Retrospective Study



Efficacy Analysis of Temporary Spinal Cord **Stimulation in the Treatment of Refractory Postherpetic Neuralgia**

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Background: Spinal cord stimulation can be considered in PHN patients if conservative treatment is not effective. However, the long-term pain outcomes of temporary (7-14 days) spinal cord stimulation (tSCS) in refractory PHN patients with a course of more than 3 months have not been documented.

Objectives: To investigate the efficacy of tSCS as a treatment for refractory PHN.

Study Design: Retrospective study.

Setting: Pain Department in a university hospital.

Methods: A total of 52 patients with refractory PHN were treated with tSCS between March 2018 and February 2021. Their medical records were collected, and the patients were divided into 3 groups according to the course of their disease into the medium-term group, long-term group and ultra-long-term group. The changes in the numeric rating scale (NRS) scores, Pittsburgh sleep quality index (PSQI) responses, pain relief rate, postoperative efficiency and patients' use of analgesics were recorded before the operation, 3 days, 10 days, one month, 3 months, 6 months and 12 months after the operation.

Results: The average NRS scores, the maximum NRS scores and the PSQI scores at 3 days, 10 days, one month, 3 months, 6 months and 12 months after the operation were significantly lower than those before the operation (P < 0.05). The average NRS scores and the maximum NRS scores of all groups increased significantly from one month to 6 months compared to those at 10 days after the tSCS treatment, and they decreased significantly at 12 months compared with 6 months post-operation. The average NRS scores of the medium-term and long-term group were significantly lower than that of the ultra-long-term group at 1-3 months after the operation, and the maximum NRS scores at one month, 3 months and 12 months after the operation were also significantly lower in the medium-term and long-term group compared to the ultra-long-term group. The average PSQI scores at 1-12 months after the operation were not significantly higher than that at 10 days after the operation, but it decreased significantly at 12 months compared with 6 months after the operation. Among the 3 groups, the PSQI scores of the medium-term and longterm group were significantly lower than those of the ultra-long-term group at 6 months after the operation. The postoperative pain relief rate ranged from 41.51%-59.81%, and the total effective rate was 42.31%-69.23%, and there was no significant difference among the 3 groups. Some patients still needed analgesics at 12 months after the operation, but the number of patients who were taking medications post-operation was significantly lower than that before the operation.

Limitations: This is a single-center retrospective study with the inability to completely control for variables. Additionally, the number of cases is small and the follow-up duration is short.

Conclusion: tSCS can be used as a safe and effective method to relieve refractory PHN, and the curative effect is substantially higher in patients with a disease course of 3-12 months compared to that in patients with a course of more than 12 months.

Key words: Refractory post-herpetic neuralgia, temporary spinal cord stimulation, numeric rating scale, Pittsburgh sleep quality index, postoperative efficiency

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ost-herpetic neuralgia (PHN) is defined as the pain that lasts for one month or more after the recovery from herpes zoster (HZ). Due to the differences in treatment and prognosis, pain that lasts more than 3 months after recovery from HZ is clinically known as refractory PHN (1,2). It is estimated that 5% - 30% of HZ patients experience pain that lasts for months, years or even a lifetime (3). Treatment of refractory PHN is still difficult in clinical practice. Current treatment of PHN uses analgesic drugs, but when its curative effect is unsatisfactory, it is necessary to consider neurointerventional techniques. Neuroregulatory techniques such as nerve pulse radiofrequency therapy and spinal cord or peripheral nerve stimulation might produce better analgesic effect and restore nerve function in patients with refractory PHN (4-6). The limited clinical data shows that the efficacy of neuromodulation techniques was higher in patients with herpetic neuralgia compared to diseases. Among these methods, temporary spinal cord stimulation (tSCS) has the advantages of a short cycle, low cost, few serious complications, and high patient compliance. However, there is no conclusion on the efficacy of tSCS in refractory PHN patients. This paper uses retrospective analysis to analyze the related indicators and observe the curative effect of tSCS on patients with refractory PHN.

