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A Comparative Study Of Famciclovir Versus Acyclovir In The Treatment Of Herpes Zoster

KEYWORDS: Herpes zoster, Famciclovir ,Acyclovir

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ABSTRACT *Background:Varicella is the primary infection resulting from exogenous exposure of a susceptible individual to varicella zoster virus whereas herpes zoster is the reactivation of endogenous infection that persisted in latent form within sensory ganglia after an earlier varicella.Famciclovir a new antiviral agent was approved for the management of acute herpes zoster.Materials And Methods:A total of 100 patients presented with rash ,diagnosed clinically were included in the study ,50 patients for each drug that is acyclovir and famciclovir were treated respectively.Results:Out of 100 patients ,majority were in 3rd ,4th and 5thdecade.Thoracic segment was involved in 50% of patients.Common adverse effects in both groups was nausea,it was 12% ,out of them 4% with famciclovir group and 8% with acyclovir group.Time taken for complete healing of the lesions was 20 days in famciclovir group and 27 days in acyclovir (p value >0.01)*

Conclusion:Safety profile and complete healing were comparatively better in famciclovir group

Itroduction:

Herpes zoster (HZ) (shingles)[1] is a disease of great antiquity known since ages and is caused by varicella zoster virus which also causes a different clinical entity varicella. The words "Herpes Zoster" are derived from "Herpus" meaing to creep and zoster means "Girdle"[2]. Herpes Zoster is an acute cutaneous viral infection caused by the reactivation of VZV, a herpes virus that is the cause of varicella. HZ was presented with crops of vesicles on an erythematous base in dermatomal pattern and an intractable neuropathic pain[3].

Famciclovir[4] , a prodrug of penciclovir has the advantage of simpler dosage regimen and its triphosphate has longer intracellular half life in infected cell. The present was study was undertaken to compare the safety profile and efficacy of oral famciclovir and acyclovir.

Materials And Methods:

A study population included 100 patients presented with typical rash, diagnosed clinically as herpes zoster, selected from the dermatology outpatient Department of Govt General hospital attached to Medical College, from November 2010 – October 2012 , all the patients were followed up for 6 weeks .All patients irrespective of age presented within 72 hrs of appearance of rash willing for investigations and follow up were selected .Exclusive criteria include pregnancy lactation, malignancy on chemotherapy ,chronic steroid therapy and immune suppressive status. A detailed clinical history including age, sex , socio economic status,occupation , history of chicken pox, chronic disease, immune suppression, prodromal symptoms and duration of rash , recorded in all cases.General examination and systemic examination was conducted and routine investigations,Tzanck smear and others were done whenever necessary .Patients were randomly allocated into group acyclovir and group Famciclovir. Oral acyclovir 800 mg 5 times a day for 5 days was given to group Acyclovir and oral famciclovir 500 mg two times a day for 5 days was given to group famciclovir. All patients were evaluated for pain and healing of the cutaneous lesions on Day 5 after initiation of therapy and every week thereafter for a period of 6 weeks . Primary variables evaluated at each visit were, the time taken for full crusting, compete healing of the lesions and subsidence of acute pain. Safety assessment was done by the number and percentage of patients reporting at least one adverse effect during the protocol.

Statistical analysis was done between two groups by unpaired t test and categorical data was analyzed by chi square test.

Results:

A total of 100 patients were enrolled in the study comparing 52 males and 48 females . Majority of patients (63%) were in 3rd ,4th ,5th decade . Mean age in acyclovir and famciclovirgropus were 40.6 and 40.7 respectively.The youngest patient was 15 years and oldest was 84 year old man. 56% of patients had the diseasein the months of May, june ,August,September. In both the groups thoracic segment 56% was the predominant site of involvement followed by 5th cranial nerve, lumbar ,sacral region withCC=0.188 P=0.45.

