


A Comparison of Short-Term Peripheral Nerve Stimulation and Pulsed Radiofrequency in the Treatment of Postherpetic Neuralgia

Junfei Xu*, Yongyong Ding*, Bing Liu, Xuehai Wu, Xiaofeng Yang, Yi Liu, Hong Deng 

Department of Pain, The First People's Hospital of Zunyi City, Zunyi, Guizhou Province, 563000, People's Republic of China

*These authors contributed equally to this work

Correspondence: Hong Deng, Email dengqiao303@163.com

Objective: To compare the application effects of short-term peripheral nerve stimulation (st-PNS) and pulsed radiofrequency (PRF) technology in postherpetic neuralgia (PHN).

Methods: A retrospective analysis was conducted on the clinical data of 127 PHN patients from our hospital. Based on the treatment interventions received, patients were divided into a control group (n=63, treated with PRF) and an observation group (n=64, treated with st-PNS). The clinical treatment effects, pain conditions, sleep quality, inflammatory factors [interleukin-6 (IL-6)] levels, quality of life levels, and complication rates were compared between the two groups.

Results: The observation group showed significantly higher total treatment effectiveness (93.75%) compared to the control group (80.95%) ($P < 0.05$). VAS and PSQI scores were significantly improved at 1 week, 1 month, and 3 months post-treatment in both groups ($P < 0.05$), with the observation group consistently showing better outcomes. Additionally, IL-6 levels decreased significantly, and SF-36 scores improved more in the observation group ($P < 0.05$). No significant difference was found in complication rates between the two groups ($P > 0.05$).

Conclusion: Compared to PRF treatment, the st-PNS treatment method further improves patients' pain and sleep quality, reduces inflammatory responses, and enhances quality of life, while also demonstrating better safety.

Keywords: short-term peripheral nerve stimulation, pulsed radiofrequency technology, postherpetic neuralgia, application effects, comparative study

Introduction

Herpes zoster (HZ) is an acute viral dermatological disease caused by the reactivation of varicella-zoster virus (VZV) latent in nerve ganglia.¹ It is primarily characterized by a rash distributed along a single nerve segment and severe neuralgia. Although the rash of HZ usually heals within a few weeks, about 20% of patients develop postherpetic neuralgia (PHN), a persistent or intermittent neuralgia that can last for months or even years.² The pathogenesis of PHN is complex, involving nerve damage, inflammation triggered by viral reactivation, immune responses, and pathological changes in the central nervous system.³ Due to the diversity of its pathological mechanisms, PHN treatment remains a clinical challenge. Traditional treatments include medications (such as anticonvulsants, antidepressants, opioids), nerve blocks, physical therapy, and psychological interventions, but their effectiveness varies, and they often come with significant side effects.^{4,5}

In recent years, with the rapid development of neuromodulation technologies, short-term peripheral nerve stimulation (st-PNS) and pulsed radiofrequency (PRF) technology have gradually gained attention in the treatment of PHN. Both methods have shown certain efficacy in clinical applications,^{6,7} but further research is needed to compare their specific effects and advantages. This study aims to compare the clinical effects of these two technologies in the treatment of PHN through a retrospective analysis, providing more references and optimized treatment options for clinical management of PHN.

Materials and Methods

This study was approved by the medical ethics committee the First People’s Hospital of Zunyi City. Informed consent was obtained from all study participants. All the methods were carried out in accordance with the Declaration of Helsinki.

Baseline Profiles

A retrospective analysis was conducted on the clinical data of 127 PHN patients treated at our hospital between February 2022 and March 2024. Inclusion criteria: ① All patients met the clinical diagnostic criteria for PHN;⁸ ② Pain duration >1 month with minimal improvement in pain after standard basic treatment (VAS score ≥ 4); ③ Age ≥ 18 years, no gender restriction; ④ Complete and authentic clinical data available for analysis. Exclusion criteria: ① Severe dysfunction of vital organs; ② Severe abnormalities in coagulation, hematopoietic, and endocrine functions; ③ Concurrent malignant tumors; ④ Concurrent spinal deformities or lesions; ⑤ Severe infections; ⑥ Allergic reactions or contraindications to the study medications or methods; ⑦ Concurrent cognitive impairment, consciousness disorders, and/or mental illnesses. Based on the treatment interventions received, patients were divided into a control group (n=63) and an observation group (n=64). (Table 1)