METHODS

Participants

Refractory PHN patients who received tSCS treatment between March 2018 and March 2021 were selected for this retrospective analysis. All patients were informed of the risks and expected effects of the operation, after which they voluntarily chose to undergo tSCS and signed a written informed consent form. All the data for this study came from hospitalization medical records and telephone follow-up questionnaires at different time points. A total of 52 patients, who met the inclusion criteria of this study, were selected and their basic information was summarized. The patients were divided into 3 groups according to the course of their disease: the medium-term group (had a course of less than 6 months), the long-term group (had a course of 6-12 months) and the ultra-long-term group (had a course of more than 12 months) (Table 1).

The inclusion criteria for this study were as follows:

1) History of HZ and definite nerve injury segments with unilateral lesions; 2) disease course ≥ 3 months;

3) preoperative average Numeric Rating Scale (NRS) score \geq 5; 4) poor efficacy of previous standardized treatments, such as large oral doses of analgesics, with intolerable adverse reactions (such as dizziness and nausea), and poor efficacy of previous interventional therapies such as acupuncture, nerve block, and nerve pulse radiofrequency.

The exclusion criteria for this study were as follows: 1) stimulation time of tSCS is less than 7 days; 2) combined with poorly controlled psychological or mental disorders such as severe anxiety and depression; 3) surgical contraindications such as severe infection, coagulation dysfunction or intraspinal lesions; 4) unable to accurately describe the pain type and NRS score, loss of follow-up immediately after operation, or undergoing other minimally invasive interventional surgeries during the follow-up period.

Operation and Program-controlled Mode

1) tSCS operation: the electrode implantation was performed by the deputy chief physician and chief physician according to the standard procedure. Operators used Tuohy epidural needles for the epidural puncture and implanted an 8-contact electrode (Medtronic 3873) into the patient's epidural cavity under real-time C-arm fluoroscopy guidance. The electrode was placed on the affected side of the target spinal dorsal horn corresponding to the nerve segment of the pain area (Fig. 1) (7). The electrode was then connected to the cable (Medtronic 355531) and the stimulator (Medtronic 37022), and the electrode position was fine-tuned according to test results from electrical stimulation.

2) tSCS program-controlled mode: The program-controlled mode of low-frequency electrical stimulation was used for all patients. The specific parameters of the doctor's program controller (Medtronic 8840) were as follows: 60-100Hz frequency, 60-300 µs pulse width, and 0.5V-3.5V voltage. Physicians adjusted the voltage intensity and program control parameters in real-time based on the changes in the pain response of patients. The ideal numbness and picotement distribution of electrical stimulation is the key to obtain sufficient curative effect (8).

Precautions

The patients were placed on bed rest for 24 hours after the operation, and were advised to avoid torso overextension, flexion or rotation so as to prevent electrode displacement. Patients took postoperative analgesic drugs as needed, and if their reported NRS

Table 1. General characteristics of the patients (n = 52).

Demographic Information	Total(n = 52)	Medium- term (n = 27)	Long term(n = 16)	Ultra-long term(n = 9)
Gender (n, men/women)	26/26	15/12	8/8	3/6
Age (yrs, x ± SEM)	68.96 ± 1.24	68.0 ± 1.61	73.06 ± 2.40	64.56 ± 2.39
Course of disease (mons, x ± SEM)	7.33 ± 0.88	3.63 ± 0.14	7.44 ± 0.34	18.22 ± 2.84
Regulation time (days, x ± SEM	10.5 ± 0.18	10.19 ± 0.24	10.94 ± 0.36	10.67 ± 0.41
Side (n, left/right)	18/34	8/19	6/10	4/5
Involved dermatome (n, cervical/thoracic/lumbosacral)	14/31/7	8/16/3	6/8/2	0/7/2
Comorbidity (n, yes/no)	39/13	17/10	15/1	7/2

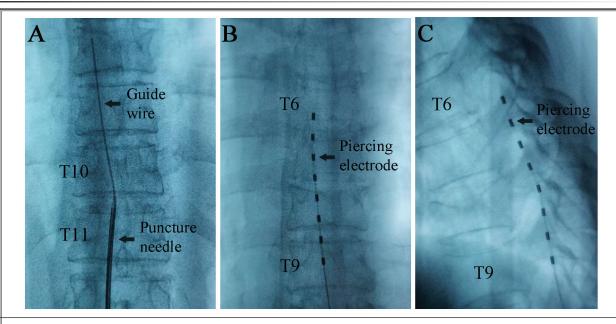


Fig. 1. Intraoperative x-ray images of tSCS in a patient with T10 neuralgia on the left side. (A) anteroposterior radiographs of the puncture needle (the needle entered the epidural cavity from the left side of the T10/T11 intervertebral space); (B) anteroposterior radiographs of the 8-contact electrode (the electrode tip was located on the left side of the inferior margin of the T6 vertebral body); (C) lateral radiographs of the electrode (the electrode was located on the dorsal side of the spinal cord in the spinal canal).

