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Article

Botulinum Toxin Type A Combined with Fire Needling for Postherpetic Neuralgia: A Randomized Controlled Trial

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Abstract: Objective: To compare the efficacy and safety of subcutaneous botulinum toxin type A (BTX-A) injection, fire needling, and their combination in patients with postherpetic neuralgia (PHN), with particular attention to whether the combined regimen sustains its benefit over six months. **Methods:** In this randomized controlled trial, 99 patients with PHN attending the outpatient and inpatient services of the Department of Rehabilitation Medicine, Gaoming District People's Hospital of Foshan, between January 2024 and March 2025 were allocated 1:1:1 by a random number table to group A (subcutaneous BTX-A, n = 33), group B (fire needling, n = 33), or group C (BTX-A plus fire needling, n = 33). All patients received oral gabapentin 300 mg/d as background therapy. The primary outcome was pain intensity on the visual analogue scale (VAS) at 3 d, 15 d, 1 month, 3 months and 6 months. Secondary outcomes were the Self-Rating Scale of Sleep (SRSS), the proportion of patients achieving ≥50% reduction in VAS, the Patient Global Impression of Change (PGIC), the distribution of efficacy grades, and adverse events. **Results:** Ninety patients completed the study (30 per group). Mixed-effects models showed significant group × time interactions for both VAS and SRSS (both $p < 0.001$). VAS differed among groups at every post-treatment time point (all $p < 0.001$). From day 15 onward, VAS was lower in group C than in groups A and B (all $p < 0.001$), whereas groups A and B did not differ at any time point (all $p > 0.05$). At 6 months, VAS was 1.34 ± 0.64 in group C, 2.99 ± 1.13 in group A and 2.88 ± 0.98 in group B (both $p < 0.001$). The 6-month responder rate was 100.0% (30/30) in group C, 66.7% (20/30) in group A and 76.7% (23/30) in group B ($p < 0.001$). SRSS was lowest in group C at every time point, reaching 37.30 ± 4.94 at 6 months ($p < 0.001$). At 6 months, 30 patients (100.0%) in group C reported a PGIC of "improved" or better, compared with 21 (70.0%) in group A and 24 (80.0%) in group B ($p = 0.006$). Adverse events were mild in all three groups and no serious adverse event occurred. **Conclusion:** Subcutaneous BTX-A injection and fire needling each relieve pain and improve sleep in PHN, with comparable efficacy. The combined regimen acts faster and achieves a higher peak response, with no attenuation over six months of observation.

Keywords: postherpetic neuralgia; botulinum toxin type A; fire needling; combined therapy; randomized controlled trial

1. Introduction

Postherpetic neuralgia (PHN) is neuropathic pain persisting for more than one month after the rash of herpes zoster has healed, and is the most common sequela of herpes zoster [1]. Its incidence rises with age, reaching 20–30% among patients with herpes zoster over 60 years old [2], and the burden among older adults in China is increasing [3]. The pain is usually continuous and burning, or paroxysmal and shooting, and is often accompanied by allodynia. Sleep disturbance, low mood, and reduced capacity for work and social activity are common, and in some patients the condition lasts for years.

First-line pharmacotherapy for PHN comprises the α2-δ ligands (gabapentin and pregabalin), tricyclic antidepressants and 5% lidocaine patches [4]. Gabapentin is the most widely used background drug in China, but

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its overall analgesic response rate as monotherapy is only 27.6–33.3% [5], and sedation, dizziness and peripheral oedema limit dose escalation. Nerve blocks, pulsed radiofrequency and spinal cord stimulation are reasonably effective, but they require equipment and expertise, are costly, and are difficult to deliver in primary care [6]. For primary-level hospitals, what is lacking is an adjunctive approach that is simple, inexpensive and practically deliverable.

Botulinum toxin type A (BTX-A) cleaves synaptosomal-associated protein 25 (SNAP-25), inhibiting the release of substance P, calcitonin gene-related peptide (CGRP) and glutamate from peripheral nerve terminals, thereby blocking the peripheral transmission of nociceptive signals and reducing central sensitization. Several randomized controlled trials have shown an analgesic effect in PHN [7–9]. Xiao et al. [10] conducted a parallel, double-blind, single-dose, placebo-controlled study and confirmed that subcutaneous BTX-A reduced VAS in PHN and that the effect was maintained to 12 weeks. Most of these studies, however, examined only short-term outcomes (within 12 weeks); how long the effect of BTX-A lasts has been reported inconsistently [11], and neither the dose–response relationship of a single injection nor the optimal interval for repeat treatment has been settled.

Fire needling is an external therapy of traditional Chinese medicine in which a red-hot needle is thrust rapidly into tender points. Traditionally it is held to warm and unblock the channels and to "open the gate" to drive out pathogenic factors; the *Lingshu·Guanzhen* states that "cui needling means needling with a heated needle to treat bi syndrome". Contemporary work suggests that the local thermal effect of fire needling raises the pain threshold, improves microcirculation, reduces the release of inflammatory mediators and promotes repair of damaged nerves [12,13]. Fire needling and filiform fire needling have been reported to improve pain and sleep in PHN [14,15], but most studies are single-centre and small, and none has made a direct comparison with a Western medical treatment. Both the magnitude of the effect and the mechanism therefore remain unclear.

BTX-A acts on transmitter release from peripheral nerve terminals, whereas fire needling acts on local tissue and the microcirculation. Combining the two might yield a faster onset, a higher peak effect, and protection against the waning of efficacy seen with single-modality treatment after a few months. No study has yet compared the combination directly with either modality alone.