Methods

Control Group

In the PRF group, patients were positioned in the supine position, and the surgical site was exposed. Under C-arm fluoroscopic guidance, the right supraorbital foramen was identified. After local anesthesia with 0.5% lidocaine, a single-use radiofrequency ablation needle was inserted under imaging guidance into the right supraorbital notch. A radiofrequency electrode was connected, and impedance was tested. Sensory stimulation was performed using a 50 hz current until a sensory response was elicited. The voltage was then set to 0.5V to reproduce a numbness and pain sensation in the ophthalmic branch of the trigeminal nerve. Pulsed mode was used with a needle tip temperature of 42°C. Two 2 hz, 60-second thermal coagulation treatments were applied. During the procedure, patient responses were closely monitored and adjustments were made as necessary. Postoperatively, patients returned to the ward for local ice application and bed rest for 2 hours. The treatment continued for one week.

st-PNS Group (Observation Group)

In the st-PNS group, patients were also placed in the supine position, with the surgical site exposed. After local anesthesia with 0.5% lidocaine, the puncture point was identified above the right lateral canthus. Under C-arm fluoroscopic guidance, an

Table 1 Comparison of Basic Data ($(\bar{x} \pm s)$, n [%])

	Control (n=63)	Observation (n=64)	t/x ²	P
Gender	–	–	0.067	0.794
Male	30 (47.62)	29 (45.31)	–	–
Female	33 (52.37)	35 (54.69)	–	–
Age (years)	65.37±6.89	64.93±7.14	0.353	0.724
Disease Course (months)	16.74±4.63	16.95±4.51	0.258	0.796
Nerve Segment	–	–	0.183	0.668
Trigeminal Nerve	10 (15.87)	12 (18.75)	–	–
Cervical Nerve	18 (28.57)	16 (25.00)	–	–
Thoracic Nerve	28 (44.45)	27 (42.19)	–	–
The baseline data of the two groups were comparable (P>0.05), as detailed in Table 1. Lumbar Nerve	7 (11.11)	9 (14.06)	–	–
Side	–	–	0.207	0.649
Left Side	36 (57.14)	34 (53.12)	–	–
Right Side	27 (42.86)	30 (46.88)	–	–

8-contact electrode was inserted along the eyebrow arch and bone direction. The electrode (Medtronic, Model: Medtronic Pisces-Quad 3487A-28) was slowly advanced to the supraorbital nerve exit, and the needle was withdrawn. The electrode lead was then connected to an external stimulator. The stimulation parameters were adjusted according to the patient's tolerance and the area covered by the electrode. Typically, the stimulation amplitude was set between 5–10 V, pulse width between 200–500 ms, frequency between 25–70 hz, with stimulation lasting 5–10 seconds and interstimulus intervals of 8–15 seconds. Once the stimulation current covered the pain distribution area of the ophthalmic branch of the trigeminal nerve, the electrode was fixed in the right temporal region, just above the eye. Imaging was used to confirm electrode placement, after which the patient was returned to the ward for 2 hours of bed rest. During the treatment, the current intensity was adjusted based on the patient's pain levels, current tolerance, and the area of skin affected by the pain. The electrode was removed after one week of treatment. Routine intravenous antibiotic prophylaxis was administered to prevent infection.

Outcome Measures

Clinical Treatment Effect

The therapeutic efficacy was assessed based on pain improvement at three months post-treatment. A significant effect was defined as a reduction in the Visual Analog Scale (VAS) score of more than 75% following treatment. An effective outcome was indicated by a VAS score reduction between 30% and 75%, while an ineffective outcome was characterized by a reduction of less than 30%. The total effective rate was calculated as 100% minus the proportion of ineffective cases relative to the total number of cases.

Pain Status

VAS scores were utilized to evaluate pain levels prior to treatment and at one week, one month, and three months post-treatment. The VAS scores range from 0 to 10, with higher scores reflecting greater pain intensity.