pain score was \geq 7, a temporary intramuscular injection of 5 mg of dizosin was given every 12 hours at most. Continuous electrical stimulation of tSCS is typically applied for 7-14 days (9). After stopping stimulation, the electrode was removed if the pain in the patient's lesion area was not aggravated.

Observation and Evaluation Index

The NRS score was categorized as no pain (0 point), mild pain (1-3 point), moderate pain (4-6 point), severe pain (7-9 point) and intolerable pain (10 point). Patient's reported NRS scores 4 times a day: in the morning, in the midday, in the evening and before bedtime.

The average NRS score (the sum of all NRS scores within 24 hours/4) and the maximum NRS score waw recorded before the operation, and 3 days, 10 days, one month, 3 months, 6 months and 12 months after the operation.

The Pittsburgh Sleep quality Index (PSQI) was used to evaluate the sleep quality of patients at each time point. The index consists of 18 self-evaluation items belonging to 7 sub-categories. The score of each subcategory ranges from 0-3 making the total score 0-21. The higher the score, the worse the patient's sleep quality.

Pain relief rate (%) was calculated as: (preoperative average NRS score - postoperative average NRS score) /

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preoperative average NRS score \times 100 is the pain relief rate. A pain relief rate > 75% is considered an excellent effect, 50% \le pain relief rate \le 75% is considered a good effect, 25% \le pain relief rate < 50% is considered poor effect, and pain relief rate < 25% is considered invalid.

Postoperative efficiency (%) was calculated as: (excellent effect + good effect) / total number of cases × 100.

The amount and types of analgesics used by patients were recorded before operation, and 10 days, one month, 3 months, 6 months and 12 months after the operation. The conventional drugs prescribed to patients included anticonvulsant drugs (prebelin and gabapentin), antidepressant drugs (amitriptyline and Duloxetine), opioid drugs, and their compound preparations (paracetamol oxycodone, paracetamol tramadol, tramadol, and oxycodone) (10).

Serious adverse events or operative complications during hospitalization of all patients were also recorded.

Statistical Analysis

Statistical differences were analyzed using the SPSS 25.0 software (SPSS Company). Data was presented as mean \pm standard error (x \pm SEM). The t-test was used to compare the normal distribution of age, regulation time, etc., among the study groups. The GEE test was used to compare the data that was not normally distributed, such as the NRS score, the PSQI score, etc. The counting data was expressed as a percentage (%). The postoperative efficiencies of the groups were compared using the Fisher test, and the pain relief rate was compared using the Friedman test. The criterion for statistical significance was P < 0.05.

RESULTS

General characteristics of patients

There was no significant difference in the gender, age and stimulation time of each group (P > 0.05) (Table 1). However, most patients had HZ lesions in their right side, patients' pain segments were most commonly in the thoracic nerve, and most patients had definite comorbidity such as heart, lung, or kidney diseases, diabetes, malignant tumors, infectious diseases or immune system diseases. The differences in in terms of the lesion side, involved dermatome and comorbidity of the groups were statistically significant (P < 0.05).

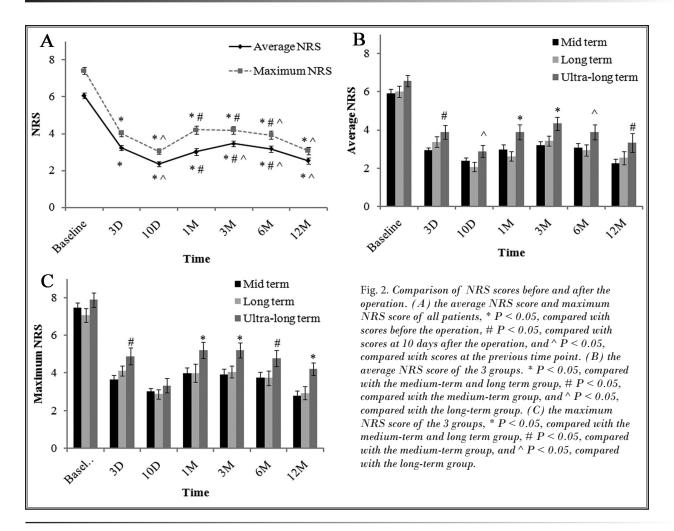
Surgical Procedures and Related Adverse Events

