Randomized Controlled Trial

Short-Term Supraorbital Nerve Stimulation and Pain Relief for Acute and Subacute Ophthalmic Herpetic Neuralgia: A Randomized Controlled Crossover Trial

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Background: Herpes zoster ophthalmicus (HZO) is a kind of refractory disease, and treating it is important for preventing postherpetic neuralgia (PHN). But the evidence surrounding the current treatment options for these conditions is controversial, so exploring reasonable clinical treatment strategies for HZO is necessary. Neuromodulation is an excellent modality for the treatment of various neuropathic pain conditions. This trial was designed to evaluate the effectiveness of short-term supraorbital nerve stimulation (SNS) and the supraorbital nerve block (SNB) for HZO.

Objectives: To determine whether short-term SNS relieves acute and subacute ophthalmic herpetic neuralgia.

Study Design: This prospective randomized controlled crossover trial compared short-term SNS to SNB.

Setting: The operating room of a pain clinic.

Methods: Patients with acute or subacute ophthalmic herpetic neuralgia were recruited. The patients were randomly assigned to receive either SNS or SNB. The primary outcome being measured was each patient's Visual Analog Scale (VAS) score at 4 weeks. The secondary outcomes under measurement were the proportion of patients who achieved ≥ 50% pain relief, sleep quality, medicine consumption, and adverse events. Crossover after 4 weeks was permitted, and patients were followed up to 12 weeks.

Results: Overall, 50 patients were included (n = 25/group). At 4 weeks, the patients who received SNS achieved greater pain relief, as indicated by their significantly different VAS scores from those of the SNB group (mean difference: -1.4 [95% CI, -2.29 to -0.51], $P < 0.05$). Both groups showed a significant decrease in pain level from the baseline (all $P < 0.05$). Overall, 72% and 44% of the SNS and SNB patients experienced ≥ 50% pain relief, respectively (OR: 0.31 [95% CI, 0.09 to 0.99], $P < 0.05$), and 68% and 32% of SNS and SNB patients, respectively, had VAS scores < 3 (OR: 0.22 [95% CI, 0.07 to 0.73], $P < 0.05$). Compared to the SNB group, the SNS group had better sleep quality, lower ophthalmic neuralgia, a lower proportion of further treatment, and lower analgesic intake. Overall, 18 patients received SNS alone, and 16 patients crossed over from SNB to SNS. The VAS scores, sleep quality, ophthalmic neuralgia, and trend of medicine intake were not significantly different between the groups (all $P > 0.05$). No serious complications occurred.

Limitations: This study was nonblind.

Conclusions: Short-term SNS is effective for controlling acute or subacute ophthalmic herpetic neuralgia. Combining SNS with SNB yields no additional benefits.

Key words: Herpes zoster ophthalmicus, postherpetic neuralgia, ophthalmic herpetic neuralgia, supraorbital nerve, neuromodulation, peripheral nerve stimulation, supraorbital nerve stimulation, supraorbital nerve block

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Herpes zoster (HZ) is a painful rash caused by reactivation of the latent varicella-zoster virus (VZV) in the dorsal root ganglia or cranial nerve ganglia (1). HZ pain can be divided into 3 phases (2,3): acute herpetic neuralgia, subacute herpetic neuralgia, and postherpetic neuralgia (PHN). Acute herpetic neuralgia occurs within a month after the onset of the rash, while subacute herpetic neuralgia occurs from one to 3 months after the rash onset. PHN is defined as pain in a dermatomal distribution that is sustained for at least 90 days after the rash (4). Approximately 95% of the adult US population is latently infected with VZV and can therefore develop HZ (1). The incidence and prevalence of PHN varies by region. Approximately a fifth of patients with HZ have PHN, and 15% report pain at 2 years (5).

Herpes zoster ophthalmicus (HZO) is defined as the involvement of HZ in the ophthalmic division of the fifth cranial nerve (6). The special anatomical structure and pathological characteristics cause HZO refractoriness. Furthermore, the risk of PHN associated with HZO is over twice that associated with nonophthalmic zoster (7). PHN carries direct, indirect, and psychosocial costs, posing a substantial national and individual burden, which highlights the importance of PHN prevention (8). The most common intervention for this condition is the epidural administration of corticosteroids and local anesthetics, but evidence of this procedure's effectiveness is controversial (9). Spinal cord stimulation (SCS) has been proven to be effective in the treatment of herpetic neuralgia (10), but it is impractical to use for HZO. Peripheral nerve simulation (PNS) is an excellent modality for the treatment of various neuropathic pain conditions and is used to complement SCS (11). The usual indications for PNS are similar to those for SCS, although whether PNS and SCS have the same mechanism is uncertain.