We therefore conducted a randomized controlled trial comparing subcutaneous BTX-A, fire needling and their combination, with follow-up to six months, to assess short- and medium-term effects on pain and sleep, to evaluate patient-perceived benefit using the ≥50% responder rate and the PGIC, and to determine whether the benefit of the combined regimen is maintained to six months.

2. Methods

2.1. Study Design and Ethics

This was a single-centre, three-arm, parallel, randomized controlled trial conducted in the Department of Rehabilitation Medicine, Gaoming District People's Hospital of Foshan, between January 2024 and December 2025, with follow-up closing in September 2025. The protocol was approved by the Medical Ethics Committee of the hospital (approval No. GMQRM-2024-011). All patients gave written informed consent before enrolment.

2.2. Participants

Inclusion criteria: (1) meeting the diagnostic criteria for PHN [1], i.e., pain persisting ≥ 1 month after healing of the herpes zoster rash; (2) age ≥ 50 years, either sex; (3) baseline VAS ≥ 4; (4) alert and able to understand and complete the rating scales; (5) no analgesic treatment of any kind (including non-steroidal anti-inflammatory drugs, opioids and nerve blocks) within 7 d before enrolment; (6) willingness to participate and provision of written informed consent.

Exclusion criteria: (1) severe cardiac, cerebral, hepatic or renal disease, or malignancy; (2) acute herpes zoster with unhealed rash; (3) special forms of herpes zoster (ophthalmic, otic or meningeal); (4) disorders of the neuromuscular junction such as myasthenia gravis, motor neuron disease or Lambert–Eaton syndrome; (5) known hypersensitivity to components of the BTX-A preparation, intolerance of fire needling, or keloid diathesis; (6) skin infection, ulceration or open wound at the treatment site; (7) pregnancy or lactation; (8) coagulopathy or current anticoagulant therapy; (9) BTX-A treatment within the preceding 3 months; (10) poor compliance or an expectation of being unable to complete 6-month follow-up.

Withdrawal criteria: patients found after enrolment not to meet the inclusion criteria were excluded. Serious adverse events, the need to add another analgesic modality, voluntary withdrawal, or loss to follow-up were counted as discontinuation. Data collected before discontinuation were retained and analysed on an intention-to-treat basis.

2.3. Randomization and Blinding

A statistician not involved in clinical care generated the randomization sequence with SPSS 22.0. Opaque sealed envelopes were prepared in a 1:1:1 ratio and opened in order of enrolment. Because fire needling produces marked heat and pain, blinding of operators and patients was not feasible; only the assessor was blinded. VAS, SRSS and PGIC were rated by an independent rehabilitation therapist unaware of group assignment, and data entry and statistical analysis were performed independently by third parties.

2.4. Interventions

All patients received background therapy: gabapentin capsules (Jiangsu Enhua Pharmaceutical Co., Ltd., Xuzhou, China; approval No. H20052318) 300 mg orally once nightly, with the dose held constant throughout the observation period; mecobalamin 0.5 mg three times daily; and no other analgesic agents during treatment.

Group A (BTX-A)

Lyophilized BTX-A for injection (Lanzhou Institute of Biological Products Co., Ltd., Lanzhou, China; approval No. S10970037), 100 U per vial, was stored at 2–8 °C and reconstituted immediately before use with 0.9% sodium chloride to 50 U/mL. With the patient in a comfortable position and the painful area fully exposed, the most tender points and the borders of the allodynic area were marked with methylene blue. A 1 mL syringe with a 4-gauge needle was used to inject at multiple intradermal and superficial subcutaneous points along the course of the affected dermatomal nerve, predominantly proximal to the nerve distribution, at 5 U per point and approximately 2 cm between points, to a total of 50–100 U (maximum 100 U). Pressure was applied after injection and patients were observed for 30 min before discharge. A single treatment was given, with no repeat injection during the observation period.

Group B (fire needling)

He's fire needles (Beijing He's Acupuncture Instrument Co., Ltd., Beijing, China; 0.5 mm × 25 mm) were used. With the patient seated or supine and the painful area exposed, distinct tender points were marked with gentian violet, and the area within a 2 cm radius of each point constituted the needling field. After routine disinfection with povidone-iodine, the anterior third of the needle was heated in the outer flame of an alcohol lamp until white-hot and then thrust rapidly into the point (depth 2–3 mm, withdrawal after approximately 0.1 s), once per point, with 5–8 points treated per session, twice weekly. Treatment was given once daily on days 1 and 2, then every other day; five sessions constituted one course and two courses (10 sessions) were given. After treatment, pressure was applied with a sterile dry cotton ball and the area was kept dry for 24 h. No lidocaine was applied.

Group C (combination)

Fire needling was performed first, exactly as in group B. Immediately afterwards, BTX-A was injected as in group A, with injection sites at least 1 cm from that day's fire-needling points. BTX-A was given once and fire needling was completed as two courses per the group B protocol.

The observation period was 6 months in all groups. If VAS reached ≥7 and the patient requested relief, paracetamol (≤2 g/d) was permitted as rescue analgesia and the amount recorded; such patients were not withdrawn, but were counted in the rescue analgesia rate.

2.5. Outcomes

Primary outcome

Pain intensity, measured with a VAS: patients marked their current pain on a 10 cm horizontal scale, where 0 indicated no pain and 10 intolerable pain. Assessments were made before treatment (baseline) and at 3 d, 15 d, 1 month, 3 months and 6 months after treatment.

Secondary outcomes

(1) Sleep: the Self-Rating Scale of Sleep (SRSS) [16], comprising 10 items each scored 1–5. The raw score ranges from 10 to 50 and the standard score, obtained by doubling the raw score, from 20 to 100; higher scores indicate worse sleep disturbance. Assessed at the same time points as VAS.