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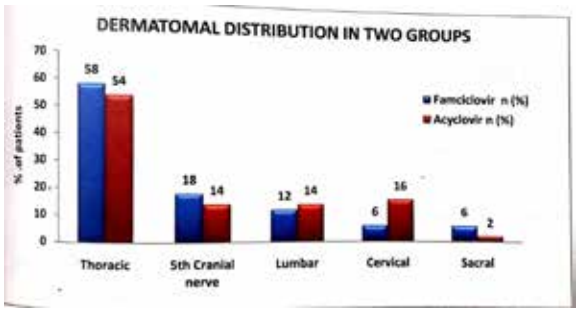


.All the patients (100%) presented with eruptions and crusted lesions and 50% of patients with prodromal symptoms (Table 1).

Table 1 : Type Of Lesions Present On Screening Visit : Day1

Variable	No.	Drug		CC	P
		Famciclovir n (%)	Acyclovir n (%)		
Papules	<5	6(12)	3(6)	0.225	0.15
	5-10	28 (56)	35 (70)		
	11-15	13 (26)	6(12)		
	16-20	3(6)	6(12)		
Vesicles	5-10	5(10)	4(8)	0.154	0.66
	11-15	11(22)	16(32)		
	16-20	23 (46)	17 (34)		
	21-25	8(16)	8(16)		
	26-50	3(6)	5(10)		
Crusts	0	19(38)	20 (40)	0.071	0.78
	1-4	25 (50)	22 (44)		
	5-6	6(12)	8(16)		
Pain	1-3	6(12)	8(16)	0.069	0.79
	4-6	36 (72)	33 (66)		
	7-10	8(16)	9(18)		

Majority of the patients had crusted lesions at the end of 5 days .The common adverse effect reported in both groups was nausea 12% .Mean time taken for crusting of the lesions in both the groups was 10 days.(Table 2).

Table 2 : 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)

The mean time taken for complete healing of lesions in Famciclovir group was 20 days and 27 days in Acyclovir group,which is statistically significant ($p< 0.01$) in Acyclovir group (Fig 2,3) (Table 3).

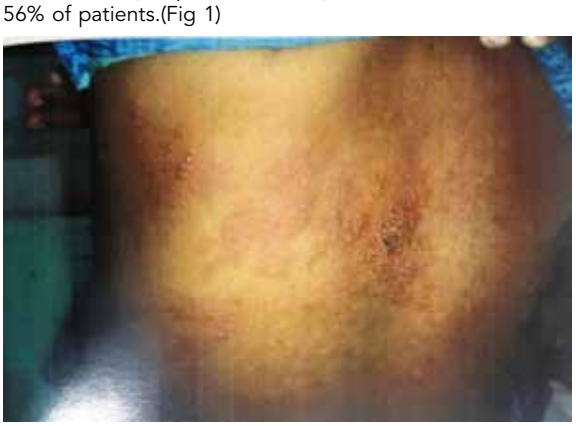
Table 3: Mean Time For Complete Healing Of Lesions In Two Groups

Drug	Dermatome	Mean healing value	SD	N
Famciclovir	1. Thoracic	21.93	3.18	29
	2. 5,h cranial nerve	22.33	3.50	9
	3. Lumbar	21.17	2.86	6
	4. Sacral	20.00	0.0	3
	5. Cervical	20.00	0.0	3
	Total	21.68	3.02	50
Acyclovir	1. Thoracic	23.89	3.54	27
	2. 5lh cranial nerve	25.00	3.42	7
	3. Lumbar	26.00	2.65	7
	4. Sacral	20.00	0.0	1
	5. Cervical	25.13	3.18	8
	Total	24.46	3.38	50

The common complication was depigmentation in 16 % cases 8 % in each group. 5% of patients developed post herpetic neuralgia, three in acyclovir group and two belonged to famciclovir group.