The possibility of PNS's positive effects on HZO has yet to be clarified. Therefore, this open randomized trial was designed to quantify the effectiveness of short-term supraorbital nerve stimulation (SNS) and the supraorbital nerve block (SNB) with dexamethasone and lidocaine during the acute or subacute phase of HZO as a method of PHN prevention.

Methods

Study Design

The study was a randomized controlled crossover trial for patients with acute or subacute ophthalmic herpetic neuralgia. The patients were randomly assigned in a one-to-one ratio to short-term SNS or SNB. Given the nature of the process, it was impossible to blind patients and doctors during the trial.

This study was approved by the Human Ethics Committee of the First Affiliated Hospital of China Medical University, Shenyang, China (No. AF-SOP-07-1.1-01) and was registered with the Chinese Clinical Trial Registry Web site (www.chictr.org.cn) in May 2018 (Registration No.: ChiCTR 1800016258). The study was conducted according to the tenets of the Declaration of Helsinki. Written informed consent was obtained from all patients. Because recruitment was slow, we extended the study until October 2021 for completion.

Objective

The study was undertaken to determine whether short-term SNS relieved acute and subacute ophthalmic herpetic neuralgia.

Setting

The study was performed in the pain clinic or operating room of the centers in which this trial was undertaken.

Inclusion and Exclusion Criteria

Patients presenting with HZO at the pain clinic were examined by a pain management physician and asked to participate in the study. The research assistant evaluated eligibility and enrolled the patients according to the following criteria: (1) age ≥ 18 years, (2) moderate to severe pain after conservative management; (3) HZO diagnosis from a dermatology or ophthalmic clinic that administered treatment through antiviral therapy during the acute stage, and the pain area involved only the first branch of trigeminal nerve; (4) disease course lasting between 14 days and 2 months; (5) voluntary participation and signing of the informed consent form.

The main exclusion criteria were as follows: (1) pregnancy; (2) serious disease, systemic or local infection, coagulation dysfunction, or consciousness disorder that rendered the patient unable to tolerate treatment or cooperate with follow-up; (3) allergy to study drugs; and (4) previous history of any kind of intervention that could affect the herpetic neuralgia.

Sample Size Calculation

The sample size was calculated using the PASS 15 software program (NCSS Statistical Software, LLC). Our

primary hypothesis was that the patients in the SNS group would experience greater pain relief than the patients in the SNB group. Each group had a sample size of 24 patients who achieved an 85.63% power to detect an intergroup difference with a proportion of 0.4. The test statistic used was the one-sided Z-test with unpooled variance. The significance level of the test was 0.025. The final sample size needed was 25 patients per group.

Randomization and Crossover Period

A randomization sequence was created using a predictive analytics software program, SPSS™ Statistics 26 (IBM™), and the patients were randomly assigned in a one-to-one ratio to either the SNS group or the SNB group. Each treatment lasted 2 weeks, and outcome parameters were evaluated at the end of the treatment period. After a 2-week washout period that reduced the carryover effect, the patient decided whether to cross over to the other intervention spontaneously if they had insufficient pain relief (less than 50% improvement) or if they were dissatisfied with the first treatment. If the patient requested further treatment, the other intervention was given, and patients who did not cross over still received follow-up.

Description of Interventions

SNS was performed under x-ray fluoroscopy guidance according to previously described methods (12). The patient was placed in a supine position, and a needle was used to puncture the area above the lateral canthus. Following sterilization and local anesthesia, a lead (Model: 18366901, St. Jude Medical) was placed subcutaneously, covering both the supraorbital and supratrochlear nerves (Fig. 1a). After the position of the lead was confirmed, stimulation was programmed with the following settings: tonic mode with a constant current amplitude of 2–10 mA (adjustable for patient comfort), a pulse width of 200–500 μs, and a frequency of 40 Hz. The duration of the stimulation was 10 days.

The SNB was performed under ultrasound guidance, and the puncture target was the supraorbital notch or supraorbital foramen, passed through by the supraorbital nerve (Fig. 1b). We administered 2 mL of 0.5% ropivacaine (AstraZeneca) twice daily, supplemented with 5 mg dexamethasone in the first injection. This treatment lasted for 10 days.

