

Comparative Study of Oral Acyclovir and Oral Famciclovir in the treatment of Herpes Zoster

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Abstract

Background: Herpes zoster is a common viral infection, mostly affect elderly and immune compromised patients. Specific treatment includes antivirals. Most commonly used drug is acyclovir.

Material and Methods: One hundred patients were prescribed to receive oral Acyclovir or oral Famciclovir on alternate basis after diagnosis of Herpes zoster. **Ac:** Oral Acyclovir 800 mg 5 times a day for 7 days. **Fa:** Oral Famciclovir 500 mg 3 times a day for 7 days. Patients in each group were evaluated on day 5 after initiation of therapy and every week thereafter for a period of six weeks.

Results: A total of one hundred patients of herpes zoster were studied with fifty patients in each group of acyclovir and famciclovir. Majority of patients (63%) were in the 3rd, 4th and 5th decade. The mean age was 40 years. There were 52 male and 48 female patients. Majority of patients (56%) had the disease in the months of May, June, August and September. Thoracic segment (56%) was the predominant site of involvement the median time taken for full crusting of lesions in both the groups was 10 days. The median time taken for complete healing of lesions in famciclovir group was 21 days and in acyclovir group 28 days. The median time taken for subsidence of pain in famciclovir group was 21 days and in the acyclovir group it was 28 days. The most common complication was dyspigmentation in 16% cases. 5% of patients had PHN, 3 in acyclovir group and 2 belonged to famciclovir group.

Conclusion: We can conclude that famciclovir can be a better option in the treatment of herpes zoster in view of all the above mentioned facts and it has got a convenient dosage schedule as well.

Key Words: Herpes Zoster, Famciclovir, Acyclovir, Old age, Varicella zoster Virus

Introduction

Herpes Zoster (Shingles) is a localized disease characterized by unilateral radicular pain and grouped vesicular eruptions, which is generally limited to the dermatome innervated by a single spinal or cranial sensory ganglion.^[1] It occurs as a result of reactivation of varicella zoster virus (VZV) that had persisted in latent form within sensory ganglion following an earlier attack of varicella. Triggers for reactivation include advancing age due to immune senescence, comorbidities (malignancies and HIV infection) and immuno suppressive treatment.^[2] ACYCLOVIR (9-[(2-hydroxyethoxy) methyl]) has been approved by food and drugs administration (FDA) as an oral antiviral therapy for the treatment of acute herpes zoster. The inhibitory activity of acyclovir is highly selective due to its affinity for the enzyme thymidine kinase encoded by VZV.^[3] FAMCICLOVIR, (2-[2-(2-amino-9-purine-9-yl)ethyl]-1,3-propanedioldiacetate) a new antiviral agent was approved for marketing by FDA in June 1994 for the management of acute herpes zoster. It is an orally administered prodrug of antiviral agent penciclovir.^[4] The present work is aimed to find out, whether to any extent, Famciclovir, and Acyclovir is capable of making one get rid of the discomfort, annoyance and fretfulness due to Herpes Zoster and subsequent post herpetic neuralgia(PHN).

Materials and Methods

A total of 100 cases of newly diagnosed herpes zoster patients, irrespective of age, sex and socioeconomic status, attending department of Dermatology, Venereology and Leprology of Rajendra Institute of Medical Sciences, Ranchi from October 2012 to September 2013 were enrolled in the study. Immunocompetent patients irrespective of age, Within 72 hrs of rash, Patients willing for investigations, treatment and regular follow up after taking consent were included in the study. Those Patients not capable of coming for follow up, Patients with malignancy on chemotherapy, Pregnant and nursing patients, Patients receiving chronic steroid therapy and Patients with immunosuppressive status were excluded from the study. Patients were allocated for Acyclovir and Famciclovir treatment randomly.

A detailed clinical history, examination and relevant investigations like routine investigations, Tzanck smear and wherever required other investigations were carried out according to pre-structured proforma.

Efficacy assessment

Patients were evaluated for pain and healing of the cutaneous lesions on day 5 after initiation of therapy and every week there after for a period of six weeks.