(2) ≥50% responder rate: a reduction in VAS of ≥50% from baseline was defined as a response, and the responder rate was calculated at each time point, in line with the IMMPACT core outcome framework for PHN [17].

(3) Patient Global Impression of Change (PGIC): assessed at 6 months on a 7-point scale (1 = much improved, 2 = improved, 3 = minimally improved, 4 = no change, 5 = minimally worse, 6 = much worse, 7 = very much worse). Grades 1–2 were defined as "substantially effective".

(4) Efficacy grades: at 6 months, patients were graded by the percentage reduction in VAS as clinically cured (≥75%), markedly effective (50–74%), effective (25–49%) or ineffective (<25%). The total effective rate was (clinically cured + markedly effective + effective)/total × 100%.
(5) Rescue analgesia rate and change in gabapentin dose.
(6) Safety: all adverse events during treatment and follow-up were recorded, including injection-site pain, local swelling, ecchymosis, transient muscle weakness, needling pain, local erythema, pruritus, pigmentation, dizziness and somnolence. Causality was judged and severity graded as mild, moderate or severe. Blood count, urinalysis, liver and renal function, coagulation profile and electrocardiography were performed before and after treatment.

2.6. Quality Control

All fire needling was performed by the same acupuncture physician with more than five years of fire-needling experience, and all BTX-A injections by the same attending physician. Assessors received uniform training and used standardized instructions for the VAS and SRSS; inter-rater agreement was checked in a random 10% sample and the intraclass correlation coefficient was 0.91. Data were recorded on case report forms, entered independently in duplicate, checked, and the database locked after logical verification.

2.7. Statistical Analysis

Analyses were performed with SPSS 22.0 and R 4.3.1. Continuous variables are presented as mean ± SD. Comparisons among more than two groups used one-way analysis of variance. Within-group comparisons of each time point against baseline used the paired *t* test or the Wilcoxon signed-rank test according to the Shapiro–Wilk test for normality, with the LSD procedure for multiple comparisons; pairwise between-group comparisons were additionally verified with the Mann–Whitney U test. Categorical variables are presented as n (%) and compared with the χ^2 test or Fisher's exact test; ordinal variables were compared with the Kruskal–Wallis H test. To exploit the longitudinal data and account for within-patient correlation, the primary efficacy analysis used a linear mixed-effects model with group, time and group × time interaction as fixed effects and a random intercept for each patient; the interaction was tested by likelihood ratio. Two-sided $p < 0.05$ was considered statistically significant. Sample size was estimated from pilot data: an expected 6-month VAS difference of 0.8 between the combination and monotherapy groups with a pooled SD of 1.0, $\alpha = 0.05$ (two-sided) and power of 0.80 required 26 patients per group; allowing for 20% attrition, 33 patients were enrolled per group.

3. Results

3.1. Patient Disposition and Baseline Characteristics

Of 124 patients with PHN screened, 25 were excluded (13 did not meet the inclusion criteria, 8 declined to participate and 4 were receiving other analgesic therapy), and 99 were randomized, 33 per group. Nine patients discontinued (group A, 3: 2 lost to follow-up, 1 withdrew consent; group B, 3: 2 lost to follow-up, 1 referred to surgery; group C, 3: 2 lost to follow-up, 1 withdrew because of an adverse event), an attrition rate of 9.1% with no difference among groups ($\chi^2 = 0.000$, $p = 1.000$). Ninety patients completed 6-month follow-up and were analysed, 30 per group (Figure 1).

The three groups did not differ significantly in sex, age, disease duration, site of lesions, baseline VAS or baseline SRSS (all $p > 0.05$) and were therefore comparable (Table 1).

Thirty-three patients were randomized to each group; three discontinued in each group, and 30 per group completed 6-month follow-up and were analysed.