Discussion:

The present study of 100 patients of Herpes zoster,majority 63% were in 3rd,4th and 5thdecade.The overall mean age was 40 years. More than 90% of patients presented with classical zoster.Thoracic segment was the predominant site of involvement.Similar findings were observed in study of Dubey et al[5].Nigam et al[6] noted 60% of patients in 2nd ,3rd 4th decade in their study of 53 patients. Choudary et al[7] observed 54% of patients in their study of 230 patients to be second and 3rddecade . Youngest case reported in present study was 15 years. The youngest reported in the literature was 3 months. The oldest reported in our study was 84 years. In the study of sehgalet al[8], 82 years old person was the oldest. In present study 52 patients were male , 48 patients were females. Goh et al[9] in their study found equal incidence in men and women . In the studies of sehgal et al[8], Nigametal[6] and Dubey et al[4] were found varied male : female ratio. The variables in the sex distribution was due to variation in the number of males and females attending to outpatient department .majority of cases were seen in the months of May, June, August and September .Choudary et al[7] noted increased incidence in the months of August September and October . Some other studies observed there was no seasonal variation[10,11]. In both the groups thoracic segment in was involved in 56% of patients.(Fig 1)



.Fig1

In the present study all the patients were presented with eruptions vizpapule,vesicle,pustule (100%), pain in 80% ,burning sensation in 50%,fever in 11%, and headache in 10% were other symptoms. Prodromal symptoms like parasthesia, pain, itching and malaise were present in 50% of patients.(Table 1). In studies of Dubeyet al[4], pain was the presenting symptom in 97% of cases. Sehgal et al[8] observed skin eruptions in 91%.When compared to other studies, the incidence of prodromal symptoms were comparatively less in our study. The distribution of the lesions on screening visit day one were comparable in each group , thus the patients presented with 5- 10 papules and 16-20 vesicles and 1-4 crusted lesions which was in accordance with study of shen et al. majority of our patients had crusted lesion at the end of 5 days. There are no available studies to compare the observations of present study. In Acyclovir group complete healing was seen in mean time of 27 days (Fig 2,3),fig 2

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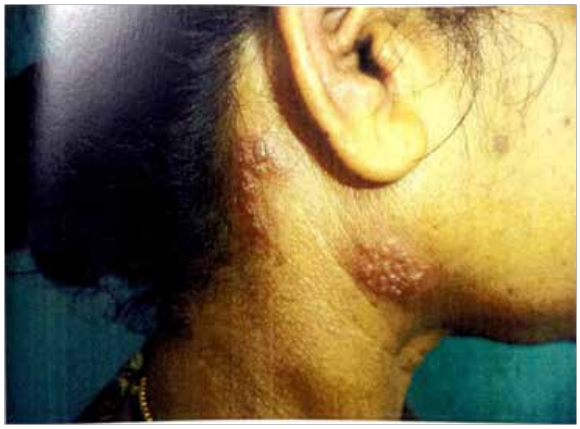


