and age between the two groups were not statistically significant ($P > 0.05$). The difference between the NRS scores of the two groups before treatment was not statistically significant ($P > 0.05$) (see Table 1).

When compared with pre-treatment levels, the NRS scores of the two groups at 1, 4, 8, and 12 weeks after treatment decreased significantly, and the differences were statistically significant ($P < 0.05$). At each time point after treatment, the NRS score was significantly lower in group B than in group A, and these differences were also statistically significant ($P < 0.05$) (see Table 2).

There was no significant difference in the degree of sleep disturbance between the two groups before treatment ($P > 0.05$). The sleep disturbance score for group B was significantly lower than that for group A at 1 and 12 weeks after treatment ($P < 0.05$), and the differences between the two groups were statistically significant ($P < 0.05$) (see Table 3).

DISCUSSION

PHN is a type of intractable pain disorder that affects middle-aged and elderly patients, and most cases result in moderate or severe pain. As a pseudomonopolar afferent neuron of sensation of the body and most of the organs, the DRG of the spinal nerve is the first receptor that mediates the signals of pain, temperature, touch, and position, and it serves as a key conduction integration site for the initiation and nociceptive stimulation of PHN. Therefore, the DRG of the spinal nerve is an important therapeutic target for neuropathic pain.[5-7]

DRG PRF can act highly selectively on the conduction branch of pain fibers and block signal transmission to the superior nerve, rendering pain signals unable to enter the brain by destroying the pain conduction pathway. Due to the resulting lack of feeling or experiencing pain, this would accordingly achieve nerve analgesia and anti-inflammatory effects and effectively reduce the damage caused to nerve tissues. This mechanism has been considered to be the biological effect of the PRF electric field on the synaptic activity and

Table 1: Baseline data of patients before treatment

Group	n	Gender (Male/Female)	Age	NRS score
Group A	39	19/20	70.1±12.2 (60~82)	7.6±1.2 (6~9)
Group B	39	17/22	71.4±10.3 (61~82)	7.5±1.4 (6~9)
p value		$P > 0.05$	$P > 0.05$	$P > 0.05$

Note: NRS, numerical rating scale.

Table 2: Comparison of NRS score before and after treatment between the two groups

Time	Group A	Group B
Before treatment	7.6±1.2 (6~9)	7.5±1.4 (6~9)
1 week after treatment	5.3±1.3* (4~7)	3.3±1.6*Δ (2~5)
4 week after treatment	4.7±1.2* (3~6)	3.4±1.2*Δ (2~5)
8 week after treatment	4.5±1.3* (3~6)	3.0±1.5*Δ (2~5)
12 week after treatment	4.2±1.1* (3~5)	2.8±1.3*Δ (1~4)

Note: NRS, numerical rating scale. *Compared to before treatment, P <0.05; ΔCompared to group A, P <0.05.

cytokines of neurons.[8] The radiofrequency needle point forms a high-voltage field around the DRG of the spinal nerve to produce a series of follow-up biological effects after PRF stimulation on the DRG. These include a decrease in substance P in the DRG and dorsal horn of the spinal cord, an increase in β-endorphin and other analgesic substances in the brain tissue, and inhibition of hyperactivity and central sensitization of nociceptive neurons in the spinal dorsal horn. Furthermore, this may activate the brainstem's descending inhibition system by inhibiting the nociceptive afferent of C-fiber and stimulating the central process of the DRG through the peripheral process of the DRG of the spinal nerve, thereby finally producing a long-lasting analgesic effect.

PRF can inhibit the ectopic discharge of nerves to relieve pain without damaging the nerves, which can also repeatedly and effectively prevent the recurrence of pain. PRF is a type of "neuromodulation therapy," and it can promote the recovery of injured nerves, representing one of the most effective methods of minimally invasive treatment for neuropathic pain.[9-11] The analgesic mechanism of PRF in DRG is not the destruction of nerve structure caused by temperature, but the regulation mechanism of the DRG being stimulated by the pulse current. This can avoid damage to the pain and tactile fibers from thermal coagulation and lead to the occurrence of complications such as numbness. As yet, no reports have been published on the complications of PRF-related nerve injury.

The procedure and effects of treatments for PHN remain very complex. To date, there is no method to completely relieve patients' pain.[12] When patients have severe pain, their sleep is seriously disturbed; they often find it difficult to fall asleep all night or wake up just after falling asleep. PRF treatment of dorsal root ganglion pulse combined with "cocktail" nerve block therapy can effectively relieve patients' pain and improve their sleep quality. Applying a reasonably comprehensive treatment and regular usage of analgesic drugs can block the process of neuropathic pain and inhibit the transmission of the associated signals to the center, thereby achieving the effect of alleviating severe pain.[13,14] Clinicians striving to mitigate pain should shift from a passive to an active approach and assess their patients in good time their pain level. This will help them to develop an understanding of the pain curves of patients and to provide analgesics and the corresponding psychological guidance at the right time, instead of delaying treatment until the pain becomes intolerable to the patient. This could not only greatly reduce the pain of patients, but also stabilize the analgesic effect.[6]

West *et al*. reported that PRF is a viable treatment option for long-term relief of intractable residual and phantom limb pain.[15] Rana *et al*. reported that it may be a non-neurodestructive pain management technique for tumors involving peripheral nerves.[16] Unlike previous investigations, the current study aimed to investigate the clinical efficacy of DRG PRF combined with pain management for treating PHN. Our results provide further support for the use of PRF for pain management.

Table 3. Comparison of sleep disturbance scores of two groups at different time points before and after treatment

Group	n	Before treatment	1 week after treatment	12 weeks after treatment
Group A	39	7.4±1.2 (6~8)	4.6±1.3 (3~6)	2.6±0.8 (2~4)
Group B	39	7.6±1.5 (6~8)	3.2±1.4 (2~5)	1.1±0.6 (0~2)
p value		*P* >0.05	*P* <0.05	*P* <0.05

The present study has some limitations. First, while it was a randomized controlled study, it was not blinded. Second, it was a single-center clinical trial; multi-center clinical trials with a larger sample size are needed in the future.

In conclusion, our findings indicate that DRG PRF with pain management is a safe and effective treatment approach that can quickly alleviate the pain symptoms of elderly PHN patients. It is thus recommended as a treatment for PHN in the elderly.

DISCLOSURE

Conflict of interest: None

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