



EFFICACY OF TOPICAL ACYCLOVIR IN TREATMENT OF HERPETIC KERATITIS

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Article Info <i>Received 15/06/2015</i> <i>Revised 27/06/2015</i> <i>Accepted 12/07/2015</i> Key words: Herpetic keratitis, Topical Acyclovir, Efficacy.	ABSTRACT Herpetic keratitis is a major cause of corneal blindness in the world. Several commercially available topical and oral antiviral drugs are currently available, oral antiviral drugs alone are not always effective in Herpetic keratitis. Thus, there had been a need for safe and effective topical antiviral agents against Herpetic keratitis. This study aimed to evaluate the efficacy of topical ophthalmic acyclovir applied five times daily as a treatment for herpes keratitis. 48 patients of Herpes simplex ocular disease who attended the outpatient department were included in study. Topical Acyclovir was found to be effective antiviral agent for the treatment of Herpetic keratitis showing an efficacy of 73 % of cases. In this study topical Acyclovir therapy was not effective in the treatment of stromal disease. Topical therapy is a potentially effective modality in herpetic keratitis.
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INTRODUCTION

Viral keratitis is commonly caused by Herpes simplex virus and Herpes zoster virus. The Herpes simplex virus remains significant ocular pathogen despite the existence of highly specific antiviral agents. India being an agricultural country with poor socio economic condition of the people and lack of literacy, associated with indiscriminate and widespread use of antibiotic and corticosteroids leading to a steep rise in the incidence of viral keratitis, posing a big problem as an aetiological agent in causing permanent blindness [1-3].

Specific antiviral agents and refinements in surgical technique have improved the prognosis for patients with Herpes simplex keratitis the condition persists and poses a therapeutic challenge to ophthalmologists because no therapy has been devised to block reactivation of virus. Present treatment is only effective in eliminating replicating virus or suppressing an immune response to viral antigens. Prophylactic therapy is also impractical because of long intervals between recurrent episodes of disease. Delay in treatment, frequent recurrences and mistreatment can all result in visual impairment [4].

Due to present increased awareness of viral lesions and also better clinical facilities in examining outpatient cases by corneal staining and examining under slit lamp better microbiological techniques of growing organism in vitro and using specific antiviral drugs more cases are being treated positively. HSV follicular conjunctivitis and keratoconjunctivitis occur mainly in adults between the ages of 20 to 40 years i.e, the period of life exposed to more stress, strain and trauma. Alterations of host immune status like as in fever, sore throat with common cold, menstruation, surgical procedures act as frequent recurrence triggers in HSV [5].

The only natural reservoir of HSV is man with sources of infection being children with primary disease, adults with recurrent disease and children and adults as healthy asymptomatic carriers, Transmission of virus appears to be primarily by direct contact. Organisms are also introduced through some herbal medicines when applied to the eye for some eye problem and also by unhygienic removal of foreign bodies. The incubation period between contact and disease is from 3 -9 days [6].



HSV involves predominantly the anterior segment and includes Herpes simplex virus shedding in tear films in the absence of the disease, dendritic ulcers, stromal keratitis with overlying epithelial disease, and stromal keratitis with underlying endothelial diseases. Management of viral keratitis is by medical line of treatment using antivirals, cycloplegics, antibiotics to combat secondary infections steroids for deep forms of keratitis (2) surgical line where in superficial keratectomy, conjunctival hooding or penetrating keratoplasty to be done. Many cases even treated successfully need partial or full thickness keratoplasty to restore the vision lost by scarring [7].

Acyclovir (9-2 hydroxy methyl guanine) is a purine analogue. This new generation antiviral agent was described first during 1978. The drug is more specific in affecting viral particle as it is activated only by virus induced thymidine kinase and converted to an acyclomonas - phosphate form and then to a triphosphate form . This triphosphate form selectively inhibits virus induced DNA polymerase [8,9].

Since the introduction of acyclovir in the last decade the visual prognosis of herpetic keratitis has improved dramatically. Benefits with this drug include rapid restoration of epithelial keratitis, reduction of disturbances in ocular surface epithelia and a decreased incidence of necrotizing or subsequent corneal melting compared to other antiviral agents Acyclovir is an extremely safe drug. The adverse effects namely stinging and punctate keratopathy .Orally it cause nausea, vomiting abdominal pain. Phlebitis and local injection site irritation. Effect on renal function due to crystallization and deposition of the drug in the kidneys of patients whose hydration or renal function are inadequate.

The aim of this study is to evaluate the efficacy of the anti-viral agent Acyclovir in the treatment of Herpetic Keratitis

MATERIAL AND METHODS

A clinical study was conducted to evaluate the efficacy of Acyclovir in selected cause of Herpes simplex keratitis. The diagnosis of viral origin in cases of corneal ulcer was made on the basis of clinical appearance and by way of exclusion of bacterial and fungal etiopathogenesis. 48 patients of Herpes simplex ocular disease who attended the outpatient department of ophthalmology, in our Hospital.