The adverse events that occurred during hospitalization included one mild case of cerebrospinal fluid leakage (the wound healed after the puncture point was sutured) and one case of pneumothorax (the wound healed without special treatment). There were no other serious complications such as intraoperative nerve or spinal cord injuries, hematoma, postoperative infections or wire breakages. Intraoperative images of typical cases are shown in Fig. 1.

Comparison of NRS Scores

Compared with those before the operation, the average NRS scores reported by all groups' patients decreased significantly after the operation (P < 0.05) (Fig. 2A). The average NRS score and the maximum NRS score of all groups at 10 days post-operation were significantly lower than those at 3 days after the operation (P < 0.05). However, the NRS scores of all groups at one month, 3 months and 6 months post-operation were significantly higher than those at 10 days after the operation (P < 0.05). The average NRS score of all groups at 3 months post-operation was significantly higher than that at one month post-operation, but the average NRS score and the maximum NRS score at 6 months and 12 months after the operation were significantly lower than those at previous time points (P < 0.05).

Among the 3 groups, the average NRS scores and the maximum NRS scores reported by the medium-term and long-term groups were significantly lower than those of the ultra-long-term group (P < 0.05). However, there was no difference in the average NRS scores and the maximum NRS scores of the medium-term and long term groups (P > 0.05). Compared with the ultra-longterm group, the average NRS scores of the mediumterm and long-term groups were significantly lower at 1-3 months after the operation (P < 0.05) (Fig. 2B). Additionally, compared to the ultra-long-term group, the long-term group had a significantly lower average NRS score at 10 days and 6 months post-operation (P < 0.05), and the medium-term group had a significantly lower average NRS score at 3 days and 12 months post-operation (P < 0.05). In terms of the maximum NRS score, the medium-term and long-term groups had significantly lower scores than the ultra-long-term group at one month, 3 months and 12 months after the operation (P < 0.05) (Fig. 2C). Meanwhile at 3 days and 6 months post-operation, the maximum NRS score of



the ultra-long-term group was significantly higher than that of the medium-term group, but significantly lower than that of the long-term group.

Comparison of PSQI scores

The average PSQI scores of patients from all groups after the operation were significantly lower than those before the operation (P < 0.05) (Fig. 3A). The PSQI score at 10 days post-operation was significantly lower than that at 3 days after the operation for all groups. At one month post-operation, the PSQI score of all groups was slightly higher than that at 10 days post-operation, but this increase was not statistically significant (P > 0.05). The PSQI score of all groups decreased slowly starting 3 months post-operation, and this decrease became significant at 12 months after the operation (P < 0.05). However, for all groups, there was no significant difference in the PSQI score at other time points after the operation compared with 10 days post-operation (P > 0.05).

0.05). Comparing groups, the PSQI scores of the long-term group were lower than that of the ultra-long term group at one month and 6 months after the operation (P < 0.05) (Fig. 3B). At 6 and 12 months post-operation, the PSQI scores of the medium-term group were significantly lower than that of the ultra-long-term group (P < 0.05).

Pain Relief Rate and Postoperative Efficiency

The pain relief rates of all groups at 3 days, 10 days, one month, 3 months, 6 months and 12 months after the operation were 45.45%, 59.81%, 49.19%, 41.51%, 45.37% and 57.21%, respectively. Among them, the pain relief rate at 10 days post-operation was significantly higher than that at 3 days after the operation, and the pain relief rates at one month, 3 months and 6 months post-operation were significantly lower than that at 10 days post-operation (P < 0.05) (Fig. 4Aa). The pain relief rate at 12 months post-operation was

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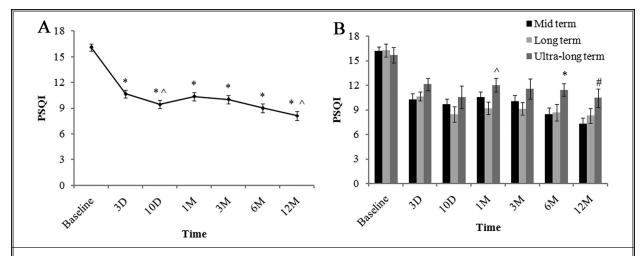