Systemic analgesic therapy with anticonvulsants (pregabalin) and opioids was given in both groups if there was insufficient pain control, and dosage modifications according to the pain severity were allowed.

Outcome Measurement

The primary outcome measures were the Visual Analog Scale (VAS) scores at one week and 2, 4, 5, 6, 8, and 12 weeks after the initiation of treatment. The secondary outcome measures were the proportion of patients who achieved at least 50% pain relief as estimated using the VAS scores, the proportion of patients who achieved at least 50% ophthalmic neuralgia relief, sleep quality evaluated with the Pittsburgh Sleep Quality Index (PSQI) (13), further treatment (change in the use of SNS and SNBs), and drug therapy as determined by anticonvulsant and opioid consumption. Adverse events were recorded throughout the study period. Baseline data on age, gender, and disease course were collected prior to randomization.

Pain relief was assessed using the standard 10-point VAS, with a score of 0 representing no pain at all and a score of 10 representing the highest pain level. For the baseline and follow-up measurements, the VAS scores were measured using the averaged self-reported pain within the past 24 hours. Quality of sleep was evaluated with the PSQI, a tool for assessing sleep quality over a one-month period. The PQSI includes 19 questions for assessing 7 different components: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction. The scores were then added to determine the total PSQI score, ranging from 0 to 21, with higher scores indicating worse sleep quality.

Pregabalin and opioids (translated into a daily oral dose of the morphine equivalent) were allowed to be combined, and for analysis, the patient's mean consumption of the medication over the preceding 7 days was measured in milligrams and recorded on each follow-up visit. Adverse events and medicine-related side effects were monitored and documented during the entire study period and immediately reported to the researchers.

Statistical Analysis

All statistical analyses were performed using SPSS Statistics 26 (IBM™). For descriptive statistics, continuous variables were presented as the mean, SD, median, and range depending on data distribution; meanwhile, categorical variables were presented as frequencies and percentages. Intergroup comparisons were performed using independent or paired t-tests (or nonparamet-

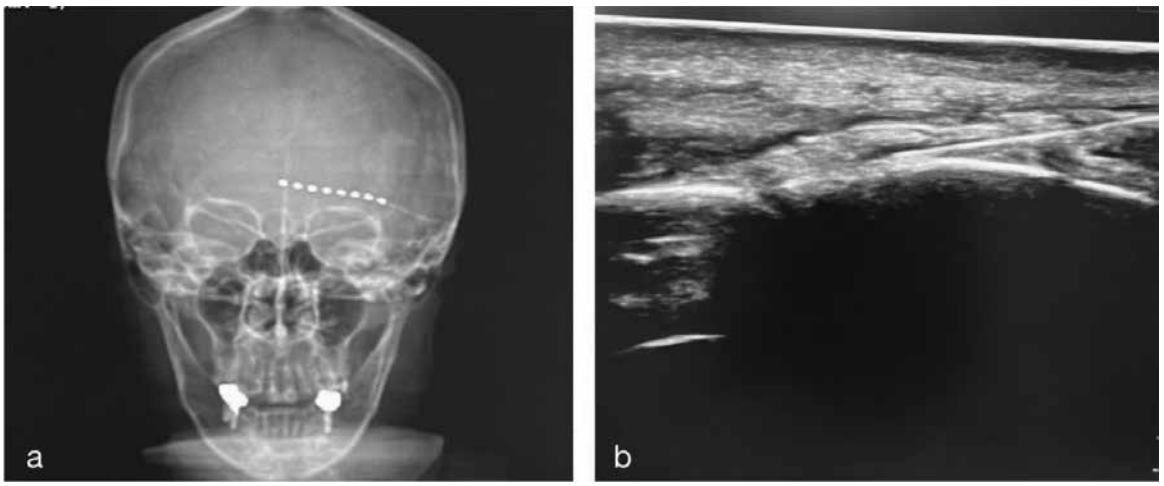

Fig. 1. *Pictures of intervention.*
a: X-ray fluoroscopy of supraorbital nerve stimulation; b: Ultrasound image of supraorbital nerve block

ric tests) for continuous variables and Pearson's chi-squared test (or Fisher's exact test) for categorical variables, following the intent-to-treat (ITT) principle. The choice of parametric and alternative tests was reported in the results. Given the extent of patient crossover at 4 weeks, the Phase II analyses were limited to the patients treated with SNS and with SNB-SNS. Continuous and binary variables were expressed as the mean differences and the odds ratios, respectively. Two-tailed *P*-values < 0.05 were considered indicative of statistical significance for intra- and intergroup comparisons.