The primary variables evaluated at each visit were, the time taken for the full crusting of the lesions, lesions were defined to be fully crusted when all the papules and vesicles in the affected dermatome had resolved and crusts had appeared. The time taken for complete healing of the lesions, healing was defined as the first time in which a patient had no papules, vesicles or crusts and after these did not develop at any later visit. The time taken for the subsidence of acute pain: The pain was assessed by visual analogue scale (the visual analogue score was): No pain was given as score 0, Worst ever felt pain was given score 10 Score, 1-3 was considered as mild pain, Scores 4-6 as moderate pain and Scores 7-9 as severe pain. Routine Investigations like complete Haemogram, Random Blood Sugar, Liver function test, Urine microscopy. One hundred patients were prescribed to receive oral Acyclovir or oral Famciclovir on alternate basis. **Ac:** Oral Acyclovir 800 mg 5 times a day for 7 days. **Fa:** Oral Famciclovir 500 mg 3 times a day for 7 days. Patients in each group were evaluated on day 5 after initiation of therapy and every week thereafter for a period of six weeks.

Safety assessments: The number and percentage of patients reporting at least 1 adverse event during the treatment protocol were assessed. Drug related adverse events were defined as those adverse events that were related or possibly related to the study therapy or as being of unknown causality.

Statistical analysis: This is a randomized single blind controlled study. Comparison between the 2 groups was done by Unpaired T test. Categorical data was analysed by Chi-square test.

Results

A total of one hundred patients of herpes zoster were studied with fifty patients in each group of acyclovir and famciclovir. Majority of patients (63%) were in the 3rd, 4th and 5th decade. The mean age was 40 years. There were 52 male and 48 female patients. The youngest patient was 15 years and oldest was 84 years. Majority of patients (56%) had the disease in the months of May, June, August and September. All the patients had eruptions in the form of papules, vesicles & pustules. Thoracic segment (56%) was the predominant site of involvement. Pain was moderate in nature in majority of patients during first day of visit. Majority of patients had crusted lesions at the end of 5 days. The most common adverse effect reported in both the groups was nausea (12%). Both the drugs were well tolerated and safety profile was slightly higher in famciclovir group. The median time taken for full crusting of lesions in both the groups was 10 days. The median time taken for complete healing of lesions in famciclovir group was 21 days and in acyclovir group 28 days [Table 1]. The median time taken for subsidence of pain in famciclovir group was 21 days

and in the acyclovir group it was 28 days. The mean values for full crusting in different dermatomes in both the groups were statistically insignificant ($p>0.01$). The mean values for full complete healing in different dermatomes in both the groups were statistically significant ($p<0.01$). The mean values for subsidence of acute pain in different dermatomes in both the groups were statistically significant ($p<0.01$) [Table 2]. The most common complication was dyspigmentation in 16% cases. 5% of patients had PHN, 3 in acyclovir group and 2 belonged to famciclovir group.

Table 1: Primary Variables: Time Taken for Full Crusting, Complete Healing and Subsidence of Acute Pain

Groups	Full crusting	Complete healing	Subsidence of acute pain
Famciclovir	10 days (8-11 days)	20 days (20-27 days)	20 days (20-27 days)
Acyclovir	10 days (8-11 days)	27 days (20-27 days)	27 days (20-27 days)

Table 2: Mean Time taken for Full Crusting, Complete Healing and Subsidence of Acute Pain in two groups

	Drug	Mean (days)	SD	t-value*	P-value
Full crusting	Fm	10.3	0.7	0.67	0.51
	Ac	10.1	0.8		
Healing	Fm	21.7	3.0	4.34	<0.01, S
	Ac	24.5	3.4		
Subsidence of Pain	Fm	22.6	3.4	3.52	<0.01, S
	Ac	24.9	3.1		

*un paired t test Fm = Famciclovir Ac = Acyclovir S= Significant

Discussion

HERPES ZOSTER is a disease of great antiquity caused by varicella zoster virus (VZV) which is also a pathogen for a different clinical entity varicella (chicken pox). Pathogenesis of herpes zoster is not fully understood. During the course of varicella, VZV spreads from lesions in the skin and mucosal surface into the sensory nerve endings. From there it travels centripetally along these nerve fibres until it reaches the dorsal ganglion cells. In the ganglia the virus establishes a latent infection that persists for life.^[5] Herpes zoster occurs most often in dermatomes in which the rash of varicella achieves the highest density. When host resistance falls below a critical level, reactivated virus can no longer be contained. Virus multiplies and spreads within the ganglion, causing necrosis and intense inflammation, a process that is accompanied by severe neuralgia.^[6,7] In the present study of 100 patients of herpes zoster, majority of patients (63%) were in 3rd, 4th and 5th decade. This is in conformity with the study of Dubey et al who also observed the majority of patients (74%) in their study of 107 cases to be in 3rd, 4th and 5th decade. Chaudhary et al observed 54% of patients in their study of 230 patients to be in 2nd and 3rd decade.^[8] In the present study 52 patients (52%) were males and 48 patients (48%) were females. However, Sehgal et al found the disease in 68.7% males and 31.3% females.^[9] The variation in the sex distribution in some of the studies could be due to variation in the number of females and males attending the outpatient department. In the present study majority of cases (56%) were seen in the months of May, June, August and September. Nigam et al found increased incidence during March, April, August, September and December.^[10] Thoracic segment was the predominant site of involvement in 56% of cases followed by cranial (16%), lumbar (13%), cervical (11%) and sacral (4%). Sehgal et al in their study noted involvement of thoracic segment in 52.5%