Fig. 3. Comparison of PSQI scores before and after the operation (n=52). (A) the PSQI score of all patients, * P<0.05, compared with scores at 10 days after the operation, and ^ P<0.05, compared with scores at the previous time point. (B) the PSQI score of the 3 groups, * P<0.05, compared with the medium-term and long-term group, # P<0.05, compared with the medium-term group, and ^ P<0.05, compared with the long-term group.

significantly higher than that at 3 and 6 months after the operation (P < 0.05). Although the pain relief rate in the ultra-long-term group was low, there was no significant difference in the pain relief rate among the 3 groups (P > 0.05) (Fig. 4Ab).

The postoperative efficiency of all groups at 3 days, 10 days, one month, 3 months, 6 months and 12 months after the operation were 48.08% (effective for 25 patients/invalid for 27 patients), 69.23% (36/16), 53.85% (28/24), 42.31% (22/30), 44.23% (23/29), and 62.75% (32/19), respectively. For all groups, the efficiency rate at 10 days post-operation was significantly higher than that at 3 days after the operation. However, the efficiency rates decreased significantly at 3 and 6 months post-operation compared with that at 10 days postoperation (P < 0.05) (Fig. 4Ba). The efficiency rate of all groups at 12 months post-operation was significantly higher than that at 3 months after the operation (P < 0.05), but it was not significantly higher than that at 6 months post-operation. Additionally, there was no significant difference in the postoperative efficiency among the 3 groups (P > 0.05) (Fig. 4Bb).

The Use of Analgesics.

Compared to pre-operation, the number of patients using opiods decreased gradually at each time point after the tSCS operation in all groups. Additionally, among all groups, the number of anticonvulsant and antidepressant users decreased at one, 3, 6 and 12

months after operation (P < 0.05) (Fig. 5). Only a small proportion of patients across all groups still needed to take painkillers at 12 months post-operation (only 7 out of 52 patients needed to use anticonvulsants, 1 out of 21 patients needed to use antidepressants, and 3 out of 24 patients needed to use opioids).

DISCUSSION

PHN often occurs in elderly patients with HZ who also have a variety of other complications, low immunity, and poor nerve repair function (11). The average age of the patients in this study was 68 years old, and most of the patients were also experiencing other complications at the time of this study. There was no significant difference in the age of patients in the 3 groups. Additionally, in this study, there was no significant correlation between the age of patients and the course of their PHN. In this study, the average electrode placement time for tSCS was 10.5 days, and there was no statistical difference in the regulation time of electrical stimulation among the 3 groups. In 1993, Shimoji et al (12) reported that SCS provided a better analgesic effect for neuropathic pain in the neck and trunk. However, in this study, the thoracic nerve was found to mostly be involved in PHN (12). PHN occurs mostly in the thoracolumbar region, but the efficacy of tSCS on PHN at different nerve segments remains to be observed (13). There were no serious complications such as spinal cord injury, nerve injury, or large electrode

