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Original Article

Shaoyao Gancao decoction for neuropathic pain: a systematic review and meta-analysis of postherpetic neuralgia

Jinfeng Zhao, Fengyun Wang, Fang Wang, Ling Ma

Department of Dermatology, TCM Hospital of Wenjiang District, Chengdu 611130, Sichuan, China

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Abstract: Objective: To systematically evaluate the efficacy and safety of Shaoyao Gancao Decoction (SGD) for neuropathic pain (NP), with a focused analysis on postherpetic neuralgia (PHN), the most evidence-rich subtype, and to provide evidence for clinical decision-making. Methods: Randomized controlled trials (RCTs) on SGD for PHN were retrieved from databases up to March 2026. Two reviewers independently screened literature, extracted data, and assessed risk of bias using the Cochrane tool. Meta-analyses were performed using RevMan 5.3, and effect sizes were expressed as odds ratio (OR) or mean difference (MD) with 95% confidence intervals (CIs). Results: Fifteen RCTs involving 1,188 patients with PHN (594 per group) were included. Compared with conventional Western medicine alone, the addition of SGD significantly improved the overall response rate (OR=5.42, 95% CI: 3.40-8.64, P<0.0001), reduced Visual Analogue Scale (VAS) pain score (MD=-1.33, 95% CI: -1.68 to -0.99, P<0.0001), improved Pittsburgh Sleep Quality Index (PSQI) score (MD=-2.23, 95% CI: -2.85 to -1.62, P<0.0001), and lowered the incidence of adverse events (OR=0.34, 95% CI: 0.21-0.56, P<0.0001). Subgroup analyses by treatment duration (14 and 28 days) showed consistent analgesic effects and overall efficacy. Pain Rating Index (PRI) and Present Pain Intensity (PPI) scores were also significantly improved in the SGD group (both P<0.0001). Although high heterogeneity was observed in VAS (I^2=97%), subgroup and sensitivity analyses suggested that the pooled results remained robust. Given that PHN represents a common NP subtype, SGD may have potential therapeutic value for broader NP conditions. Conclusion: Current evidence supports SGD as an adjunctive therapy for PHN, with good efficacy and safety. Its potential value for other NP types (such as diabetic peripheral neuropathy, chemotherapy-induced neuropathy) warrants further research.

Keywords: Shaoyao Gancao decoction, neuropathic pain, postherpetic neuralgia, systematic review, meta-analysis, randomized controlled trial, clinical efficacy, safety

Introduction

Herpes zoster (HZ) is caused by reactivation of the varicella-zoster virus (VZV) in the dorsal root ganglia and is a relatively common clinical condition. It is characterized by unilateral vesicular clusters along affected peripheral nerves and is frequently associated with severe neuropathic pain. The acute phase typically lasts one to three weeks after infection [1]. Postherpetic neuralgia (PHN) is a common and troublesome long-term complication following VZV infection and may persist for over a month after resolution of the skin lesions [2]. The incidence of PHN increases significantly with age, reaching approximately 20% to 50% among people aged 60 years and older [3]. Clinically, PHN is characterized by spontaneous ongoing pain, hyperalgesia, allodynia, and neuropathic pruritus [4], which may further lead to sleep disorders, depression, reduced social functioning, and substantial impairment in quality of life. In severe cases, multi-modal integrated interdisciplinary management is required, posing a considerable economic burden on both patients and healthcare systems [5].

Currently, pharmacological management of PHN mainly includes calcium channel ligands (e.g., gabapentin and pregabalin), tricyclic antidepressants, opioids, and local anesthetics [6]. Although these agents can help alleviate acute

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pain, they are not universally effective. Many patients experience inadequate response to single-drug therapy due to the complex and heterogeneous nature of neuropathic pain. In addition, prolonged use of opioids may be associated with tolerance and dependence, while other drugs may be limited by side effects that compromise tolerability and adherence [7, 8]. Therefore, identifying alternative or adjunctive therapies with improved safety profiles and satisfactory efficacy is of great importance.

Neuropathic pain (NP) is a type of pain caused by lesion or disease affecting the somatosensory nervous system, and PHN represents one of the most common and well-studied subtypes of NP [9]. Shaoyao Gancao Decoction (SGD) originates from *Treatises on Cold Damage Diseases* (*Shang Han Lun*) written by Zhang Zhongjing during the early Eastern Han Dynasty. It consists of *Paeonia lactiflora Pall.* and *Glycyrrhiza uralensis Fisch*. SGD is a representative traditional Chinese medicine (TCM) formula that can relieve spasm and alleviate pain, and it has also been widely used in the management of muscle spasms and other internal disorders [10].

Recent pharmacological studies have suggested multiple mechanisms underlying the analgesic effects of SGD. Paeoniflorin and glycyrrhizin are thought to inhibit voltage-gated calcium channel activity in dorsal root ganglion neurons, reduce the expression of pro-inflammatory factors such as interleukin-1β (IL-1β) and tumor necrosis factor-α (TNF-α) in the spinal cord, and modulate glutamatergic synaptic transmission [11-13]. Additionally, studies on neuromuscular and synaptic regulation suggest that co-administration of paeoniflorin and glycyrrhizin may exert synergistic pharmacological effects, which may provide a mechanistic basis for the compatibility of the two herbs in SGD [14]. Animal studies have further demonstrated that SGD can alleviate mechanical allodynia and thermal hyperalgesia in neuropathic pain models, with effects comparable to pregabalin [15]. Collectively, these findings provide a solid theoretical basis supporting the potential clinical application of SGD in the management of NP, specifically PHN.

Recent clinical studies have investigated the application of SGD in PHN management. Several randomized controlled trials (RCTs) have reported that, when combined with conventional Western medical treatment, SGD may further reduce Visual Analogue Scale (VAS) pain scores, shorten time to pain relief, decrease opioid consumption, improve sleep quality, and enhance patient satisfaction [16-18]. In addition, SGD has demonstrated a favorable safety profile, with only mild gastrointestinal adverse events reported and no severe treatment-related adverse events observed in clinical practice. However, evidence remains limited by several methodological shortcomings, including small sample sizes, heterogeneity in study designs, and inconsistent assessment standards. These limitations reduce the overall robustness and generalizability of the findings. Although several systematic reviews have attempted to synthesize the available evidence, their conclusions remain preliminary. Some earlier reviews did not include studies published after 2022, and certain relevant databases were not comprehensively searched. In addition, the number of included RCTs in previous meta-analyses was relatively small, with a maximum of eight RCTs, which may have introduced potential selection bias and limited the reliability of pooled estimates [19].

Based on these considerations, we conducted a systematic review and meta-analysis of the efficacy and safety of SGD in the treatment of PHN. By comprehensively searching major international and domestic databases up to 2026, this study aims to provide a more updated and rigorous synthesis of the available evidence.

Materials and methods

Literature search

This systematic review and meta-analysis was registered in the International Platform of Registered Systematic Reviews and Meta-Analysis Protocols (INPLASY). The Registration ID is INPLASY202660017.

A structured database search was conducted in PubMed, Web of Science, Embase, Cochrane Library, CNKI, Wanfang Data Knowledge Service Platform, and the VIP Chinese Science and Technology Journal Database. The search strategy combined subject headings (e.g., MeSH terms where applicable) and free-text terms.

English search terms included: "Shaoyao Gancao Decoction", "Shaoyao Gancao Tang", "Paeonia lactiflora", "Glycyrrhiza uralensis", "SGD", herbal pairs involving Paeonia and Glycerrrhiza, botanical mixtures for Paeonia lactiflora and Glycerrrhiza uralensis, TCM, Chinese herbal medicine, phytotherapy; and disease-related terms such as "post-herpetic neuralgia", "PHN", "herpes zoster", "shingles", "acute herpes zoster', "neuralgia", and "postherpetic pain".

