DOI: https://doi.org/10.53350/pjmhs22164329

ORIGINAL ARTICLE

A Comparative Study to Evaluate the Efficacy of Valacyclovir and Famcyclovir in the Management of Herpes Zoster in a Tertiary Care Hospital of Khyber Pakhtunkhwa

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ABSTRACT

Objective: To evaluate the efficacy of valacyclovir and famcyclovir in the management of herpes zoster in a tertiary care hospital of Khyber Pakhtunkhwa.

Design of the Study: It was a randomized controlled Trial.

Study Settings: The study was conducted at Department of Pharmacology over 1 year from March 2020 to March 2021 at DHQ Teaching Hospital, Kohat.

Material and Methods: Patients were divided into two groups to valacyclovir 1000mg thrice daily or Famciclovir 500mg thrice daily in a 1:1 ratio was given to patients for a period of seven days. Seven days after treatment began, patients underwent pain and healing of the cutaneous lesions evaluations, which continued for three weeks. On the 7th day of treatment, patients were given a Visual analogue scale to assess their level of pain.

Results of the Study: In the famciclovir therapy group, the percentages of patients reporting mild, moderate, or severe pain were 0 percent, 63.9 percent, and 30.6 percent by the end of day seven. Valacyclovir therapy was associated with just 1%, 69%, and 12.33 % of patients reporting mild to moderate pain correspondingly.

Conclusion: The result showed that both the interventions are effective and safe for treating acute herpes zoster. Famciclovir in comparison to valacyclovir demonstrated a significant advantage for the complete cessation of herpes zoster associated pain. Both the intervention had virtually equivalent efficacy in complete healing of herpes zoster

Keywords: Valacyclovir, Famciclovir, Herpes Zoster, Efficacy

INTRODUCTION

Viral herpes zoster (HZ) is characterised by a unilateral dermatome rash and pain due to the reactivation and amplification of endogenous varicella zoster virus (VZV) dormant in sensory ganglia due to basic varicella infection (VZI).[1,2] Varicella zoster virus reactivation is the cause of herpes zoster, also known as shingles. People over the age of 50 are more likely to acquire herpes zoster because of immunosenescence, although it can affect anyone, especially those with a reduced cell-mediated immunity owing to any condition or medication.[3] Herpes zoster has been linked to complications involving the cerebral, splanchnic, motor nerves and ophthalmic. However, post-herpetic neuralgia is the most frequent complication.[4,5] Ophthalmic zoster infection can cause permanent damage to the eyes, including blindness. Approximately 4 to 6 cases per 1000 individuals of general population have been observed every year.[6] HZ vulnerability rises with age, with 25% of persons over the age of 50 developing HZ-related problems. The incidence has been demonstrated to be higher in women than in men, although others have either found no statistical difference in the incidence rate between the genders or have reported a male predominance.[7,8]

Varicella zoster virus (VZV) reactivation risk factors include previous exposure to the virus, age 50, immunosuppressive drugs, immunocompromised state, organ transplantation or bone marrow transplantation, HIV/AIDS, cancer, psychologic stress, trauma and chronic steroid therapy.[9,10]

The pharmacotherapy of herpes zoster comprises, antiviral, anti-inflammatory agents, and analgesics. The three most commonly used antiviral agents for treatment of HZ are acyclovir, valacyclovir and famciclovir.[11] Valacyclovir and famciclovir are the oral pro- drugs of acyclovir and penciclovir, respectively. Because of their nucleoside analogue active moieties, the intracellular dynamics and target site mechanism of action in preventing varicella zoster virus dsDNA replication are unique.[12]

The rationale of this study was to determine efficacy of these drugs in clinical use so that physicians can make a well informed choice about which drug to prescribe.

MATERIALS AND METHODS

The hospital's ethics committee gave its clearance before the study could begin. This randomized controlled trial study was conducted at Department of Pharmacology over 1 year from March 2020 to March 2021 at DHQ Teaching Hospital, Kohat. After informing patients of the study's procedures, they were asked to sign a written consent for. A sample size of 72 patients was calculated using the online WHO calculator with a significance level of 10 % (α error), relative precision of 70% and confidence interval of 95%. Patients of both genders age 18 to 75 years within 72 hours of onset of rash were enrolled in this trial. Patients with history of complicated herpes zoster virus (HZV) such as, severe dispersed infection (> 20 lesions outer the primary affected dermatome), visceral involvement, known hypersensitivity to famciclovir, acyclovir, penciclovir, valacyclovir were excluded.

Patients were divided into two groups to valacyclovir 1000mg thrice daily or Famciclovir 500mg thrice daily in a 1:1 ratio was given to patients for a period of seven days. Seven days after treatment began, patients underwent pain and healing of the cutaneous lesions evaluations, which continued for three weeks. On the 7th day of treatment, patients were given a Visual analogue scale to assess their level of pain. Between the two groups pain intensity was compared. The clinician assessed severity of rash of all included patients as mild (<25 lesions), moderate (25–50 lesions), or severe (>50 lesions). The data was entered and analysed using SPSS version 19.0, which is the most recent version available. Continuous variables were described with the help of the mean, standard deviation (SD), and range. To summarise categorical data, frequency and percentages were used. A 0.05 p-value was found to be statistically significant in this study.