Results

Study Population

Among the 97 patients screened, 50 patients with HZO were enrolled (Fig. 2), and 48 of the patients (96%) who completed the Phase I trial proceeded to the Phase II trial and completed both initial treatment phases. Twenty-three of the patients proceeded to the crossover phase. Meanwhile, 2 patients did not complete the treatment after one or 2 SNB sessions for personal reasons.

The baseline patient characteristics are summarized in Table 1. There were no significant intergroup differences in age, gender, or location and duration of pain.

Primary Outcomes at 4 Weeks

The difference between the groups' VAS scores (Fig. 3) was statistically significant at one week (mean difference -1.52 [95% CI, -2.36 to -0.68], $P < 0.05$), 2 weeks (mean difference -1.64 [95% CI, -2.47 to -0.81], $P < 0.05$), and 4 weeks (mean difference -1.4 [95% CI, -2.29 to -0.51], $P < 0.05$). Both groups showed significantly lower VAS scores after treatment than at the baseline (all $P < 0.05$).

Secondary Outcomes at 4 Weeks

Table 2 summarizes the secondary outcomes at 4 weeks. The proportion of responders (50% or more pain relief from the baseline VAS scores) was 72% (18 of 25) in the SNS group and 44% (11 of 25) in the SNB group (OR: 0.31 [95% CI, 0.09 to 0.99], $P < 0.05$). Seventeen of the 25 (68%) patients in the SNS group and 8 of the 25 (32%) patients in the SNB group had VAS scores of ≤ 3 at 4 weeks (OR: 0.22 [95% CI, 0.07 to 0.73], $P < 0.05$). Compared to the SNB group, the SNS group experienced better sleep quality (mean difference in global PSQI score: -3.24 [95% CI, -5.9 to -0.58], $P < 0.05$). The SNS group also exhibited a trend toward lower analgesic drug intake (based on the daily oral dose of the morphine equivalent and the proportion of patients using medication). For ophthalmic neuralgia, 10 of the 18 (55.6%) patients in the SNS group and 4 of the 16 (25%) patients in the SNB group achieved 50% or more pain relief ($P = 0.09$). At the end of Phase I, 28% (7 of 25) of the patients in the SNS group and 64% (16 of 25) of the patients in the SNB group crossed over for further treatment ($P < 0.05$). There were no adverse treatment-related events or complications requiring hospitalization or emergency treatment in either group. Transient pain aggravation and upper eyelid swelling were common adverse reactions, which were

