



RANDOMIZED CONTROL TRIAL- COMPARISON OF TOPICAL ACYCLOVIR AND GANCICLOVIR IN THE TREATMENT OF HSV EPITHELIAL KERATITIS

Ophthalmology

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ABSTRACT

Purpose- This research was conducted to study the efficacy of topical ganciclovir 0.15% gel and topical acyclovir 3% ointment in HSV epithelial keratitis and to compare the two drugs. **Material and methods-** It was a single blinded Randomized Control Trial with a sample size of 50. Cases in acute stage of HSV keratitis were enrolled and randomly divided into Group I and Group II. Group I patients received topical ganciclovir and patients in Group II were given topical acyclovir. Efficacy of both the drugs was compared. **Results-** The percentage of ulcers completely healed by Day 14 was 90.90% in Group I and 85.00% in Group II. The mean ulcer healing time in group I was 8.59 days and in group II was 11.20 days which was not statistically significant ($p=0.085$). There was no significant difference between the mean BCVA on logMAR scale in both the groups. **Conclusion-** Both the drugs were equally efficacious in the treatment of HSV keratitis with similar improvement in BCVA.

KEYWORDS

Ganciclovir 0.15% gel, Acyclovir 3% ointment, HSV epithelial keratitis

INTRODUCTION

Globally it is estimated that there are 1,000,000 new cases and 9,000,000 recurrent episodes of ocular Herpes simplex Virus (HSV) each year. It is also estimated that ocular HSV is responsible for visual disability in 1,000,000 people worldwide each year. [1]

HSV infection may manifest as epithelial, stromal or endothelial keratitis. The epithelial form typically manifests as branching epithelial defects ('dendrites'). The resulting dendritic keratitis is associated with corneal scarring and decreased corneal sensation. [2] Dendrites can progress to geographic ulcers, a type of large (amoeboid) epithelial defect with fimbriated edges. Stromal keratitis may be necrotising (infectious) or Immune/interstitial (non-infectious) keratitis. The endothelial involvement manifests as endothelitis that may be disciform, diffuse or linear.

The antiviral drugs commonly used in the treatment of HSV epithelial keratitis are Ganciclovir and Acyclovir ointments. Cellular enzymes convert these drugs to triphosphate form. Ganciclovir triphosphate and acyclovir triphosphate are competitive inhibitors of deoxy guanosine triphosphate (dGTP) incorporation into DNA and preferentially inhibit viral rather than host cellular DNA polymerase. [3]

MATERIALS AND METHODS

Our study was a single blinded Randomized Control Trial conducted to study the efficacy of topical ganciclovir and topical acyclovir in HSV epithelial keratitis and to compare the two drugs.

Patients:

We included all cases of HSV epithelial keratitis coming to the OPD and cornea clinic of the Department of Ophthalmology, KGMU during the study period. The patients having superadded bacterial infection and those not willing to participate in the study were excluded. Every eligible patient was enrolled in the study after taking an informed consent. Single blinded randomized sampling of study subjects was done into Group I and Group II. Group I patients received topical ganciclovir and Group II patients received topical acyclovir.

History, Examination And Follow Up:

We performed detailed history taking and examination of all the subjects on day 1 and on follow up visits which were done on day 3, 7, 14, 21, 45 and 90. Also the patient was advised to visit us in case of recurrence even after this period. Thorough ocular examination was performed on each visit. This included Best corrected visual acuity (BCVA), slit lamp examination, corneal sensations and fluorescein staining of cornea. The largest dimension of the ulcer was measured after staining and the ulcer size recorded at each visit. The treatment with topical ganciclovir and topical acyclovir was given for 1 week

after complete healing of the epithelial defect. The maximum duration for which the drug was administered was 6 weeks.

Outcome was assessed in terms of efficacy of the drugs. The criteria for assessment of efficacy were-

- Ulcers completely healed by Day 14 (%)
- Median and mean ulcer healing time
- Improvement in BCVA after treatment

The data was been analysed by using Unpaired t test, Paired t test and Chi square test. Categorical variables have been presented in number and percentage (%) and continuous variables have been presented as mean, SD and median. Quantitative variables have been compared using unpaired t-test and paired t test. Qualitative variables have been compared using Chi-Square test. A p value of <0.05 has been considered statistically significant.

RESULTS

The study enrolled 50 subjects out of which 25 were assigned group I who received treatment with topical ganciclovir and 25 were allocated Group II who were treated with topical acyclovir. However 2 subjects in group I were lost to follow up and 1 subject in this group was withdrawn from the study due to worsening of the corneal epithelial defect on day 14 of follow up. Similarly 3 subjects in group II were lost to follow up and 2 subjects had to be withdrawn from the study due to worsening of the corneal epithelial defect on day 14. So finally data from 42 subjects was documented and analysed, of which 22 were in group I and 20 were in group II.

The age and gender distribution of the study population has been summarized in Table 1 and 2 respectively. The comparison of efficacy of the two drugs as illustrated by percentage of ulcers completely healed by Day 14, median and mean ulcer healing time and improvement in BCVA after treatment has been shown in Table 3, 4 and 5 respectively.

