Journal of Pain Research

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REVIEW

Efficacy and Safety of Pulsed Radiofrequency Combined with Platelet-Rich Plasma in the Treatment of Postherpetic Neuralgia: A Systematic Review and Meta-Analysis

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Background: Herpes zoster-associated neuralgia (HZN) is a disease caused by the reactivation of the varicella-zoster virus (VZV) that is latent within the spinal nerves, with a major impact on patients' quality of life. The objective of this study is to evaluate the efficacy and safety of Pulsed Radiofrequency (PRF) combined with Platelet-Rich Plasma (PRP) in the treatment of HZN, comparing it with PRF alone.

Methods: A thorough search was conducted on multiple databases. Several clinical studies from the inception of each database up to December 2024 were included in the study. The primary clinical outcome was the postoperative pain intensity score. Secondary clinical outcomes encompassed sleep quality, the utilization of rescue analgesics postoperatively, and the incidence of adverse events.

Results: The final analysis incorporated a total of seven studies, encompassing 568 subjects. With regard to the alleviation of pain, PRF combined with PRP therapy has shown more significant pain relief for HZN when compared with conventional PRF therapy. The combination of PRF and PRP therapy has been demonstrated to be more efficacious in enhancing patients' sleep quality. With regard to the administration of postoperative rescue analgesics, the dosage of such medication was found to be lower in cases where PRF was combined with PRP therapy. The incidence of adverse events was consistent across both groups.

Conclusion: The PRF - PRP is more effective than the traditional radiofrequency pulse therapy in treating HZN. This combination has been demonstrated to enhance sleep quality and reduce the necessity for postoperative rescue analgesics. The potential for this approach extends to its utilization as a novel therapeutic modality for HZN.

Keywords: herpes zoster, postherpetic neuralgia, pulsed radiofrequency, platelet-rich plasma

Introduction

Herpes zoster (HZ) is a skin disease caused by the infection of the spinal cord and cranial nerves by the varicella-zoster virus (VZV). It is characterized by vesicular eruptions along the affected dermatomes, accompanied by burning, stabbing pain.[1] The annual incidence of HZ ranges from 4.28/1000 person-years across all age groups, with a higher incidence observed in elderly patients due to declining immunity.[2] The classification of HZN is as follows: acute herpes zoster neuralgia (AHN; within 1 month post-rash), subacute herpes zoster neuralgia (SHN; within 3 months post-rash), and post herpetic neuralnia (PHN; beyond 3 months post-rash).[3] Postherpetic neuralgia (PHN) has been identified as the most common and severe complication of shingles.[4] Consequently, there is a necessity to proactively investigate efficacious therapeutic methodologies with a view to enhancing the management of pain and reducing the prevalence of HZN, thus leading to an enhancement in patients' quality of life.

Current treatment options for HZN encompass pharmacological interventions, nerve blocks, and minimally invasive surgical interventions.[5] Pharmacological treatment is frequently regarded as the primary intervention for patients in the

Received: 4 July 2025
Accepted: 23 December 2025
Published: 30 December 2025

acute phase; nevertheless, drug treatment has no effect on many patients[6] and can also cause some adverse reactions, such as nausea, vomiting, dizziness, and somnolence can ensue.[7] Although the efficacy of nerve block therapy in alleviating pain is well-documented, its relatively brief duration of action is a salient drawback.[8]

Pulsed Radiofrequency (PRF) is a neuromodulation technique that has been shown to effectively alleviate pain, improve sleep, and reduce the dosage of oral medications in patients.[9] However, it should be noted that standard PRF has limitations, including poor long-term pain relief and high recurrence rates.[10] It is therefore essential to investigate novel treatment modalities with the aim of enhancing the therapeutic effects of PRF. Platelet-Rich Plasma (PRP) constitutes a concentrated preparation of platelets and plasma obtained from autologous blood through centrifugation, resulting in a platelet concentration that exceeds baseline levels. PRP has been demonstrated to elicit the release of a variety of bioactive factors and adhesion proteins, thereby instigating the process of tissue repair.[11] PRP has been demonstrated to release a number of bioactive factors, which have been shown to exhibit neuro-regenerative and analgesic effects.[12] A number of studies have indicated that the combination of PRP and PRF in the treatment of postherpetic neuralgia (PHN) can yield superior outcomes in terms of reduced pain scores and enhanced sleep quality when compared to conventional radiofrequency treatment.[13] Nevertheless, it is important to note that the majority of trials may be subject to bias, which can impede the ability to draw definitive conclusions.

The objective of this study is to conduct a systematic review and meta-analysis of randomized controlled trials to explore the efficacy and safety of combined treatment with PRF and PRP for pain related to herpes zoster. Clinical recommendations for treatment options for patients with herpes zoster-related pain will be provided.

Methods

This review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, as detailed in supplementary material 1. The study protocol was registered in PROSPERO (CRD420250632902).

Search Strategy

We perform a complete search in several databases. This search encompassed relevant English and Chinese studies from inception through to December 2024. A search was conducted of the Chinese Clinical Trial Registry and ClinicalTrials.gov, with a view to identifying unpublished studies. Papers were searched using the keywords: ("PRP" OR "platelet-rich plasma") AND ("postherpetic neuralgia" OR "zoster related neuralgia" OR "zoster related pain" OR "herpetic neuralgia" OR "herpes zoster") AND ("pulsed radiofrequency" OR "pulsed neuromodulatory" OR "PRF" OR "pulsed" OR "radiofrequency").

Inclusion Criteria

The following criteria were used for inclusion:1) study design: this paper brings together a number of published trials that examined the use of a combination of PRF with PRP to treat patients diagnosed with HZN. 2) Study subjects: HZN patients. 3) Intervention measures: The experimental group received a combination of PRF and PRP treatment. The subjects in the control group received standard PRF treatment. 4) Outcomes: Postoperative pain scores (VAS/NRS), the Pittsburgh Sleep Quality Index(PSQI), the dosage of postoperative analgesics, and adverse events. The following criteria were used to determine exclusion from the study: Firstly, the study will encompass both animal studies and in vitro studies. Secondly, patients suffering from herpes zoster in combination with other chronic pain conditions. Thirdly, trials should be conducted on non-surgical treatments and procedures other than PRF treatment. 4) Research for which the full text could not be obtained. The fifth issue pertains to studies that have been conducted with incomplete data.