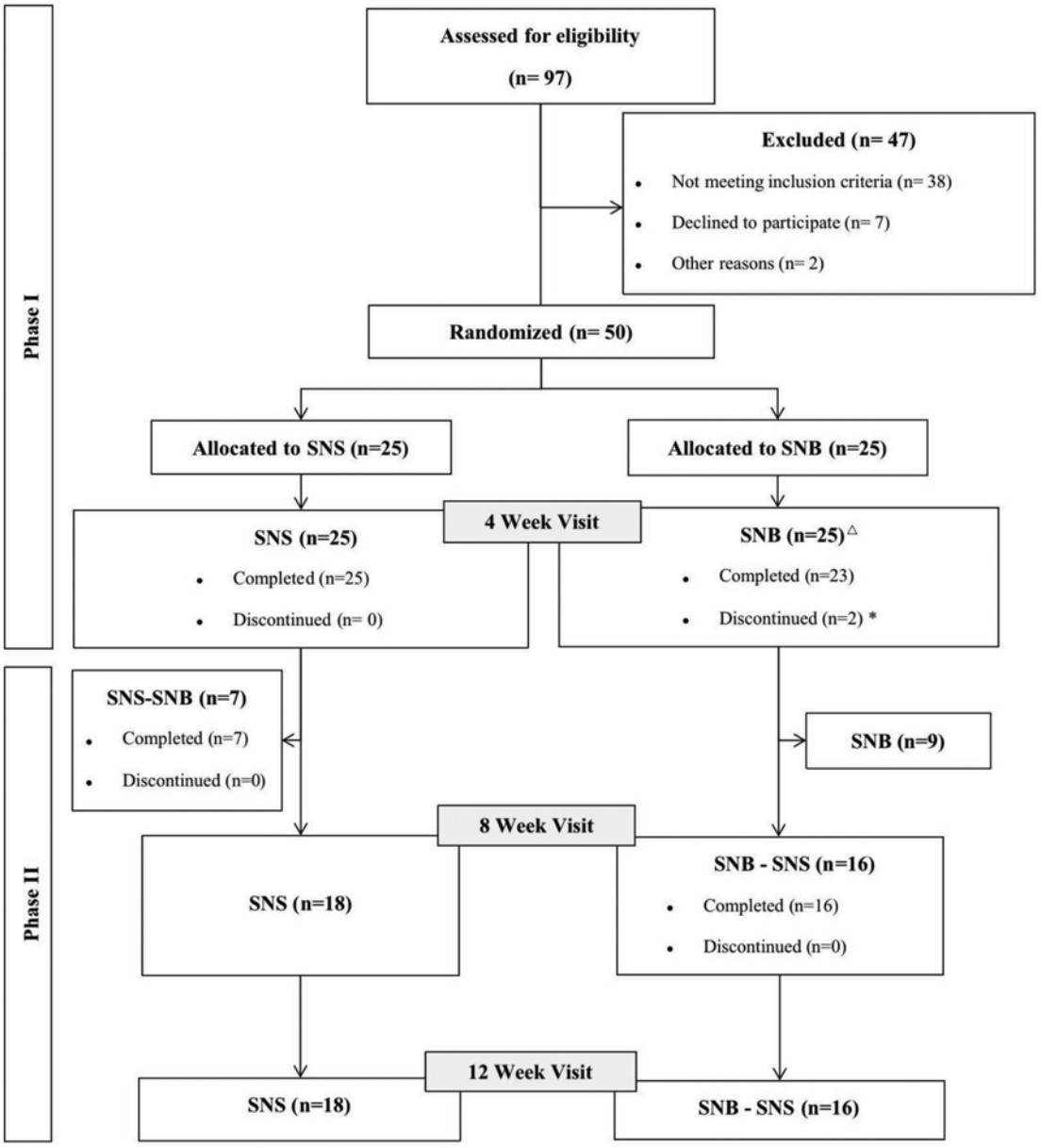

Fig. 2. *CONSORT flow-diagram*.
Δ: Follow-up is completed regardless of whether SNB is completed or not. *: Patients are unable to complete the whole treatment process after one or 2 SNB sessions.
SNS, supraorbital nerve stimulation; SNB, supraorbital nerve block

relieved within one to 2 days after clinical observation and management.

Outcomes at 12 Weeks

Patients at 12 weeks—that is, those receiving SNS in Phase I (SNS) and SNB patients moving to SNS in Phase II (SNB-SNS)—were evaluated. Fig. 4 shows the trends in both groups' VAS scores at each visit. Both groups showed a significant decrease from the baseline VAS scores at 5, 6, 8, and 12 weeks after treatment (all $P < 0.05$). The difference in VAS scores between the SNS group and the SNB-SNS group was statistically significant at 5 weeks ($P < 0.05$) but not at 6, 8, or 12 weeks.

Table 3 summarizes the other outcomes that ap-

Table 1. *Baseline clinicodemographic patient characteristics*.

	SNS Group (n = 25)	SNB Group (n = 25)	Intergroup Difference (*P*-value)
Age (years), mean (SD)	72.64 (8.34)	71.76 (9.48)	0.73
Age group (years), n (%) < 60 60-69 70-79 ≥ 80	 1 (4) 9 (36) 8 (32) 7 (28)	 2 (8) 9 (36) 8 (32) 6 (24)	0.94
Gender, n (%) Male Female	 14 (56) 11 (44)	 13 (52) 12 (48)	0.78
Location of pain, n (%) Frontoparietal Frontoparietal + eye	 7 (28) 18 (72)	 9 (36) 16 (64)	0.54
Pain duration (days), mean (SD)	33.52 (13.55)	33.28 (12.70)	0.95
Phase of pain, n (%) Acute (< 30 days) Subacute (≥ 30 days)	 9 (36) 16 (64)	 12 (48) 13 (52)	0.39

An intergroup *P*-value of < 0.05 is considered statistically significant.
SNS, supraorbital nerve stimulation; SNB, supraorbital nerve block; SD, standard deviation