Table 1. Demographic details.

Patient details		Number of patients	Percentage (%)
Gender	Males	30	62.5
	Females	18	37.5
Age groups (years)	1-10	3	6.25
	11-20	6	12.5
	21-40	25	52
	41-60	12	25
	61 and above	2	4.25

Clinical procedure

At the initial examination each patient was questioned on the following points by present or past occurrence of extraocular herpes(2) Time of onset of ocular symptoms and a description of them (3) previous treatment with antiviral drugs or corticosteroids.

A complete and detailed local examination of both eyes which included slit lamp biomicroscopic study was carried out. The establishment of viral aetiology was done by way of exclusion. Particular attention was paid to note the characteristic pattern of the corneal lesion with fluorescein stain. In every case conjunctival swabs were taken to rule out bacterial growth. Corneal scrapings were taken for KOH smear to rule out fungal growth.

Negative reports of culture and KOH smear were favored to label the viral aetiology. Corneal sensation was checked with a fine wisp of sterile cotton in all cases to support the diagnosis.

This iris, pupils, was recorded in each eye prior to the onset of treatment and at subsequent visits. The general examination as conducted in all cases to rule out systemic diseases nutritional status and general health.

The type of corneal lesions was evaluated on the basis of the pattern of staining with flourescein. Patients with superficial punctate lesions of the cornea, dendrite geographic or stromal lesions were noted.

Therapy

Each patient was instructed to use 5 mm strip of 3% Acyclovir ointment in inferior conjunctival fornix of the involved eye five times daily. Supportive cycloplegic and vitamin therapy was also given. The keratitis was treated when epithelial and stromal odema had regressed and when there was no activity of any kind in the anterior chamber. Topical 0.1% dexamethsone was given to patients of stromal keratitis in the event of failure response with Acyclovir.

RESULTS

In present study 48 patients with Herpes simplex were included. Diagnosis was made by the characteristic finding, symptomatology fluorescein staining, and corneal sensation and slit lamp biomicroscopy. Exclusion of fungal and bacterial growth was done to support the diagnosis. This study included various types of dendritic, geographic and stromal keratitis.



Occupation	Manual laborers	23	47.9
	Students	10	20.8
	House wives	8	10.0
	Mechanics	6	12.8
Residence	Rural	32	66.6
	Urban	16	33.3

In a present study males are predominantly affected of 62.5% .age interval of 21-40% are more affected wit 52% . manual labourers more affected more of 47.9% and rural people are common group effected.

Table 2. Incidence of types of lesions

Types of lesions	Number of patients	Percentage (%)
Cutaneous Herpes	4	8.3
Recurrent Herpes	10	20

4 patients had history of cutaneous herpes and 10 patients and history of recurrence.

Table 3. Characteristic of corneal lesion.

Type of lesion	Number of patients	Percentage(%)
Dendritic	28	58.3
Geographic	16	33.3
Stromal	4	8.3

Evaluation of the corneal lesions revealed that dendritic keratitis was the most common variety.

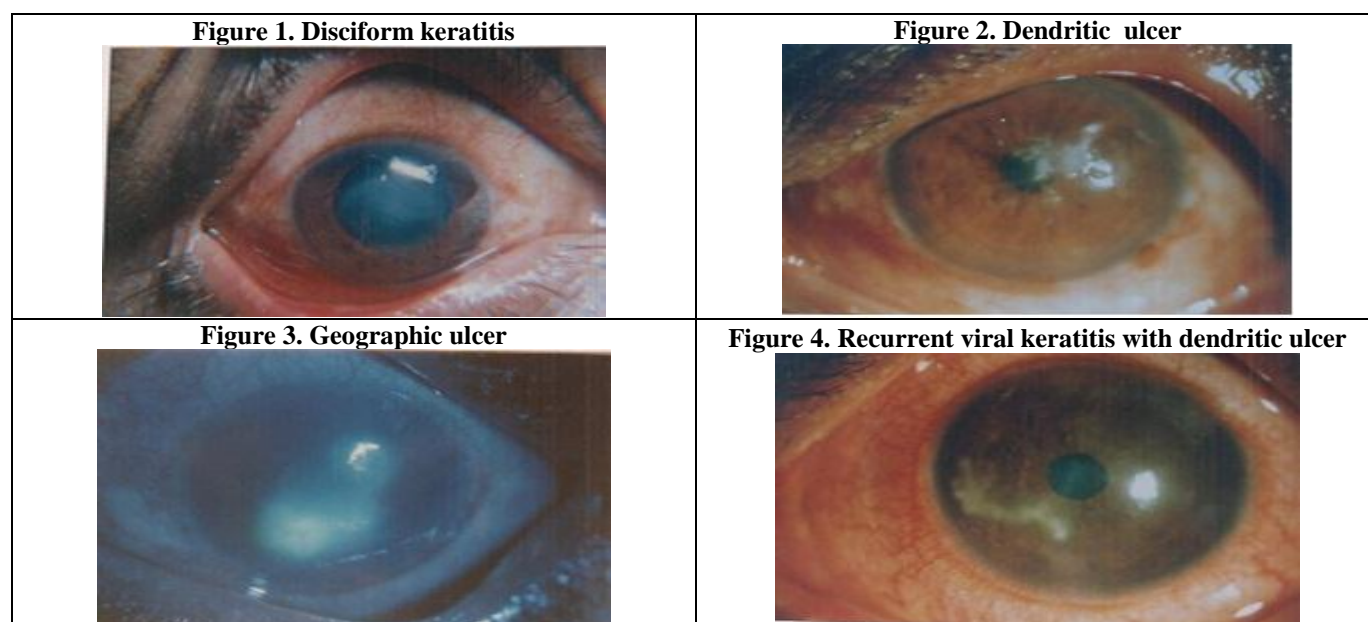
Table 4. Incidence of previous treatment