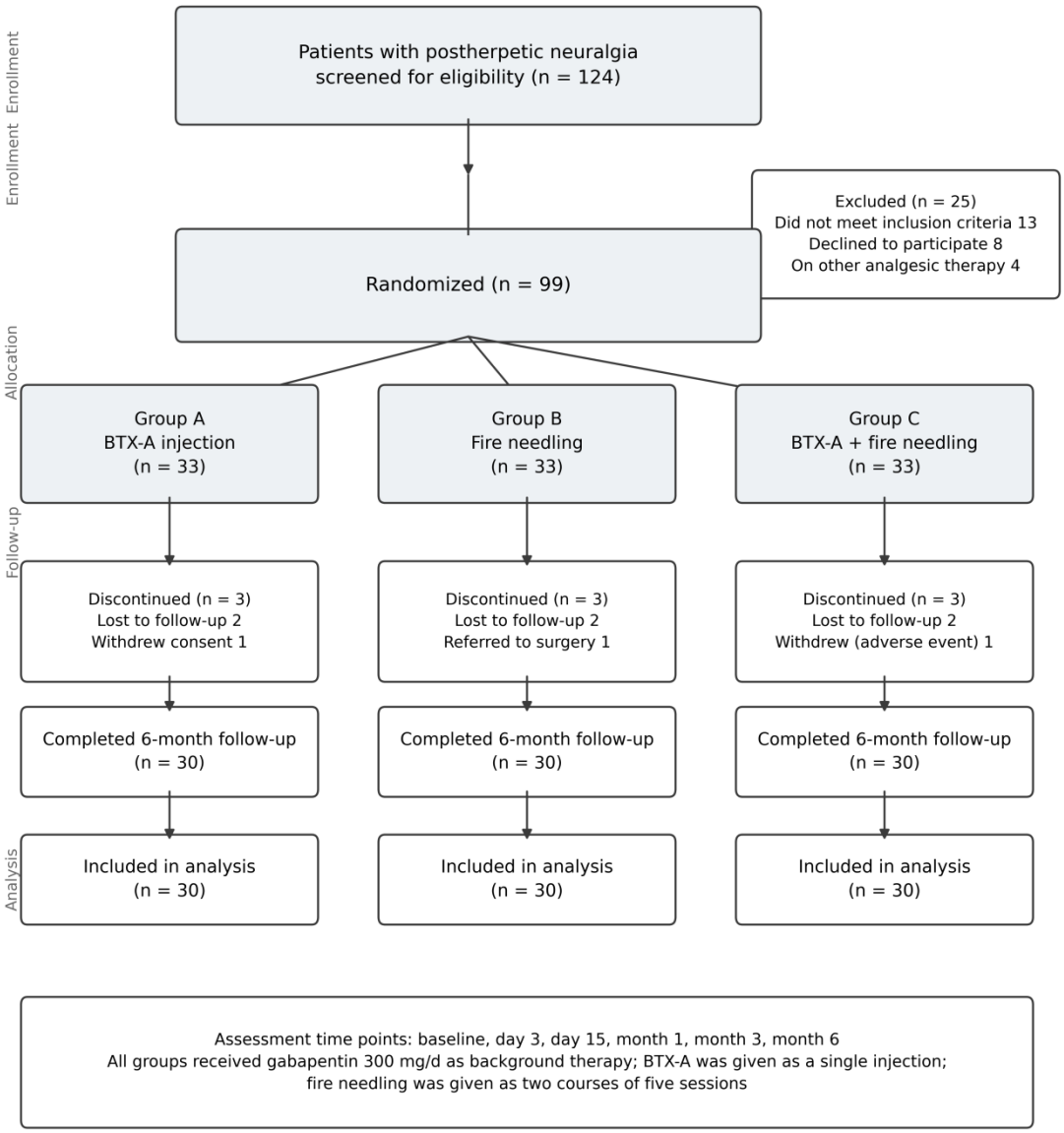


Figure 1. Patient screening, randomization and follow-up.

Table 1. Baseline characteristics of the three groups.

Characteristic	Group A (n = 30)	Group B (n = 30)	Group C (n = 30)	F/χ^2	p
Sex, male/female, n	16/14	13/17	13/17	0.804	0.669
Age, years	69.0 ± 7.7	65.9 ± 8.4	65.2 ± 7.8	1.930	0.151
Disease duration, d	85 ± 50	76 ± 39	85 ± 40	0.430	0.652
Site of lesions, n				9.477	0.148
Thoracodorsal	12	12	10		
Lumbosacral	12	7	15		
Cranial	4	8	1		
Limbs	2	3	4		
Baseline VAS	6.76 ± 1.01	6.98 ± 1.04	6.46 ± 1.11	1.842	0.165
Baseline SRSS	65.27 ± 7.51	63.63 ± 8.16	62.08 ± 8.99	1.123	0.330

Note: VAS, visual analogue scale; SRSS, Self-Rating Scale of Sleep (standard score). Values are mean ± SD. Sex and site of lesions were compared with the χ^2 test; other variables with one-way ANOVA.

3.2. Pain Intensity (VAS)

In the linear mixed-effects model, the main effect of group (LR $\chi^2 = 95.95$, $p < 0.001$), the main effect of time ($p < 0.001$) and the group × time interaction (LR $\chi^2 = 44.00$, df = 10, $p < 0.001$) were all statistically significant,

indicating that the trajectories of pain reduction differed among the three groups (Figure 2A). Individual trajectories are shown in Figure 3.

VAS differed among groups at every post-treatment time point (all $p < 0.001$). On pairwise comparison, VAS at 3 d was already lower in group C than in group A ($p = 0.003$) and group B ($p < 0.001$), while groups A and B did not differ ($p = 0.282$). At 15 d, 1 month, 3 months and 6 months, VAS in group C was lower than in groups A and B (all $p < 0.001$), and groups A and B never differed (all $p > 0.05$). The Mann–Whitney U test gave consistent results (Table 2). At 6 months, VAS was 1.34 ± 0.64 in group C, 2.99 ± 1.13 in group A and 2.88 ± 0.98 in group B (Table 3).

In groups A and B, VAS was lowest at 3 months (2.86 ± 1.06 and 2.91 ± 0.99, respectively) and rose slightly by 6 months (2.99 ± 1.13 and 2.88 ± 0.98). In group C, VAS was 1.05 ± 0.66 at 3 months and 1.34 ± 0.64 at 6 months, so the curve was essentially flat. The change in VAS between 3 and 6 months did not differ among groups ($F = 1.892$, $p = 0.157$); the rebound was too small to separate statistically at this sample size, and its clinical relevance will require longer follow-up.