Table 1: Age Distribution Of Study Population And Intergroup Comparison Of Age Distribution Using Chi Square Test And Unpaired T Test

Age Group (years)	TOTAL (N=42)		Group I (n=22)		Group II (n=20)	
	No.	%	No.	%	No.	%
Below 18 years	4	9.5	2	9.1	2	10
18 to 35 years	12	28.6	5	22.7	7	35
36 to 50 years	13	31.0	9	40.9	4	20
51 to 60 years	8	19	4	18.2	4	20
Above 60 years	5	11.9	2	9.1	3	15

$\chi^2=2.367$; $p=0.669$			
Mean + SD	40.17±16.090	39.33 ± 15.363	40.05 ± 16.599
Median	40.00	41.00	41.11
p value=0.883			

Table 2: Gender Distribution Of Study Population And Intergroup Comparison Of Gender Using Chi Square Test

Gender	TOTAL (N=42)		Group I (n=22)		Group II (n=20)	
	No.	%	No.	%	No.	%
Male	27	4.3	11	50	16	80
Female	15	35.7	11	50	4	20
$\chi^2=4.107$; $p=0.043$						

Table 3: Percentage Of Ulcers Completely Healed By Day 14 in Group I and Group II

	Groups	N	Mean	Std. Deviation	Median	P value
Ulcer healing time (in Days)	Group I (GANCICLOVIR)	22	8.5909	4.28351	7.00	0.085
	Group II (ACYCLOVIR)	20	11.2000	5.27756	14.00	

Table 4: Intergroup Comparison Of Ulcer Healing Time Using Unpaired T Test

	N	Number of ulcers completely healed by day 14	Percentage of ulcers completely healed by day 14
Group I (GANCICLOVIR)	22	20	90.90
Group II (ACYCLOVIR)	20	17	85.00

Table 5: Intergroup Comparison Of BCVA (log MAR) Using Unpaired T Test

	Group I (GANCICLOVIR) (N=22)		Group II (ACYCLOVIR) (N=20)		P value
	Mean	Std. Deviation	Mean	Std. Deviation	
BCVA DAY 1	1.2800	.52445	1.0760	.52140	0.214
BCVA DAY 3	1.2336	.52501	1.0670	.52976	0.312
BCVA DAY 7	1.1382	.55119	1.0290	.53769	0.520
BCVA DAY 14	.9936	.56966	.9020	.57502	0.607
BCVA DAY 21	.8164	.56571	.8520	.57584	0.841
BCVA DAY 45	.6827	.54147	.7280	.60900	0.800
BCVA DAY 90	.6427	.54027	.6490	.62655	0.972

DISCUSSION

This randomized control trial enrolled 50 subjects out of which 25 were assigned group I who received treatment with topical ganciclovir and 25 were allocated Group II who were treated with topical acyclovir. However few subjects were lost to follow up and some were withdrawn from the study due to worsening of the corneal epithelial defect on day 14 of follow up. So finally data from 42 subjects was documented and analysed, of which 22 were in group I and 20 were in group II.

The demographic profile of viral keratitis as evident from this study is that the incidence is higher among males as compared to females. 64.3% of our subjects were males and 35.7% were females (Table 2). The mean age of presentation as computed by this study is 40.17±16.090 (Table 1).

The follow up visits in our study were on day 3, 7, 14, 21, 45 and 90 after the first visit on day 1. The ulcer size on each visit was recorded. In our study, the percentage of ulcers that completely healed by Day 14 was 90.90% in Group I and 85.00% in Group II (Table3). In a study performed at four centers (Tunis, Dakar, Sousse, and Bamako) in Africa, the rate of healing, i.e. percentage of ulcers healed on Day 14 was 82.6% for the Ganciclovir 0.15% group and 72.7% for the

Acyclovir 3% group. The difference between the two groups was not statistically significant. [4] Our findings corroborate with these findings. The median ulcer healing time in group I was 7 days and that in group II was 14 days. We also calculated the mean ulcer healing time of both the groups, which was 8.5909 days for group I and 11.2000 days for group II. This difference was not statistically significant with $p=0.085$ (Table 4). Similar results were shown in a study conducted in Pakistan, the median time to healing was 7 days with Acyclovir 3% and 6 days with Ganciclovir 0.15%. The difference between the two groups was not statistically significant. [5] Mean BCVA on each follow up visit was recorded and no statistically significant difference was found between both the groups. The mean BCVA on day 1 was $1.2800 \pm .52445$ in group I and $1.0760 \pm .52140$ in group II with $p=0.214$ that was not statistically significant. The mean BCVA of group I and group II on day 3 was $1.2336 \pm .52501$ and $1.0670 \pm .52976$ respectively, on day 7 was $1.1382 \pm .55119$ and $1.0290 \pm .53769$ respectively, on day 14 was $.9936 \pm .56966$ and $.9020 \pm .57502$ respectively, on day 21 was $.8164 \pm .56571$ and $.8520 \pm .57584$ respectively and on day 45 was $.6827 \pm .54147$ and $.7280 \pm .60900$ respectively. The final mean BCVA on day 90 was $.6427 \pm .54027$ in group I and $.6490 \pm .62655$ in group II the difference between the two being not statistically significant with $p=0.972$ (Table 5). None of the previously performed studies on viral keratitis have compared the effect of two topical antiviral agents on best corrected visual acuity.

CONCLUSION

Topical ganciclovir 0.15% gel and topical acyclovir 3% ointment are equally efficacious in the treatment of viral keratitis with respect to the percentage of the ulcers completely healed by day 14 and the ulcer healing time.

The improvement in best corrected visual acuity in the subjects with viral keratitis is similar with both topical ganciclovir and topical acyclovir and is in proportion with the healing of the ulcer.

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