Sleep Quality

The Pittsburgh Sleep Quality Index (PSQI) was employed to assess sleep quality before treatment and at one week, one month, and three months post-treatment. PSQI scores can range from 0 to 21, with higher scores indicating poorer sleep quality.

Inflammatory Factor Levels

Blood samples (3 mL) were collected from fasting participants before treatment and one week post-treatment. The supernatant was separated via standard centrifugation and analyzed using enzyme-linked immunosorbent assay (ELISA) to measure interleukin-6 (IL-6) levels.

Quality of Life Levels

The Short Form 36 (SF-36) Health Survey was administered prior to treatment and one week post-treatment to evaluate the patients' quality of life. This instrument comprises eight dimensions, with scores ranging from 0 to 100, where higher scores correlate with improved quality of life.

Incidence of Complications

The occurrence of complications—including pneumothorax, hematoma, local infection, peripheral nerve injury, spinal cord injury, and skin numbness—was meticulously recorded by designated medical personnel during treatment and throughout the three-month follow-up period.

Statistical Analysis

GraphPad Prism 8 was used for graphing; SPSS 22.0 was used for data analysis. Measurement data were described using ($\bar{x} \pm s$), and comparisons between groups were made using independent sample t-tests, while paired t-tests were used for comparisons within the same group. Repeated measures analysis of variance was used to compare different time points between the two groups. Count data were described using n (%), and chi-square tests were used for analysis. $P < 0.05$ indicated statistically significant differences.

Table 2 Comparison of Clinical Treatment Effects [n (%)]

Group (n)	Significant Effect	Effective	Ineffective	Total Effective Rate
Control (n=63)	24 (38.09)	27 (42.86)	12 (19.05)	51 (80.95)
Observation (n=64)	29 (45.31)	31 (48.44)	4 (6.25)	60 (93.75)
χ^2	–	–	–	4.722
P	–	–	–	0.029

Results

Comparison of Baseline Data Between the Two Groups

In the comparison of baseline data between the two groups, no significant differences were observed in terms of gender, age, duration of illness, and distribution of affected nerve segments. This similarity in baseline characteristics indicates that both groups were comparable at the time of enrollment, which enhances the validity and reliability of the subsequent treatment effect comparisons. Such homogeneity in baseline demographics is crucial for accurately assessing the efficacy of the treatment modalities being studied.

Comparison of Clinical Treatment Effects

The total effective treatment rate in the observation group (93.75%) was significantly higher than that in the control group (80.95%) ($P < 0.05$), as shown in Table 2, as shown in Table 2.

Comparison of Pain Conditions

VAS scores at 1 week, 1 month, and 3 months post-treatment were significantly lower than pre-treatment scores in both groups ($P < 0.05$). Furthermore, the observation group showed significantly lower VAS scores than the control group at all time points ($P < 0.05$), as illustrated in Figure 1.

Comparison of Sleep Conditions

The PSQI scores at 1 week, 1 month, and 3 months after treatment were significantly reduced compared to baseline in both groups ($P < 0.05$). At these time points, the observation group demonstrated significantly lower PSQI scores than the control group ($P < 0.05$), as shown in Figure 2.

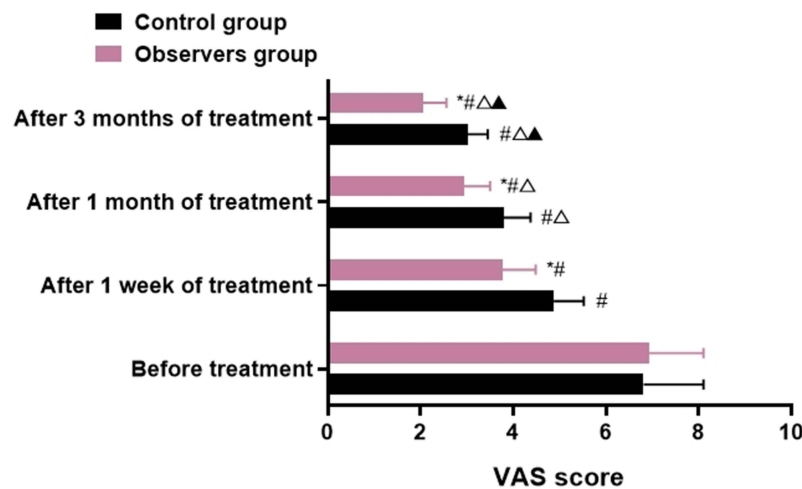


Figure 1 Comparison of Pain Conditions ($\bar{x} \pm s$).