Chinese search terms included: "Shaoyao Gancao Tang", "Shaoyao Gancao", "Shaoyao Gancao Tang combined with or modified for the treatment of postherpetic neuralgia", modified Shaoyao Gancao Tang, integrated therapy; as well as disease terms such as "postherpetic neuralgia", "herpes zoster", and "PHN". No restrictions were applied regarding publication language, study form, or publication status.

Inclusion and exclusion criteria

Inclusion criteria: (1) Study design: RCTs, irrespective of blinding or allocation concealment status. (2) Participants: Patients with clinically diagnosed PHN, based on internationally or domestically recognized diagnostic criteria, without restrictions on sex, age, ethnicity, disease duration, or affected site. (3) Interventions: The placebo group received standard Western medical care (e.g., antiviral agents, analgesics, and neurotrophic agents), placebo, sham interventions, or other non-SGD TCM interventions (e.g., different prescriptions, acupuncture). The experimental group received SGD, either alone or in combination with conventional Western medications. There were no restrictions regarding dosage form (decoctions, powder, or pills), dosage regimen, or treatment duration. (4) Outcomes: Primary outcomes included pain-related indices, including VAS, numeric rating scales (NRS), and other validated pain assessment tools. Secondary outcomes included total clinical efficacy, sleep quality (Pittsburgh Sleep Quality Index; PSQI), quality of life measures, and incidence of adverse events. At least one pain-related outcome was required for study inclusion.

Exclusion criteria: (1) Patients with acute HZ without progression to PHN. (2) Pregnant or lactating women, or other special populations. (3) Non-RCT studies, including basic research, case reports, case series, reviews, systematic reviews, or meta-analyses. (4) Duplicate publications. (5) Studies for which full-text articles could not be obtained after multiple attempts.

Literature screening and data extraction

Two scholars independently screened all retrieved studies for eligibility according to the predefined inclusion and exclusion criteria. First, duplicate records were removed using EndNote. Then, titles and abstracts were screened to exclude irrelevant studies. The full texts of potentially eligible articles were then retrieved and assessed for final inclusion. Any disagreements between the two reviewers were resolved by consultation with a third reviewer to reach consensus. The following information was collected: (1) basic study characteristics, including title, first author, journal, and year of publication; (2) study content, including study design, sample size, baseline demographic data, and disease duration; (3) treatment details, including treatment regimens, drug composition, dosage, and duration of therapy; (4) outcome measures, including pain intensity, overall clinical efficacy, and side effects.

Quality assessment

The methodological quality of included RCTs was assessed using the Cochrane Risk-of-Bias Tool (ROB 1.0). The following seven domains were evaluated: (1) random sequence generation; (2) allocation concealment; (3) blinding of participants and staff; (4) blinding of outcome assessment; (5) incomplete outcome data; (6) selective reporting; and (7) other sources of bias. Each domain was judged as "low risk", "high risk", or "unclear risk" based on the given information. The risk-of-bias summary and corresponding graphical representations were generated using RevMan 5.3 software.

Statistical analysis

Statistical analyses were performed using RevMan 5.3 software. For dichotomous outcomes, effect sizes were expressed as odds ratios (ORs) with 95% confidence intervals (CIs). For continuous outcomes, mean differences (MD) with 95% CIs were calculated.

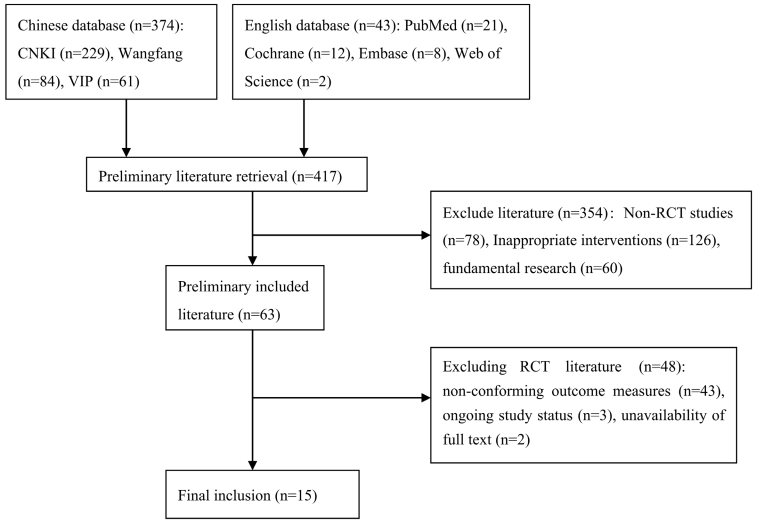

Figure 1. Literature search and selection process.

Heterogeneity among studies was assessed the chi-square test and quantified using the I^2 statistic. If $P>0.1$ and $I^2<50\%$, a fixed-effect model was used; otherwise, a random-effects model was applied. In cases of substantial heterogeneity, subgroup analysis or sensitivity analyses were conducted to explore potential sources of variability. Publication bias was assessed using funnel plots. A two-sided *P* value <0.05 was considered statistically significant.

Results

Literature inclusion results

According to the predefined search strategy, a total of 417 studies were initially identified from multiple databases. Specifically, 374 articles were retrieved from Chinese databases (CNKI: 229; Wanfang Data: 84; VIP: 61), and 43 articles were retrieved from English databases (PubMed: 21; Cochrane Library: 12; Embase: 8; Web of Science: 2). After removal of duplicates and initial screening of titles and abstracts, 354 studies were excluded due to irrelevance (including non-RCTs, mismatched treatments, absence of PHN populations, and non-clinical studies such as basic science or reviews), leaving 63 potential candidate articles (56 Chinese and 7 English). Of these, 48 studies were further excluded due to lack of relevant outcome indicators, insufficient methodological information, inaccessibility of full texts, incomplete or unusable data, or duplicated publications. Ultimately, 15 RCTs [20-34] met the inclusion criteria and were included. The detailed study selection process is illustrated in **Figure 1**.

Characteristics of included studies

A total of 15 RCTs [20-34], all published in Chinese, were included in this analysis. These trials involved 1,188 patients with PHN, with 594 allocated to the experimental group and 594 to the control group.

The control group received conventional Western medical treatments, including gabapentin, methylcobalamin, Vitamin B1, pregabalin, acyclovir, diclofenac sodium, and amitriptyline. Treatment regimens varied across studies in terms of dosage, combination strategies, and durations.

The intervention groups received SGD, either alone or in combination with other therapies: SGD alone in 1 study [22]; SGD combined with Western pharmacotherapy in five studies [21, 27, 29, 31, 34]; SGD combined with Western drugs and acupuncture-related therapies (e.g., electroacupuncture, fire needling, and filiform needling) in four studies [23, 25, 30, 32]; SGD in conjunction with other TCM (e.g., bloodletting therapy, auricular therapy, and topical herbal applications) in 5 studies. Treatment duration across studies ranged from approximately 1 week to several weeks, with variability among protocols.

