Am J Transl Res 2026;18(2):1310-1319
www.ajtr.org /ISSN:1943-8141/AJTR0167976

Original Article

Effect of famciclovir combined with nerve block on acute pain in patients with herpes zoster

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Received August 7, 2025; Accepted December 29, 2025; Epub February 15, 2026; Published February 28, 2026

Abstract: Aims: To evaluate the efficacy of famciclovir in combination with nerve block treatment for managing acute pain in patients with herpes zoster. Methods: This retrospective study included 200 patients with acute pain due to herpes zoster, admitted to our hospital between January 2021 and January 2025. Participants were divided into two groups: the observation group (n = 108; famciclovir combined with nerve block therapy) and the control group (n = 92; nerve block therapy alone), according to their treatment protocols. Pain intensity was assessed using the Visual Analog Scale (VAS) at baseline, Day 3, Day 7, and Day 14. Secondary outcomes included inflammatory markers, sleep quality (Pittsburgh Sleep Quality Index [PSQI], Sleep Disturbance Scale [SDS], Epworth Sleepiness Scale [ESS], and Insomnia Severity Index [ISI]), adverse events, and clinical outcomes, such as rash resolution and postherpetic neuralgia (PHN) incidence. Results: The observation group experienced greater reductions in VAS scores on Days 3, 7, and 14 compared with the control group ($P < 0.001$), indicating better pain relief. Inflammatory markers, including C-reactive protein (CRP), interleukin-6 (IL-6), procalcitonin (PCT), tumor necrosis factor-α (TNF-α), and white blood cell count (WBC), were significantly lower in the observation group ($P < 0.001$ for all), indicating a stronger anti-inflammatory response. Sleep quality also improved significantly in the observation group, evidenced by reductions in PSQI, SDS, ESS, and ISI scores ($P < 0.001$ for all). The incidence of adverse events was similar between the two groups ($P > 0.05$), with no severe events. In addition, the observation group also showed better clinical manifestations, including higher rates of pain relief ($P = 0.001$) and rash resolution ($P < 0.001$), as well as a lower incidence of PHN ($P < 0.001$). Conclusion: The combination of famciclovir and nerve block therapy substantially improves pain relief, reduces inflammatory responses, and enhances clinical outcome without increasing the risk of adverse events.

Keywords: Famciclovir, nerve block, acute pain, herpes zoster, pain management

Introduction

Herpes zoster (HZ), or popularly known as shingles, is a painful condition caused by the reactivation of varicella-zoster virus (VZV), following a previous episode of varicella (chickenpox) [1]. Upon reactivation, the virus transmits along the sensory nerves, leading to painful vesicular eruptions in a particular dermatome [2]. HZ predominantly affects elderlies and immunocompromised individuals, with epidemiological data showing a notable rises in incidence among individuals over 50 years of age [3, 4]. In addition to the rash, HZ is also accompanied by acute pain, which can be disabling and substantially impair patients' quality of life. This pain may persists for couple of weeks and is primarily attributed to inflammation and damage of the affected nerves [5, 6]. If not properly managed, this acute pain might progress to postherpetic neuralgia (PHN), a chronic pain condition that is difficult to treat. PHN represents a major contributor to disease burden, as it leads to prolonged suffering and greatly impairs daily activities [7]. Thus, effective pain control during an acute stage of HZ is important for preventing PHN and improving overall patient outcomes.

Famciclovir is a commonly used antiviral gent for the pharmacologic treatment of HZ by inhibiting VZV replication. Although famciclovir is effective in reducing viral load, its direct analgesic effect on acute HZ-induced pain remains limited [8-10]. Accordingly, additional analgesic regimens are often required, including the

https://doi.org/10.62347/JWBN6636

opioids, nonsteroidal anti-inflammatory drugs (NSAIDs), and corticosteroids; however, these agents are associated with potential side effects and clinical limitations, particularly in the elderly or immunocompromised patients [11, 12].