RESULTS

Famciclovir and valacyclovir groups had mean ages of 57.00 and 59.06 years, respectively, according to the study's results. There was no statistically significant difference in the age distribution between the two groups (p=0.639). Both groups had a similar

distribution of gender. Both groups were dominated by male patients. In the famciclovir group, 55.6% of patients had diabetes mellitus, hypertension, HIV, cancer, and concurrent diabetes mellitus and hypertension; in the valacyclovir group, 58.3% had these diseases. The co-morbid condition did not differ statistically significantly between the two groups (p=0.906).

In the famciclovir therapy group, the percentages of patients reporting mild, moderate, or severe pain were 0 percent, 63.9 percent, and 30.6 percent by the end of day seven. Valacyclovir therapy was associated with just 1%, 69%, and 12.33 % of patients reporting mild to moderate pain correspondingly. Both groups showed no statistically significant differences at the start of day 7.

Table 1: According to the type of therapy, the demographics of the patients

Parameters		Famciclovir	Valacyclovir	P-value
Age	-	57.00 ± 18.508	59.06 ± 18.222	0.639
Gender	Male	29(80)	32(88)	0.814
	Female	7(20)	4(12)	
Lesion duration	<48 h	16(44.4)	16(44.4)	
	48-72 h	20(55.6)	20(55.6)	
Comorbidities	Diabetes mellitus	19.4	22.2	0.906
	Hypertension	11.1	8.3	
	HIV	5.6	8.3	
	Cancer	16.4	11.1	

Table 2: Severity of Pain

VAS score	Famciclovirn (%)	Valacyclovirn (%)	Total (%)	P value
Mild	0 (0.0)	1 (2.8)	1 (1.4)	0.994
Moderate	23 (63.9)	25 (69.4)	48 (66.7)	0.401
Severe	11 (30.6)	12 (33.3)	23 (31.9)	0.801

Table 12: primary variables: mean time taken for full crusting and complete healing

Groups	Drugs	Weeks (Mean±SD)	P Value
Full crusting	Famciclovir	3.48±0.51	0.51
	Valacyclovir	3.52±0.54	
Complete healing	Famciclovir	3.50±0.507	0.66
	Valacyclovir	3.56±0.558	

DISCUSSION

Herpes zoster is a devastating disease because of its painful symptoms. The majority of patients complained of pain before as well as throughout the acute rash phase, according to our research. Post Herpetic Neuralgia (PHN) may be more common in the elderly and difficult and expensive to treat adequately if pain persists after a rash has healed. As a result, preventing or reducing the likelihood of chronic pain is of even greater importance.[14]Zoster sufferers in their fifth decade were the most common demographic in the current investigation, which is consistent with the findings of Degreef et al.[15] Shafran et al. conducted a comparable study in which the average patient was 55 years old.[16]

About 55.6 percent of the patients in this study were men in both of the categories. According to Goh et al. males and females have equal prevalence to develop the condition.[17] The zoster virus and diabetes mellitus appear to be linked, according to two studies.[18,19] However, no previous investigation has found a link between hypertension and HZ. Patients with weakened immune systems, such as those with cancer or HIV, have a higher risk of contracting herpes zoster because of their weakened defences.[20] In the present study 5.6% and 8.3% of patients were HIV positive in famciclovir and valacyclovir group respectively.

In the both treatment group the 50% of the patient were initiated with antiviral within 48 hours of lesion appearance and 50% were initiated before 72 hour of the lesion appearance. It has been established to initiate the treatment within 72 hours of rash onset but unlikely to be helpful after lesions have crusted to increase the rate of healing and decrease pain.[21,22]

When the severity of pain was compared, visual analog score of mild and severe pain declined on day 7th in the both treatment group. However visual analog score moderate pain was noted to increase in both the treatment group. Our these finding are in line with the results of the study of Mostofa et al.[23]. In both the group each patient were healed by the end of week 4 (28 days). The result corresponds to study which showed minimal differences between these agents with regard to time to complete healing .[24] The study showed median time to complete healing was 20 and 21 days with famciclovir group.

Our study had some limitations, such as a small number of patients seen throughout the study period. Longer-term and larger-scale investigations yield more accurate results. However, patients admitted of using pain medicines despite our advice that they not do so early on the day of the follow-up.

CONCLUSION

The result showed that both the interventions are effective and safe for treating acute herpes zoster. Famciclovir in comparison to valacyclovir demonstrated a significant advantage for the complete cessation of herpes zoster associated pain. Both the intervention had virtually equivalent efficacy in complete healing of herpes zoster.

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