Data Extraction

The authors ZWL and CCZ respectively extracted the documents by searching the titles, abstracts and full texts of the research studies, in order to determine whether these documents should be included in this review. The process of extracting data is as follows: The data to which the article refers has been independently extracted. The following basic information must be provided: the author's name, the publication year, the sample size, and the follow-up time. The following characteristics of the subjects studied have been documented: age, gender and average disease duration.

Thirdly, the interventions and controls were examined, which included PRF settings and PRP extraction in the experimental group, and PRF settings in the control group. The primary clinical outcomes encompassed VAS or NRS scores following treatment within the experimental or control group, while secondary outcomes included sleep quality as assessed by the PSQI, the necessity for rescue analgesics post-surgery, and the occurrence of adverse events.

Quality Assessment

The Cochrane Risk of Bias tool (RoB 2) was employed to assess the methodological quality and risk of bias in the included studies, considering selection bias, execution bias, detection bias, attrition bias, reporting bias, and other biases. In accordance with the stipulated methodology, the evaluation of bias was conducted and categorized as "low risk", "high risk", or "unclear risk".

Data Analysis

The meta-analysis was conducted utilizing the Review Manager statistical software (RevMan version 5.4). The dichotomous data was reported using relative risk (RR) and 95% confidence intervals (CI), while the continuous variables were quantitatively analyzed using mean difference (MD) or standardized mean difference (SMD) and 95% CI. The pain assessment involves NRS and VAS scoring sheets, so the SMD method is chosen; PSQI, emergency drug rescue quantity, and adverse events are selected as MD. The pain intensity score, the PSQI and he amount of first aid analgesicst were considered continuous type data. While adverse events were considered as dichotomous data. The chi-square test and I^2 test were utilized to assess the heterogeneity of the included studies. In instances where heterogeneity was identified among the studies, characterized by $P < 0.10$ and $I^2 > 50\%$, a random-effects model was employed. Conversely, a fixed-effects model was utilized to derive the pooled effect of the results when heterogeneity was not present. A sensitivity analysis was conducted using the "leave-one-out" method to identify the origin of significant heterogeneity. The level of significance was set at $P < 0.05$.

Results

The selection process for the study resulted in the selection of seven trials that were published between 2021 and 2024, with a total of seven trials in the final selection,[14–21] as detailed in Table 1. The screening process is illustrated in Figure 1. All subjects were diagnosed with HZN and received either PRF combined with PRP therapy or PRF therapy

Table 1 Baseline Characteristics of Included Studies

Study	Inclusion Criteria	Age (Mean ±SD)	Mean Course of Disease	Parameters	Outcomes	Baseline Scores (Mean ±SD)	Intervention	Follow-Up
Xin et al 2024[14]	1. T≤3months 2. NRS≥6 3. accept	P: 56.34±6.45 C: 55.82 ±6.67	P: 1.83±0.49months C: 1.95±0.52months	P: sensory stimulation: <0.3V,50Hz treatment parameters: 45V,2Hz,42°C,120s+2mL PRP C: sensory stimulation: <0.3V,50Hz treatment parameters: 45V,2Hz,42°C,120s+2mL NS	1. NRS 2. PSQI 3. rescue drug dose 4. adverse events	P:7.32±0.64 C:7.21±0.58	P: PRF+PRP C: PRF	4w
Wu et al 2023[15]	1. T≥1months 2. VAS≥5 3. accept	P: 64.52±3.41 C: 65.04 ±3.43	P: 8.54±1.65months C: 8.33±1.42months	P: sensory stimulation: 0.2–0.4V,50Hz treatment parameters: 45V,2Hz,42°C,120s+2mL PRP C: sensory stimulation: 0.2–0.4V,50Hz treatment parameters: 45V,2Hz,42°C,120s	1. NRS remission rate 2. PSQI 3. Alginogenic factor 4. inflammatory factor 5. adverse events	/	P: PRF+PRP C: PRF	4w

(*Continued*)

https://doi.org/10.2147/JPR.S548797

Table 1 (Continued).

Study	Inclusion Criteria	Age (Mean ±SD)	Mean Course of Disease	Parameters	Outcomes	Baseline Scores (Mean ±SD)	Intervention	Follow-Up
Zhang et al 2023[16]	1. NRS≥4 2. accept	P: 67.4±5.9 C: 66.8±5.8	P: 5.7±1.8months C: 5.7±1.9months	P: sensory stimulation: 0.3–0.5V,50Hz treatment parameters: 45V,2Hz,45°C,240s for 3 times +2mL PRP C: sensory stimulation: 0.3–0.5V,50Hz treatment parameters: 45V,2Hz,45°C,240s for 3 times +2mlNS	1. NRS 2. PSQI 3. adverse events	p:7.6±1.0 C:7.7±1.3	P: PRF+PRP C: PRF	24w
Xing et al 2023[17]	1. T≥3months 2. VAS≥4 3. accept	P: 53.66 ±10.05 C: 56.92 ±8.64	P: 6.82±1.57months C: 7.08±2.19months	P: sensory stimulation: 0.5V,50Hz treatment parameters: 45V,2Hz,42°C,120s for 2 times +2mL PRP C: sensory stimulation: 0.5V,50Hz treatment parameters: 45V,2Hz,42°C,120s for 2 times +2mL NS	1. VAS 2. PSQI 3. HAMD 4. DLQL 5. adverse events	P:7.02±1.57 C:6.87±2.14	P: PRF+PRP C: PRF	8w
Sun et al 2023[18]	1. T 1–3months 2. VAS>6 3. accept	P: 53.66 ±10.05 C: 56.92 ±12.6 C: 65.2±12.6	P: 48.4±13.9days C: 48.1±13.9days C: 48.0±12.6days	P: sensory stimulation: 0.5V,50Hz treatment parameters: 45V,2Hz,42°C,120s for 2 times +4mL PRP C1: sensory stimulation:0.5V,50Hz treatment parameters:45V,2Hz,42°C,120s for 2 times C2: mecobalamin-500mg for 3 times; gabapentin-300mg	1. VAS 2. PSQI	P:7.8±1.1 C1:7.8±1.0 C2:7.8±1.0	P: PRF+PRP C1: PRF C2: drug therapy	8w
Yuan et al 2022[19]	1. T≤3months 2. VAS≥5 3. accept	P: 70.11 ±12.15 C: 69.34 ±10.32	P: 2.07±0.93months C: 2.21±1.52months	P: sensory stimulation: <0.3V,50Hz treatment parameters: 50V,2Hz,900s +3mL PRP C: sensory stimulation<0.3V,50Hz treatment parameters: 50V,2Hz,900S+3mL NS	1. VAS 2. PSQI 3. adverse events	P:7.23±1.78 C:7.32±1.93	P: PRF+PRP C: PRF	12w
Xu et al 2021[20]	1. T≤1week 2. NRS≥6	P: 67.0±6 C: 65.0±5	P: 6.1±1.7months C: 6.4±1.4months	P: sensory stimulation: 0.3V,50Hz treatment parameters: 45V,2Hz,42°C,240s+1mL PRP C: sensory stimulation: 0.3V,50Hz treatment parameters: 45V,2Hz,42°C,240s+5mL NS	1. NRS 2. PSQI 3. rescue drug dose 4. adverse events	P:7.5±1.2 C:7.6±1.5	P: PRF+PRP C: PRF	12w