In recent years, nerve block interventions have emerged as promising adjunctive treatment for HZ-induced acute pain. By administrating local anesthetics around the affected nerves, nerve block therapy interrupts nociceptive signal transmission and provides rapid and substantial pain relief. Such procedures have proven effective in reducing acute pain intensity and decreasing the risk of developing PHN [13, 14]. The combination of nerve block with antiviral treatment, including famciclovir, represents a synergistic approach that not only suppresses viral replication but also achieves both immediate and long-term pain relief, thereby reducing reliance on systemic analgesics, lowering the incidence of PHN, and ultimately improving patient outcomes.

Despite these anticipated beneficial effects, the clinical efficacy of combining famciclovir with nerve block therapy has not been fully elucidated. This study aimed to assess the effectiveness of famciclovir combined with nerve block therapy in the management of acute pain in patients with HZ, with a focus on pain alleviation and PHN prevention.

Methods

Patient selection

This retrospective study included 200 patients with acute HZ-induced pain who were admitted to The First People's Hospital of Jiashan between January 2021 and January 2025. Based on the treatment protocol, patients were divided into two groups: the observation group (n = 108; famciclovir combined with nerve block therapy) and the control group (n = 92; nerve block therapy alone). Strict inclusion and exclusion criteria were applied to ensure the reliability of the retrospective analysis. This study was approved by the Ethics Committee of The First People's Hospital of Jiashan.

Inclusion criteria: (1) a diagnosis of HZ confirmed by clinical examination and laboratory tests [15]; (2) presence of acute pain due to HZ; (3) age ≥ 18 years; and (4) hospitalization during the acute phase of the disease. Exclusion criteria: (1) a history of hypersensitivity or contraindications to famciclovir or local anesthetics; (2) severe immunosuppressive conditions, including HIV/AIDS or ongoing chemotherapy; (3) neurological disorders unrelated to HZ; (4) incomplete medical records or failure to complete the assigned treatment.

Treatment details and data extraction

In the control group, patients received standardized nerve block therapy. The specific type of nerve block was selected according to the anatomical distribution of the HZ lesions. For lesions located on the trunk, paraspinal or intercostal nerve blocks were performed; for facial lesions, trigeminal nerve branch blocks (e.g., supraorbital, maxillary, or mandibular branch) were applied; and for limb lesions, peripheral nerve blocks corresponding to the affected dermatome were used. All nerve block procedures were performed by trained anesthesiologists under strict aseptic conditions. After identification of the target nerve region using anatomical landmarks, a local anesthetic agent was injected near the affected sensory nerve pathway under ultrasound guidance (when appropriate) to interrupt pain transmission. Lidocaine (Jiangsu Hualu Pharmaceutical Co., Ltd., Product No. H2008423) was administered at a dose of 10 mg as a single injection on the day of admission. Patients were monitored continuously after the procedure to detect adverse events.

In the observation group, patients received nerve block treatment combined with oral famciclovir (AstraZeneca AB; Product No. H20140763). Famciclovir was administered at a dose of 0.25 g/day for 7 consecutive days, and the nerve block therapy was the same with the control group. The antiviral therapy aimed to suppress viral replication and reduce viral load, while nerve block therapy was intended to alleviate acute herpes zoster-related pain. Both treatments were administered under clinical supervision, and patients were regularly monitored to ensure treatment safety.

Key variables collected included demographic details (age, sex), clinical characteristics (comorbidities, lesion location), baseline pain intensity measured using the Visual Analog

Scale (VAS), and inflammatory markers including C-reactive protein (CRP), Interleukin-6 (IL-6), procalcitonin (PCT), tumor necrosis factor-alpha (TNF-α), and white blood cell count (WBC). In addition, sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI), Sleep Disturbance Scale (SDS), Epworth Sleepiness Scale (ESS), and Insomnia Severity Index (ISI). Clinical outcomes, including pain relief, rash resolution, PHN incidence, and recurrence, were also recorded at multiple time points (Day 3, Day 7, Day 14, and 6-month follow-up). Adverse events, including gastrointestinal, neurological, dermatological, and general health disturbances, were noted, along with any severe events that led to hospitalization. All data were anonymized and reviewed by a team of clinicians for accuracy.