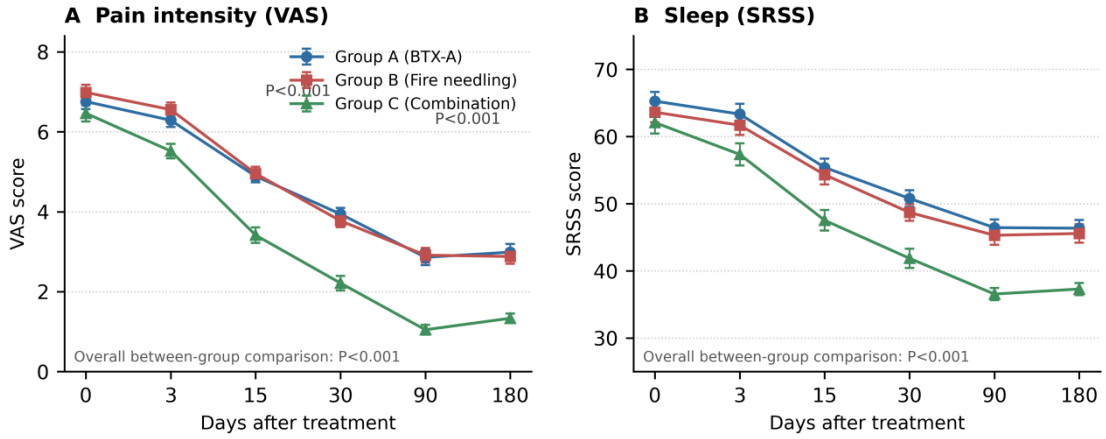


Figure 2. Time course of VAS and SRSS in the three groups. Data are mean ± SEM. (**A**) VAS score; (**B**) SRSS standard score. Between-group comparisons by one-way ANOVA.

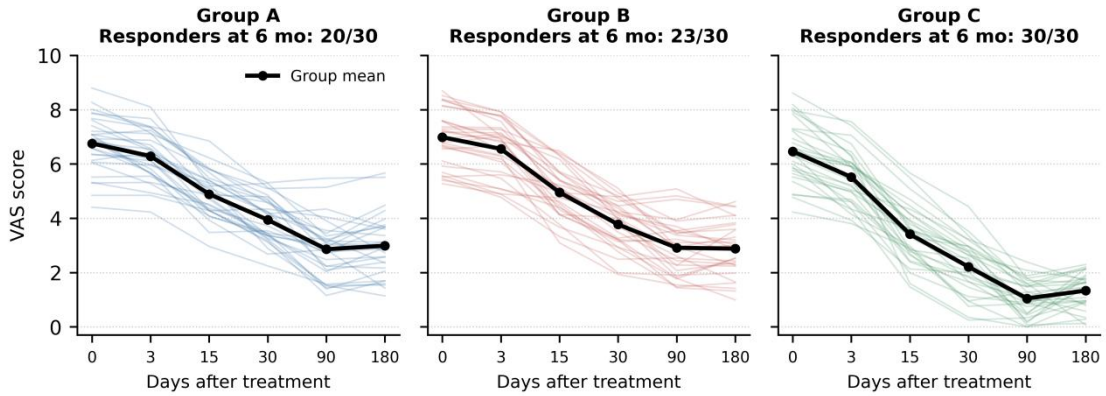


Figure 3. Individual pain trajectories in the three groups. Thin lines represent individual patients and the thick black line the group mean; the number of 6-month responders is given in each panel title.

Table 2. VAS scores at each time point in the three groups.

Time Point	Group A (n = 30)	Group B (n = 30)	Group C (n = 30)	*F*	*p*
Baseline	6.76 ± 1.01	6.98 ± 1.04	6.46 ± 1.11	1.842	0.165
3 d	6.29 ± 0.91	6.55 ± 0.99	5.52 ± 0.99 ab	9.333	<0.001
15 d	4.89 ± 0.83 c	4.95 ± 0.92 c	3.41 ± 1.07 abc	25.454	<0.001
1 month	3.94 ± 0.83 c	3.77 ± 0.86 c	2.21 ± 0.99 abc	33.804	<0.001
3 months	2.86 ± 1.06 c	2.91 ± 0.99 c	1.05 ± 0.66 abc	39.667	<0.001
6 months	2.99 ± 1.13 c	2.88 ± 0.98 c	1.34 ± 0.64 abc	29.095	<0.001

Note: Values are mean ± SD. a: $p < 0.05$ vs group A; b: $p < 0.05$ vs group B; c: $p < 0.05$ vs baseline within the same group.

Table 3. Within-group change in VAS and SRSS and 6-month outcomes.

Variable	Group A (n = 30)	Group B (n = 30)	Group C (n = 30)	F/χ^2	*p*
Reduction in VAS	3.77 ± 1.59	4.10 ± 1.42	5.13 ± 1.48 ab	6.684	0.002
Reduction in VAS, %	54.5 ± 19.0	57.7 ± 17.0	78.0 ± 12.3 ab	18.945	<0.001
Reduction in SRSS	18.92 ± 8.12	18.06 ± 7.67	24.78 ± 8.76 ab	5.978	0.004
VAS ≤ 3, n (%)	16 (53.3)	17 (56.7)	30 (100.0) ab	19.459	<0.001
PGIC ≥ improved, n (%)	21 (70.0)	24 (80.0)	30 (100.0) ab	10.080	0.006
Rescue analgesia, n (%)	7 (23.3)	6 (20.0)	1 (3.3)	5.259	0.072

Note: a: $p < 0.05$ vs group A; b: $p < 0.05$ vs group B. All values refer to the 6-month time point; reductions in VAS and SRSS are mean ± SD. PGIC, Patient Global Impression of Change.

3.3. Sleep (SRSS)

SRSS declined over time in all three groups (each time point vs baseline, all $p < 0.001$), and the group × time interaction was significant (LR $\chi^2 = 57.78$, $p < 0.001$). SRSS already differed among groups at 3 d ($F = 4.027$, $p = 0.021$): it was lower in group C than in group A ($p = 0.010$) but did not differ from group B ($p = 0.051$). From day 15 onward, SRSS in group C was consistently lower than in groups A and B (all $p < 0.01$), and groups A and B did not differ at any time point (all $p > 0.05$) (Table 4, Figure 2B).