alone, followed by post-treatment assessments. Four trials included patients whose disease duration exceeded three months, for the other three experiments, the patients involved all had their illnesses lasting for less than three months. The average age of the patients ranged from 43.61 years to 82.26 years. The average duration of the trials ranged from 5.8 days to 5.5 months. In the six experiments, the intensity of the pain was evaluated using the 10-point visual analogue scale (VAS) or numerical rating scale (NRS), and the efficacy of pain relief was reported in one trial, both pre- and post-treatment. The evaluation of sleep quality was conducted by means of the PSQI in all of the included trials. The administration of rescue analgesic dosages was documented in two trials. Adverse events were reported in all trials. The follow-up period of the trials included in the study ranged from 1 week to 24 weeks.

Bias Risk Assessment

Six of the trials were assessed as having "low risk" for random sequence generation because the participants were grouped using a digital randomization method; one trial was assessed as having "high risk" for random sequence

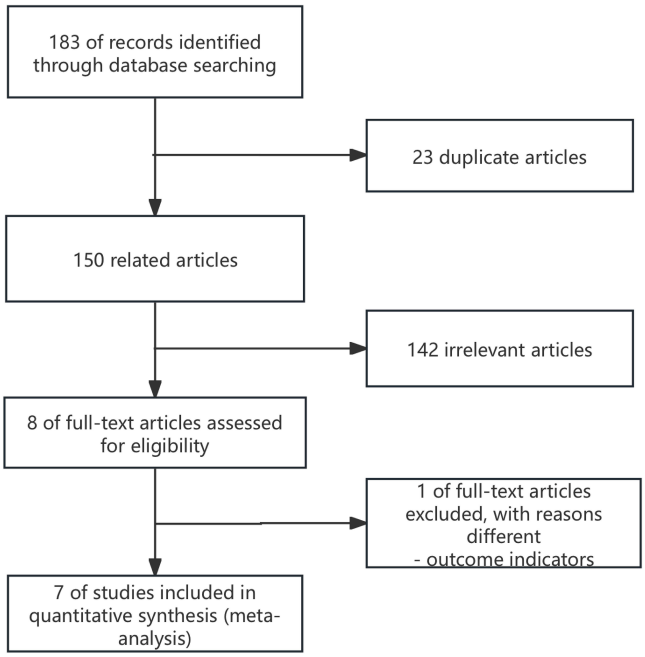

Figure 1 Study Screening Flowchart.

generation because the study was a retrospective study. Due to the lack of information, six of the trials were regarded as having "unclear risk" for allocation concealment; one trial was rated as having "high risk" for this project. The evaluation of the seven trials revealed that they all exhibited a "low risk" classification with respect to participant blinding. The findings of three trials indicated the presence of performance bias, attributable to a paucity of information concerning personnel blinding and outcome assessment. Four trials were assessed as "low risk" for performance bias because personnel and participants were blinded to group assignment due to well-designed sham PRP and PRP groups. The assessment of detection bias was categorised as "unclear risk" in all trials, a decision that was made due to an absence of pertinent information. Patient attrition occurred in three trials without explanation, raising concerns about attrition bias. Four trials were classified as "low risk" due to the absence of incomplete outcome data. The included trials did not demonstrate any instances of selective reporting; however, it should be noted that six of these trials did not disclose any conflicts of interest or funding sources. This has given rise to concerns regarding the potential presence of other biases. The presence of publication bias could not be ascertained due to the inclusion of a maximum of ten studies. Since no more than 10 studies were included, publication bias would not be assessed. A comprehensive overview of the findings is provided in Figure 2.

Primary Outcome Measure

NRS Score

Before the intervention, no statistically significant differences were observed between the two groups (SMD =0.02, 95% CI: −0.16 to 0.20, P=0.79, Figure 3a), there was no heterogeneity within the group (I2 = 0%, P = 0.95), and no sensitivity analysis was conducted.

One week after treatment, there was no statistically significant difference between the two groups (SMD = −0.38, 95% CI: −0.92 to 0.15, P = 0.16, Figure 3b). Due to high heterogeneity (I2 = 79%, P = 0.003), by excluding the studies of Sun et al and Zhang et al, the heterogeneity was resolved (I2 = 0%, P = 0.92), and the effect size remained significant (SMD=0.09,95% CI −0.26 to −0.44, P=0.62).

After two weeks of treatment, there was a statistically significant difference between the two groups (SMD =−0.54, 95% CI −0.77 to −0.32, P<0.00001, Figure 3c), (I2=0%, P=0.85) there was no heterogeneity within the group (I2=0%, P=0.85), and no sensitivity analysis was conducted.