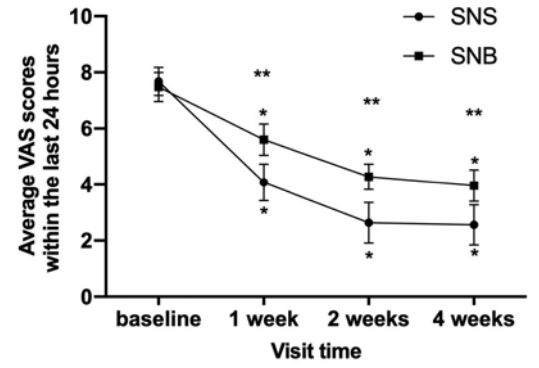

Fig. 3. *VAS pain scores over time in the SNS and SNB groups*.
*: $P < 0.05$ compared to baseline. **: Intergroup difference *P*-value < 0.05. Error bars indicate 95% CIs.
VAS, Visual Analog Scale; SNS, supraorbital nerve stimulation; SNB, supraorbital nerve block; CI, confidence interval

peared at 12 weeks after the treatment. Both groups showed decreased PSQI scores from the baseline ($P < 0.001$), and there was no significant intergroup difference at 12 weeks ($P = 0.37$). The proportion of patients using medication was also not significantly different between the 2 groups. For ophthalmic neuralgia, 10 of the 15 (66.67%) patients in the SNS group and 6 of the 11 (54.55%) patients in the SNB-SNS group achieved 50% or more pain relief ($P = 0.69$). Throughout the entire trial, there were no adverse treatment-related events or complications requiring hospitalization or emergency treatment.

Discussion

The current study demonstrates that short-term SNS is effective and well-tolerated for the management of acute and subacute ophthalmic herpetic neuralgia. Furthermore, the analgesic effect of combined short-term SNS and SNB is similar to that of short-term SNS alone.

Rigorous evidence for the benefit of nerve blocks or glucocorticoid injections as ophthalmic herpetic neuralgia treatments is lacking; therefore, increasing attention has been paid to neuromodulation as a method of managing neuropathic pain. SCS that used permanent pulse generator implants was associated with successful analgesia in PHN and acute herpetic neuralgia patients in a previous study (14), but the medical cost was high. Unfortunately, herpetic neuralgia involving the cranial nerves is not a condition eligible for SCS. Dunteman reported 2 cases of permanent implantation of PNS for the treatment of ophthalmic postherpetic neuralgia (15). In our study, the main purpose of Phase I was to compare the analgesic effect of short-term SNS to that of SNB on patients with ophthalmic herpetic neuralgia. At 4 weeks, the SNS group achieved more pain relief and better sleep quality than did the SNB group, although both groups experienced significant analgesic effects. The SNB group's VAS scores decreased gradually after the nerve blocks, whereas the SNS group's VAS scores significantly decreased immediately in the first week after treatment. Most patients described that the original pain area became numb as soon as the electrical stimulation worked, and a satisfactory analgesic effect soon followed. This favorable effect of SNS on neuropathic pain is consistent with previously reported findings (12,16).

The treatment duration of our percutaneous short-term SNS was no more than 2 weeks, but the pain did not recur during the 4-or-more-week follow-up. The continuous analgesic effect was also observed in SCS. Yanamoto et al investigated the effects of temporary SCS or spinal nerve root stimulation on patients with early PHN (within one to 6 months of onset), and 21 of 33 (63.6%) cases achieved > 50% pain relief at 6 months after treatment (17). Dong et al reported consistent conclusions in acute/subacute herpetic neuralgia (10).

Recent literature reported temporary PNS as a potential treatment for chronic pain that is refractory to conventional treatment measures. This approach has shown promising results in improving conditions such as lower back pain and peroneal neuropathy (18).

The role of SCS and PNS in preventing PHN is considered related to the mechanisms of neuropathic pain and neuromodulation. Neuropathic pain is caused by the altered and disordered transmission of sensory signals into the spinal cord after a lesion or disease of the somatosensory nervous system develops (19). Acute effects may lead to abnormal pain responses in the central nervous system, and the pathophysiology of the condition involves ectopic activity in damaged or adjacent nerves, changes in the dorsal root ganglion (DRG) or central pathways, peripheral and central sensitization, and a range of molecular mechanisms (20). The sustained analgesic effect of PNS is likely mediated through both central and peripheral mechanisms. PNS activates Aβ fibers at peripheral locations and activates inhibitory dorsal interneurons, leading to the inhibition of Aδ and C fibers, which in turn inhibits the afferent transmission of pain signals to the higher central nervous system (21).

