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Famciclovir Versus Acyclovir in The Management of Herpes Zoster: Effects on Rash Healing, Pain, And Post-Herpetic Neuralgia

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ABSTRACT

Background: Herpes zoster, commonly known as shingles, results from the reactivation of latent varicella-zoster virus (VZV) residing in dorsal root ganglia following primary infection. Early initiation of antiviral therapy has been shown to reduce viral replication, accelerate lesion healing, decrease acute pain severity, and lower the risk of PHN. Acyclovir and famciclovir are commonly used antiviral agents; however, differences in pharmacokinetics, dosing convenience, and clinical outcomes necessitate comparative evaluation. **Objective**: To compare the efficacy and tolerability of Famciclovir and Acyclovir in treating Herpes Zoster. **Methods:** This randomized, open-label, prospective, parallel-group study was conducted in 60 patients with clinically diagnosed herpes zoster. Participants were randomly allocated into two equal groups. One group received oral famciclovir 500 mg three times daily, while the other group received oral acyclovir 800 mg five times daily, both for a duration of seven days. Patients were followed up regularly to assess time to complete rash healing, reduction in pain intensity using standardized pain scales, development of post-herpetic neuralgia, and occurrence of adverse drug reactions. Data were analyzed using appropriate statistical tests, with a p-value <0.05 considered statistically significant. **Results:** Patients treated with famciclovir demonstrated significantly faster rash healing compared with those receiving acyclovir (7.2 ± 1.8 days vs 9.1 ± 2.2 days; p = 0.003). Pain reduction was also more pronounced in the famciclovir group, with a 78% decrease in pain scores compared to a 65% reduction in the acyclovir group (p = 0.01). Furthermore, the incidence of post-herpetic neuralgia was significantly lower among patients treated with famciclovir (10%) compared with those treated with acyclovir (26%; p = 0.04). **Conclusion:** Famciclovir demonstrated superior efficacy compared with acyclovir in the treatment of herpes zoster, with faster lesion healing, greater pain relief, and a lower incidence of post-herpetic neuralgia. Its favorable tolerability and convenient dosing make famciclovir a preferred antiviral option for the management of herpes zoster.

Keywords*: Acyclovir, Antiviral therapy, Famciclovir, Herpes zoster, Post-herpetic neuralgia.*

INTRODUCTION

Herpes zoster (HZ) or shingles is a neurocutaneous disorder caused by reactivation of latent varicella-zoster virus in the sensory dorsal root ganglia.[1] The incidence and severity of HZ increase with advancing age and immunosuppression, and the condition is associated with significant morbidity and impairment of quality of life.[2] Among its complications, postherpetic neuralgia (PHN) remains the most debilitating, characterized by persistent neuropathic pain lasting months or years after rash resolution due to sustained neuronal inflammation and damage.[3]

Early initiation of antiviral therapy—preferably within 72 hours of rash onset—is a critical determinant of clinical outcome.[4] Antiviral treatment limits viral replication, accelerates cutaneous healing, reduces the intensity and duration of acute pain, and lowers the risk of developing PHN. Consequently, timely and effective antiviral therapy is central to the management of acute HZ.[5]

Acyclovir and famciclovir are widely used guanosine nucleoside analogues that exert antiviral activity through selective inhibition of viral DNA polymerase after intracellular phosphorylation.[6] Acyclovir has long been considered a standard treatment for HZ; however, its clinical utility is limited by poor oral bioavailability (approximately 15–30%) and the requirement for frequent dosing (800 mg five times daily). These pharmacokinetic limitations may adversely affect patient adherence, particularly in elderly individuals, thereby potentially compromising therapeutic outcomes.[7,8]

Famciclovir, the oral prodrug of penciclovir, offers several pharmacological advantages over acyclovir. It demonstrates substantially higher oral bioavailability (>70%), prolonged intracellular half-life of the active metabolite, and a more convenient dosing schedule (three times daily).[9] These properties may translate into improved compliance, enhanced antiviral efficacy, and better clinical outcomes, including reduced pain burden and lower incidence of PHN.[10] Despite these theoretical advantages, comparative evidence evaluating the clinical effectiveness of famciclovir versus acyclovir remains limited, particularly in diverse and resource-constrained populations.

The present prospective study was therefore designed to compare the efficacy, safety, and tolerability of famciclovir and acyclovir in adults with acute herpes zoster. Clinical outcomes assessed included time to complete rash healing, reduction in pain intensity, and incidence of postherpetic neuralgia, using standardized and clinically relevant measures.