Note: Compared with the control group at the same time point, * $P < 0.05$; compared with the same group before treatment, # $P < 0.05$; compared with the same group 1 week after treatment, $\Delta P < 0.05$; compared with the same group 1 month after treatment, $\blacktriangle P < 0.05$.

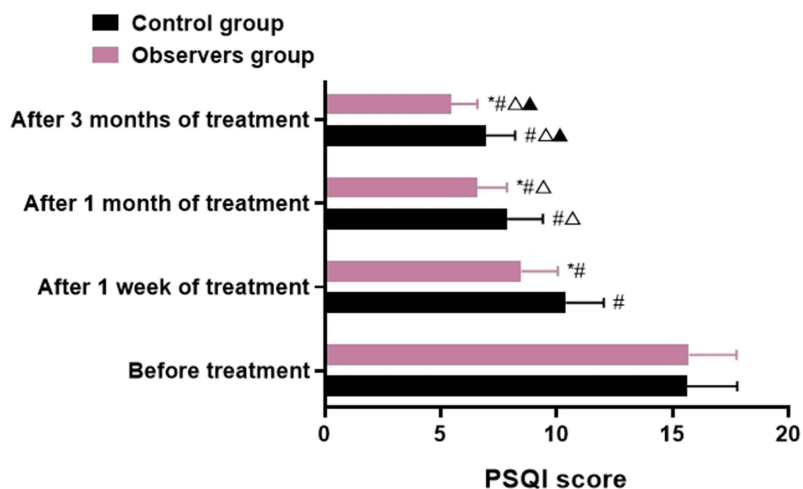


Figure 2 Comparison of Sleep Conditions ($\bar{x} \pm s$).

Note: Compared with the control group at the same time point, * $P < 0.05$; compared with the same group before treatment, # $P < 0.05$; compared with the same group 1 week after treatment, $\Delta P < 0.05$; compared with the same group 1 month after treatment, $\blacktriangle P < 0.05$.

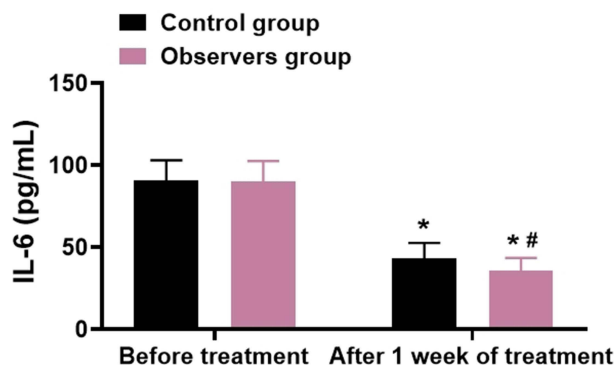


Figure 3 Comparison of Inflammatory Factors ($\bar{x} \pm s$).

Note: Compared to before treatment, * $P < 0.05$; between groups, # $P < 0.05$.

Comparison of Inflammatory Factors

The levels of IL-6 in both groups decreased 1 week after treatment compared to before treatment, with a greater change observed in the observation group ($P < 0.05$), as shown in Figure 3.

Comparison of Quality of Life

The SF-36 scores in both groups increased 1 week after treatment compared to before treatment, with a greater change observed in the observation group ($P < 0.05$), as shown in Figure 4.

Comparison of Complication Incidence

The overall incidence of complications in the control group was 6.35%, lower than that in the observation group (10.94%), but no statistically significant difference was observed ($P > 0.05$), as shown in Table 3.