At 6 months, SRSS had fallen to 46.35 ± 6.78, 45.57 ± 7.56 and 37.30 ± 4.94 in groups A, B and C, reductions of 18.92 ± 8.12, 18.06 ± 7.67 and 24.78 ± 8.76, respectively; the reduction in group C was greater than in groups A and B (both $p < 0.05$). At 6 months, VAS and SRSS were strongly correlated ($r = 0.811$, $p < 0.001$), as they were at 1 month ($r = 0.709$, $p < 0.001$), so improvement in sleep largely followed the relief of pain.

Table 4. SRSS standard scores at each time point in the three groups.

Time Point	Group A (n = 30)	Group B (n = 30)	Group C (n = 30)	*F*	*p*
Baseline	65.27 ± 7.51	63.63 ± 8.16	62.08 ± 8.99	1.123	0.330
3 d	63.34 ± 8.47	61.69 ± 7.88	57.35 ± 8.98 a	4.027	0.021
15 d	55.40 ± 7.22c	54.32 ± 7.91c	47.53 ± 8.33 abc	8.901	<0.001
1 month	50.78 ± 6.73c	48.70 ± 6.74c	41.87 ± 7.88 abc	12.796	<0.001
3 months	46.44 ± 6.69c	45.30 ± 7.78c	36.55 ± 4.92 abc	20.344	<0.001
6 months	46.35 ± 6.78c	45.57 ± 7.56c	37.30 ± 4.94 abc	17.751	<0.001

Note: Values are mean ± SD. a: $p < 0.05$ vs group A; b: $p < 0.05$ vs group B; c: $p < 0.05$ vs baseline within the same group.

3.4. ≥50% Responder Rate

The responder rate differed among groups at every time point (Table 5, Figure 4A). At 15 d it was 40.0% (12/30) in group C, higher than in group A (0/30) and group B (3.3%, 1/30) ($p < 0.001$). At 1 month it reached 90.0% (27/30) in group C, compared with 26.7% (8/30) in group A and 40.0% (12/30) in group B ($p < 0.001$). At 6 months it was 100.0% (30/30) in group C, 66.7% (20/30) in group A and 76.7% (23/30) in group B ($\chi^2 = 11.459$, $p = 0.003$); group C was higher than both groups A and B ($p = 0.002$ and $p = 0.016$), and groups A and B did not differ ($p = 0.567$). In groups A and B the responder rate peaked at 3 months (73.3% and 76.7%) and then fell by 6 months, whereas in group C it reached 100% at 3 months and was maintained to 6 months.

Table 5. responder rate and PGIC in the three groups, n (%).

Variable	Group A (n = 30)	Group B (n = 30)	Group C (n = 30)	χ^2	*p*
Responders at 15 d	0 (0.0)	1 (3.3)	12 (40.0)ab	23.916	<0.001
Responders at 1 month	8 (26.7)	12 (40.0)	27 (90.0)ab	26.809	<0.001
Responders at 3 months	22 (73.3)	23 (76.7)	30 (100.0)ab	9.120	0.010
Responders at 6 months	20 (66.7)	23 (76.7)	30 (100.0)ab	11.459	0.003
PGIC grade 1	12 (40.0)	10 (33.3)	22 (73.3)	—	—
PGIC grade 2	9 (30.0)	14 (46.7)	8 (26.7)	—	—
PGIC grade 3	6 (20.0)	5 (16.7)	0 (0.0)	—	—
PGIC grade 4	3 (10.0)	1 (3.3)	0 (0.0)	—	—
PGIC ≥ improved	21 (70.0)	24 (80.0)	30 (100.0)ab	10.080	0.006

Note: a$P < 0.05$ vs group A; b$P < 0.05$ vs group B. Response was defined as a ≥50% reduction in VAS from baseline. PGIC grades 1–4 are much improved, improved, minimally improved and no change.

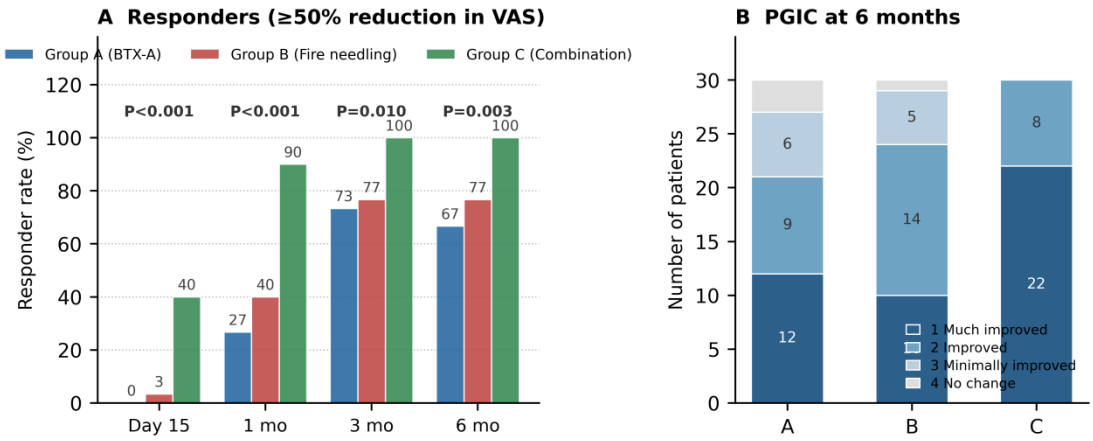


Figure 4. Responder rate and PGIC distribution at 6 months. (**A**) proportion of patients with a ≥50% reduction in VAS from baseline at each time point; (**B**) distribution of PGIC grades (1–4) at 6 months.