Outcome measures

Pain intensity was the primary outcome of the study and was measured using the VAS [16]. Pain was measured at baseline and on Days 3, 7, and 14. Patients were asked to rate their pain on a scale ranging from 0 (no pain) to 10 (the worst pain possible). A greater reduction in VAS score was indicative of more effective pain management. Secondary outcomes included inflammatory markers, quality of sleep, adverse events, and clinical manifestations. Inflammatory markers were assessed at baseline and during follow-up visits. Serum levels of IL-6, PCT, and TNF-α were measured using enzyme-linked immunosorbent assay (ELISA). CRP was determined by immunoturbidimetric assay, and WBC count was measured using an automated hematology analyzer. All assays were conducted in accordance with the manufacturers' instructions and standard laboratory protocols. Significant reductions in these markers were regarded as evidence of an anti-inflammatory effect of treatments.

Sleep quality was evaluated using four validated scales: the PSQI [17], SDS [18], ESS [19], and ISI [20]. The PSQI was used to evaluate the subjective sleep quality, the SDS quantifies sleep disturbances, the ESS assesses daytime sleepiness, and the ISI measures the severity of insomnia. All sleep-related assessments were conducted at baseline and on Day 14 to evaluate changes following treatment. Adverse events were also monitored throughout the study period and recorded at each visit. These events were categorized as gastrointestinal (e.g., nausea, vomiting, abdominal pain), neurological (e.g., headache, dizziness), dermatological (e.g., skin rash, itching), or general health disturbances (e.g., fatigue, fever). The incidence, severity, and the association with treatment were documented, and any severe adverse events requiring hospitalization were recorded. Clinical outcomes were measured based on the percentage of patients achieving pain relief (VAS score ≤ 3), complete rash resolution (disappearance of vesicular lesions), and the incidence of PHN (pain persisting for more than 3 months after rash resolution). These outcomes were assessed on Day 14 and at 6-month follow-up to determine short and long-term therapeutic effects.

Statistical analysis

Data were analyzed using SPSS 25.0. Continuous variables were presented as means ± standard deviations, while categorical variables were presented as frequencies and percentages. Comparisons between groups for continuous variables were performed using the independent-samples t-test or Mann-Whitney U test, as appropriate. Categorical variables were compared using the chi-square test or Fisher's exact test. Changes in pain scores, inflammatory markers, and sleep quality over time were assessed using repeated-measures analysis of variance (ANOVA). A p-value of < 0.05 was considered statistically significant for all analyses.

Results

Comparison of baseline clinical characteristics between the two groups

The two groups were comparable in terms of age, gender distribution, comorbidities, or mean duration of acute pain (all $P > 0.05$). In addition, the distribution of lesion locations, including the trunk, face, or extremities did not differ significantly between the two groups ($P > 0.05$) (**Table 1**). These results suggest that the groups were well-matched at baseline, allowing for a reliable comparison of the treatment outcomes.

Table 1. Comparison of baseline clinical characteristics between the two groups

Characteristics	Observation Group (n = 108)	Control Group (n = 92)	t/χ^2	P
Age (mean ± SD)	56.06 ± 9.56	54.86 ± 10.82	0.831	0.407
Sex			0.029	0.864
Male	48 (44.4%)	42 (45.7%)		
Female	60 (55.6%)	50 (54.3%)		
Comorbidities (Hypertension)	36 (33.3%)	32 (34.8%)	0.047	0.829
Comorbidities (Diabetes)	25 (23.1%)	24 (26.1%)	0.232	0.630
Mean duration of acute pain (days)	6.88 ± 1.54	7.24 ± 1.73	1.554	0.122
Lesion location				
Extremities	25 (23.1%)	14 (15.2%)	1.991	0.158
Face	18 (16.7%)	20 (21.7%)	0.831	0.362
Trunk	65 (60.2%)	58 (63.0%)	0.171	0.679