Discussion

PHN is a chronic neuropathic disorder primarily characterized by persistent pain, and its pathogenesis involves complex interactions between the central and peripheral nervous systems. PHN often develops following the infection of the spinal dorsal root ganglia by VZV, leading to extensive viral replication, sensory nerve fiber damage, and disruption of the spinal cord’s inhibitory function. This process results in the transmission of excessive excitatory signals to the central

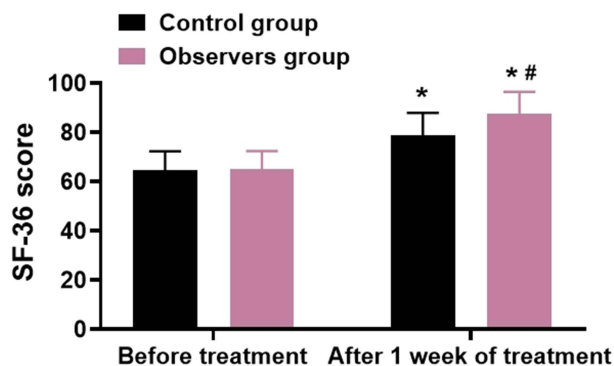


Figure 4 Comparison of Quality of Life ($\bar{x} \pm s$).
Note: Compared to before treatment, * $P < 0.05$; between groups, # $P < 0.05$.

nervous system, which, in turn, activate sympathetic efferent fibers and increase the excitability of primary receptors. Consequently, patients experience continuous burning, cutting, or stabbing pain, often accompanied by severe neuralgia.^{9–11} Despite the availability of traditional treatments such as oral medications, topical agents, and nerve blocks, their efficacy in managing PHN remains limited.^{12,13}

Recently, neuromodulation techniques like st-PNS and PRF have emerged as promising alternatives for pain management in PHN patients. These techniques target excessive neuronal excitability through different mechanisms. For st-PNS, short-term electrical stimulation is applied around the nerve to regulate nerve conduction and reduce abnormal excitability. Mechanistically, st-PNS achieves pain relief by blocking the transmission of pain signals, inducing the production of endogenous opioids to elevate the pain threshold, and exerting an anti-inflammatory effect that reduces pro-inflammatory cytokines and alleviates neural inflammation.^{14–16} On the other hand, PRF works by intermittently applying high-frequency electromagnetic waves to the nerve, altering neuronal membrane potentials to reduce pain transmission. PRF also induces plastic changes in neurons, reducing their sensitivity to pain, and generates a mild thermal effect that modulates nerve function without causing tissue damage.^{17,18}

In this study, we compared the effectiveness of st-PNS and PRF in treating PHN. Our results showed that st-PNS provided a significantly higher total effective treatment rate compared to PRF. Specifically, the VAS and PSQI scores in the observation group (st-PNS) were significantly lower than those in the control group (PRF) at 1 week, 1 month, and 3 months post-treatment. Additionally, the SF-36 scores, which assess overall quality of life, were significantly higher in the st-PNS group at 1 week after treatment. These findings suggest that both st-PNS and PRF effectively relieve pain and improve sleep quality, but st-PNS appears to offer more pronounced benefits in terms of pain relief and overall well-being. The mechanisms behind these differences may be explained by the ability of st-PNS to directly act on damaged peripheral nerves through electrical stimulation. This stimulation suppresses abnormal neuronal discharge, rapidly blocks pain signal transmission, and likely plays a role in inducing neuroplastic changes within the central nervous system. These long-term changes in neural networks may contribute to sustained pain relief, even after the stimulation ends.^{19,20} In contrast, while PRF also modulates nerve function and reduces pain sensitivity, its effect may not be as direct or long-lasting as st-PNS.