Another significant finding was that both the SNS and SNB groups showed reductions in ocular pain. A total of 55.6% and 25% of patients in the SNS group and SNB group, respectively, achieved at least 50% ocular pain relief at 4 weeks. The HZO involves at least one branch of the ophthalmic division of the trigeminal nerve, namely, the frontal, lacrimal, and nasociliary branches (22). Because the nasociliary branch innervates the globe, ocular pain develops if this branch is affected. The mechanism

Table 2. *Secondary outcome measurements at 4 weeks.*

	SNS Group	Intragroup Difference *P*-value	SNB Group	Intragroup Difference *P*-value	Mean Difference (95% CI)	Odds Ratio (95% CI)	Intergroup Difference *P*-value
Proportion, n	25		25				
Pain relief ≥ 50%, n (%)	18 (72)		11 (44)			0.31 (0.09 to 0.99)	0.045 (a)
VAS ≤ 3, n (%)	17 (68)		8 (32)			0.22 (0.07 to 0.73)	0.011 (a)
PSQI, n	25		25				
Baseline, mean (SD)	13.44 (3.64)	< 0.001 (b)	14 (2.86)	<0.001 (b)	-0.56 (-2.42 to 1.3)		0.548
4 weeks, mean (SD)	6.52 (5.01)		9.76 (4.3)		-3.24 (-5.9 to -0.58)		0.018 (b)
Ophthalmic neuralgia, n	18		16				
Ophthalmic pain relief (≥ 50%), n (%)	10 (55.6)		4 (25)			0.27 (0.06 to 1.15)	0.092
Morphine (oral equivalent daily mg), n	25		25				
Baseline, median (IQR)	40 (25 to 95)	<0.001	30 (20 to 45)	0.0.858			0.056
4 Weeks, median (IQR)	20 (0 to 30)		30 (25 to 50)				0.004 (d)
Drug therapy	(c)						
Opioids: Baseline, n (%)	22 (88)		23 (92)			0.07 (0.01 to 0.58)	0.004 (e)
4 Weeks, n (%)	13 (52)		22 (88)				
Anticonvulsants: Baseline, n (%)	23 (92)		22 (88)			0.45 (0.1 to 2.07)	0.459
4 Weeks, n (%)	17 (68)		19 (76)				
Further treatment, n	25		25				
Crossover, n (%)	7 (28)		16 (64)			4.57 (1.38 to 15.11)	0.011 (a)
Adverse events, n	25		25				
Total, n (%)	3 (12)		8 (32)				
Transient pain aggravation, n (%)	2 (8)		0			3.45 (0.79 to 15.01)	0.088
Transient upper eyelid swelling, n (%)	1 (4)		8 (32)				

$P < 0.05$ indicates a statistically significant difference.
(a): Pearson χ2 test; (b): t-test, $P < 0.05$; (c): Wilcoxon signed-rank test, $P < 0.05$; (d): Mann-Whitney U test, $P < 0.05$; (e): Fisher's exact test, $P < 0.05$.

by which SNS reduces ocular pain intensity is unclear. The supraorbital nerve innervates not the globe but the forehead area. Thus, we speculate that SNS may produce total suppression in the excitability of the ophthalmic nerve and decreased nociceptive input to the trigeminal ganglion. These effects in turn reduce the allodynia in all the areas dominated by the trigeminal ganglion (23). Clinically, we found that some HZ patients in whom the trigeminal nerve's first branch was involved had slight ophthalmic symptoms such as keratitis, iritis, and visual impairment; thus, we supposed that the eye pain was the referred pain. A possible cause of this effect is that descending facilitatory pathways dominate over inhibitory pathways (24), and relieving the forehead pain may result in the secondary relief of referred eye pain.

We investigated whether a combination of SNB and SNS could achieve an effect equal to or better than SNS alone at the 12-week follow-up in Phases I and II. Nerve blocks consisting of local anesthetics and glucocorticoids decrease repetitive painful stimuli and inflammation during the acute phase of HZ and attenuate the central sensitization and development of neuropathic pain (25), and PNS can exert an identical or better effect. Our results showed that the VAS scores at follow-up visits did not significantly differ between the 2 groups, indicating that combination therapy did not provide additional clinical benefits and that SNS could be considered as a replacement for the injection of local anesthetics and glucocorticoids.