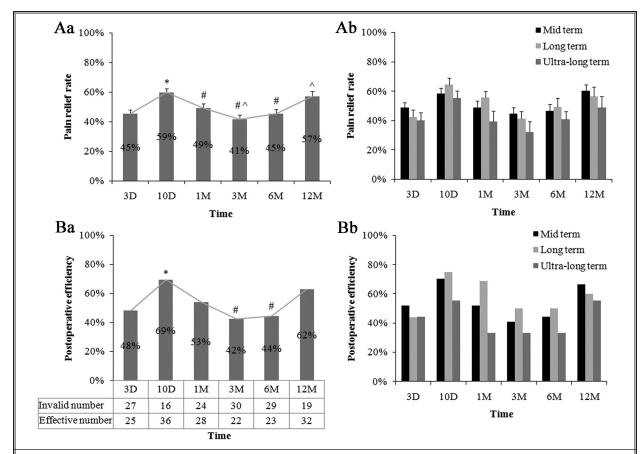


Fig. 4. Comparison of the pain relief rate (A) and postoperative efficiency (B) at each time point after the operation. (Aa) pain relief rate of all patients, *P < 0.05, compared with that at 3 days after the operation, #P < 0.05, compared with that at 10 days after the operation, $\P < 0.05$, compared with that at the previous time point, and $\P < 0.05$, compared with that at 3 months after the operation; (Ab) pain relief rates of the 3 groups; (Ba) postoperative efficiency of all patients, $\P < 0.05$, compared with that at 3 days after the operation, $\P < 0.05$, compared with that at 10 days after the operation, $\P < 0.05$, compared with that at the previous time point, and $\P < 0.05$, compared with that at 3 months after the operation; (Bb) postoperative efficiency of the 3 groups.

displacement in this study. In this study, only 3.85% (2/52 cases) of patients experienced mild complications like cerebrospinal fluid leakage or pneumothorax. Furthermore, since the range of motion of the patients' thoracic vertebra was limited, there was less electrode displacement observed.

At 10 days after the operation, the average NRS score of all groups was lower than 3, the pain relief rate was 59.81%, the postoperative efficacy was as high as 69.23%, and the PSQI score was gradually decreasing during the tSCS treatment. The results indicated that the tSCS had a significant real-time analgesic effect on refractory PHN patients and produced a significant improvement in patients' sleep quality. A clinical study by Yanamoto and Murakawa (14) also showed that

tSCS could significantly alleviate the pain and improve the sleep quality of PHN patients. During the follow-up period from one to 12 months after the operation, the NRS score and PSQI score of the patients enrolled in this clinical study were still significantly lower than those before the operation (14). In 2016, Yang et al (16) published a study showing that the quality of life of PHN patients had significantly improved even at 7 days after the tSCS operation. Moreover, the study found that the analgesic effect of tSCS persisted to a certain extent even at the 3-month follow-up period (16). This is consistent with the results of this current study in which PHN patients could still maintain analgesia for a period of time after the removal of the tSCS treatment electrodes. The prolonged analgesic effect of tSCS may

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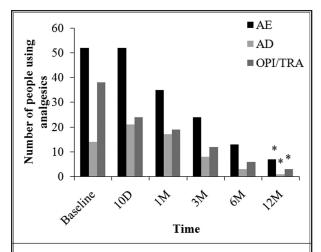


Fig. 5. The number of patients using analysis before and after operation (n=52). * P < 0.05, compared with that before the operation in the same group.

be related to the fact that SCS inhibits peripheral and central sensitization, further promoting nerve regeneration (17-21).

Through the postoperative follow-up, it was found that the average NRS score of all groups was higher and the pain relief rate of all groups decreased significantly between 1-6 months after the operation. The pain relief rate across all groups was only 41.51% at 3 months. The postoperative efficiency between 3-6 months (ranging from 42.31%-44.23%) was also significantly lower than that at 10 days post-operation. However, at 12 months after the operation, the pain relief rate and postoperative efficiency had increased, but it was still lower than that at 10 days post-operation. In a previous study, Huang et al. also observed that refractory PHN patients had a rebound phenomenon after tSCS treatment (22). However, patients with acute and subacute herpetic neuralgia did not experience this significant decrease in curative effect after the removal of the tSCS treatment electrodes (23,24). The refractory PHN patients in the current study experienced a reduction in analgesic effect of tSCS after the electrodes were removed, which might be because the tSCS is unable to completely reverse the neuropathic injury of the structurally damaged nerves that the patients may have.

Current literature compares the treatment of patients in the acute, subacute, or PHN phase of herpes zoster-related pain, but the surgical efficacy in patients with different PHN courses has rarely been compared (22). In terms of the average and maximum NRS score, there were differences in the medium-term and long-term groups compared with the ultra-long-term

group, especially at 1-3 months after the operation. At 6 months after the operation, the all patients in the medium-term and long-term groups had significantly better sleep quality than those in the ultra-long-term group. And at 12 months post-operation, the pain relief and sleep quality of all patients in the mediumterm group were significantly better than that of the ultra-long-term group. On the other hand, the pain relief rate and postoperative efficiency of patients in the ultra-long-term group were lower than those of the other groups, but this difference was not statistically significant. A study published by Kurklingsky et al (27) in 2018 reported that more patients received long-term pain relief from tSCS than permanent SCS. However, those patients received tSCS soon after the resolution of HZ lesions, which have prevented them from developing chronic pain sensitization and thus allowed them to achieve better outcomes from tSCS (14,25,26). Patients in the early stages of PHN, tSCS can have better efficacy compared to permanent SCS. This supports the results of the current study which demonstrates that tSCS could relieve pain and improve sleep quality better in refractory PHN patients with a course of less than 12 months compared to patients with a course of more than 12 months. This suggests that refractory PHN patients can still consider tSCS operation within the first year of disease course.

