Oral Acyclovir to Treat Herpes Zoster: A Prospective Case Control Study

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This was a case control prospective study carried out to see the effectiveness and safety of oral acyclovir in the treatment of acute Herpes Zoster. Each group consisted of 15 patients. Acyclovir treated group received 400mg acyclovir 5 times daily for 5 days. The patients were followed up to 3 months. Acyclovir was shown to reduce the days of new lesion formation within the affected dermatome after day 0 (P<0.01). No other statistical difference was demonstrated between two groups although pain was reduced in a larger proportion of acyclovir recipients (71% VS 53%) during therapy. Acyclovir was well tolerated and not associated with any undesirable symptoms.

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Introduction

Herpes zoster is a common infection in general medical practice and may give rise to considerable morbidity, including intractable post herpetic neuralgia. Acyclovir is a specific inhibitor of the DNA polymerase of all five members of the human herpes virus family and thus the drug is potentially useful for the treatment of many herpes virus associated disease. Acyclovir is the drug of choice for the treatment of primary and recurrent genital herpes and also for mucocutaneous HSV infection in immuno-compromised hosts.[1,2,3]

Treatment of Herpes Zoster has been a greater challenge because vericella zoster virus strain are about ten fold less sensitive than HSV type-2 isolates. Double blinded controlled studies have shown intravenous acyclovir in a dosage of 5mg/kg three times a day[4,5] and 500 mg/sq.m[6] to be effective in the treatment of acute herpes zoster by modifying rash development and lessening pain.[4,5,6] But intravenous therapy is not practical for most patients and may be associated with side effects.

Acyclovir administered by mouth is only partially absorbed giving mean plasma concentration of around 3 μMol/L following nine four hourly doses of 200 mg and 5.2 μMol/L following nine four hourly doses of 400mg.[7] Most vericella zoster strains tested have been sensitive to acyclovir in vitro with ED_{50s} less than 4 μMol/L.[8] In vitro data suggests that vericella zoster virus is sensitive to concentrations of acyclovir that have been safely attained by oral acyclovir.[8] This controlled trial of oral acyclovir for the treatment of acute herpes zoster in otherwise normal adults was carried out to see its effectiveness and safety.

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Methods

This was a case control prospective study, carried out at Comilla, during the year 2007. Patient selection: Immune competent patients of different ages having a clinical diagnosis of acute herpes zoster were included into the study. Patients were excluded if his rash had been present for 72 hours or more, who had received antiviral therapy, pregnant lady, serum creatinine level >2mg/dI, serum bilirubin level >30 μMol/L.

After obtaining informed consent, we took a medical history and performed physical examination. On entry (Day 0) the age, sex, length of prodrome and duration of rash was noted. Distribution of rash was charted together with the stage of lesion development in terms of macule/papule, vesicle/pustule, ulceration or crust. The severity of rash was assessed by an approximate lesion count <50 or > 50. The severity of pain was noted as nil, mild to moderate and severe.

Every alternate patient were given acyclovir (virux), two 200 mg tablets at four hourly interval omitting the middle of the night dose (five does in 24 hours) and continued for five days, other alternate patients were treated without acyclovir and served as control.

Efficacy and tolerance were evaluated in both control and acyclovir treated group daily until full crusting had taken place or up to 21 days which ever was sooner. In daily examination lesions were examined with respect to location, total number of new lesion, erythema and area of involvement. The time to cessation of new lesion formation was recorded and the time of first scab formation and complete scabbing and healing also noted. Progression of zoster within or outside the dermatome was also noted.

Haematological and biochemical tests including Hb%, serum creatinine, serum bilirubin were done on day 0 and on day 5 after completion of acyclovir therapy. Any new complains of patient noted. All patients were later followed up at one and at three months.

Results

A total of 30 patients entered the study, of whom 15 received acyclovir treatment and 15 treated without acyclovir. One acyclovir patient withdrew from the study because he started homeopathy. Thus 29 patients were analysed for efficacy and safety.

Sex and duration of rash were compared between the two groups using t-test. No difference were found at the 5% level of significance. (Table I). The rash progression was analysed and two groups compared according to the following parameters: a) mean days to cessation of new lesion formation b) mean days to loss of vesicles c) mean days to first crust formation and d) mean days to full crusting.

