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ORIGINAL ARTICLE

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

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ABSTRACT:
Introduction: The purpose of this study is to determine whether Acyclovir and Famciclovir can, in any way, relieve the pain, irritation, and anxiety associated with Herpes Zoster and the ensuing post herpetic neuralgia (PHN). **Materials and Methods:**A thorough clinical history, physical examination, and pertinent investigations, such as routine tests and Tzanck smears, were performed in accordance with pre-structured proforma when necessary. Patients were evaluated for pain and healing of the cutaneous lesions on day 5after initiation of therapy and every week there after for a period of six weeks. One hundred patients were prescribed to receive oral Acyclovir or oral Famciclour on alternate basis. Comparison between the 2 groups wasdone by Unpaired T test. Categorical data was analysed by Chi-square test. **Results:** In both groups, the average values for complete crusting in various dermatomes were not statistically significant ($p>0.01$). In both groups, the mean values for full and complete healing in distinct dermatomes were statistically significant ($p<0.01$). In both groups, the average values for the subsidence of acute pain in several dermatomes were statistically significant ($p<0.01$). **Conclusion:**It can be concluded that famciclovir can be a better option in the treatment ofherpes zoster in view of all the above mentioned factsandithas gotaconvenientdosagescheduleas well.
Keywords: Acyclovir, Famciclour,Varicella Zoster virus (VZV),

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INTRODUCTION

It happens as a result of the varicella zoster virus (VZV), which had survived an earlier varicella infection in sensory ganglions in a latent form. Reactivation can be triggered by immunosuppressive treatments, co-morbidities (HIV infection and cancer), and aging brought on by immunological senescence.[1] The Food and Drug Administration (FDA) has authorized ACYCLOVIR (9-[(2-hydroxyethoxy) methyl]) as an oral antiviral medication for the management of acute herpes zoster. Acyclovir has a strong affinity for the thymidine kinase enzyme that is encoded by VZV, which makes its inhibitory effect very specific.[2] In June 1994, the FDA approved FAMCICLOVIR, 2-[2-(2-amino-9-purine-9-yl)ethyl]-1,3-propanedioldiacetate, a novel antiviral medication, for marketing use in the treatment of acute herpes zoster. It is a prodrug of the antiviral medication penciclovir taken orally.[3]

Relieving chronic pain is an unmet issue in the care of people with acute zoster. For many people, the discomfort goes away as soon as the skin in the affected area heals normally. Nonetheless, even after the lesions have healed, some individuals still feel agony. As the most prevalent complication of herpes zoster, the pain is usually referred to as postherpetic neuralgia, which is also one of the most incurable pain diseases.[4,5] As people age, the incidence of PHN rises significantly. In addition, it affects elderly patients more severely and lasts longer than it does younger ones. For patients and doctors alike, the condition is undoubtedly the most upsetting aspect of the illness process. Acyclovir has been the prescribed oral antiviral medication for treating patients with acute herpes zoster for a long time, although there is still debate over its impact on postherpetic neuralgia.[6,7] In June 1994, the FDA approved famciclovir, a novel antiviral medication, for sale in order to treat acute herpes zoster. This oral penciclovir formulation is well absorbed (77% bioavailable) and effective against VZV. It phosphorylates to the antiviral molecule famciclovir triphosphate, which selectively activates it in virus-infected cells.

The fact that famciclovir triphosphate stays in virus-infected host cells longer than acyclovir triphosphate may be a potentially significant therapeutic aspect. A good intracellular halflife of penciclovir triphosphate in VZV-infected cells and consistent oral bioavailability indicate that famciclovir may provide clinically significant benefits over existing therapies for the treatment of herpes zoster.[8]

MATERIALS AND METHODS

Patients with immunocompetence, regardless of age, Patients who were willing to participate in the study

after giving their consent and who had rash within 72 hours were included in the study. Excluded from the study were patients who were unable to attend follow-up appointments, patients receiving chemotherapy for cancer, patients who were pregnant or breastfeeding, patients on long-term steroid therapy, and patients who were immunosuppressed. Patients were randomized to receive medication with either Famciclovir or Acyclovir.