This study provides direct comparative clinical data on famciclovir and acyclovir in the management of acute herpes zoster within a real-world clinical setting. By simultaneously evaluating rash healing, pain relief, and PHN prevention, the study offers a comprehensive assessment of therapeutic outcomes and adds region-specific evidence to guide rational antiviral selection in routine clinical practice.

MATERIALS AND METHODS

Study Design and Setting: This randomized, open-label, parallel-group, comparative clinical study was conducted in the Departments of Pharmacology and Dermatology at Sree Mookambika Institute of Medical Sciences, Kulasekharam, over a period spanning January 2024 to June 2025.

Study Population and Sample Size: A total of 60 patients with clinically diagnosed herpes zoster were enrolled in the study and randomly allocated into two groups of 30 participants each.

Inclusion Criteria: Adults aged 18–65 years presenting within 72 hours of onset of herpes zoster rash and willing to provide written informed consent were included.

Exclusion Criteria: Patients with immunocompromised states, renal or hepatic impairment, pregnancy or lactation, known hypersensitivity to study drugs, or those receiving concurrent antiviral therapy were excluded from the study.

Study procedure: After obtaining written informed consent, patients meeting the inclusion criteria were enrolled and randomly allocated into two treatment groups. Baseline demographic and clinical details, including rash distribution and pain intensity, were recorded. Group A received oral famciclovir 500 mg three times daily for 7 days, while Group B received oral acyclovir 800 mg five times daily for the same duration. Patients were advised regarding drug compliance and monitored for adverse drug reactions throughout the treatment period. Follow-up assessments were conducted at regular intervals to document time to complete rash healing and changes in pain intensity using the Visual Analog Scale (VAS). All participants were reassessed at 4 weeks after treatment completion to evaluate the occurrence of postherpetic neuralgia.

Outcome Measures: The primary outcome measure was time to complete rash healing. Secondary outcome measures included reduction in pain intensity assessed using the Visual Analog Scale (VAS) and the incidence of postherpetic neuralgia at 4 weeks of follow-up.

Statistical Analysis: Data were analyzed using SPSS version 25.0. Continuous variables were analyzed using Student's *t*-test, and categorical variables were compared using the Chi-square test. A p-value of <0.05 was considered statistically significant.

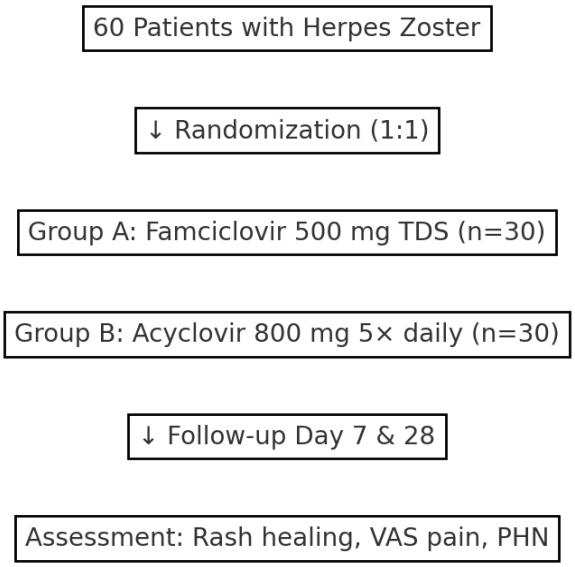

Fig 1: Study Design Flowchart

RESULTS

The demographic and baseline clinical characteristics of the study participants are summarized in Table 1. Both treatment groups were comparable at baseline with respect to age, sex distribution, and time since rash onset, with no statistically significant differences observed.

Parameter	Famciclovir (n=30)	Acyclovir (n=30)	p-value
Age (years), mean ± SD	48.5 ± 11.2	47.3 ± 10.6	0.61
Sex (M:F)	17:13	16:14	0.79
Time since rash onset (hours), mean ± SD	48.6 ± 12.5	50.2 ± 13.1	0.57

Table 1: Demographic and Baseline Characteristics

Comparison of treatment outcomes is presented in Fig 2 and Table 2. Patients treated with famciclovir demonstrated significantly faster rash healing compared with those receiving acyclovir (7.2 ± 1.8 vs 9.1 ± 2.2 days; p = 0.003). Pain reduction was also significantly greater in the famciclovir group (78%) than in the acyclovir group (65%; p = 0.01). The visual gap between bars underlines clinically meaningful analgesic superiority of Famciclovir. In addition, the incidence of postherpetic neuralgia at 4 weeks was significantly lower in the famciclovir group (10%) compared with the acyclovir group (26%; p = 0.04).