fig 2

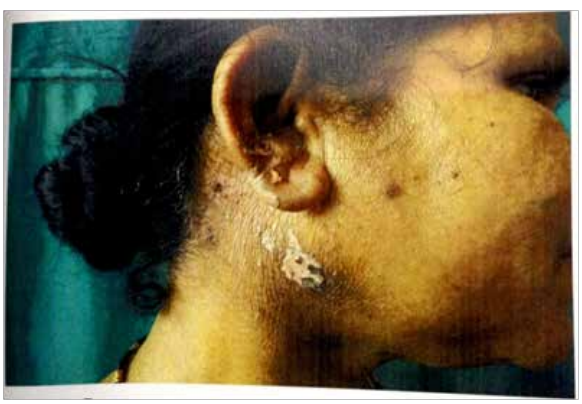


Fig 3

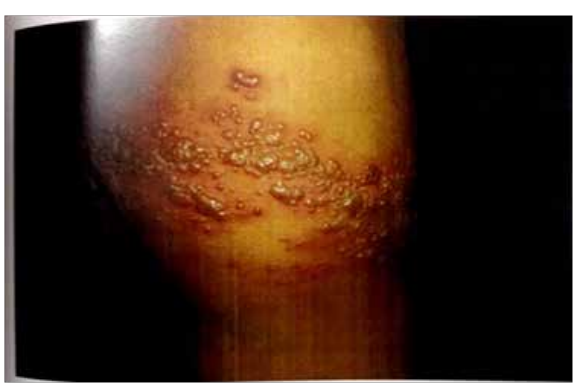


fig 4

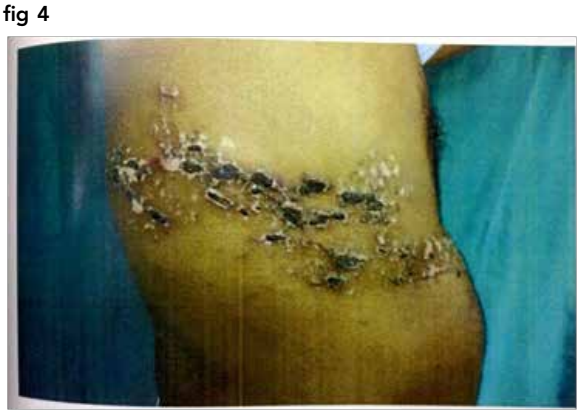
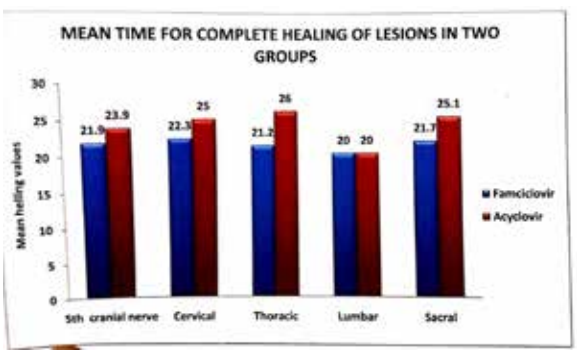


fig 5

In present study, most common adverse effects reported in both groups was nausea seen in 6 patients, and 4 were in acyclovir group and 2 were in famciclovir group. Similarly Shenet al[12] also observed a higher proportion of adverse effects in patients of acyclovir group were 14/28 (50%) thanfamciclovir 4/27 (14.8%). Thus, compared to other available studies in the present study both the drugs were well tolerated.

The median time taken for full crusting of lesions in both groups was 10 days . In the study of Shafran et al[13] it was 7 days in both groups and in Shen et al[12] , it was 11 days in famciclovir group and 10 days in acyclovir group. According to Tyringet al[14] the median time for full crusting of lesions was 8 days in famciclovir group .Thus there is variation of full crusting of lesions in different studies. In the present study the mean time taken for complete healing of lesion in famciclovir group was 20 days and it was 27 days in acyclovir group which is statistically significant (p value< 0.01).(Table 3 and Bar Diagram).



Shen et al[9] found similar findings,Tyring et al[11] observed complete healing was 20 days in famciclovir group and 21 day in acyclovir group. Shafranet al[10] observed 20 days in bothe the groups. The subsidence of acute pain in our study was 20 days ,infamciclovir group and in acyclovir group 27 days . Same was observed in the study ofShen et al[9] and in other study of Tyring et al[11] found 14 days in 14 days in Famciclovir group and 17 days in acyclovir group.Shafran et al found 17 days in both the groups which was significantly less.

Regarding complications in our study , depigmentation was seen in 16% of patients whereas choudary et al[6] observed in 15 % of patients. Post herpetic neuralgia seen in 5 % of patients in which 3 % on Acyclovir group and 2 % in famciclovir group .Similar results were seen in Niganet al[5] study.

Conclusion:

Present comparative study showed most of the patients presented with classical zoster with moderate pain . Thoracic segment was involved in 56 %of patients .Crusted lesions were seen in majority of patients at the end of 5 days after initiation of chemotherapy. There was no significant adverse effects in both groups. Safety profile was slightly better in famciclovir group and also complete healing was much earlier in famciclovir group.

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