A thorough clinical history, physical examination, and pertinent investigations, such as routine tests and Tzanck smears, were performed in accordance with pre-structured proforma when necessary.

EFFICACY ASSESSMENT

Patients were evaluated for pain and healing of thecutaneouslesionson day 5afterinitiation of therapyandeveryweekthereafterforaperiodofsixweeks.

The primary variables evaluated at each visit were, thetime taken for the full crusting of the lesions, lesionswere defined to be fully crusted when all the papulesandvesicles in theaffecteddermatomehadresolvedand crusts had appeared. The time taken for completehealing of the lesions, healing was defined as the first time in which a patient had nopapules,vesiclesorcrusts and after these did not develop at any later visit.The time taken for the subsidence of acute pain: Thepain was assessed by visual analogue scale (the visualanalogue score was): No pain was given as score 0,Worst ever felt pain was given score 10 Score, 1-3 wasconsidered as mild pain, Scores 4–6 as moderate painand Scores 7-9 as severe pain. Routine Investigationslike complete Haemogram, Random Blood Sugar, Liver function test, Urine microscopy. One hundred patients were prescribed to receive oral Acyclovir or oral Famciclour on alternate basis.

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

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

RESULTS

The most common site of involvement (56%) was the thoracic region. Most patients experienced considerable pain on their initial visit day. After five days, the majority of patients developed crusted lesions. Nausea was the most frequent side effect (12%) reported in both groups. Both medications were well tolerated, with the famciclovir group having a somewhat better safety profile. Ten days was the median amount of time needed for both groups' lesions to fully crust. According to Table 1, the median duration required for lesions to fully heal was 21 days for the famciclovir group and 28 days for the acyclovir group.

Table1: Primary Variables: Time Taken for Full Crusting, Complete Healing and Subsidence of Acute Pain

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

In both groups, the average values for complete crusting in various dermatomes were not statistically significant ($p>0.01$). In both groups, the mean values for full and complete healing in distinct dermatomes were statistically significant ($p<0.01$). In both groups, the average values for the subsidence of acute pain in several dermatomes were statistically significant ($p<0.01$) [Table 2].

Table2: 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	11.4	0.9	0.69	0.52
	Ac	11.2	0.6		
Healing	Fm	22.9	4.1	5.31	<0.01, S
	Ac	25.3	4.8		
Subsidence of Pain	Fm	23.8	4.9	4.51	<0.01, S
	Ac	25.7	4.3		

*unpaired t test Fm=Famcyclovir Ac=Acyclovir S=Significant

DISCUSSION

It's unclear exactly how herpes zoster pathogenesis works. Varicella virus (VZV) travels from lesions in the skin and mucosal surface into the sensory nerve terminals during the illness. It then moves along these nerve fibers in a centripetal direction until it reaches the dorsal ganglion cells. The virus creates a latent infection in the ganglia that lasts a lifetime.[9]The