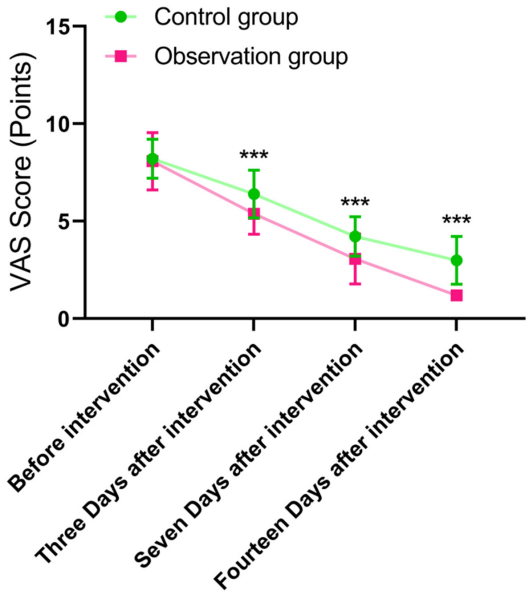

Figure 1. Comparison of VAS scores between the two groups. ***P < 0.001, compared to the control group. Note: VAS: Visual Analog Scale.

Comparison of VAS scores between the two groups

At baseline, both groups exhibited similar VAS scores. However, three days after intervention, the observation group demonstrated a significantly greater reduction in pain intensity compared to the control group (P < 0.001). This trend continued on Day 7, where the observation group showed a more pronounced decrease in VAS scores, further emphasizing the superior pain relief provided by the combination of famciclovir and nerve block therapy. On Day 14, the observation group maintained a significantly lower VAS score compared to the control group (P < 0.001) (**Figure 1**).

Comparison of inflammatory indicators between the two groups

At follow-up, the observation group demonstrated significantly lower serum levels of CRP, IL-6, and PCT compared with the control group (**Figure 2A-C**) (P < 0.001), indicating a stronger anti-inflammatory response. Additionally, TNF-α levels and WBC were more pronouncedly reduced in the observation group compared with the control group (**Figure 2D**, **2E**) (both P < 0.001), further supporting the enhanced inflammatory control provided by the combination of famciclovir and nerve block therapy.

Comparison of sleep quality between the two groups

The PSQI and SDS scores significantly decreased in the observation group across all follow-up points, with the most pronounced reduction observed at day 14 (P < 0.001) (**Figure 3A**, **3B**). The ESS exhibited a comparable trend, with the observation group demonstrating a marked reduction in daytime sleepiness (P < 0.001) (**Figure 3C**). Similarly, the ISI scores significantly improved in the observation group, reaching the most significant decrease at day 14 (P < 0.001) (**Figure 3D**). These results indicate that the combination of famciclovir and nerve block therapy provides a more effective improvement in sleep quality, as reflected by greater reductions in PSQI, SDS, ESS, and ISI scores, compared to nerve block therapy alone.