In a 2020 study by Huang et al (22), only 37.5% of PHN patients had VAS scores less than 2 at 12 months after tSCS. In this study, the average PHN duration of patients was 640.3 ± 173.6 days (22). Meanwhile, a 2018 literature review showed that 54 patients underwent tSCS within 6 months of HZ symptoms resolution, of which 42 patients (77.8%) achieved long-term relief during the 3.2 months follow-up period (27). In this paper, at 12 months post-operation, the postoperative efficiency was 62.75%, and the pain relief rate was 57.21% (27). Comparing the results of these two studies to the current study (in which the average PHN duration of patients is 7.33 ± 0.88 months) shows that patients with a longer the course of herpetic neuralgia, experience a lesser long-term analgesic effect from tSCS (28,29).

Other studies have shown that tSCS treatment was less efficient in producing long-term pain relief compared to permanent SCS in PHN patients (30). In a literature review, Kurklingsky et al (27) summarized 16 studies about permanent SCS treatment of PHN, and showed that the average pain relief rate was 79.0% during an average follow-up period of 50.8 months.

However, only 47.1% (120/255) of patients experienced long-term remission (50% decrease in VAS scores), and some patients still needed medication-assisted treatment (27). Another literature review analyzed 12 papers reporting the tSCS treatment of 134 PHN patients with an average follow-up time of 12.85 months (31). Of these 134 PHN patients, 91 patients (67.9%) achieved long-term pain relief, and the average improvement rate was 61.4% (31). In this study, the pain relief rate of refractory PHN patients rebounded to 57.21% at 12 months after the operation, and the postoperative efficiency also increased to 62.75% (31). Additionally, the number of patients regularly taking analgesics continued to decline during the follow-up period, and at 12 months post-operation, the number was significantly lower than that before the operation (31). Prospective studies in which PHN patients were treated with tSCS and other minimally invasive interventional therapies show that the efficacy and safety of tSCS was better than the other therapies (32-34). Therefore, considering the above factors, although the long-term pain relief rate and postoperative efficiency of tSCS treatment is not high, due to the current limited therapies, refractory PHN patients within 12 months of PHN course might find that tSCS is still worth trying to achieve better long-term relief.

Limitations

This is a single-center retrospective study with a relatively small number of cases and a follow-up time of only 12 months after tSCS. Thus, a multicenter study with a larger patient cohort might reveal more insight into PHN treatment. This study also does not compare tSCS with other minimally invasive treatments. In future studies, the therapeutic effect of different electrode placements and the neural regulation mode on PHN treatment should be researched.

CONCLUSION

The results of this study suggest that tSCS treat-

ment could reduce the pain degree and the improve sleep quality of refractory PHN patients in 12 months after the operation. This implies that tSCS could be used as a safe and effective therapy for refractory PHN. The therapeutic effect of tSCS in PHN patients within 12 months of PHN course was better than that in patients with more than 12 months of PHN course. However, the long-term pain relief rate and postoperative efficiency were low within 12 months of follow-up after tSCS. Thus, further investigation is needed to determine an effective way to reduce the pain experienced by refractory PHN patients.

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Author Contributions

Xin Li conducted the study including data collection and analysis, statistical analysis, data interpretation, and wrote the manuscript; Yaping Wang interpreted the data and reviewed and edited the manuscript; Kai Chen performed data collection and statistical analysis; Dingquan Zou designed the study, interpreted the data and wrote the manuscript; All authors approved the final manuscript and agree with its submission.

Compliance with Ethics Guidelines

This observational data collection adhered to the ethical principles of the Declaration of Helsinki. This study is a prospective data collection without any intervention, which complies with the ethical guidelines of the Declaration of Helsinki and is approved by the Ethics Committee of second Xiangya Hospital of Central South University (No.2022-543, date of registration: 2022-06-20).

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