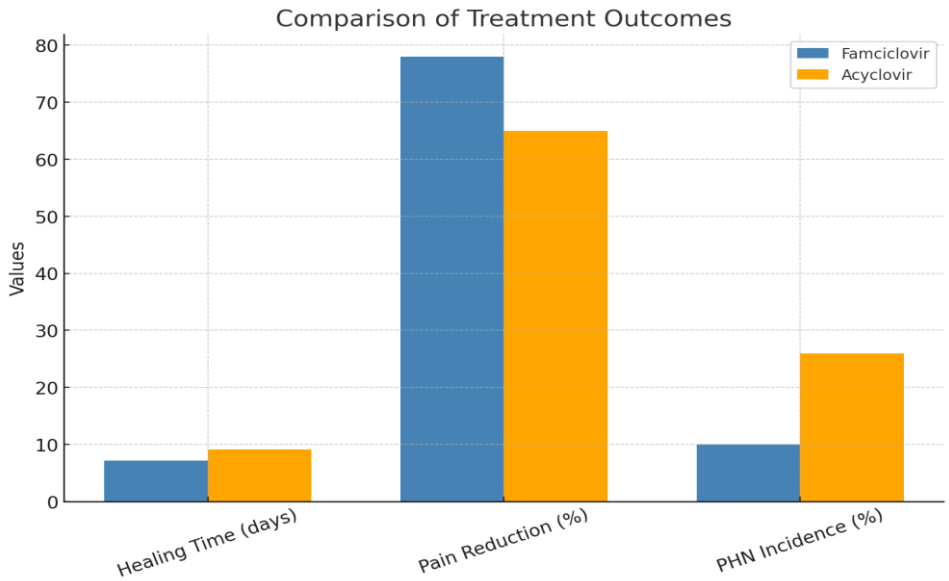

Fig 2: Comparison of Treatment Outcomes

Outcome	Famciclovir	Acyclovir	Difference	p-value
Rash healing time (days), mean ± SD	7.2 ± 1.8	9.1 ± 2.2	−1.9	0.003
Pain reduction (%)	78%	65%	+13%	0.01
PHN at 4 weeks (%)	10%	26%	−16%	0.04

Table 2: Clinical Efficacy Outcomes

The incidence of postherpetic neuralgia is detailed in Fig 3, Table 3. PHN was observed in 3 patients (10%) in the famciclovir group compared with 8 patients (26%) in the acyclovir group, indicating a statistically significant reduction in chronic neuropathic pain with famciclovir treatment. This visual difference reinforces that earlier viral control with Famciclovir reduces nerve damage, thereby preventing chronic pain development. The distribution pattern confirms the clinical advantage of Famciclovir in long-term neural outcomes.

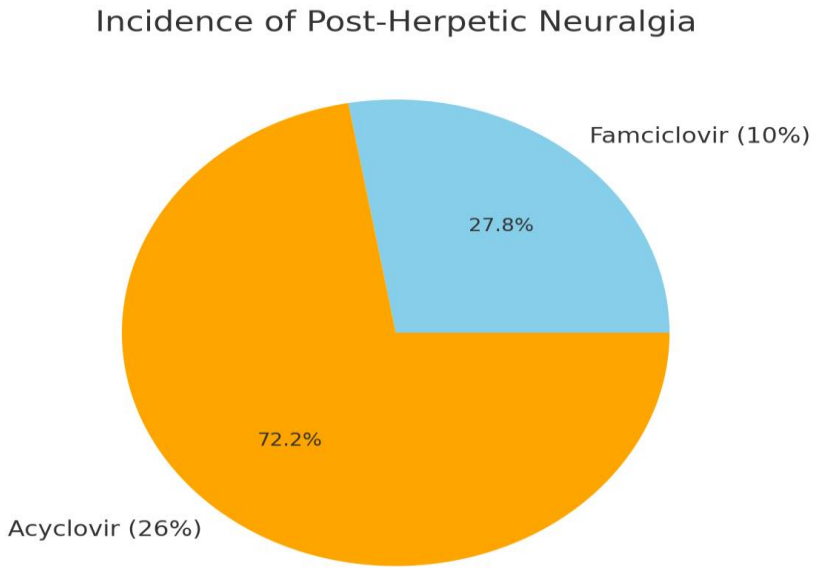

Figure 3: Incidence of Post-Herpetic Neuralgia

PHN Outcome	Famciclovir (n=30)	Acyclovir (n=30)	p-value
PHN present, n (%)	3 (10%)	8 (26%)	0.04
PHN absent, n (%)	27 (90%)	22 (74%)	