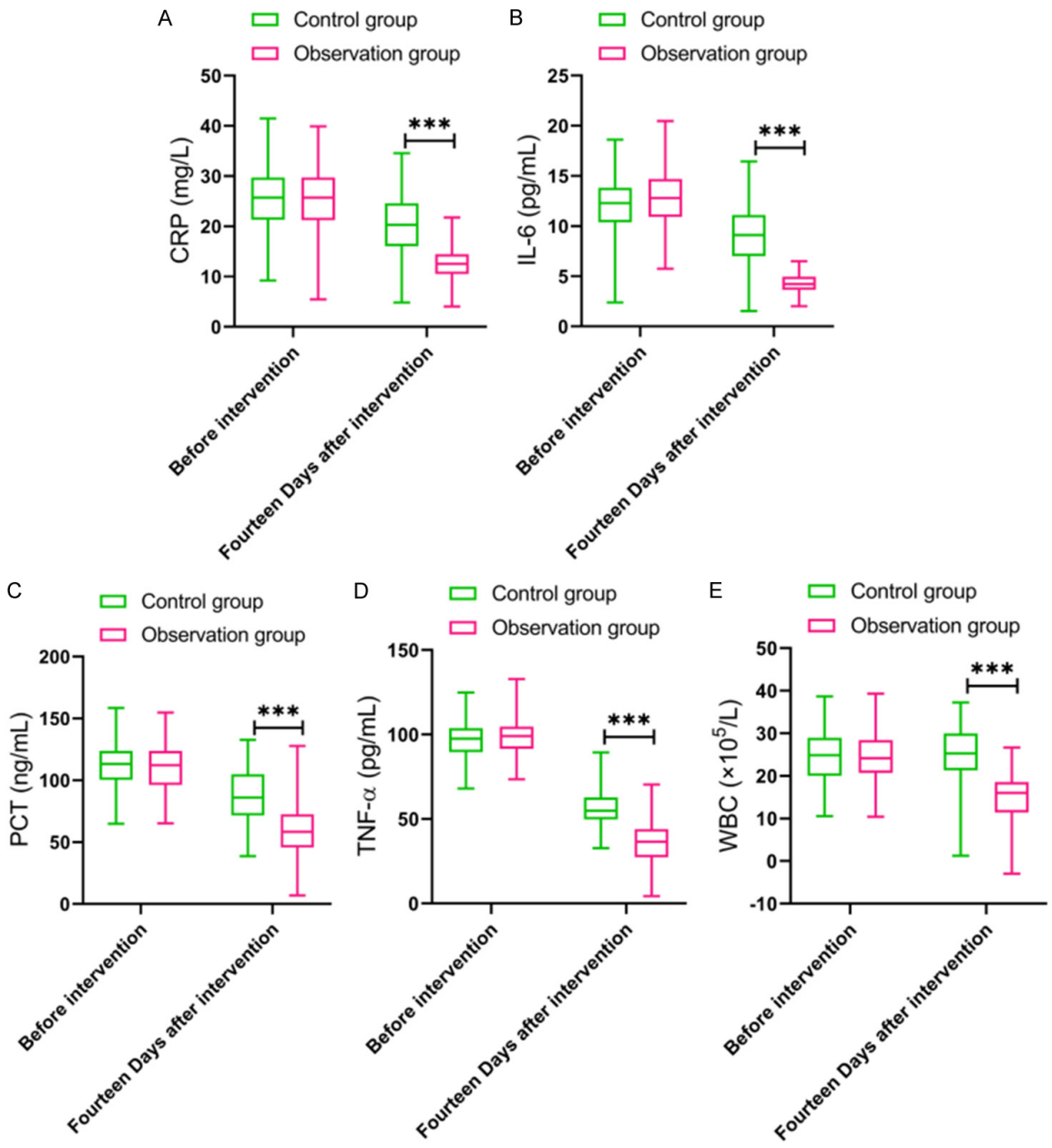

Figure 2. Comparison of inflammatory marker levels between the two groups. (A) CRP, (B) IL-6, (C) PCT, (D) TNF-α, (E) WBC. ***P < 0.001, compared to the control group. Note: CRP: C-reactive protein; IL-6: Interleukin 6; PCT: Procalcitonin; TNF-α: Tumor necrosis factor alpha; WBC: White blood cells.

Comparison of adverse events between the two groups

The overall incidence of adverse events was comparable between the two groups (25.0% vs. 32.6%; P = 0.235). Gastrointestinal symptoms were the most common adverse events, including nausea (6.5% vs. 9.8%; P = 0.391), vomiting (2.8% vs. 4.3%; P = 0.547), and abdominal pain (1.9% vs. 3.3%; P = 0.525). Neurological adverse events, including headache and dizziness, were also equally distributed between both groups (P = 0.807). Dermatological events, including skin rash and pruritus, were relatively uncommon, and didn't differ significantly between groups (P = 0.557). The incidence of general health disorders (e.g., fatigue and fever) was marginally higher in control group, but didn't reach statistical significance (P = 0.167). Severe adverse events were