of cases followed by cervical in 20%, lumbosacral in 18.8% and cranial in 8.8%.^[9] In the present study pain was moderate in nature in majority of patients. Majority of patients had crusted lesions at the end of five days. In the present study, the most common adverse effect reported in both groups was nausea seen in 6 (12%) patients, out of them 2 (4%) were in famciclovir group and 4 (8%) were in acyclovir group. In famciclovir group, 48 (96%) patients had no adverse effects and drug was well tolerated. Adverse effects were slightly higher in Acyclovir group with 4 (8%) patients having nausea and 1 (2%) patient having constipation. Shen et al^[11] observed that higher proportion of patients in the acyclovir group had adverse effects 14/28 (50%) than famciclovir group 4/27 (14.8%). Renal adverse effects were more in acyclovir group (17.9%) followed by gastrointestinal (14.3%), metabolic adverse effects were more in famciclovir group (7.4%) followed by gastro intestinal and renal (3.7%) in each. In the present study, the median time taken for full crusting of lesions in both the groups was 10 days. Shen et al^[9] found the median time taken for full crusting to be 11 days in famciclovir group and 10 days in acyclovir group. As per Shafran et al^[12] the median time for full crusting was 7 days in both the groups. According to Tyring et al^[13] the median time for full crusting of the lesions was 8 days in famciclovir and 9 days in Acyclovir group. Thus, there is a variation in full crusting between different studies.

In the present study, the median time taken for complete healing of lesions in famciclovir group was 20 days and was 27 days in acyclovir group, which is statistically significant ($p < 0.01$). Shen et al^[11] found the median time for complete healing of lesions in famciclovir group to be 20 days and 27 days in acyclovir group. The findings in the present study are in concurrence with the above study. In the study of Tyring et al^[13] median time for complete healing of lesions was 20 days in famciclovir group and 21 days in

acyclovir group, where they found slight variation in the duration in comparison to the present study where famciclovir was found to be more effective. Shafran et al^[11] observed the median time for complete healing of the lesions to be 20 days in both the groups, i.e. there was no much difference. In the present study, the median time taken for subsidence of acute pain in famciclovir group was 20 days and in acyclovir group was 27 days. In the study of Shen et al^[11] the median time taken for subsidence of acute pain in famciclovir group was 20 days and 27 days in acyclovir group, which is similar to the observations of the present study. Shafran et al^[12] observed the median time taken for subsidence of acute pain in both groups to be 17 days which is significantly less. Tyring et al^[13] found the median time for subsidence of acute pain in famciclovir group to be 14 days and acyclovir group to be 17 days. In the present study, dyspigmentation was seen in 16% patients. In the study of Chaudhary et al^[14] 15% patients had dyspigmentation. In the present study, post herpetic neuralgia was seen in 5% of patients: 3% in acyclovir and 2% in famciclovir group. Sehgal et al observed, 11% incidence of post herpetic neuralgia in their study and similar results were seen in the study of Nigam et al.^[10] Thus, the dyspigmentation varies from study to study and probably depends upon the severity of the lesions.

Conclusion

There were no significant adverse effects seen which could alter the modality of treatment with both the drugs. Safety profile was slightly better in the famciclovir group. There was no difference in the median time in the crusting of lesions but complete healing was seen much earlier in famciclovir group. Similarly subsidence of acute pain was seen much earlier in patients treated with famciclovir. Dyspigmentation was the most common finding seen after healing of the lesion and it was more often seen among patients who reported to treatment late. The incidence of post herpetic neuralgia in general was less probably because of early onset of disease in majority of the patients and it was less in famciclovir group compared to acyclovir group. It can be concluded that famciclovir can be a better option in the treatment of herpes zoster in view of all the above mentioned facts and it has got a convenient dosage schedule as well.

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