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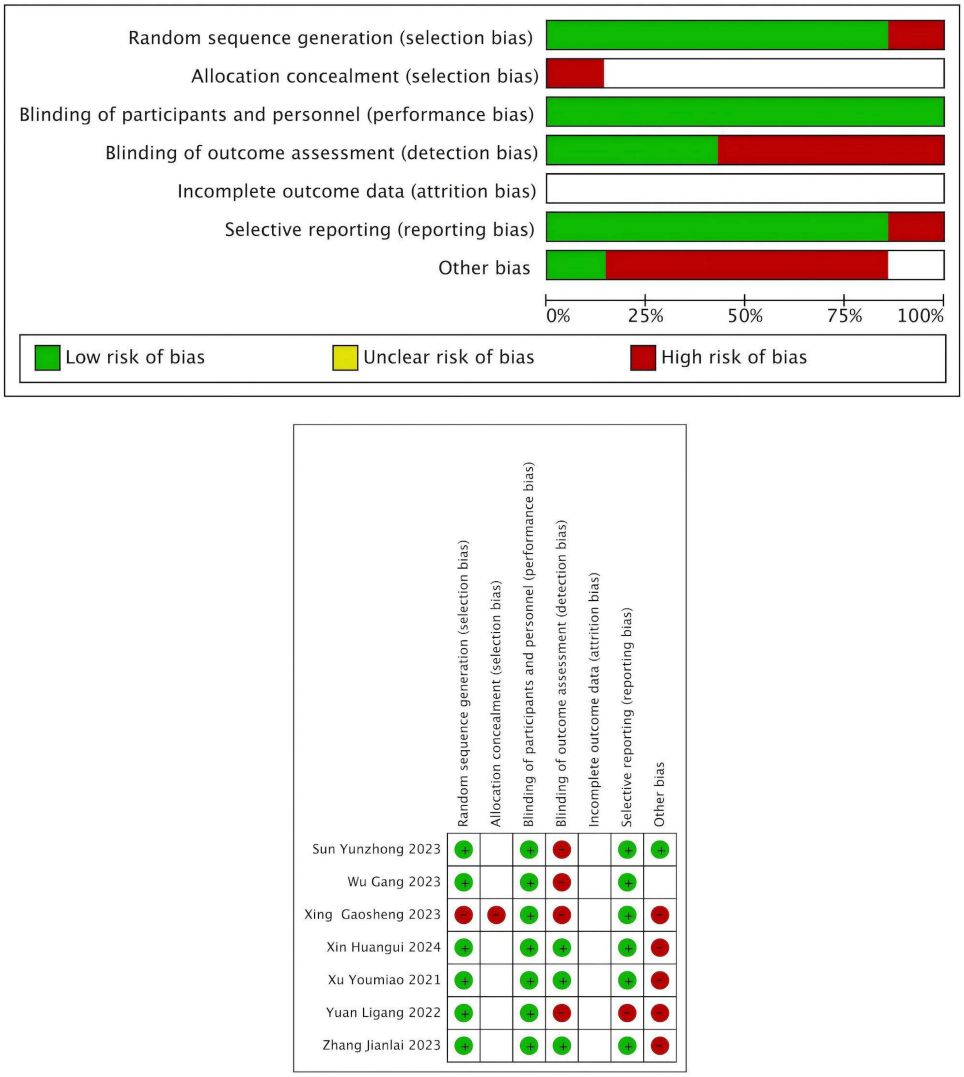

Figure 2 Assessment of Bias Risk.

After four weeks of treatment, there was a statistically significant difference between the two groups (SMD=−0.64, 95% CI −1.17 to −0.10, P=0.02, Figure 3d), due to high heterogeneity (I2=87%, P<0.00001, by excluding the studies of Xing et al and Xu et al, the heterogeneity was resolved (I2=0%, P=0.52), and the effect size remained significant (SMD= −0.61,95% CI −0.85 to −0.37, P<0.00001).

After eight weeks of treatment, there was a statistically significant difference between the two groups (SMD =−1.12, 95% CI −1, 36 to −0.87, P<0.00001, Figure 3e), there was low heterogeneity within the group (I2=37%, P=0.19).

After twelve weeks of treatment, there was a statistically significant difference between the two groups (SMD =−1.43, 95% CI −1.74 to −1.12, P<0.00001, Figure 3f), there was no heterogeneity within the group (I2=0%, P=0.46).

Secondary Outcome Measures

Sleep Quality

Seven of the included studies reported PSQI scores in order to assess patients' sleep quality. Before the intervention, no statistically significant differences were observed between the two groups (MD =0.31, 95% CI −0.19 to 0.80, P=0.22, Figure 4a), there was no heterogeneity within the group (I2=0%, P=0.94).

After two weeks of treatment, there was a statistically significant difference between the two groups (MD =−1.57, 95% CI −2.51 to −0.63, P=0.001, Figure 4b), there was moderate heterogeneity within the group (I2=63%, P=0.04), by