largest density of varicella rash is found in dermatomes where herpes zoster most frequently occurs. Reactivated viruses cannot be contained once host resistance reaches a certain point. The virus grows and spreads inside the ganglion, leading to acute neuralgia along with necrosis and severe inflammation.[10,11] The bulk of the 100 herpes zoster patients in the current study (63%) were in their third, fourth, and fifth decades of life. This is consistent with a research by Dubey et al. that found that most patients (74%) in their analysis of 107 cases were in their third, fourth, or fifth decade. In their study of 230 patients, Chaudhary et al. found that 54% of the patients were in their second or third decade.[12] 52 patients (52%) and 48 patients (48%) were male and female in the current study. Sehgal et al. discovered the illness in 31.3% of females and 68.7% of males.ThirteenThe differences in the proportion of males and females visiting the outpatient department may be the cause of the variations in the sex distribution observed in some of the studies. In 56% of instances, the thoracic segment was the primary location of involvement, with cranial (16%), lumbar (13%), cervical (11%), and sacral (4%), following in order. In 52.5% of patients, the thoracic segment was involved, followed by the cervical (20%), lumbosacral (18.8%), and cranial (8.8%) regions in Sehgal et al.'s study.Thirteen Most of the patients in the current study had moderate to severe pain. After five days, the majority of patients developed crusted lesions. In the current study, nausea was the most often reported side effect in both groups, with 6 (12%) patients experiencing it; 2 (4%) of these patients were in the famciclovir group and 4 (8%) were in the acyclovir group. 48 individuals (96%) in the famciclovir group experienced no side effects, and the medication was well tolerated. The Acyclovir group saw a slightly greater rate of adverse effects, with 4 (8%) and 1 (2%) patients experiencing nausea and constipation, respectively. Shen et al. (2015) found that more patients in the acyclovir group—14 out of 28; or 50%—than in the famciclovir group—4 out of 27; or 14.8%—experienced side effects. Adverse effects on the kidneys were more common in the acyclovir group (17.9%), followed by gastrointestinal problems (14.3%), and metabolic problems were more common in the famciclovir group (7.4%), with gastrointestinal and renal problems (3.7%) in each case. The current study found that it took a median of 10 days for both groups' lesions to fully crust. The median time for complete crusting was determined to be 10 days for the acyclovir group and 11 days for the famciclovir group. both groups' median times for complete crusting were seven days. report that the median duration required for the lesions to fully crust was 8 days for the famciclovir group and 9 days for the acyclovir group. As a result, there are differences in full crusting amongst research.

The present study was aimed to assess the efficacy and safety of acyclovir and famciclovir in the treatment of acute herpes zoster. At the end of each week the patients were evaluated for the primary endpoints, time taken for full crusting of the lesions, complete healing of the lesion and loss of acute pain. The secondary parameters included: assessing the primary variables in the patients aged above 60 years with each drug, and the relative efficacy of each drug in different dermatomes (cranial, cervical, thoracic, lumbar) in patients aged above 60 years were also considered. The median time taken for full crusting of the lesions in both the groups was 10 days, 4 patients in famciclovir and 6 patients in acyclovir group took more than 10 days for full crusting of the lesions. Shen et al.[13] found the median time taken for full crusting was 11 days in the famciclovir group and 10 days in a cyclovir group. The median time for full crusting was 7 days in both the groups. Our findings are in agreement with Shen et al., The median time taken for complete healing of the lesions in both the groups was 21days. 5 patients in famciclovir group and 4 patients in acyclovir group took more than 21 days. The time taken for complete healing of the lesions in the patients above 60 years, belonging to acyclovir group was considerably faster than the famciclovir group. The median time taken for loss of acute pain in both the groups was 21 days. 9 patients in famciclovir group and 17 patients in a cyclovir group to 3 weeks for loss of acute pain. The most common adverse effects reported were dyspepsia (10%), headache (9%), nausea (8%) and constipation (7%) in the decreasing order of frequency. Both the drugs were well-tolerated with no serious adverse effects. Since postherpetic neuralgia increases with increasing age, we studied the effect of these drugs in patients above 60years of age-group, with respect to the dermatome affected, full crusting, complete healing and loss of acute pain. It was observed that the patients above 60 years of age took considerably longer period for complete healing of the lesion and loss of acute pain i.e., 28 days. However, the time taken for full crusting of the lesion remained same as the lesser age-groups. There was no significant difference between the effects of drugs in different dermatomes in these patients. Thus, the dyspigmentation varies fromstudy to study and probably depends upon the severityofthe lesions.

CONCLUSION

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 ofherpes zoster in view of all the above mentioned facts and it has got a convenient dosage

scheduleas well.

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