3.5. PGIC and Efficacy Grades

At 6 months, PGIC was grade 1 (much improved) in 22 patients (73.3%) and grade 2 in 8 (26.7%) in group C, with no patient in grade 3 or 4; grades 1–4 comprised 12, 9, 6 and 3 patients in group A and 10, 14, 5 and 1 in group B (Table 5, Figure 4B). Taking grades 1–2 as "substantially effective", this was achieved by 100.0% (30/30) in group C, higher than 70.0% (21/30) in group A and 80.0% (24/30) in group B ($\chi^2 = 10.080$, $p = 0.006$). The Kruskal–Wallis test also showed a difference in PGIC distribution among groups ($H = 13.258$, $p = 0.001$), with group C better than group A ($p = 0.002$) and group B ($p < 0.001$), and no difference between groups A and B ($p = 0.875$).

When graded by percentage reduction in VAS at 6 months, group C had 17 clinically cured and 13 markedly effective patients and no effective or ineffective cases; group A had 5 clinically cured, 15 markedly effective, 7 effective and 3 ineffective; and group B had 5, 18, 5 and 2, respectively (Table 6). The distribution of efficacy grades differed among groups ($H = 19.641$, $p < 0.001$), with group C better than groups A and B (both $p < 0.001$) and no difference between groups A and B ($p = 0.541$). The total effective rate was 90.0% (27/30), 93.3% (28/30) and 100.0% (30/30) in groups A, B and C, respectively, with no significant difference (Fisher's exact test, $p = 0.278$). The difference lay in the "clinically cured" category, which was larger in group C, and in the absence of any effective or ineffective cases ($p < 0.001$).

Table 6. Efficacy grades at 6 months, n (%).

Group	Clinically Cured	Markedly Effective	Effective	Ineffective	Total Effective
A (n = 30)	5 (16.7)	15 (50.0)	7 (23.3)	3 (10.0)	27 (90.0)
B (n = 30)	5 (16.7)	18 (60.0)	5 (16.7)	2 (6.7)	28 (93.3)
C (n = 30)	17 (56.7) ab	13 (43.3)	0 (0.0)	0 (0.0)	30 (100.0)

Note: a: $p < 0.05$ vs group A; b: $p < 0.05$ vs group B. Total effective rate = (clinically cured + markedly effective + effective)/total × 100%.

3.6. Rescue Analgesia and Safety

During the observation period, rescue paracetamol was taken by 7 patients (23.3%) in group A, 6 (20.0%) in group B and 1 (3.3%) in group C; the overall difference was not significant ($\chi^2 = 5.259$, $p = 0.072$), and pairwise comparisons between group C and the two monotherapy groups were only marginal (vs group A, $p = 0.052$; vs group B, $p = 0.103$). The need for rescue analgesia appeared lower in the combination group, but at this sample size no conclusion can be drawn. The gabapentin dose remained at 300 mg/d throughout in all three groups, with no escalation.

A total of 44 adverse events were recorded in 27 patients during treatment and follow-up: 8 (26.7%) in group A, 11 (36.7%) in group B and 8 (26.7%) in group C, with no significant difference in incidence ($\chi^2 = 0.938$, $p = 0.626$). All adverse events were mild and, apart from symptomatic treatment, required no specific intervention; all resolved spontaneously within 1–7 d. There were no serious adverse events, no permanent discontinuation due to an adverse event, and no systemic botulinum toxin toxicity. Injection-site pain (6 events) and local swelling/ecchymosis (4 events) predominated in group A; needling pain (7 events), local erythema (5 events) and

pruritus (3 events) predominated in group B; the profile in group C was similar to those of the monotherapy groups (Table 7). No clinically meaningful abnormality was found in blood count, urinalysis, liver or renal function, coagulation profile or electrocardiography before or after treatment.

Table 7. Adverse events in the three groups, number of events.

Adverse Event	Group A (n = 30)	Group B (n = 30)	Group C (n = 30)
Injection-site pain	6	—	5
Local swelling/ecchymosis	4	3	2
Transient muscle weakness	1	—	1
Dizziness	2	—	1
Needling pain	—	7	4
Local erythema	—	5	3
Pruritus	—	3	1
Pigmentation	—	2	1
Patients with any adverse event, n (%)	8 (26.7)	11 (36.7)	8 (26.7)

Note: A patient could experience more than one adverse event, so the number of events exceeds the number of patients.

4. Discussion

4.1. Comparison of the Three Regimens

In this study, subcutaneous BTX-A and fire needling used alone both reduced VAS and improved sleep, and no outcome differed between them over six months. The two approaches were therefore of comparable efficacy. This is consistent with previous reports: Xiao et al. [10] found that VAS fell from 6.4 at baseline to 3.1 after BTX-A injection and remained there for 12 weeks, and the meta-analysis by Shackleton et al. [18] of several randomized trials concluded that BTX-A has a moderate analgesic effect in PHN. Fire needling has been reported to improve pain and sleep [14,15], but direct randomized comparison with a Western medical treatment has been lacking. To the best of our knowledge, this is the first randomized controlled trial to compare fire needling with BTX-A head to head.