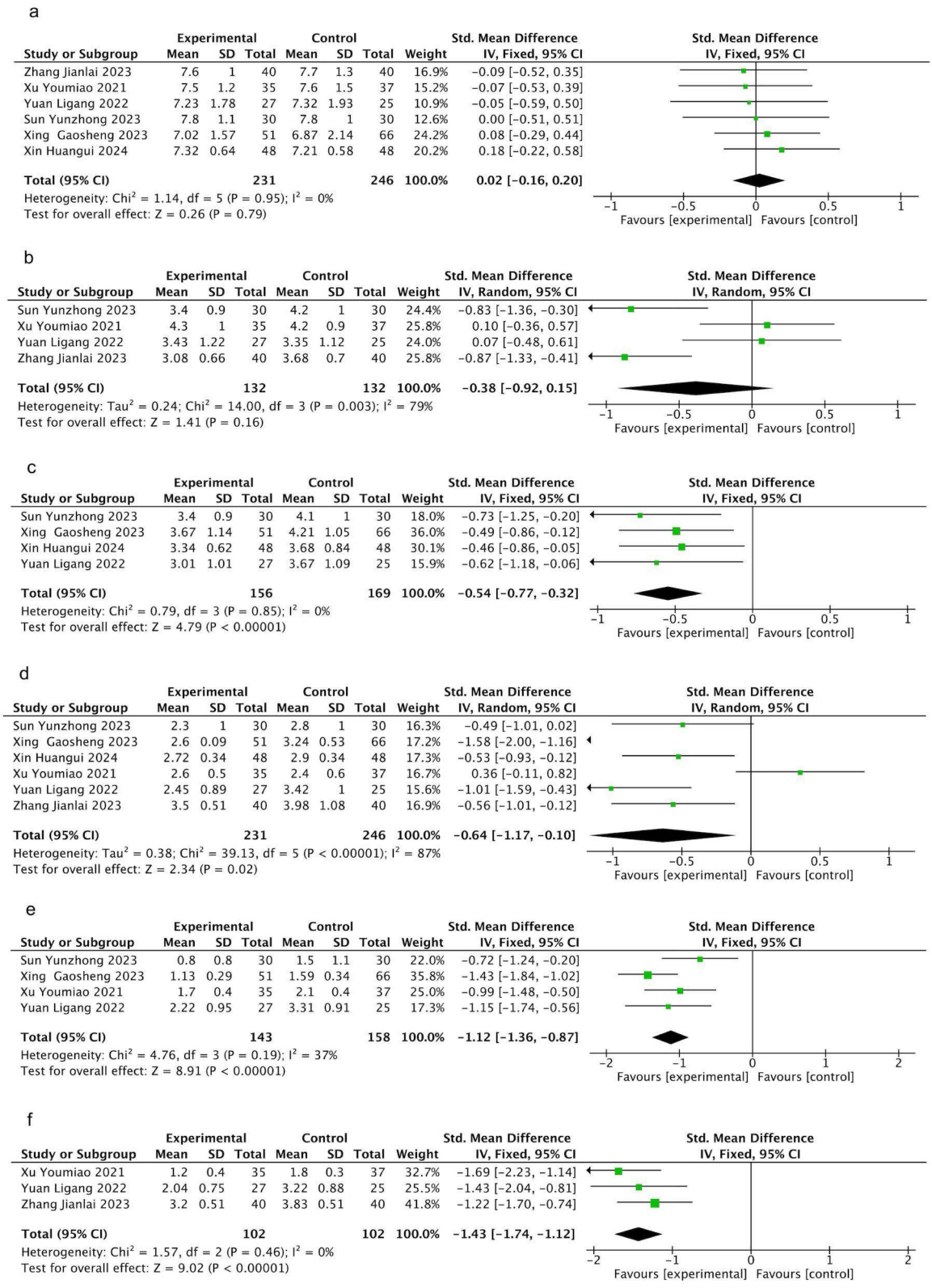

Figure 3 (**a**) Comparison of preoperative NRS/VAS scores; (**b**) Comparison of NRS/VAS scores 1 week after surgery; (**c**) Comparison of NRS/VAS scores 2 weeks after surgery; (**d**) Comparison of NRS/VAS scores 4 weeks after surgery; (**e**) Comparison of NRS/VAS scores 8 weeks after surgery; (**f**) Comparison of NRS/VAS scores 12 weeks after surgery.

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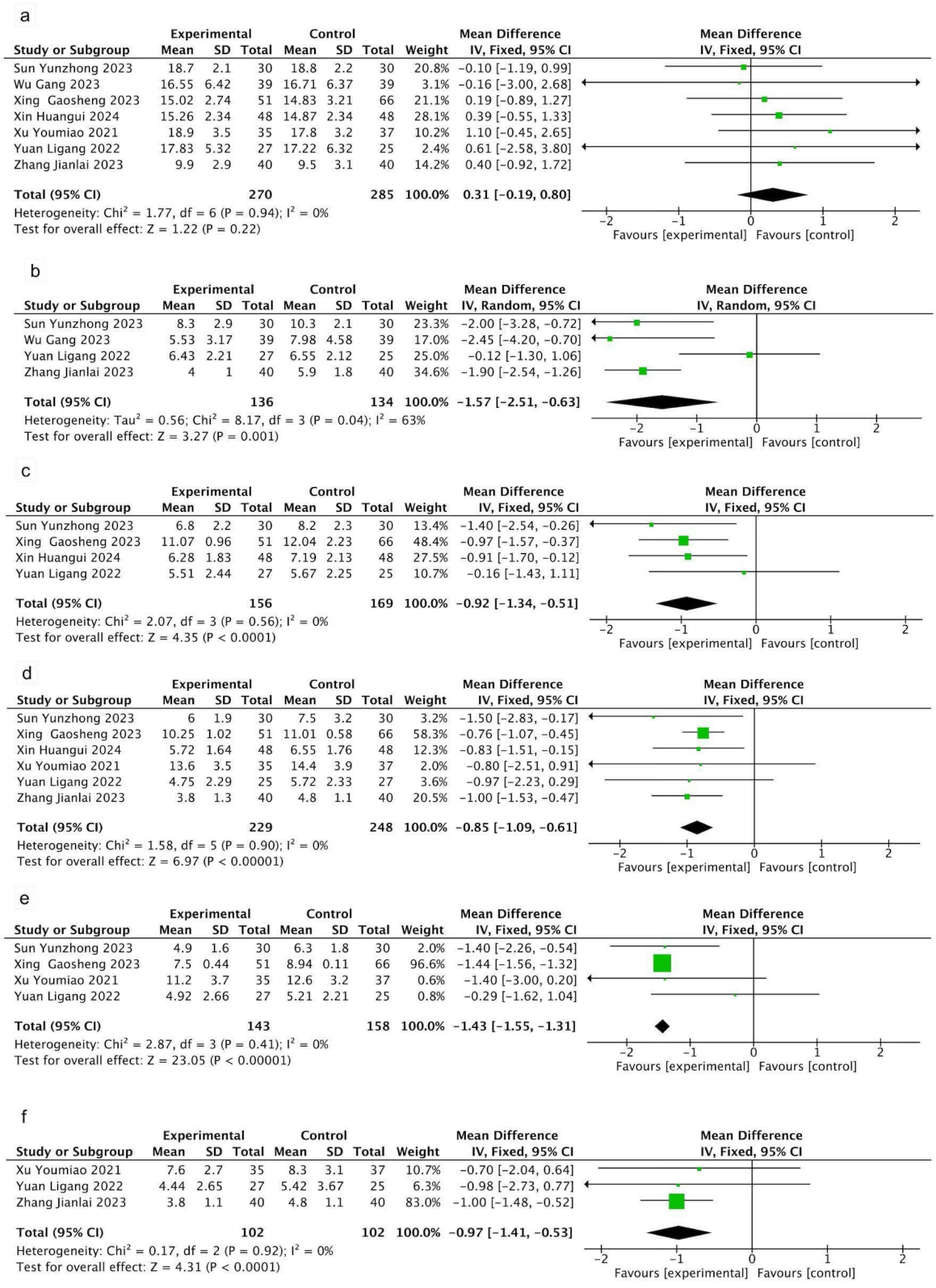

Figure 4 (**a**) Comparison of preoperative PSQI scores; (**b**) Comparison of PSQI scores 1 week after surgery; (**c**)Comparison of PSQI scores 2 weeks after surgery; (**d**) Comparison of PSQI scores 4 weeks after surgery; (**e**) Comparison of PSQI scores 8 weeks after surgery; (**f**) Comparison of PSQI scores 12 weeks after surgery.