Table 3 Comparison of Complication Incidence [n (%)]

Complication	Control (n=63)	Observation (n=64)	χ^2	P
Pneumothorax	2 (3.17)	0 (0.00)	–	–
Hematoma	1 (1.59)	2 (3.13)	–	–
Local Infection	0 (0.00)	2 (3.13)	–	–
Peripheral Nerve Injury	0 (0.00)	1 (1.56)	–	–
Spinal Cord Injury	0 (0.00)	0 (0.00)	–	–
Skin Numbness	1 (1.59)	2 (3.13)	–	–
Total Incidence	4 (6.35)	7 (10.94)	0.844	0.358

Furthermore, our study also revealed that the incidence of complications was comparable between the two groups, suggesting that both treatments are relatively safe and well-tolerated. This is important, as safety profiles play a crucial role in the clinical decision-making process for PHN management. Research has shown that an imbalance between pro-inflammatory and anti-inflammatory factors is a key contributor to persistent neuropathic pain in PHN.²¹ Interleukin-6 (IL-6), a pro-inflammatory cytokine, is significantly elevated in response to nerve injury and plays a central role in both acute and chronic inflammatory responses. IL-6 contributes to local inflammation and can exacerbate pain perception by affecting the central nervous system through the blood-brain barrier.^{22–24} In our study, we observed that the IL-6 levels in the st-PNS group were significantly lower than those in the PRF group 1 week after treatment ($P < 0.05$). This suggests that st-PNS may have a more potent effect on regulating inflammatory responses, potentially offering additional benefits in alleviating pain associated with inflammation.

Limitations: Despite the promising results, this study has some limitations. First, the sample size was relatively small ($n = 127$), which may limit the generalizability and statistical power of the findings. Second, the retrospective design of this study may introduce biases such as treatment selection and information bias, which weakens the validity of the conclusions. Third, the study was conducted at a single center, and the results may not be universally applicable across different medical institutions. Lastly, although we have observed the efficacy of st-PNS over PRF, the exact mechanisms behind the inflammatory modulation and neuroplastic changes remain unclear. Future studies should explore these mechanisms in greater depth, possibly through mechanistic investigations and larger, randomized controlled trials to validate and optimize these findings.

Conclusion

st-PNS appears to be more effective than PRF in managing PHN, with better outcomes in pain relief, sleep quality, and quality of life. Moreover, st-PNS may reduce inflammatory responses more effectively, although further studies are needed to elucidate the underlying mechanisms. We recommend that future research include larger sample sizes, multi-center trials, and more focused mechanistic studies to validate the results and refine treatment strategies.

Data Sharing Statement

All data generated or analysed during this study are included in this published article.

Ethics

This study was approved by the ethics committee of The First People's Hospital. Informed consent was obtained from all study participants. All the methods were carried out in accordance with the Declaration of Helsinki.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

There is no funding to report.

Disclosure

The authors declare that they have no competing interests.

References

1. Patil A, Goldust M, Wollina U. Herpes zoster: a review of clinical manifestations and management. *Viruses*. 2022;14(2):192. doi:10.3390/v14020192
2. Ehrenstein B. [Diagnosis, treatment and prophylaxis of herpes zoster]. *Z Rheumatol*. 2020;79(10):1009–1017. doi:10.1007/s00393-020-00915-y