Table 3: Postherpetic Neuralgia (PHN) Incidence

DISCUSSION

The present randomized, open-label comparative study demonstrated that famciclovir 500 mg administered three times daily was significantly more effective than acyclovir 800 mg given five times daily in the management of acute herpes zoster. Patients treated with famciclovir experienced faster rash healing, greater reduction in pain intensity, and a significantly lower incidence of postherpetic neuralgia (PHN) at four weeks. These findings highlight the clinical advantage of famciclovir in both acute symptom control and prevention of long-term complications.

The superior efficacy observed with famciclovir in the present study can be attributed to its favorable pharmacokinetic and pharmacodynamic characteristics. Famciclovir, a prodrug of penciclovir, has higher oral bioavailability and a prolonged intracellular half-life of its active metabolite, resulting in sustained antiviral activity within infected cells. This prolonged suppression of viral replication likely contributes to faster lesion resolution and improved control of acute neuritic pain.[11]

In contrast, acyclovir is limited by lower oral bioavailability and the requirement for frequent dosing, which may adversely affect patient adherence and lead to suboptimal viral suppression. Inadequate control of viral replication may allow continued neuronal inflammation and damage, thereby increasing the risk of persistent pain and PHN. Enhanced and sustained viral inhibition with famciclovir provides a plausible explanation for the lower PHN incidence observed in this study.[12]

The findings of the present study are consistent with earlier comparative trials. Kong J et al.[13] Junior HP et al.[14] and Liu Y et al.[15] reported shorter lesion healing times, superior pain relief, and reduced PHN rates with famciclovir compared to

acyclovir. Similarly, Oka T et al.[16] suggested that famciclovir's greater potency and longer duration of action may suppress the emergence and proliferation of resistant viral strains in vivo. They further observed that famciclovir may retain efficacy even during the early phases of acyclovir resistance.

Other studies have demonstrated comparable efficacy between the two antivirals. Gopal MG et al.[17] reported no significant difference in time to full crusting, complete healing, or resolution of acute pain between famciclovir and acyclovir, while noting that famciclovir was well tolerated and offered the advantage of a more convenient dosing regimen. Common adverse effects such as constipation, headache, nausea, and vomiting were mild and comparable between groups. The authors concluded that famciclovir provides clinical benefits through ease of administration, good tolerability, and potential reduction in PHN duration.

Similarly, Agarwal S et al.[18] found both drugs to be effective in treating herpes zoster, though famciclovir was associated with milder adverse effects and was preferred due to its superior bioavailability and simpler dosing schedule. In contrast, Peng F et al.[19] observed no significant differences in pain reduction or PHN incidence between treatment groups and noted that extending famciclovir therapy beyond one week did not confer additional benefit.

These studies, along with the current findings, support the growing evidence favoring famciclovir as a more effective antiviral option for herpes zoster. Improved adherence associated with simplified dosing schedules may further contribute to better clinical outcomes and reduce PHN-related morbidity, including chronic pain, sleep disturbances, and impaired functional status, particularly in older adults.

This study has several strengths, including complete follow-up with no dropouts, comparable baseline characteristics between treatment groups, and the evaluation of clinically relevant outcomes such as rash healing, pain reduction, and PHN incidence. These factors enhance the internal validity of the findings.

However, certain limitations must be acknowledged. The relatively small sample size and single-center, open-label design may limit the generalizability of the results. The short follow-up duration of four weeks may underestimate the true burden of PHN, and the subjective assessment of pain without blinding introduces the potential for observer and reporting bias. Additionally, the exclusion of immunocompromised patients restricts applicability to higher-risk populations.

CONCLUSION

Famciclovir demonstrated superior efficacy compared to acyclovir in the treatment of acute herpes zoster, with faster rash healing, greater pain reduction, and a lower incidence of postherpetic neuralgia. Its favorable pharmacokinetic profile and simpler dosing regimen likely enhance adherence and antiviral effectiveness. These findings support famciclovir as a preferred first-line therapy for herpes zoster in immunocompetent adults.

Funding and Conflicts of Interest

No funding was received for this study. The authors declare no conflicts of interest.

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