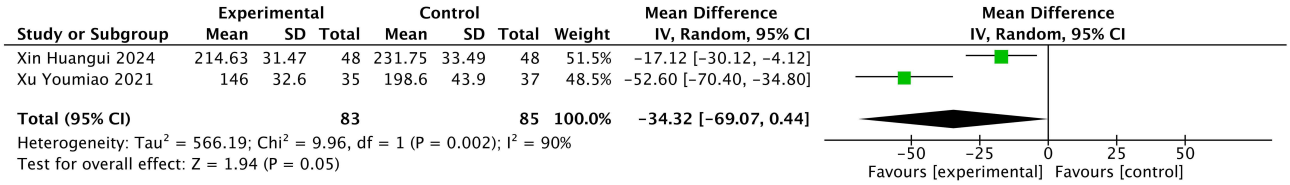

Figure 5 Comparison of Rescue Medication Dosage.

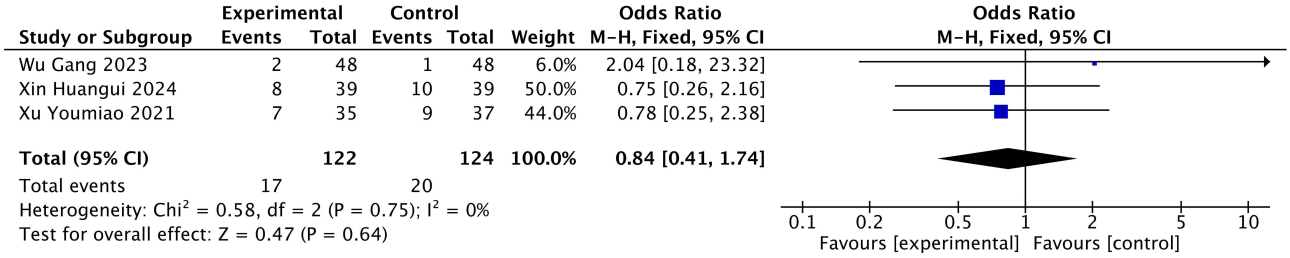

Figure 6 Comparison of Adverse Event Occurrences.

excluding the studies of Yuan et al, the heterogeneity was resolved (I2=0%, P=0.84), and the effect size remained significant (MD =−1.97, 95% CI −2.51 to −1.43, P<0.00001).

After two weeks of treatment, there was a statistically significant difference between the two groups (MD =−0.92, 95% CI −1.34 to −0.51, P<0.0001, Figure 4c), there was no heterogeneity within the group (I2=0%, P=0.56).

After four weeks of treatment, there was a statistically significant difference between the two groups (MD =−0.85, 95% CI −1.09 to −0.61, P<0.00001, Figure 4d), there was no heterogeneity within the group (I2=0%, P=0.90).

After eight weeks of treatment, there was a statistically significant difference between the two groups (MD =−1.12, 95% CI −1.36 to −0.87, P<0.00001, Figure 4e), there was low heterogeneity within the group (I2=37%, P=0.19).

After twelve weeks of treatment, there was a statistically significant difference between the two groups (MD =−1.43, 95% CI −1.74 to −1.12, P<0.00001, Figure 4f), there was no heterogeneity within the group (I2=0%, P=0).

Rescue Medication Dosage

As demonstrated in the studies conducted by Xin and Xu, there is a discrepancy in the postoperative dosage of rescue medication. The findings demonstrated that the combined group exhibited a reduced necessity for pregabalin rescue medication in comparison to the control group, exhibiting a significant discrepancy (MD −34.32, 95% CI –69.07 to −0.44, P=0.05, Figure 5), due to high heterogeneity (I2=90%, P=0.002), a sensitivity analysis cannot be conducted. It is important to note that, due to the limited number of studies available, conducting meaningful sensitivity analyses (ie, the “leave-one-out” method) is not feasible. This high degree of heterogeneity represents a significant limitation for this particular outcome.

Adverse Events

Of the seven trials that were included in the study, adverse events were reported by 568 participants. In all the trials, no serious complications were observed, including but not limited to nerve damage or intracranial infections. The adverse events that were observed included nausea, dizziness, rash, and localized skin infection. The incidence of adverse events was comparable between the combined group and the control group (MD 0.84, 95% CI 0.41 to −1.74, P=0.64, Figure 6), there was no heterogeneity within the group (I2=0%, P=0.64).

Discussion

The present meta-analysis yielded four key findings. Firstly, in comparison with the control group, PRF combined with PRP significantly alleviated pain associated with herpes zoster. Secondly, the combination therapy significantly improved

patients' sleep quality. Thirdly, it resulted in a substantial reduction in the necessity for postoperative rescue medication. Fourthly, no severe adverse events were observed, with comparable complication rates between both groups.

The development of herpes zoster-related neuralgia is the result of persistent inflammation and neuronal lesions induced by the varicella-zoster virus. This virus can alter the functions of neurons and trigger abnormal spontaneous secretion, thereby increasing the sensitivity of the peripheral nervous system and the central nervous system.[21] For the established changes in the peripheral nervous system and the central nervous system, PRF relies on microscopic or subcellular-level modulation, such as regulating synaptic plasticity, suppressing ectopic discharges, and enhancing noradrenergic and adrenergic descending suppression pathways to reverse sensitization.[22]

In recent years, there has been an increasing focus on the combined use of PRP and PRF in the treatment of postherpetic neuralgia. It has been demonstrated by clinical studies that this approach has the potential to yield favourable therapeutic outcomes.[12,23–25] PRP has been demonstrated to facilitate the release of a range of bioactive factors and adhesive proteins, thereby instigating the process of tissue repair. These active substances have been demonstrated to trigger the hemostatic cascade, synthesize new connective tissue and promote vascular reconstruction, thereby providing a theoretical basis for PRP in repairing tissue defects and facilitating wound healing.[26] The potential pathogenesis of herpes zoster-related pain includes the following: nerve damage, peripheral and central sensitization, and severe inflammatory responses. The potential therapeutic mechanisms of platelet concentrate in the treatment of herpes zoster pain may include the following points: It has been demonstrated that several growth factors in PRP exert anti-apoptotic and neuroprotective effects on mesenchymal stem cells, neurons, Schwann cells, and human neural stem cells.[27,28] Secondly, the anti-inflammatory effects of the substance in question have been demonstrated in clinical trials.[29] PRP has been demonstrated to elicit the release of a substantial quantity of anti-inflammatory factors, thereby exerting a suppressive effect on inflammatory responses. Thirdly, the analgesic effects of the substance under investigation are considered.[30] Freshly prepared platelets in PRP remain dormant; upon activation, they undergo morphological changes, promote platelet aggregation, and release intracellular α-granules, which stimulate the release of pain-modulating serotonin. The fourth point pertains to immunomodulation.[31] It has been established that platelet α-granules release two key growth factors, transforming growth factor-β (TGF-β) and platelet-derived growth factor (PDGF). The function of these two factors is to regulate immune responses. In a randomized controlled trial conducted by Rarissima et al, Studies have shown that in the treatment of knee osteoarthritis, the therapeutic effect of platelet-rich plasma (PRP) is better.[32]

In terms of pain intensity, in the treatment and management of herpes zoster-related pain, the combined application of PRF and PRP has a significant advantage over the use of PRF alone. Subgroup analyses at varying follow-up time points revealed no significant difference in pain reduction at one week post-intervention; however, significant differences were observed at two, four, eight, and 12 weeks, with the combination group demonstrating superior outcomes.