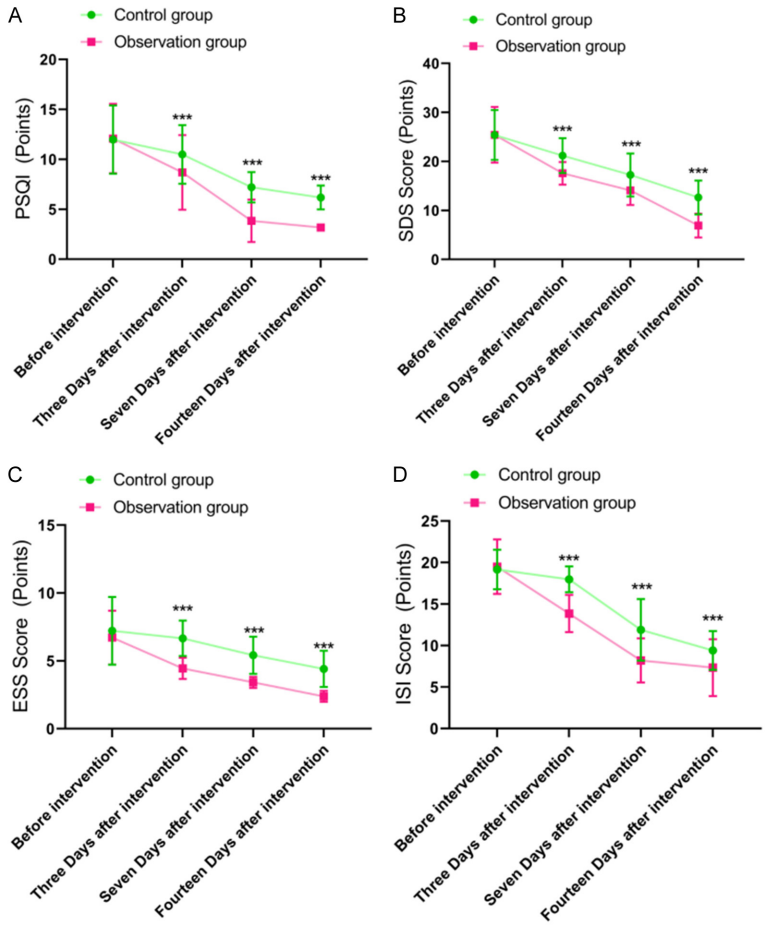

Figure 3. Comparison of sleep quality between the two groups. (A) PSQI, (B) SDS, (C) ESS, (D) ISI. ***P < 0.001, compared to the control group. Note: PSQI: Pittsburgh Sleep Quality Index; SDS: Sleep Disturbance Scale; ESS: Epworth Sleepiness Scale; ISI: Insomnia Severity Index.

rare and did not differ significantly between groups (P = 0.169). Only one patient in the observation group and two patients in the control group required hospitalization due to adverse events (P = 0.469) (**Table 2**).

Comparison of clinical manifestations between the two groups

In this study, 80.6% of patients in the observation group experienced pain relief, defined as a VAS score ≤ 3, compared to 63.0% in the control group (P = 0.006). Although a greater proportion of patients in the observation group achieved a VAS score ≤ 5 than in the control group (94.4% vs. 89.1%), this difference was not statistically significant (P = 0.167). Additionally, complete rash resolution was observed in 37.0% of the observation group versus 16.3% of the control group (P = 0.001). In addition, the proportion of patients achieving lesion reduction exceeding 50% was significantly higher in the observation group compared with the control group (78.7% vs. 65.2%, P = 0.033). None of the patients in the observation group showed no improvement in rash lesions, whereas 27.2% in the control group showed no improvement (P < 0.001).

The incidence of PHN by Day 14 was markedly lower in the observation group (3.7% vs. 15.2%; P = 0.005). Among those who developed PHN, pain severity was also significantly lower in the observation group compared to the control group (VAS = 4.73 ± 2.01 vs. 7.01 ± 2.03; P < 0.001). Furthermore, at the 6-month follow-up, PHN occurred in 5.6% of the patients in the observation group, in contrast to 21.7% of the control group (P = 0.001). The occurrence of new lesions by Day 14 was lower in the observation group, compared to the control group (5.6% vs. 16.3%, P = 0.013). Skin infections were also less frequent in the observation group (1.9% vs. 5.4%, P < 0.001) (**Table 3**).

Representative rash images before and after treatment

Figure 4 presents representative clinical images illustrating changes in HZ rashes in both the groups before and after treatment. In the observation group, patients presented with typical vesicular rashes, characterized by erythema and fluid-filled blisters at baseline (**Figure 4A**). After treatment, significant clinical improvement was observed, with a noticeable reduction in lesion size, erythema, and crust formation (**Figure 4B**). In contrast, the control group displayed a more extensive rash at baseline, with a greater density of vesicles and localized inflammation (**Figure 4C**). After treatment,