Among the included studies, 11 studies reported overall clinical efficacy [20-31]; 14 studies assessed pain reduction using VAS [21-34]; 5 studies evaluated sleep quality using PSQI [21, 23, 26, 32, 34]; and 7 studies reported adverse reactions [26, 27, 29-34]. In addition, some studies reported secondary outcomes such as TCM syndrome differentiation scores [27, 30], quality-of-life indicators [27, 29], inflammatory cytokines (IL-2, IL-6, IL-10) [21, 27, 34] and neuropeptides (NPY, substance P, β-endorphin)

Table 1. Characteristics of the included studies

Literature	Number of cases		Intervention		Outcome Measures
	Control	Experimental	Control	Experimental	
CBQ 2012 [20]	30	30	Conventional Western medicine	SGD	①
HT 2022 [21]	45	45	Conventional Western medicine	SGD+Control	① ② ④
LGF 2015 [22]	26	26	Conventional Western medicine	SGD	① ②
LJC 2019 [23]	47	47	Conventional Western medicine	SGD	① ② ④
LL 2018 [24]	37	37	Conventional Western medicine	SGD+Control	① ②
LWJ 2019 [25]	63	63	Conventional Western medicine	SGD	① ② ⑤ ⑥
LXB 2025 [26]	53	53	Conventional Western medicine	SGD	① ② ③ ④ ⑤ ⑥
LXY2021 [27]	47	47	Conventional Western medicine	SGD+Control	① ② ③
SHR 2015 [28]	38	38	Conventional Western medicine	SGD+Control	① ②
WCG 2016 [29]	43	43	Conventional Western medicine	SGD+Control	① ② ③
WYQ 2022 [30]	30	30	Conventional Western medicine	SGD+Control	① ② ③
XWM 2013 [31]	36	36	Conventional Western medicine	SGD	① ② ③
ZHC 2022 [32]	31	31	Conventional Western medicine	SGD	② ③ ④
ZXY 2018 [33]	28	28	Conventional Western medicine	SGD	② ⑤ ⑥
ZYP 2021 [34]	40	40	Conventional Western medicine	SGD+Control	② ③ ④

Define as follows: ① clinical efficacy; ② VAS scores; ③ occurrence of adverse events; ④ PSQI; ⑤ pain intensity measures and PSI values; ⑥ pain degree (PIL).

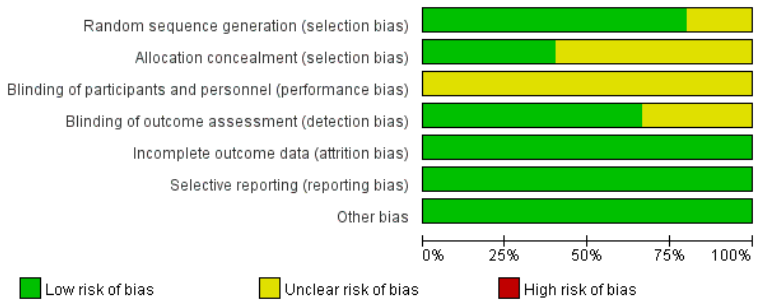

Figure 2. Risk of bias assessment (Percentage across studies).

[26, 27]. **Table 1** shows the detailed characteristics of the included studies.

Quality assessment of included studies

(1) Random sequence generation: twelve studies [20-22, 25, 26, 28-34] adopted random allocation using random number tables, thus rated as low risk; the remaining three studies [23, 24, 27] only mentioned "random" without detailed methods, rated as unclear risk of bias.

(2) Allocation concealment: six studies [22, 24, 26, 32-34] explicitly described the use of opaque, sealed envelopes for allocation concealment, and were rated as low risk of bias; the other nine studies [20, 21, 23, 25, 27-31] did not mention allocation concealment, thus rated as unclear risk of bias.

(3) Blinding of participants and personnel: none of the included studies mentioned blinding of participants or study personnel. Given the nature of the interventions (herbal decoctions combined with oral Western medications), blinding was difficult to implement in most trials. Therefore, all studies were rated as unclear risk of bias in this domain.

(4) Blinding of outcome assessment: ten studies [20-22, 24, 25, 27-30, 33] explicitly reported blinding of outcome assessors and therefore were rated as low risk of bias. The remaining five studies [23, 26, 31, 32, 34] did not specify whether assessors were blinded, and therefore was rated as unclear risk of bias.

(5) Incomplete outcome data: all included studies reported complete outcome data for all participants, with no apparent dropouts, withdrawals, or loss to follow-up, and were therefore rated as low risk of bias.

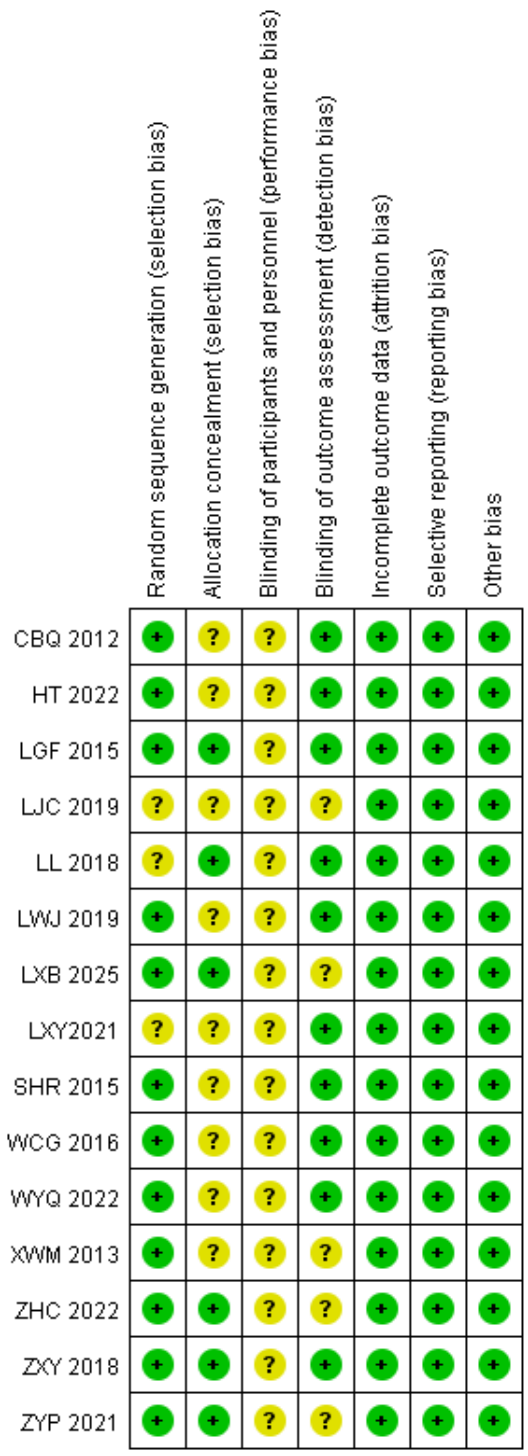

Figure 3. Risk of bias assessment (Summary per study).

(6) Selective reporting: all studies fully reported pre-specified outcome measures in the methods section, with no evidence of selective reporting bias, thus rated as low risk of bias.

(7) Other sources of biases: no additional significant sources of biases were identified in the included studies; thus, this domain was rated as low risk of bias.

The risk-of-bias evaluation was conducted using RevMan 5.3, and the details are shown in **Figures 2**, **3**.

Meta-analysis results

Overall efficacy rate

A total of 13 outcome datasets from 12 studies [20-31] reported overall therapeutic efficacy. Among them, 6 studies [22, 24, 26-28, 31] evaluated efficacy after a 14-day regimen, 6 others [20, 21, 23, 25, 26, 29] reported outcomes after 28 days, and one study [30] assessed efficacy after 21 days of treatment. No significant heterogeneity was observed among these studies (I^2=0%, P=1.00). Therefore, a Mantel-Haenszel (M-H) fixed-effect model was used. The pooled analysis demonstrated that the overall clinical response rate was significantly higher in the intervention group than in the control group [OR=5.42, 95% CI (3.40-8.64), P<0.0001].