In terms of sleep quality, the combination therapy demonstrated a significant improvement in comparison to PRF administered as a standalone treatment. Subgroup analyses confirmed improvements at all follow-up intervals (1, 2, 4, 8, and 12 weeks), with the combination group showing superior results. With regard to the administration of postoperative rescue analgesia, the combination group demonstrated a significantly reduced requirement for such medications. There was no significant difference in the incidence of adverse events between the two groups.

It has been demonstrated by several studies that PRF is an efficacious treatment for herpes zoster-related neuralgia.[33] However, some patients experience inadequate pain relief after PRF alone, with some even developing PHN.[34] The findings of our meta-analysis suggest that the combination of platelet-rich fibrin (PRF) and platelet-poor plasma (PRP) is more efficacious than PRF alone in the therapeutic management of pain associated with shingles, based on the superiority of the former in terms of pain reduction.

It is widely acknowledged that elderly patients, defined as those over the age of 60, constitute the demographic most susceptible to HZ infection. Greater attention should be paid to this population, as age-related declines in renal function and altered pharmacokinetics/pharmacodynamics may lead to an increased prevalence of drug-related adverse effects. In this meta-analysis, no serious complications were observed, and the adverse events reported by the experimental group were comparable to those of the control group. Consequently, for the majority of patients experiencing shingles-related pain, the combination of PRF and PRP is a relatively safe and well-tolerated approach.

It has been established through the course of numerous studies that the combination of PRF and PRP is an efficacious treatment for shingles-related pain. In a similar vein, the article offers substantiated evidence that lends credence to the efficacy and safety of this joint therapy.

Strengths and Limitations

This meta-analysis demonstrates several advantages. Firstly, as far as we know, this is the first comprehensive quantitative study on the effects and safety of the combined application of PRF and PRP in the treatment of shingles-related pain, while other meta-analyses mainly focus on other treatment methods for improving postherpetic neuralgia. Secondly, we conducted subgroup analyses for patients at different follow-up time points. Thirdly, the review was conducted in accordance with the standards set out by the Cochrane Collaboration. The evaluation by two independent authors can reduce systematic errors.

Nevertheless, it should be noted that the present meta-analysis is not without its limitations. Firstly, the majority of the primary outcomes demonstrated considerable heterogeneity, which may be attributed to the varying ages and disease durations of the combined group and the control group, resulting in some inconsistencies in this meta-analysis. Secondly, most of the included studies were followed for less than three months, so their long-term effect could not be determined. Thirdly, the number of experimental cases included in the study was relatively small. Finally, this study has limitations including poor blinding.

Conclusion

The combination of PRF and PRP has been proven to be a safe and effective treatment modality, with superior outcomes in the management of postherpetic neuralgia when compared with PRF alone. This combination has also been demonstrated to enhance sleep quality and reduce the necessity for postoperative rescue analgesics.

Consent for Publication

The authors confirm that all content in this review is publicly accessible.

Acknowledgments

This study was supported by the National Clinical Key Specialty Construction Project-Oncology department (2023-GJZK-001), the Clinical Key Specialty of Zhejiang Province Anesthesiology (2023ZJZK001), the Zhejiang Provincial Traditional Chinese Medical Innovation Team of China under Grant No. (2022-19), Zhejiang Clinovation Pride-Herpes zoster neuralgia (CXTD202502014), the Key Supported Discipline of Jiaxing Medical Science - Anesthesiology (2023-ZC-001).

Disclosure

The authors report no conflicts of interest in this work.

References

1. Zhao C, Lu Z, Hua B, et al. Predictive value of current perception threshold for prognosis of pulsed radiofrequency in patients with acute herpetic neuralgia. *J Pain Res*. 2024;17:3241–3253. doi:10.2147/JPR.S472535
2. Zhang Z, Liu X, Suo L, et al. The incidence of herpes zoster in China: a meta-analysis and evidence quality assessment. *Hum Vaccin Immunother*. 2023;19(2):2228169. doi:10.1080/21645515.2023.2228169
3. Singer D, Thompson-Leduc P, Ma S, et al. Herpes zoster burden in patients with asthma: real-world incidence, healthcare resource utilisation and cost. *BMJ Open Respir Res*. 2024;11(1). doi:10.1136/bmjresp-2023-002130
4. Adriaansen EJM, Jacobs JG, Vernooij LM, et al. 8. Herpes zoster and post herpetic neuralgia. *Pain Pract*. 2024;25(1).
5. Luo G, Zhang Z, Zhu J, et al. Association between the risk of relapse and the type of surgical procedure for herpes zoster-related pain. *Pain Physician*. 2021;24(8):E1227–1236.
6. Peng F, Xia TB. Effects of intradermal botulinum toxin injections on herpes zoster related neuralgia. *Infect Drug Resist*. 2023;16:2159–2165. doi:10.2147/IDR.S401972
7. Tang J, Zhang Y, Liu C, et al. Therapeutic strategies for postherpetic neuralgia: mechanisms, treatments, and perspectives. *Curr Pain Headache Rep*. 2023;27(9):307–319. doi:10.1007/s11916-023-01146-x
8. Thouaye M, Yalcin I. Neuropathic pain: from actual pharmacological treatments to new therapeutic horizons. *Pharmacol Ther*. 2023;251:108546. doi:10.1016/j.pharmthera.2023.108546
9. De la Cruz J, Benzecry Almeida D, Silva Marques M, et al. Elucidating the mechanisms of pulsed radiofrequency for pain treatment. *Cureus*. 2023;15(9):e44922. doi:10.7759/cureus.44922