Table 2. Comparison of adverse events between the two groups

Adverse events	Observation group (n = 108)	Control group (n = 92)	χ^2	*p*-value
Total adverse events (n, %)	27 (25.0%)	30 (32.6%)	1.411	0.235
Total gastrointestinal events (n, %)	12 (11.1%)	16 (17.4%)	1.627	0.202
Nausea	7 (6.5%)	9 (9.8%)	0.736	0.391
Vomiting	3 (2.8%)	4 (4.3%)	0.363	0.547
Abdominal pain	2 (1.9%)	3 (3.3%)	0.405	0.525
Total neurological events (n, %)	8 (7.4%)	6 (6.5%)	0.060	0.807
Total dermatological events (n, %)	6 (5.6%)	7 (7.6%)	0.345	0.557
Total general health disturbances (n, %)	6 (5.6%)	10 (10.9%)	1.906	0.167
Fatigue	4 (3.7%)	7 (7.6%)	1.458	0.227
Fever	2 (1.9%)	3 (3.3%)	0.405	0.525
Total severe adverse events (n, %)	2 (1.9%)	5 (5.4%)	1.888	0.169
Hospitalization due to adverse events (n, %)	1 (0.9%)	2 (2.2%)	0.524	0.469

Table 3. Comparison of clinical manifestations between the two groups

Parameters	Observation group (n = 108)	Control group (n = 92)	t/χ^2	*p*-value
Pain relief (VAS ≤ 3 at day 14) (n, %)	87 (80.6%)	58 (63.0%)	7.642	0.006
Pain relief (VAS ≤ 5 at day 14) (n, %)	102 (94.4%)	82 (89.1%)	1.906	0.167
Complete rash resolution (n, %)	40 (37.0%)	15 (16.3%)	10.711	0.001
Partial rash improvement (n, %)	68 (63.0%)	52 (56.5%)	0.859	0.354
No rash improvement (n, %)	0 (0%)	25 (27.2%)	33.540	< 0.001
Number of rash lesions decreased by > 50% (n, %)	85 (78.7%)	60 (65.2%)	4.532	0.033
Postherpetic neuralgia (PHN) at day 14 (n, %)	4 (3.7%)	14 (15.2%)	8.041	0.005
PHN severity (VAS) at day 14 (among PHN patients)	4.73 ± 2.01	7.01 ± 2.03	7.952	<0.001
PHN at 6-month follow-up (n, %)	6 (5.6%)	20 (21.7%)	11.505	0.001
Presence of new lesions at day 14 (n, %)	6 (5.6%)	15 (16.3%)	6.108	0.013
Skin infection (n, %)	2 (1.9%)	5 (5.4%)	13.342	<0.001

rash resolution was slower, with remaining erythema and some residual vesicles (**Figure 4D**), indicating less effective healing compared to the observation group.

Discussion

In this study, we evaluated treatment efficacy of famciclovir in combination with nerve block therapy for the management of acute pain in patients with herpes zoster. Our results indicate that the combined therapy offers significant benefits compared with nerve block therapy alone, especially in pain relief and PHN prevention. In particular, patients in the observation group exhibited greater reductions in pain intensity, higher rates of the rash healing, and lower rates of PHN during early follow-up, suggesting that the combination strategy not only targets viral replication but also enhances symptomatic pain control, thereby potentially reducing overall disease burden.

Our findings are generally consistent with previous reports on the individual therapeutic efficacies of famciclovir and nerve block treatment in herpes zoster. Famciclovir is a well-established antiviral drug that suppresses VZV replication and has been shown to shorten the duration and severity of HZ rashes [21]. However, despite its antiviral efficacy, famciclovir alone has a limited analgesic effect during the acute stage, underscoring the necessity for additional pain-control interventions. Nerve blocks, which involves the injection of local anesthetics around the affected nerves, provides rapid analgesia by inhibiting nociceptive signal transmission [22, 23]. Our study extends