3. Gruver C, Guthmiller KB. Postherpetic neuralgia, in StatPearls. 2024. StatPearls Publishing Copyright © 2024, StatPearls Publishing LLC.: Treasure Island (FL) ineligible companies. Disclosure: Kevin Guthmiller declares no relevant financial relationships with ineligible companies.
4. Menaldi SL, Halim PA, Kurniawan K. Efficacy of gabapentinoids for acute herpes zoster in preventing postherpetic neuralgia: a systematic review of randomized controlled trials. *Dermatol Online J.* 2022;28(5). doi:10.5070/D328559238
5. Warner BE, Goins WF, Kramer PR, et al. A guide to preclinical models of zoster-associated pain and postherpetic neuralgia. *Curr Top Microbiol Immunol.* 2023;438:189–221. doi:10.1007/82_2021_240
6. Kim K, Jo D, Kim E. Pulsed radiofrequency to the dorsal root ganglion in acute herpes zoster and postherpetic neuralgia. *Pain Physician.* 2017;20(3):E411–e418. doi:10.36076/ppj.2017.E418
7. Kurklinsky S, Palmer SC, Arroliga MJ, et al. Neuromodulation in postherpetic neuralgia: case reports and review of the literature. *Pain Med.* 2018;19(6):1237–1244. doi:10.1093/pm/pnx175
8. Fan HR, Zhang E-M, Fei Y, et al. Early diagnosis of herpes zoster neuralgia: a narrative review. *Pain Ther.* 2023;12(4):893–901. doi:10.1007/s40122-023-00510-4
9. Gierrhmühlen J, Braig O, Rehm S, et al. Dynamic of the somatosensory system in postherpetic neuralgia. *Pain Rep.* 2018;3(6):e668. doi:10.1097/PR9.0000000000000668
10. Kennedy PGE. The spectrum of neurological manifestations of varicella-zoster virus reactivation. *Viruses.* 2023;15(8):1663. doi:10.3390/v15081663
11. Lu L, Mei L, Li X, et al. Metabolomics profiling in predicting of post-herpetic neuralgia induced by varicella zoster. *Sci Rep.* 2023;13(1):14940. doi:10.1038/s41598-023-42363-z
12. Liu Y, Xiao S, Li J, Long X, Zhang Y, Li X. A network meta-analysis of randomized clinical trials to assess the efficacy and safety of antiviral agents for immunocompetent patients with herpes zoster-associated pain. *Pain Physician.* 2023;26(4):337–346. doi:10.36076/ppj.2023.26.337
13. Jiang X, Li Y, Chen N, et al. Corticosteroids for preventing postherpetic neuralgia. *Cochrane Database Syst Rev.* 2023;12(12):Cd005582. doi:10.1002/14651858.CD005582.pub5
14. Lee M, Kiernan MC, Macefield VG, et al. Short-term peripheral nerve stimulation ameliorates axonal dysfunction after spinal cord injury. *J Neurophysiol.* 2015;113(9):3209–3218. doi:10.1152/jn.00839.2014
15. Wan CF, Song T. Short-term peripheral nerve stimulation relieve pain for elder herpes zoster ophthalmicus patients: a retrospective study. *Neuromodulation.* 2021;24(6):1121–1126. doi:10.1111/ner.13288
16. Früh A, Sargut TA, Hussein A, et al. Peripheral nerve stimulation for the treatment of chronic knee pain. *Sci Rep.* 2023;13(1):15543. doi:10.1038/s41598-023-42608-x
17. Ma J, Wan Y, Yang L, et al. Dual-neuromodulation strategy in pain management of herpes zoster ophthalmicus: retrospective cohort study and literature review. *Ann Med.* 2023;55(2):2288826. doi:10.1080/07853890.2023.2288826
18. Song Y, Yu Z, Guan J, et al. Efficacy of high-voltage pulsed radiofrequency in zoster-associated pain: a meta-analysis and systematic review. *Anesthesiol Res Pract.* 2023;2023:8479293. doi:10.1155/2023/8479293
19. Quirke T, Sleator RD. A beginner's guide to genomics in complex neurological disorders. *Innov Discov.* 2024;1(4):29. doi:10.53964/id.2024029
20. Wang C, Dou Z, Yan M, et al. Efficacy and safety of pulsed radiofrequency in herpes zoster related trigeminal neuralgia: a systematic review and meta-analysis. *J Pain Res.* 2023;16:341–355. doi:10.2147/JPR.S396209
21. Han R, Guo G, Ni Y, et al. Clinical efficacy of short-term peripheral nerve stimulation in management of facial pain associated with herpes zoster ophthalmicus. *Front Neurosci.* 2020;14:574713. doi:10.3389/fnins.2020.574713
22. Tse MMY, Liu TW, Leung SH, Tang SK. Development and evaluation on web-based pain management program for older adults. *J Mod Nurs Pract Res.* 2023;3(3):14. doi:10.53964/jmnp.2023014
23. Schmader K. Herpes Zoster. *Clin Geriatr Med.* 2016;32(3):539–553. doi:10.1016/j.cger.2016.02.011
24. Lin D, Zhong C, Jiang Q, et al. Serum interleukin-6 levels are increased in post-herpetic neuralgia: a single-center retrospective study. *An Bras Dermatol.* 2023;98(2):202–207. doi:10.1016/j.abd.2022.03.007