Sub-group analyses were performed according to treatment duration. Among studies with a 14-day treatment period [22, 24, 26-28, 31], no significant heterogeneity was detected (I^2= 0%, P=0.97), and a fixed-effects model was used. The pooled results showed that the intervention group achieved a significantly higher overall response rate than the control group (OR=4.71, 95% CI: 2.42-9.15, P<0.0001). Similarly, no significant heterogeneity was identified among studies with a 28-day treatment duration [20, 21, 23, 25, 26, 29] (I^2=0%, P=0.93). Meta-analysis using a fixed-effects model revealed a significantly higher overall response rate in the intervention group (OR= 6.19, 95% CI: 3.02-12.69, P<0.0001). In the study by Wang et al. [30], the overall response rate after 21 days of treatment was significantly higher in the intervention group than the control group (OR=6.00, 95% CI: 1.17-30.72, P=0.03). The corresponding forest plot is presented in **Figure 4**.

Pain outcomes

Visual analogue scale (VAS): A total of 14 studies [21-34] evaluated pain intensity using VAS.

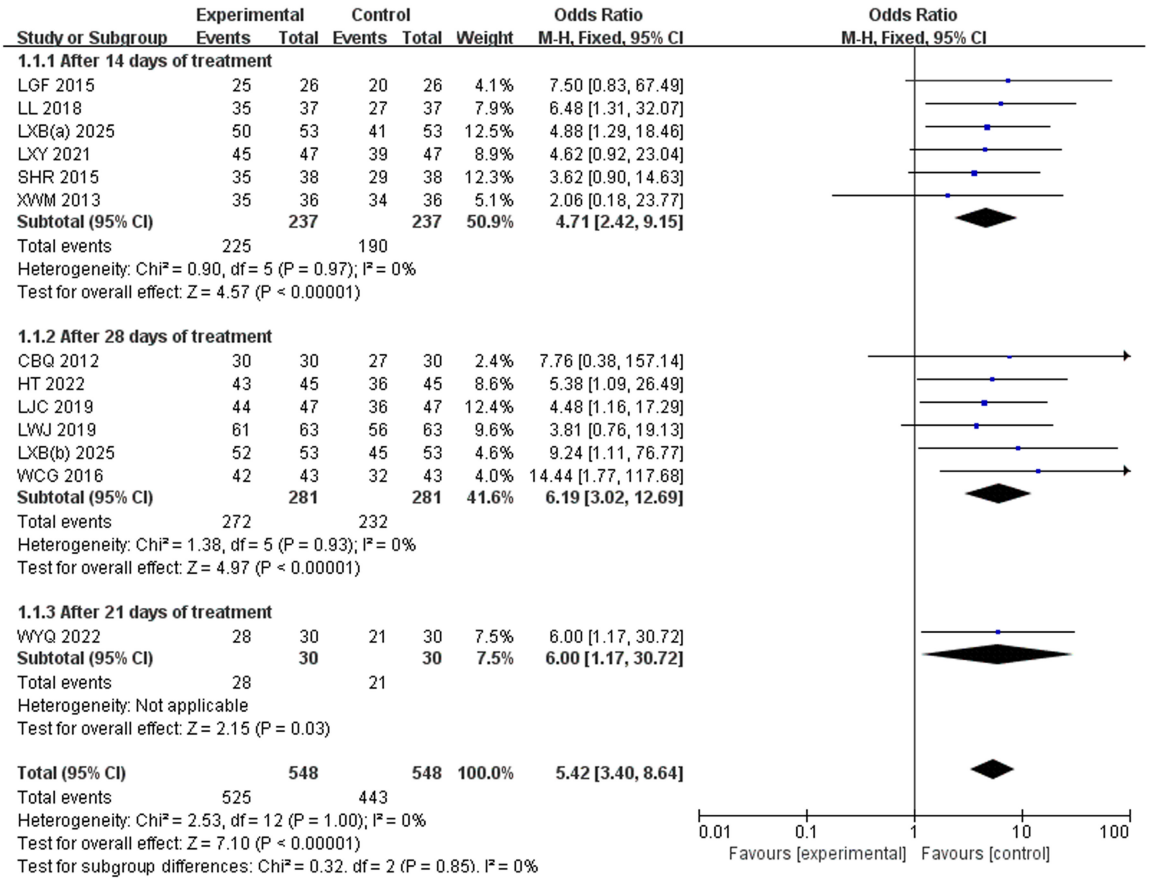

Figure 4. Forest plot of overall therapeutic efficacy.

Among these, 9 studies [22, 24-29, 31, 32] reported VAS outcomes after 14 days of treatment, 7 studies [21, 23, 26, 29, 32-34] reported VAS outcomes after 28 days of treatment, and one study [30] evaluated VAS scores after 21 days of intervention. Substantial heterogeneity was observed across the included studies (I^2=96%, P<0.0001). Therefore, an inverse-variance (IV) random-effects model was used for the meta-analysis, and the pooled analysis showed that post-treatment VAS scores were significantly lower in the intervention group than in the control group [MD=-1.33, 95% CI (-1.68 to -0.99), P<0.0001].

Subgroup analyses were subsequently performed according to treatment duration. Substantial heterogeneity remained in the 9 studies [22, 24-29, 31, 32] with a 14-day treatment duration (I^2=97%, P<0.0001). The random-effects model was used in the meta-analysis, and the results showed significantly lower VAS values in the intervention group compared with the control group [MD=-1.32, 95% CI (-1.92 to -0.71), P<0.0001]. Similarly, studies with a 28-day treatment duration [21, 23, 26, 29, 32-34] demonstrated high heterogeneity (I^2=87%, P<0.0001). A random-effects model was used in this analysis, and the VAS scores in the intervention group were significantly lower than those in the control group (MD=-1.42, 95% CI [-1.76, -1.07], P<0.0001). In the study conducted by Wang et al. [30], VAS scores after 21 days of treatment were significantly lower in the intervention group than in the control group [MD=-0.84, 95% CI (-1.11 to -0.57), P<0.0001]. Detailed results are shown in **Figure 5**.

Pain rating index (PRI) and present pain intensity (PPI): Three studies [24, 25, 32] assessed analgesic efficacy using PRI or PPI. Substantial heterogeneity was observed across these three studies (I^2=92%, P<0.0001). Therefore, IV random-effects models were applied. Meta-analysis showed that both PRI and PPI scores