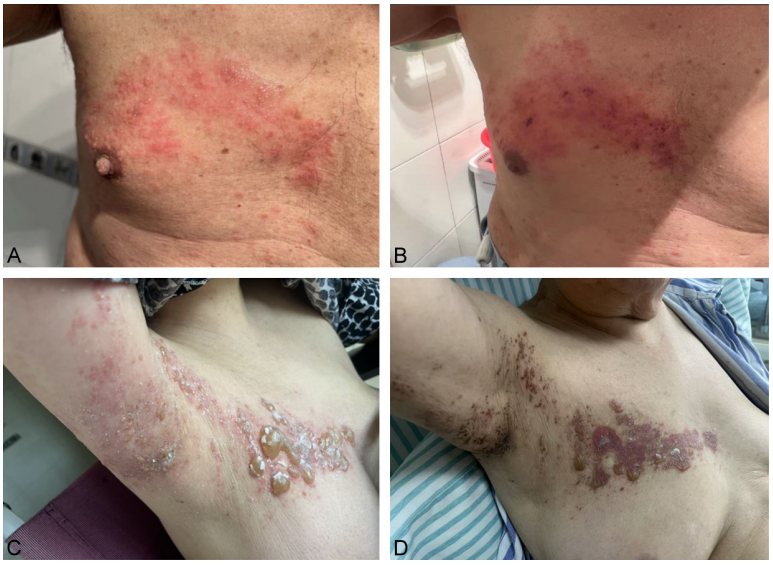

Figure 4. Representative rash images of patients with herpes zoster in both groups before and after treatment. A. Observation group - Pre-treatment; B. Observation group - Post-treatment; C. Control group - Pre-treatment; D. Control group - Post-treatment. The images illustrate the typical clinical features of herpes zoster lesions at baseline and the extent of lesion resolution following treatment in both groups.

this to a combination of antiviral famciclovir and immediate analgesic effect of nerve block therapy providing better clinical results than either therapy alone.

Mechanistically, the combination therapy exerts synergistic effects on both acute pain control and viral replication. Famciclovir suppresses VZV replication, thereby limiting virus-induced inflammation, while nerve block interrupts nociceptive signal transmission along affected nerves. In this study, patients receiving combined therapy exhibited significantly lower levels of CRP, IL-6, PCT, and TNF-α, suggesting suppressed inflammatory activity. In addition, famciclovir combined with nerve blocks may reduce the risk of developing PHN, a long-term complication associated with persistent inflammation and nerve injury [24].

It is especially remarkable that this combination therapy effectively lowers the incidence of PHN. PHN is among the most debilitating sequelae of HZ that characterized by chronic neuropathic pain. Previous studies have suggested that early initiation of antiviral therapy may reduce the risk and severity of PHN [25-27]. Consistently, our results demonstrated a significantly lower incidence of PHN in the observation group during the follow-up period. This finding indicates that antiviral therapy combined with nerve blocks may play a beneficial role in mitigating the long-term consequences of HZ, ensuring a higher quality of life among patients.

In addition to clinical outcomes, this study examined the effects of combination therapy on sleep-related outcomes. The sleep quality of HZ patients is generally poor, especially in those affected by severe pain, which intensifies fatigue and leads to daytime sleepiness. The observation group showed significant improvements across all assessed sleep-related parameters, including the PSQI, SDS, ESS, and ISI scores. This enhancement in sleep quality highlights the overall superiority of combination therapy, which greatly contributes to patient well-being beyond mere pain alleviation [28]. Collectively, the results suggest that combination therapy not only alleviates the acute pian of HZ but also mitigates secondary sleep disturbances that are often overlooked, yet have substantial impacts on overall quality of life.

Despite these inspiring findings, several limitations of this study should be acknowledged. First, the retrospective design restricts the ability to draw definite causal conclusions. Although baseline characteristics were well balanced between the two groups, the lack of randomization may have introduced section biases that could influence the outcome. Further large-scale randomized controlled trials are necessary to validate our results and minimize bias. Second, longer-term follow-up data are needed to better assess the durability of treatment effect, especially for the prevention of PHN and HZ recurrence. In addition, rare side effects of famciclovir or nerve block treatment may not have been fully captured, underscoring the need for studies with larger sample sizes.

Conclusion

This study provides evidence supporting the effectiveness of famciclovir combined with nerve block treatment for the management of

HZ-induced acute pain. This combination therapy not only enhances pain relief and accelerates rash resolution but, more importantly, reduces the incidence of PHN, providing an encouraging modality for the treatment of herpes zoster.

Disclosure of conflict of interest

None.

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