10. Chen R, Xu X, Yu Y, et al. High-voltage pulsed radiofrequency improves ultrastructure of DRG and enhances spinal microglial autophagy to ameliorate neuropathic pain induced by SNI. *Sci Rep*. 2024;14(1):4497. doi:10.1038/s41598-024-55095-5
11. Dos Santos RG, Santos GS, Alkass N, et al. The regenerative mechanisms of platelet-rich plasma: a review. *Cytokine*. 2021;144:155560. doi:10.1016/j.cyto.2021.155560
12. Wang S, Liu Z, Wang J, et al. Platelet-rich plasma (PRP) in nerve repair. *Regen Ther*. 2024;27:244–250. doi:10.1016/j.reth.2024.03.017
13. Sun YZ, Guo XL, Zhao L, et al. Evaluation and prediction of the therapeutic effect of radiofrequency combined with platelet-rich plasma in the treatment of herpes zoster ophthalmicus of trigeminal nerve by current perception threshold measurement. *Chin J Pain Med*. 2024;30(07):534–538.
14. Xin H. Clinical efficacy of platelet-rich plasma injection combined with pulsed. radiofrequency therapy in patients with acute/subacute postherpetic neuralgia. *Fujian Med J*. 2024;46(03):53–55. doi:10.20148/j.fmj.2024.03.016
15. Wu G. Clinical observation on combined pulsed radiofrequency and autologous platelet-rich plasma perineural injection for postherpetic neuralgia. *Xinjiang Med*. 2023;53(12):1446–1449.
16. Zhang J, Wang X, Song Y. Clinical observation on combined radiofrequency ablation of dorsal root ganglion and platelet-rich plasma injection for post-herpetic neuralgia. *Shanxi J Med*. 2023;52(21):1611–1615.
17. Xing G, Zhang J, Tang Q. Clinical efficacy of CT-guided intervertebral foramen puncture radiofrequency thermocoagulation combined with platelet-rich plasma injection for refractory post-herpetic neuralgia in the upper thoracic region. *J Clin Exp Med*. 2023;22(18):1964–1968.
18. Sun Y, Guo X, Zhao L, et al. CT-guided pulsed radiofrequency combined with platelet-rich plasma injection for the treatment of subacute postherpetic neuralgia. *Chin J Pain Med*. 2023;29(01):69–73.
19. Yuan L, Wan C. Clinical efficacy of combined pulsed radiofrequency of the dorsal root ganglion and platelet-rich plasma injection for acute/subacute postherpetic neuralgia. *J China Med Univ*. 2022;51(08):752–755.
20. Xu Y, Yang X, Liu T. Clinical study on combined pulsed radiofrequency and platelet-rich plasma therapy for herpes zoster in the elderly. *Chin J Mod Med*. 2021;31(08):65–69.
21. Pacifico P, Coy-Dibley JS, Miller RJ, et al. Peripheral mechanisms of peripheral neuropathic pain. *Front Mol Neurosci*. 2023;16:1252442. doi:10.3389/fnmol.2023.1252442
22. Moussa WM, Khedr W, Elsawy M. Percutaneous pulsed radiofrequency treatment of dorsal root ganglion for treatment of lumbar facet syndrome. *Clin Neurol Neurosurg*. 2020;199:106253. doi:10.1016/j.clineuro.2020.106253
23. Zhou Z, Hu X, F YAN, et al. Observation on the effect of platelet-rich plasma combined with drugs in the treatment of herpes zoster neuralgia. *Int J Neurosci*. 2024;134(6):628–634. doi:10.1080/00207454.2022.2138381
24. M TD, Gao XM, Yang L, et al. Clinical effect of percutaneous transcavernous injection of platelet-rich plasma into the trigeminal ganglion for treating postherpetic neuralgia of the trigeminal nerve. *Chin J Pain Med*. 2022;18(01):52–57.
25. Huang LR, Guo JN, Lv YN, et al. Observation on the therapeutic effect of intramuscular injection of platelet-rich plasma in treating post-herpetic neuralgia. *Chin J Pain Med*. 2021;27(08):631–634.
26. Vladulescu D, Scurtu LG, Simionescu AA, et al. Platelet-Rich Plasma (PRP) in dermatology: cellular and molecular mechanisms of action. *Biomedicines*. 2023;12(1):7. doi:10.3390/biomedicines12010007
27. Zhang Y, Yi D, Hong Q, et al. Platelet-rich plasma-derived exosomes boost mesenchymal stem cells to promote peripheral nerve regeneration. *J Control Release*. 2024;367:265–282. doi:10.1016/j.jconrel.2024.01.043
28. Cheng PG, Yang KD, Huang LG, et al. Comparisons of cytokines, growth factors and clinical efficacy between platelet-rich plasma and autologous conditioned serum for knee osteoarthritis management. *Biomolecules*. 2023;13:555. doi:10.3390/biom13030555
29. Fang X, Guo JM, Liu PD. Comparison of different concentrations of platelet-rich plasma in repairing cartilage defects in rabbit knee osteoarthritis. *Chin J Tissue Eng Res*. 2021;25(35):5588–5593.
30. Yang YF, Zhong ZF, Liu YM, et al. Application progress of platelet-rich plasma in the treatment of neuropathic pain. *Chin J Pain Med*. 2024;30(01):19–27. doi:10.1186/s13020-023-00864-z
31. Ju Y, Wen CH. Current research on the treatment of post-herpes neuralgia with platelet-rich plasma. *Med Front*. 2024;14(04):45–47.
32. Raeissadat SA, Ghazi Hosseini P, Bahrami MH, et al. The comparison effects of. intra-articular injection of Platelet Rich Plasma (PRP), Plasma Rich in Growth Factor (PRGF), Hyaluronic Acid (HA), and ozone in knee osteoarthritis; a one year randomized clinical trial. *BMC Musculoskelet Disord*. 2021;22(1):134. doi:10.1186/s12891-021-04017-x
33. Zhang E, Fei Y, Xu L, et al. Effect of repeated high-voltage long-duration pulsed radiofrequency on herpetic neuralgia. *Pain Physician*. 2022;25(7):1047–1055.
34. Li HQ, Xia LJ, Jiang YH, et al. Efficacy and safety of pulsed radiofrequency combined with gabapentin in the treatment of acute herpetic neuralgia. *Zhonghua Yi Xue Za Zhi*. 2023;103(48):3954–3958. doi:10.3760/cma.j.cn112137-20230921-00517