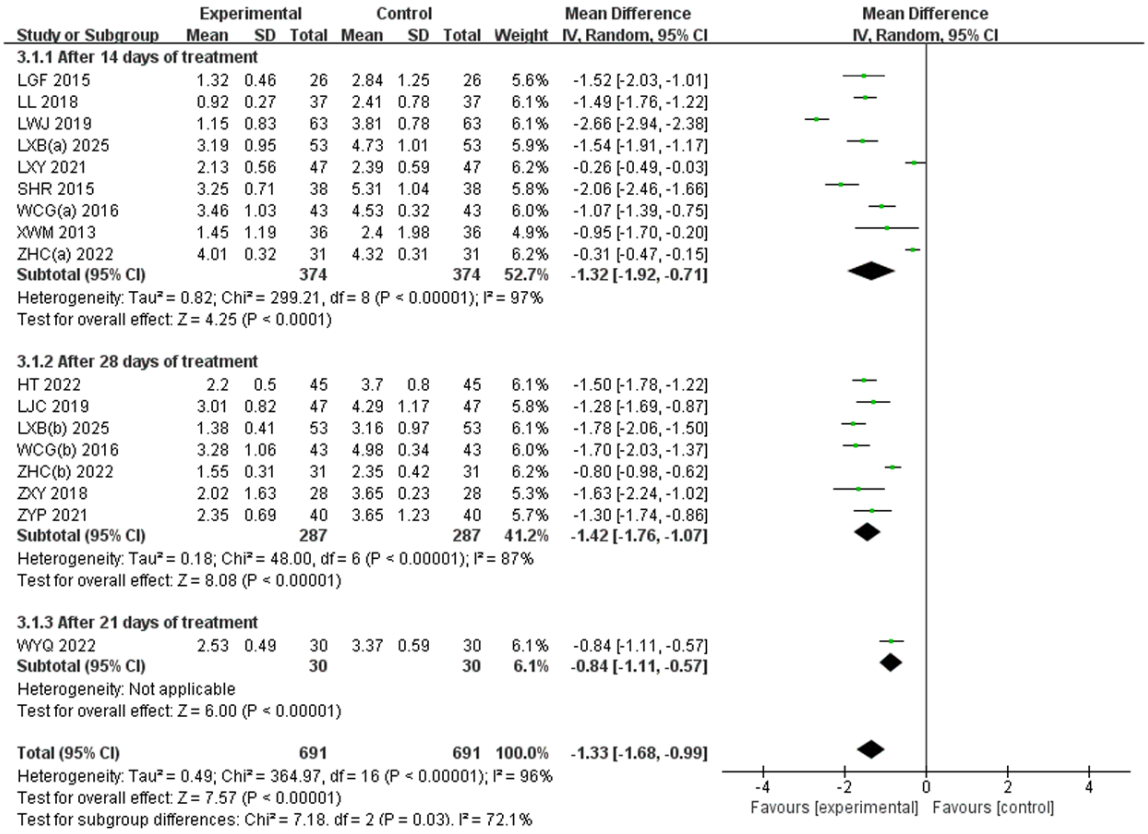

Figure 5. Forest plot of post-intervention VAS score.

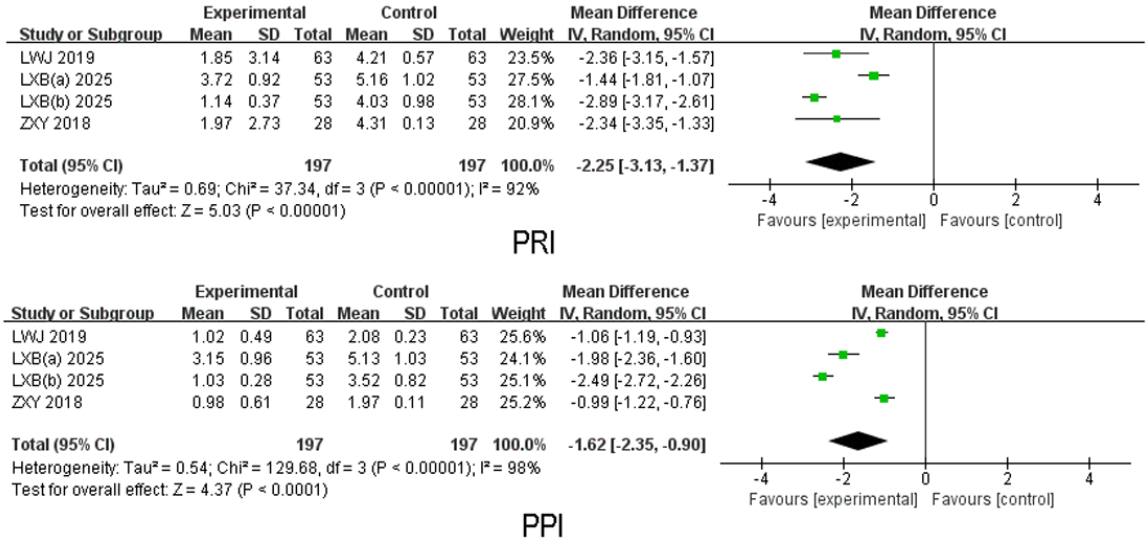

Figure 6. Forest plot of pain rating index (PRI) and present pain intensity (PPI) after treatment.

were significantly lower in the intervention group than in the control group [PRI: MD=-2.25 (95% CI: -3.13 to -1.37), P<0.0001; PPI: MD=-1.62 (95% CI: -2.35 to -0.90), P<0.0001; **Figure 6**].

Sensitivity analyses were conducted using a leave-one-out approach. Each study was sequentially excluded and the pooled effect size was recalculated. The direction and magnitude

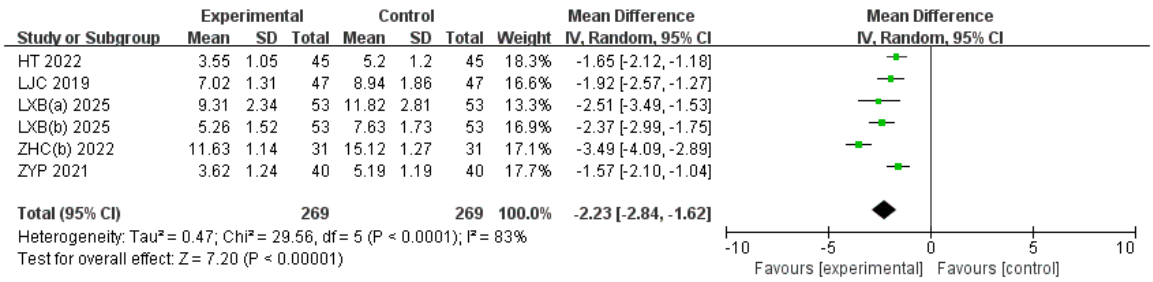

Figure 7. Forest plot of PSQI Scores after Intervention.

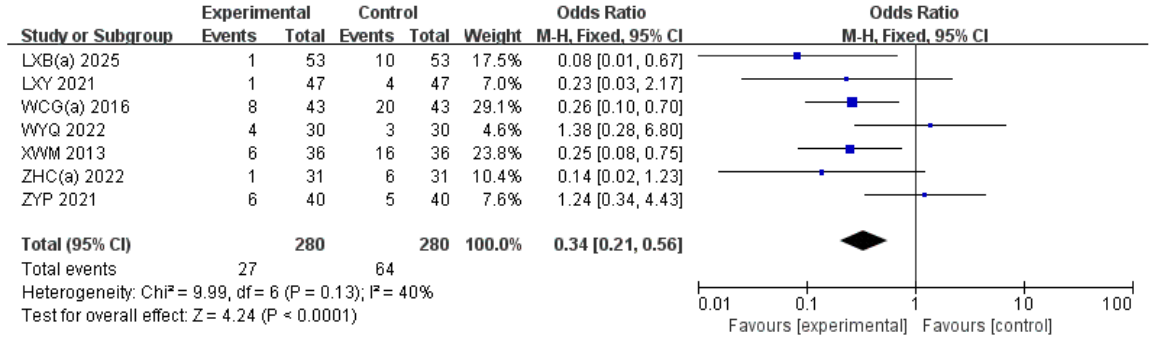

Figure 8. Forest plot of the incidence of adverse events.

of the pooled estimates remained generally stable after removal of individual studies, and all pooled 95% CIs remained statistically significant. These findings indicate that the overall results were robust and were not driven by any single study.

Sleep quality

Five studies [21, 23, 26, 32, 34] involving six datasets evaluated sleep quality using PSQI. Among them, Liu et al. [26] reported PSQI outcomes at days 14 and 28, while the remaining four studies [21, 23, 32, 34] assessed outcomes after 28 days of treatment. Moderate-to-high heterogeneity was observed among the included studies (I^2=83%, P<0.0001). Therefore, a IV random-effects model was applied in the meta-analysis. The pooled results demonstrated that PSQI values were significantly lower in the intervention group than in the control group after treatment [MD=-2.23, 95% CI: -2.85 to -1.62), P<0.00001], as shown in **Figure 7**.

Safety evaluation

Seven studies [26, 27, 29-32, 34] reported the incidence of adverse effects. Low heterogeneity was observed across studies (I^2=40%, P= 0.13), and thus a fixed-effects model was used. The results showed that the incidence of adverse events was significantly lower in the intervention group than in the control group [OR=0.34, 95% CI: 0.21-0.56), P<0.0001], as shown in **Figure 8**.