The advantage of the combination was evident from day 3, when VAS in group C was already below that of both monotherapy groups and the 15-day responder rate was 40.0%, compared with 0 and 3.3% in groups A and B. By 6 months, 100% of patients in group C had achieved a ≥50% reduction, VAS had fallen to 1.34 and patients were essentially pain-free, with 100% reporting a PGIC of grade 1–2 and no patient in the effective, ineffective or unchanged categories. VAS in groups A and B was lowest at 3 months and rose by 0.13 and 0.03 points, respectively, by 6 months (between-group comparison, $p = 0.157$), with a corresponding slight fall in responder rate (group A, from 73.3% to 66.7%); group C remained essentially flat between 3 and 6 months and the responder rate stayed at 100%. The magnitude of this rebound could not be distinguished statistically at our sample size, but its direction agrees with the pharmacological profile of single-dose BTX-A, whose effect lasts about 3–4 months [11], and it offers a lead on the question of how long the effect is maintained, which has been reported inconsistently [11]. Whether this represents true loss of efficacy will require longer follow-up.

4.2. Possible Mechanisms of Synergy

The analgesic action of BTX-A is mainly peripheral. After cleaving SNAP-25 it blocks vesicular release from the central and peripheral terminals of primary sensory neurons, reducing the release of substance *p*, CGRP and glutamate and thereby decreasing peripheral sensitization and neurogenic inflammation [7,8]. It does not act through the opioid system and does not affect sensory or motor function, so there is no central sedation or risk of dependence. Its limitations are twofold: the analgesic field is confined to the area covered by injection, and SNAP-25 in nerve terminals is resynthesized after approximately 3 months, so the effect weakens.

The action of fire needling is more localized and involves more than one pathway. A needle heated until white-hot (about 1000 °C) and inserted briefly causes a controlled local thermal injury that induces heat shock protein expression and the release of endogenous opioid peptides; it dilates local vessels and improves microcirculation, accelerating the clearance of inflammatory mediators; the intense “counter-irritant” stimulation activates large-fibre afferents and produces a gate-control effect in the dorsal horn; and it promotes local tissue repair and nerve regeneration [12,13]. These effects act quickly but depend on repeated sessions, which is consistent with the limited effect at day 3 and the rapid improvement after day 15 in group B.

The two may interact as follows. Fire needling first improves the local microenvironment and microcirculation, creating better conditions for the diffusion and uptake of BTX-A. The repeated gate-control

effect of fire needling covers the latency before BTX-A takes effect (usually 3–7 d). BTX-A, by continuously suppressing peripheral transmitter release, offsets the dependence of fire needling on the number of sessions. Group C was superior both early (day 3) and in the medium term (3–6 months), in keeping with this proposal. The proportion of clinically cured patients in group C was 56.7%, compared with 16.7% in each of groups A and B, indicating that the combination does not merely raise the mean response but brings more patients to complete relief. In a condition as refractory as PHN this difference is of practical importance.

As for sleep, SRSS fell in all three groups and at 6 months was strongly correlated with VAS ($r = 0.811$), so the improvement in sleep largely followed the relief of pain. The greater reduction in group C may reflect more complete pain relief; fire needling also has a calming effect [13], which may have contributed. The two contributions cannot be separated in this study.

4.3. Safety

No serious adverse event occurred in any group. Adverse reactions were mild and transient, with no difference in incidence among groups. Injection-site pain and ecchymosis predominated in group A, and transient muscle weakness occurred only once; there was no systemic weakness or dysphagia, indicating that a total dose of 50–100 U injected into a PHN dermatome is safe. Needling pain and local erythema predominated in group B, and the two cases of pigmentation resolved within 3 months. The adverse event profile in group C resembled those of the monotherapy groups, with no additive effect. The rescue analgesia rate in group C was only 3.3%, against 23.3% in group A and 20.0% in group B ($p = 0.072$), suggesting a more stable benefit, although this difference did not reach significance at the present sample size.

4.4. Limitations

Several limitations should be noted. The sample was small (30 per group); post hoc power analysis showed an effect size of Cohen's $d = 1.80$ for 6-month VAS with power >0.99, but this remains insufficient for subgroup analysis and for rare adverse events. Because fire needling cannot be blinded, only the assessor was blinded, and an expectancy effect on the part of patients cannot be excluded; a sham fire-needling control (blunt needle, light touch) should be considered in future. Follow-up of 6 months is short for a condition that may persist for years, and quality of life and mood (e.g., SF-36, HADS) were not assessed. Without a gabapentin-only control group, the incremental benefit of each regimen over background therapy cannot be quantified. BTX-A was given as a single injection only, and whether repeat injection or a higher dose would add further benefit was not examined. Finally, the mechanistic evidence rests on clinical measures alone, without confirmation from biological markers such as local cytokines or nerve growth factor.

4.5. Clinical implications and future directions

Treating PHN in primary care has long been hampered by effective options being expensive and affordable options being few. Fire needling is inexpensive and requires little equipment, and in this study its efficacy was comparable to that of BTX-A; used together, the two raised the ceiling of efficacy, acted faster and remained stable over 6 months. For primary-level departments with a good foundation in traditional Chinese medicine, such as rehabilitation and acupuncture departments, the combination is worth disseminating. Future work should enlarge the sample, extend follow-up beyond 12 months, add sham fire-needling and background-therapy controls, and measure local neuropeptides and inflammatory cytokines to clarify the mechanism; the optimal interval for repeat BTX-A injection, and differences in response according to disease duration and dermatomal distribution, also merit further study.

5. Conclusions

Subcutaneous botulinum toxin type A injection and fire needling are both safe and effective in postherpetic neuralgia, with comparable efficacy. Used together they act faster and produce a higher peak response, bringing more patients to complete relief of pain, with no attenuation over six months of observation. The combined regimen is worth recommending and is suitable for use in primary care.

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Conflicts of Interest

The author declares no conflict of interest.

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