Some patients did not achieve satisfactory pain relief, perhaps because our treatment ignored the semilunar ganglion. The DRG plays an important role in the development of neuropathic pain (26). Once a lack of timely management results in pathophysiological changes to the DRG, intervention for the peripheral nerves may not be sufficient to achieve remission, and the treatment target should focus on the DRG. A recent double-blind randomized clinical trial proved that pulsed radiofrequency (PRF) was effective in patients with PHN that affected the thoracic dermatomes (27), although recommending PRF for PHN was considered "inconclusive" (28). Moreover, PRF of the semilunar ganglion through the foramen ovale was associated with satisfactory results in HZO patients (29). However, the procedure is complex and high-risk, especially for elderly patients. Among the 50 patients who underwent SNS or SNB in this study, no inadvertent lead dis-

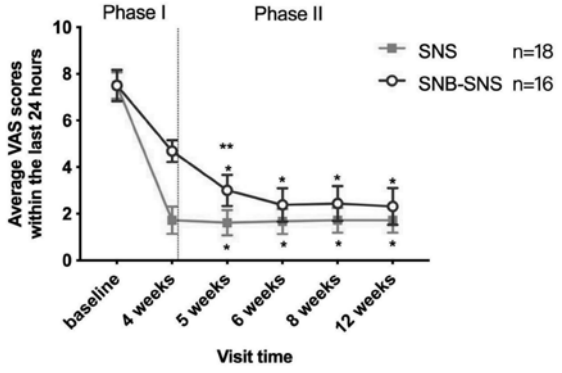

Fig. 4. *VAS pain scores over time in the SNS and SNB-SNS groups.*
*: $P < 0.05$ compared to baseline. **: Intergroup difference P-value < 0.05. Error bars indicate 95% CIs.
VAS, Visual Analog Scale; SNS, supraorbital nerve stimulation; SNB, supraorbital nerve block; CI, confidence interval

Table 3. *Outcome measures at 12 weeks.*

	SNS Group	Intragroup Difference *P*-value	SNB-SNS Group	Intragroup Difference *P*-value	Mean Difference (95% CI)	Odds Ratio (95% CI)	Intergroup Difference *P*-value
PSQI, n Baseline, median (IQR) 12 Weeks, median (IQR)	18 12 (4.75) 3 (4.25)	< 0.001[a]	16 15 (4.75) 4 (5.75)	< 0.001[a]			0.17 0.374
Ophthalmic neuralgia, n Ophthalmic pain relief (≥50%), n (%)	15 10 (66.67)		11 6 (54.55)			0.6 (0.12 to 2.97)	0.689
Drug therapy, n Opioids: Baseline, n (%) 12 Weeks, n (%) Anticonvulsants: Baseline, n (%) 12 weeks, n (%)	18 16 (88.89) 3 (16.67) 16 (88.89) 5 (27.78)	< 0.001[b] < 0.001[b]	16 15 (93.75) 4 (25) 13 (81.25) 5 (31.25)	< 0.001[b] 0.011[b]		1.67 (0.31 to 8.93) 1.18 (0.27 to 5.18)	0.681 1

$P < 0.05$ indicates a statistically significant difference.
(a): Wilcoxon signed-rank test, $P < 0.05$; (b): Fisher's exact test, $P < 0.05$.
SD, standard deviation; IQR, interquartile range.

lodgments or fractures occurred during treatment, and at no point during the trial did any patient experience complications requiring emergency treatment. These findings indicate that between PRF of the semilunar ganglion and SNS, the latter is the safer, more beneficial method of PHN prevention for elderly patients.

In our past clinical practice, the intervention for elderly patients with HZO tended to be more active and aggressive because once PHN developed, the condition would be burdensome for the patients and their families. Therefore, an SNB was initially performed during the visit to the clinic, and SNS was performed if the SNB was ineffective. If SNS did not provide adequate pain control, the patients were hospitalized and given PRF of the semilunar ganglion. The current findings show that SNS can be the first-line modality for patients with HZO and help them avoid repeated puncture. However, there is currently no evidence regarding the appropriate indication for PRF of the semilunar ganglion or SNS. Further research is needed to obtain evidence and guide clinical decision-making.

This study had some limitations. Studies of "tonic" PNS are challenging to conduct in a double-blind manner because of the operation process and the perceptible paresthesia experienced by patients. The lack of blinding makes assessments susceptible to evaluation bias. Our inclusion criteria limited the course of disease under study to 2 months because doing so was necessary to ensure that the patients were in the acute or subacute phase (within 3 months) before crossover. Because of the rare recurrence of PHN, the follow-up period was 3 months. The pain assessment in this study was not comprehensive due to the insufficient quantity or absence of records of breakout pain in patients with poor communication skills, both verbal and physical.

Conclusions

Short-term SNS is feasible and improves pain relief and sleep quality for patients with acute or subacute ophthalmic herpetic neuralgia. A combination of SNS and SNB does not provide better clinical benefits than SNS alone.

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