Other outcome indicators

Several studies presented additional outcomes, including TCM syndrome scores, quality of life assessments, inflammatory cytokines, and neuropeptides. However, due to the limited number of studies reporting each outcome (fewer than three studies per category), meta-synthesis was not feasible; therefore, a qualitative synthesis was performed.

Two studies [27, 30] evaluated TCM symptom-related outcomes. Lu et al. [27] reported that post-treatment TCM syndrome scores in the treatment group were significantly lower than those in the control group.

Two studies [27, 29] assessed quality of life outcomes. Lu et al. [27] used the World Health Organization's Quality of Life-BREF (WHOQOL-Bref) and reported significant improvements

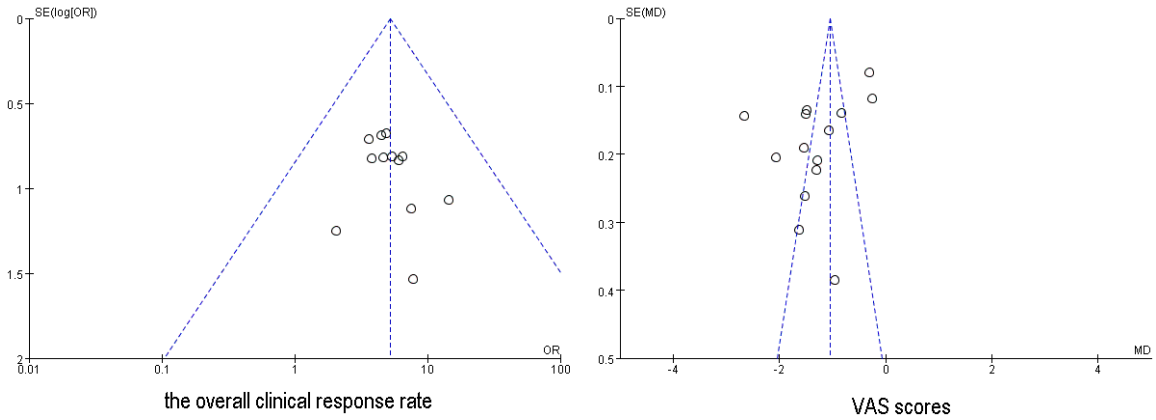

Figure 9. Funnel plot for publication bias.

across physical, mental, and social domains in the intervention group compared with the control group (P<0.05); Wang et al. [29] used a 0-10 visual analog scoring system and also found higher quality-of-life scores in the intervention group than the control group (P<0.05).

Three studies [21, 27, 34] investigated inflammatory cytokine levels. Han et al. [21] reported significantly lower IL-2 and IL-6 levels in the intervention group compared to the control group after treatment (P<0.05); Lu et al. [27] observed a significant reduction in IL-10 level in the intervention group compared to the control group (P<0.05); Zhou et al. [34] showed that IL-2, IL-6, and IL-10 level were all significantly reduced in the intervention group compared with the control group (P<0.05).

Two studies [26, 27] reported neuropeptide-related outcomes. Liu et al. [26] found that serum concentrations of NPY, substance P, β-EP, and prostaglandin E2 (PGE2) were significantly lower in the intervention group than in the control group after treatment (P<0.05); Lu et al. [27] reported that tissue expression levels of NPY, SP, and β-EP were also significantly reduced in the intervention group compared with the control group (P<0.05).

Publication bias

Funnel plots were used to assess potential publication bias for outcomes with a relatively sufficient number of included studies (**Figure 9**). For overall clinical efficacy, the distribution of studies appeared approximately symmetrical around the pooled effect estimate, with most points falling within the pseudo 95% confidence limits, suggesting no obvious evidence of publication bias. For VAS outcomes (17 effect estimates from 14 studies), The plot showed a degree of asymmetry, with several studies falling outside the pseudo 95% confidence boundaries, indicating the possibility of potential publication bias or small-study effects. For other outcomes, the number of included studies was fewer than 10; therefore, funnel plot analysis was not performed due to limited statistical power.

Discussion

HZ has become an increasingly important public health concern worldwide, with a rising incidence [35]. Evidence suggests that early intervention may shorten disease duration and reduce the severity of acute episodes, as well as decrease the risk of progression to PHN [36]. In the present study, 15 RCTs were included to systematically evaluate the efficacy and safety of SGD in the management of PHN. The pooled results indicated that, compared with conventional Western medicine alone, SGD combined therapy was associated with higher overall response rate, relieved pain intensity, improved sleep quality, and reduced incidence of adverse events.

SGD, composed of *Paeonia lactiflora* and *Glycyrrhiza uralensis*, is traditionally considered to have the effects of regulating the Liver channel, relieving spasm, calming the mind, and alleviating pain. Modern pharmacological studies have suggested that SGD relieves neuropathic pain through multiple targets and sig-

naling pathways. Paeoniflorin (PF) has been reported to alleviate neuropathic pain by inhibiting TRPV1 channel activity, modulating the PKCε-TRPV1 signaling pathway, and reducing neuroinflammation via suppression of microglial activation and inflammatory factors such as IL-6 and TNF-α [11, 37]. Glycyrrhizic acid, a major active compound of *Glycyrrhiza uralensis*, may attenuate neuro-inflammation by targeting the HMGB1-TLR4 signaling pathway [38]. In addition, the combined treatment with paeoniflorin and glycyrrhizin may exhibit synergistic interactions, which has been proposed as a pharmacological basis for the compatibility of the two herbs in SGD [39]. In addition, PF may also attenuate postoperative pain by regulating microglial activation and inhibiting the TLR4/MMP-9/IL-1β signaling cascade [40, 41]. Several studies have reported reductions in inflammatory mediators (e.g., IL-2, IL-6, IL-10) and neuropeptides (e.g., NPY, substance P, β-EP) following SGD intervention. These mechanisms are consistent with key pathological processes involved in NP, suggesting that the therapeutic effect of SGD may extend beyond PHN to other NP subtypes.

The present findings are consistent with previous meta-analyses reporting the efficacy and safety of SGD in PHN management [42]. Compared with earlier meta-analyses, which were limited by a smaller number of included trials and insufficient clinical trials, this study incorporates a larger dataset and updated literature up to March 2026, thereby providing a more comprehensive synthesis of available evidence.

Based on our investigation, SGD significantly improved sleep quality, as reflected by a reduction in PSQI scores. Insomnia-related symptoms frequently occur in PHN patients, particularly in those with long-term chronic pain, which may further exacerbate psychological distress and reduce quality of life. Furthermore, pooled safety data indicated that the incidence of adverse events was lower in the intervention group compared to the control group, suggesting a favorable safety profile when SGD is used as an adjunctive therapy.

Substantial heterogeneity was observed across included studies. To explore potential sources of variability, subgroup analyses were conducted based on treatment duration. However, significant heterogeneity persisted within both the 14-day and 28-day VAS subgroups (I^2=97% and 87% m, respectively), suggesting that treatment duration alone does not fully explain the observed variability. Potential sources of heterogeneity may include differences in SGD formulation, dosage, control interventions, and baseline pain levels, timing of outcome assessment, and methodological variability across studies. In addition, potential investigator and reporting biases may also contribute to heterogeneity. Due to a limited number of included trials, meta-regression analysis was not performed because of insufficient statistical power. Despite these limitations, subgroup analysis indicated that SGD consistently reduced VAS scores in both the 14-day and 28-day intervention groups compared with control group, suggesting a stable analgesic effect.

Regarding safety outcomes, the incidence of adverse reactions in the intervention group was significantly lower than that in the control group. Reported side effects were predominantly mild gastrointestinal symptoms, with no serious adverse events occurred. These findings suggest that SGD, as an adjunctive therapy, demonstrates a favorable safety profile in the management of PHN.

