A Comparative Study of Safety Profile and Efficacy of Acyclovir and Ganciclovir in Viral Corneal Ulcer

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ABSTRACT

Objective: The present study was conducted to evaluate the safety profile and efficacy of ganciclovir in cases of viral corneal ulcer and to compare it with acyclovir. **Material and methods:** It was a randomized controlled comparative study undertaken at the Regional Institute of Ophthalmology, Pt BD Sharma PGIMS, Rohtak, Haryana. The patients were divided into two groups of 25 each. Group I received acyclovir 3% ointment and Group II received ganciclovir 0.5% gel. Patients were followed-up weekly for 1 month. Efficacy of the drug was assessed in terms of visual acuity and extent of healing. Safety profile was assessed by development of ocular irritation, blurring of vision and iatrogenic diffuse punctate keratopathy. The observations were analyzed using unpaired and paired 't' test and Chi-square test. **Results:** By 14th day, 80% ulcers were healed in Group I while 88% were healed in Group II. The best corrected visual acuity after healing was also similar in the two groups (p = 0.730). The safety profile in terms of ocular irritation, blurring of vision and punctate keratopathy of both the drugs was found to be similar. **Conclusion:** The efficacy and safety profile of both the drugs was similar in the treatment of viral corneal ulcer.

Keywords: Acyclovir, ganciclovir, corneal ulcer

Viral keratitis is a common cause of blindness in both developing and developed countries. Even though both DNA and RNA viruses are responsible for keratitis, common corneal infections are caused by DNA viruses, the commonest ones being the herpes group viruses (Type 1, 2, 3 - varicella zoster virus [VZV]) and adenoviruses.

Congenital ocular herpes is rare. Primary ocular herpes is the first infection of a nonimmune subject with microdendrites and lymphadenopathy. Recurrent ocular herpes gets reactivated from sensory ganglia with triggering factors.

Diagnosis is mainly clinical and treatment is mostly symptomatic and with antiviral and cycloplegic drugs. Globally, there are 1,000,000 new cases each year. According to herpetic eye disease study (HEDS), herpes simplex virus (HSV) epithelial keratitis accounted for 47% of ocular herpes cases.

Previously, topical acyclovir was compared with trifluorothymidine, vidarabine and idoxuridine and with interferon.

The topical antiviral agents used in the treatment of herpetic viral keratitis include acyclovir ophthalmic ointment 3%, ganciclovir ophthalmic gel 0.15% and trifluridine ophthalmic solution 1%. Various studies have been conducted to asses and compare the efficacy, safety and tolerability of the drugs. Some of these trials have shown that acyclovir and ganciclovir are equally effective.

This study was conducted to evaluate and compare the efficacy and safety profile of ganciclovir as compared to acyclovir in viral keratitis.

MATERIAL AND METHODS

A single-blinded randomized control trial was carried out at the Regional Institute of Ophthalmology, PGIMS, Rohtak, Haryana over a period of 1 year.

Cases of acute viral corneal ulcer were included in the study. Patients with superadded bacterial infection and those appearing immune-mediated clinically were

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excluded. Patients were divided into two groups. Group I received topical acyclovir ointment 3% while Group II received topical ganciclovir gel 0.15%. Randomization was done using computer generated randomization table.

The sample size was calculated using the formula:

$$n = \frac{2(p)(1-p)(Z_B+Z_a/2)^2}{(P_1-P_2)^2}$$

where n is sample size, p is the prevalence of viral keratitis taken as 1.6%, Z_B is the desired power, i.e., typically 0.84, $Z_{a/2}$ is the desired level of statistical significance, i.e., typically 1.96 and (P_1-P_2) is the effect size taken as 0.01.

The size of each group came out to be 25, so the total sample size taken was 50. Detailed history was taken and on follow-up visits, ocular irritation and blurring of vision were assessed subjectively as 0-none, 1-mild, 2-moderate and 3-severe. The best corrected visual acuity was noted.

Corneal scraping was examined with Giemsa staining for multinucleated giant cells. Gram stain and potassium mount were used to rule out bacterial and fungal etiology. Follow-up was done on Days 1, 7, 14 and 21. Outcome was assessed in terms of safety profile and efficacy.

Assessment of safety profile

- Ocular irritation due to drug instillation.
- Blurring of vision due to drug instillation.
- Punctate keratopathy.

Assessment of efficacy

- Best corrected visual acuity (BCVA) after treatment.
- Mean ulcer healing time.
- Ulcer completely healed by Day 14 (%).

The treatment was given for 1 month with topical antiviral, lubricating eye drops, cycloplegic and antibacterial drops.

The quantitative variables were compared using unpaired 't' test between the two groups and paired 't' test for pair comparison. Qualitative variables were compared using Chi-square test. A 'p' value of <0.05 was considered statistically significant.

OBSERVATIONS AND RESULTS

The mean age of the subjects in the two groups was not significantly different (39.04 ± 16.59 years vs. 38.22 ± 14.25 years, p = 0.77). Viral corneal ulcer was found to be more common in males as compared to females (63.2% males vs. 34.6% females, p = 0.041).

The ulcer size in both the groups was not significantly different on Days 1, 7 and 14. The ulcers completely healed by Day 21 in both the groups. There was no significant difference in the ulcer size on the follow-up visits in the two groups (Table 1). By 14th day, 80% ulcers were healed in Group I while 88% healed in Group II. There was no significant difference in the time required for healing in the two groups. The ulcer healing time was almost similar in the two groups (Table 2).

The BCVA after healing was also similar in the two groups (Table 3). Blurring of vision after instillation of drug in both the groups was mild-to-moderate and similar, with p = 0.109 (Table 4). In both the groups, majority of the patients did not have ocular irritation (Table 5). The difference in the development of diffuse punctate keratopathy between the two groups was not statistically significant, with p = 0.156 (Table 6).