Comparison was made using the t-test. The results are detailed in Table II. Days of cessation of new lesion formation were significantly reduced in acyclovir treated group (p <0.0 1).

Acyclovir group has a larger proportion of subjects whose pain improved while on therapy than did the control group (71% VS 53%) as shown in table III. During follow up period, however, pain recurred or worsened in 40% acyclovir group and 50% control group patients. But the recurrence of pain was less severe in acyclovir recipients than controls. Post herpetic neuralgia defined as pain present for more than one month after the acute episode of herpes zoster was recorded in 14% of acyclovir treated and 20% of control group patients after 30 days of follow up. Pain persisted in 7% of acyclovir group and 20% of control group patients at 90 day follow up.

Variables related to safety and tolerance are detailed in Table IV. There were no significant difference between acyclovir and control group for changes in Hb%, serum creatinine, serum Bilirubin or any untoward symptoms before and after treatment with acyclovir.

Table I: Characteristics of Acyclovir and control group at entry

Characteristics	Acyclovir (n-14)	Control (n=15)
Male/female	6/8	7/8
Age (yrs)	51±13.4	52±14
Duration of Rash (Hrs)	34±19.9	33±18.2
Severity of rash		
Lesion count <50	8	7
Lesion Count >50	6	8
Primary Dermatome		
Trigeminal	3	4
Cervical	2	1
Thoracic	8	10
Lumber/sacral	1	0

Table II: Rash progression of Acyclovir and control group

Characteristics	Acyclovir (n-14)	Control (n=15)	P
Duration of lesion at entry (hrs)	34±19.9	33±19	NS
Cessation of new vesicle formation (days)	2±1	3±0.5	<0.01
Mean days to loss of vesicle	6.4±1.2	6.8±1	NS
Mean days to first crust formation	4±0.55	3.8±0.6	NS
Mean days to full crusting	7.5±1	6.8±1.5	NS

Table III: Time and non-improvement of pain in acyclovir and control group

Time	Control (n=15)	Acyclovir (n=14)
Day-0	15 (100%)	14 (100%)
Day-5	7 (46.6%)	4 (28.5%)
Day-30	3 (20%)	2 (14%)
Day-90	3 (20%)	1 (7%)

Table IV: Adverse effects during Acyclovir therapy

Effect	Acyclovir (n=14)	Control (n=15)
Increase of Serum creatinine	2	0
Reduction of Hb%	0	0
Increase of serum bilirubin	0	0
Nausea	3	1
Vomiting	1	1
Diarrhoea	0	1

Discussion

Intravenous acyclovir has been shown to have a significant effect on the development of the rash and also to lessen the acute pain in herpes zoster.[4,5] However, oral-acyclovir has been also shown to be highly effective in modifying the course of herpes zoster.[9] In the present study, oral acyclovir 400 mg five times a day has been shown to reduce the number of days of new lesion formation (p <0. 01), which is consistent with the findings of McKendrick et al.[10] There was no statistical significance in other parameters of rash progression although trends in the mean days favored the drug.

In a larger proportion of subjects pain improved while on therapy in acyclovir treated group. At 3 month follow up 7% of acyclovir and 20% of control group patient had persistent pain which highlightens that there is no significant difference between two groups regarding development of post herpetic neuralgia. Bean et al in randomized placebo controlled double blind trial showed that acyclovir did not affect the appearance of post herpetic neuralgia as also demonstrated by McKendrick et al.[6,10] In most of the studies including the present it has been shown that pain during the acute phase of the disease reduced more rapidly with acyclovir treatment. There is no difference in the associated symptoms or biochemical parameters before and after treatment with

acyclovir between the two groups.1n the study of Bean et al[6] there was transient rise of serum creatinine level in the acyclovir treated group and was associated with nausea and vomiting which may be explained by intravenous administration and inadequate hydration.

Present study suggests that oral acyclovir in a dose of 400 mg, 5 does a day is safe, effective in pain reduction in the acute phase and reduces the day of new vesicle formation. But the recurrence of pain after 5 days of treatment is suggestive of treating acute herpes zoster for longer than 5 days. Further work must be done to optimize the dosage regimen.

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