Based on the findings of this meta-analysis, several preliminary clinical implications can be proposed:

(1) Formulation principles: All included studies were based on the classical *Shanghan Lun* prescription Shaoyao Gancao Decoction, composed of *Paeoniae Radix* (15-30 g) and *Glycyrrhizae Radix* (6-10 g), with modifications according to the clinical symptoms and pain distribution of each patients. Common modifications: *Salviae Miltiorrhizae* and *Corydalis Rhizoma* are often used to promote blood circulation and relieve pain in patterns associated with blood stasis and Qi stagnation; *Viticis Fructus* is used for head and neck pain as a guiding herb to channel the effect upward; *Trichosanthis Pericarpium* is used to regulate qi and relieve chest and upper torso discomfort; and *Mori Ramulus* and *Chaenomelis Fructus* are applied to relax tendons and alleviate limb pain. These modifications are broadly consistent with the principle of “pattern differentiation combined with lesion localization” described in current expert consensus on inte-

grated traditional Chinese and Western medicine for postherpetic neuralgia.

(2) Dosage and treatment duration: SGD was generally administered orally once a day, divided into two equal doses, with a treatment duration ranging from approximately 2-4 weeks. Subgroup analyses indicated that at both 14- and 28-day treatment were associated with significant improvements in pain intensity and overall clinical efficacy, with good safety. These findings suggest that the current regimen is relatively practical in clinical application; however, optimal dosing strategies require further standardization.

(3) Target population: Existing evidence support SGD as a safe and effective adjunctive therapy for PHN, particularly in middle-aged and elderly populations, who frequently experience sleep disturbances and anxiety. Given its potential multi-target analgesic and neuroprotective effects, SGD may be considered in patients with inadequate response to, or intolerance of, conventional Western drugs. However, its use should be individualized based on syndrome differentiation and clinical judgment.

(4) Future research directions: ① Conduct large-scale, multi-center, high-quality RCTs in accordance with CONSORT guidelines to improve methodological rigor; ② Standardize SGD intervention protocols and outcome measurement systems to reduce heterogeneity and facilitate cross-study comparison; ③ Incorporate cost-effectiveness analysis and quality-of-life evaluation to provide evidence for health technology evaluation; ④ Further explore the underlying mechanisms of SGD in neuropathic pain, particularly its potential regulation of TRPV1/PKCε signaling pathways and neuroinflammation, to assess its broader applicability in different NP subtypes.

Limitations and overall conclusions

Meta-analysis is an observational research method and is therefore subject to methodological limitations and potential sources of bias. (1) Methodological flaws: although 12 trials reported the use of random number tables, only six studies described allocation concealment. In addition, none of the included studies reported blinding of participants or evaluators. Therefore, performance and assessment bias cannot be excluded. (2) Language and geographical bias: all included studies were published in Chinese, which may limit the generalizability of the findings to other populations. (3) intervention heterogeneity: Considerable variations existed across studies in SGD formulation, dosage regimens, and co-interventions, which may have contributed to heterogeneity in pooled outcomes. (4) Outcome heterogeneity and limited reporting: Several secondary outcomes (e.g., PRI, PPI, PSQI) were reported in fewer than five studies, and significant heterogeneity was observed, which may reduce the reliability of the corresponding pooled results. (5) Publication bias: Funnel plot analysis for VAS outcomes showed potential asymmetry, suggesting potential publication bias. (6) External validity: Certain patient subgroups (e.g., patients with specific lesion sites such as facial involvement or other special populations) were not included in this study, which may limit the external applicability of the findings. (7) Evidence scope limitation: Although this study offers evidence supporting the use of SGD in PHN, high-quality evidence for other neuropathic pain subtypes, such as diabetic peripheral neuropathy and chemotherapy-induced peripheral neuropathy, remains lacking. Future well-designed RCTs are needed in these populations.

In summary, adjunctive treatment with SGD in combination with conventional Western therapy appears to enhances overall therapeutic efficacy, reduce pain intensity, improve sleep quality and quality of life, and demonstrate a favorable safety profile in patients with PHN.

From a mechanistic perspective, active constituents such as paeoniflorin and glycyrrhizin may exert analgesic and neuro-modulatory effects through multiple pathways, including modulation of TRPV1 channel activity, regulation of the PKCε-TRPV1 signaling axis, and attenuation of neuroinflammation.

Disclosure of conflict of interest

None.

Address correspondence to: Jinfeng Zhao, Department of Dermatology, TCM Hospital of Wenjiang District, No. 61 Wanchun East Road, Wenjiang District, Chengdu 611130, Sichuan, China. E-mail: zhaojinfeng905@163.com

References

[1] Chinese Medical Doctor Association Dermatology Branch Herpes Zoster Expert Consensus Working Group and National Clinical Research Center for Skin and Immune Diseases. Chinese expert consensus on diagnosis and treatment of herpes zoster (2022 edition). Zhonghua Pi Fu Ke Za Zhi 2022; 55: 1033-1040.

[2] Wu X, Li B, Liu B, He L, Liu Z, Huang S, Hui K, Liu H, Cao Y, Wang S, Xu Z, Zhang C, Zhao J, Liu Y, Zhao N, Ding N and Hu J. Expert consensus on clinical protocol for treating herpes zoster with fire needling. Zhongguo Zhen Jiu 2025; 45: 1825-1832.

[3] Zhang Z, Liu X, Suo L, Zhao D, Pan J and Lu L. The incidence of herpes zoster in China: a meta-analysis and evidence quality assessment. Hum Vaccin Immunother 2023; 19: 2228169.

[4] Ma WJ. Advances in the pathogenesis and treatment of postherpetic neural pruritus. Yi Xue Li Lun Yu Shi Jian 2024; 37: 1118-1120.

[5] Chen J, Abrahamson PE, Ke Y, Ong CR, Parikh R and Shantakumar S. A systematic literature review of the epidemiology and burden of herpes zoster in selected locales in Asia Pacific. Hum Vaccin Immunother 2024; 20: 2344983.

[6] Koshy E, Mengting L, Kumar H and Jianbo W. Epidemiology, treatment and prevention of herpes zoster: a comprehensive review. Indian J Dermatol Venereol Leprol 2018; 84: 251-262.

[7] Zeng JC, Liao YZ, Li JJ, Lu LH, Li HZ, Lu LM, Li QJ, Li LX, Wang SX and Lin GH. Clinical efficacy of fire needling combined with cupping therapy on herpes zoster of acute stage and the effect on Th17/Treg immune balance. Zhongguo Zhen Jiu 2023; 43: 1128-1133.

[8] Guo Z, Xia Y and Zhang Z. Efficacy and safety of different medications compared for the treatment of postherpetic neuralgia: a network meta-analysis. Front Pharmacol 2025; 16: 1614587.

[9] Finnerup NB, Haroutounian S, Kamerman P, Baron R, Bennett DLH, Bouhassira D, Cruccu G, Freeman R, Hansson P, Nurmikko T, Raja SN, Rice ASC, Serra J, Smith BH, Treede RD and Jensen TS. Neuropathic pain: an updated grading system for research and clinical practice. Pain 2016; 157: 1599-1606.

[10] Zhang ZJ. Treatise on cold damage. Beijing: People's Medical Publishing House, 2005.

[11] Hong D and Xiao Y. Shaoyao gancao decoction: a comprehensive review of modern clinical applications and underlying pharmacological mechanism. Front Pharmacol 2025; 16: 1656217.

[12] Luo Y, Qiu Y, Zhou R, Zhang Y, Ji X, Liu Z, Li R, Zhang Y, Yang F, Hou J, Zhang S, Wang T, Song H and Tao X. Shaoyao gancao decoction alleviates the central hyperalgesia of recurrent NTG-induced migraine in rats by regulating of the NGF/TRP1/COX-2 signalling pathway. J Ethnopharmacol 2023; 317: 116781.