Table 1. Comparison of Ulcer Size on Different Follow-up Days with Unpaired *t*-test

	Group I Acyclovir (n = 25)		Group II Ganciclovir (n = 25)		P value
	Mean	SD	Mean	SD	
Day 1	4.2840	1.7804	4.3853	2.0546	0.771
Day 7	0.2800	0.4278	0.1344	0.2652	0.083
Day 14	0.0440	0.1321	0.0162	0.0824	0.447
Day 21	0.0000	0.0000	0.0000	0.0000	NA

Table 2. Comparison of Ulcer Healing Time in the Two Groups

	N	Mean (days)	SD	P value
Group I (Acyclovir)	25	10.8000	5.106	0.085
Group II (Ganciclovir)	25	7.9609	4.002	

Table 3. Comparison of BCVA (log MAR)

	Group I Acyclovir (n = 25)		Group II Ganciclovir (n = 25)		P value
	Mean	SD	Mean	SD	
Day 1	1.0650	0.4113	1.1700	0.4133	0.214
Day 7	1.0180	0.4265	1.0271	0.4411	0.420
Day 14	0.8010	0.4640	0.8825	0.4585	0.507
Day 21	0.7410	0.4658	0.7164	0.4651	0.730

Table 4. Comparison of Blurring of Vision due to Drug Instillation

Blurring of vision due to drug	Group I (n = 25)		Group II (n = 25)	
	No.	%	No.	%
None	4	16	9	36
Mild	8	32	10	40
Moderate	8	32	4	16
Severe	5	20	2	8

$\chi^2 = 5.853$; p = 0.109.

Table 5. Comparison of Ocular Irritation due to Drug Instillation

Ocular irritation due to drug	Group I (n = 25)		Group II (n = 25)	
	No.	%	No.	%
None	14	56	15	60
Mild	10	40	10	40
Moderate	1	4	0	0
Severe	0	0	0	0

$\chi^2 = 1.268$; p = 0.531.

Table 6. Comparison of Development of Diffuse Punctate Keratopathy in Two Groups

Diffuse punctate keratopathy	Group I (n = 25)	Group II (n = 25)
Absent	25 (100%)	24 (96%)
Present	0 (0%)	1 (4%)

$\chi^2 = 1.907$; p = 0.156.

DISCUSSION

In our study, the percentage of ulcers that completely healed by Day 14 was 80% in Group I and 88% in Group II. In a clinical trial, conducted in Europe, the rate of healing in ganciclovir 0.15% group was 83.3% and the rate of healing in acyclovir 3% group was 70.6%, but the difference was not statistically significant.

In another study, the healing rate of 71.05% with acyclovir and 86.1% with ganciclovir was also not statistically significant. In a multicentric study to see the relative efficacy of ganciclovir 0.15% and acyclovir 3%, there was no statistically significant difference detected in the rate of healing between the two groups (p = 0.8387).

Our findings are similar to these findings.

Mean BCVA was recorded on each follow-up and no statistically significant difference was found between the two groups (Table 3). No study could be found in literature where the BCVA was compared using these two groups. However, a clinical trial compared the effect of acyclovir and placebo with acyclovir and dexamethasone on visual acuity in herpetic disciform keratitis. The change in visual activity was similar for both the groups.

The blurring of vision due to drug instillation was graded subjectively depending upon severity as 0-none, 1-mild, 2-moderate and 3-severe. In the present study, the difference between the two groups was not found to be statistically significant (Table 4).

However, in other multicentric studies, average duration of blurring was significantly shorter in ganciclovir group when compared to acyclovir group. The difference in our study may be because of the fact that those studies are from western world and patients in our study are less literate and aware.

The ocular irritation due to drug instillation was graded subjectively from 0 to 3. Majority of the patients did not report any ocular irritation (56% in Group I vs. 60% in Group II). The difference in ocular irritation between the two groups was not statistically significant with p = 0.531 (Table 5).

In a multicentric trial, the frequency of punctate keratitis was half in ganciclovir group. Most of the previously conducted studies have shown the rates of superficial punctate keratitis to be similar in both acyclovir and ganciclovir group.

In another multicentric trial, stinging was significantly lower in ganciclovir group (p = 0.3) on 14th day. However, the duration of stinging and blurring was not statistically significant.

In this respect, some studies correlate while some do not correlate with or study.

CONCLUSION

Topical acyclovir 3% and topical ganciclovir 0.15% gel were equally effective in ulcer healing time. The ulcer healing time with topical acyclovir 3% was directly proportional to size of corneal ulcer.

The improvement of BCVA was similar in both the groups. The tolerance of the patients to topical acyclovir and ganciclovir was similar with respect to blurring of vision, ocular irritation and diffuse punctate keratitis. So, the safety profile of both the drugs (acyclovir and ganciclovir) was found to be similar.

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Cardio-obstetrics, an Upcoming Field to Check Increase in Deaths due to Heart Disease During Pregnancy

A new report published February 18, 2019 in the American Heart Association's journal *Circulation: Cardiovascular Quality and Outcomes* has urged more team-based care for mothers with cardiovascular disease and those at risk and suggested that more collaboration between cardiologists and obstetricians could help curb the nation's soaring death rate among pregnant women. According to the report, cardio-obstetrics is "a clear area of need for improved quality of care".

Nitisinone Increases Melanin in People with Albinism

A small pilot clinical study at the National Eye Institute (NEI) suggests that the drug nitisinone increases melanin production in some people with oculocutaneous albinism type 1B (OCA-1B), a rare genetic disease that causes pale skin and hair and poor vision. Increased melanin could help protect people with the condition against the sun's UV rays and promote the development of normal vision. Study results were published in *JCI Insight*.