[13] Facheng Z, Rongli Q, Li Z, Baoxiang W, Sheng Y and Mingqiu S. Shaoyao gancao decoction, an ancient classical prescription: a review on its chemical composition, pharmacology, pharmacokinetics, clinical applications, and toxicology. J Pharm Pharmacol 2025; 77: 845-865.

[14] Kimura M, Kimura I, Takahashi K, Muroi M, Yoshizaki M, Kanaoka M and Kitagawa I. Blocking effects of blended paeoniflorin or its related compounds with glycyrrhizin on neuromuscular junctions in frog and mouse. Jpn J Pharmacol 1984; 36: 275-282.

[15] Chen Y, Lu R, Wang Y and Gan P. Shaoyao gancao decoction Ameliorates Paclitaxel-Induced Peripheral Neuropathy via Suppressing TRPV1 and TLR4 Signaling expression in rats. Drug Des Devel Ther 2022; 16: 2067-2081.

[16] Hu KX, Li YF and Fang ZH. Meta analysis of modified Shaoyao Gancao Decoction in the treatment of diabetic peripheral neuropathy. J Hubei Minzu Univ (Med) 2024; 41: 40.

[17] Yuan YL. Application of Shaoyao Gancao Decoction combined with Chinese herbal hot compress package in patients with postherpetic neuralgia. Henan Med Res 2023; 32: 3395-3398.

[18] Zheng XY. Clinical observation of Shaoyao Gancao Decoction combined with stepwise acupuncture in treating postherpetic neuralgia. Shiyong Zhongyiyao Zazhi 2018; 34: 422-423.

[19] Han J and Duan XY. Meta-analysis of Shaoyao Gancao Decoction in the treatment of postherpetic neuralgia. Kunming Xueyuan Xuebao 2023; 45: 111-116.

[20] Chen BQ. Observation of the efficacy of qi and blood supplementation, blood stasis removal, and meridian unblocking therapy in treating postherpetic neuralgia. Zhongguo Zhong Yi Ji Zheng 2012; 21: 1664.

[21] Han T. Efficacy observation of Shaoyao-Gancao decoction with modifications in treating postherpetic neuralgia. Zhongguo Bao Jian Ying Yang 2022; 32: 148-150.

[22] Liu GF, Guo Q, Bao LY and Song CL. Clinical observation of Shaoyao-Gancao decoction in treating postherpetic neuralgia. Lin Chuang Yi Yao Wen Xian Dian Zi Za Zhi 2015; 2: 517-518.

[23] Li JC. Observation of the efficacy of Shaoyao-Gancao decoction combined with fire needling in treating postherpetic neuralgia. Lin Chuang He Li Yong Yao Za Zhi 2019; 12: 104-105.

[24] Li L. Self-formulated Shaoyao-Gancao decoction combined with modified Shixiao San and

local bloodletting therapy in treating postherpetic neuralgia. Shi Yong Zhong Xi Yi Jie He Lin Chuang 2018; 18: 60-61.
[25] Li WJ. Analysis of 126 cases of postherpetic neuralgia treated with Shaoyao-Gancao decoction combined with stepwise acupuncture. Pi Fu Bing Yu Xing Bing 2019; 41: 383-384.
[26] Liu XB, Ma YC and Yang B. Effect of modified Shaoyao-Gancao decoction combined with ear acupressure for postherpetic neuralgia. Zhongguo Lao Nian Xue Za Zhi 2025; 45: 1117-1121.
[27] Lu XY, Ren YW, Yang X and Zhang AH. Effects of Shaoyao-Gancao decoction with modifications on pain and serum NPY, SP levels in postherpetic neuralgia patients. Hai Nan Yi Xue 2021; 32: 31-34.
[28] Shen HR. Efficacy of internal medicine and external application of Chinese medicine combined with methylcobalamin injection in treating postherpetic neuralgia. Xin Zhong Yi 2015; 47: 220-221.
[29] Wang CG, Zhang J, Chen LP, Xie XY, Ma Q, Lei LP and Wu W. Effect of modified Shaoyao-Gancao decoction on patients with neuropathic pain and depression. Zhongguo Xian Dai Yi Sheng 2016; 54: 114-118.
[30] Wang YQ, Jin S, Fang X and Ma JF. Efficacy of electroacupuncture combined with Shaoyao-Gancao decoction in treating elderly postherpetic neuralgia with blood deficiency and hyperactivity of liver yang. Xian Dai Yi Xue Yu Jian Kang Yan Jiu (Dian Zi Ban) 2022; 6: 102-105.
[31] Xiao WM and He CY. Observation of the efficacy of modified Shaoyao-Gancao decoction in treating postherpetic neuralgia. Xin Zhong Yi 2013; 45: 76-77.
[32] Zhang HC, Lu XJ and Xiao XY. Study on the efficacy of Tongdu regulation and pain-relief acupuncture combined with Shaoyao-Gancao decoction in treating postherpetic neuralgia. Zhongguo Chu Fang Yao 2022; 20: 128-129.
[33] Zheng XY. Clinical observation of the efficacy of Shaoyao-Gancao decoction combined with stepwise acupuncture in treating postherpetic neuralgia. Shi Yong Zhong Yi Yao Za Zhi 2018; 34: 422-423.
[34] Zhou YP. Clinical efficacy and safety of Shaoyao-Gancao decoction in treating postherpetic neuralgia. Lin Chuang He Li Yong Yao Za Zhi 2021; 14: 127-129.
[35] Pan CX, Lee MS and Nambudiri VE. Herpes zoster worldwide prevalence, impact, immunisation accessibility: a theoretical analysis. Ther Adv Vaccines Immunother 2022; 10: 25151355221084535.
[36] Han J and Duan XY. Meta-analysis of Shaoyao-Gancao decoction in treating postherpetic neuralgia. Kunming Xue Yuan Xue Bao 2023; 45: 111-116.
[37] Xu F, Liu Q, Cai S, Yu Q, Zhang Y, Liu Z, Zhao H and Zhang L. Effects and mechanisms of paeoniflorin in relieving neuropathic pain: network pharmacological analysis and experimental validation. Neurochem Res 2025; 50: 160.
[38] Heidari S, Mehrizc-Sadeghi S and Hosseinzadeh A. Glycyrrhiza (family Fabaceae), the drug used in defence through defensive mediators of biological or synthetic hazards. Phytomedicine 2021; 38: 140009.
[39] Sun Q, Li L, Li J, Li SY, Zhang Y, Chen XS, Liu SS and Hua ZY. Glycyrrhizin alleviates brain injury in necrotizing enterocolitis model mice by suppressing HMGB1/TLR4 pathway. Int Immunopharmacol 2025; 150: 114294.
[40] Fan YX, Hu L, Zhu SH, Han Y, Liu WT, Yang YJ and Li QP. Paeoniflorin attenuates postoperative pain by suppressing Matrix Metalloproteinase-9/2 in mice. Eur J Pain 2018; 22: 272-281.
[41] Zhou J, Wang L, Wang J, Wang C, Yang Z, Wang C, Zhu Y and Zhang J. Paeoniflorin and albiflorin attenuate neuropathic pain via MAPK Pathway in chronic constriction injury rats. Evid Based Complement Alternat Med 2016; 2016: 8082753.
[42] Dworkin RH, Johnson RW, Breuer J, Gnann JW, Levin MJ, Backonja M, Betts RF, Gershon AA, Haanpaa ML, McKendrick MW, Nurmikko TJ, Oaklander AL, Oxman MN, Pavan-Langston D, Petersen KL, Rowbotham MC, Schmader KE, Stacey BR, Tyring SK, van Wijck AJ, Wallace MS, Wassilew SW and Whitley RJ. Recommendations for the management of herpes zoster. Clin Infect Dis 2007; 44 Suppl 1: S1-S26.