Drugs	Number of patients	Percentage (%)
Antibiotics	16	33.3
Antibiotics and steroids	2	4
No prior treatment	30	62.7

Table 5. Final status of cornea after healing

Condition of cornea	Number of patients	Percentage (%)
Without complications	35	73
Nebular opacity	6	12.5
Macular opacity	7	14.5
Leucomatous opacity	-	-

Most of the patients clinical outcome is without complications 73%



DISCUSSION

Topical Acyclovir was found to be effective antiviral agent for the treatment of Herpetic keratitis showing an efficacy of 73 % of cases. The findings in this study supports the sample evidence of excellent antiviral activity of Acyclovir reported in the literature. Two patients of geographic ulcers responded well to Acyclovir when combined with 0.1% Betnesol .

In this study topical Acyclovir therapy was not effective in the treatment of stromal disease. None of the four patients with stromal keratitis showed improvement of their clinical findings. Similar reports have appeared in the literature showing unsatisfactory results with topical Acyclovir therapy

In our study incidence was more in males with 62.5% and Patients were of all ages ranging from 1-65 years (Table-1). Of these 25 patients were of the age group 21-40 years and 14 were of the age group of 41-60 years studies correlates with study conducted by AK Khurana [10] 74.8% were males 25.2% were females (85 cases). Smith et al [11] studies showed an increased male of females ratio 1.67:1 and other the maximum incidence of viral keratitis occurred in the age group between 21-40 years [12].

An analysis of the occupational status revealed that 48% of the affected people were manual laborers (Table-1). This may probably be due to the exposure to the predisposing factors like sunlight, trauma, inadequate treatment etc. Evaluation of the corneal lesions revealed that dendritic keratitis was the most common variety. Patients from the rural areas were affected more than the urban population due to various causes like patient ignorance and lack of prompt ophthalmic help. Almost all patients had similar clinical presentations with lacrimation, redness, irritation and diminished vision of the affected eye. 4 patients had history of cutaneous herpes and 10 patients and history of recurrence. Patients who had skin lesions also had small vesicles on the lids of the affected

eye. Three of them had complete recovery without any sequelae where as one had ulceration on the lids and was treated with topical application of 5% Acyclovir cream. Studies are done on use of Acyclovir in recurrence of Herpetic keratitis which correlates with our study [13].

All the patients came for treatment 5 days or more after the onset of symptoms. 16 of them had prior simple antibiotic treatment. 2 had topical antibiotic and steroid combination. Others did not have any treatment (Table-3) . The response to topical Acyclovir therapy was excellent in dendritic ulcer with the average healing duration of 7 days. None of stromal keratitis showed any improvement with topical Acyclovir therapy after 5 days and were put on topical 0.1% Betnesol 4 times daily (Table- 4).

Out of 48 patients 25 (73%) were healed without any complications. 16 patients developed nebular opacity and were given topical steroids for two weeks after epithelial healing. 7 patients with stromal keratitis healed with macular opacity with gross diminision of vision (Table-5).

Nevertheless, the efficacy of topical acyclovir is still low and the treatment requires it to be administered five times a day to be fully effective. Other antiviral agents have a far lower efficiency than acyclovir in vitro studies and should provide an effective clinical treatment with a longer interval between doses and thus less inconvenience.

The results of this study determination of the efficacy of aciclovir show that topical acyclovir can be effective in resolving ocular surface lesions associated with Herpetic keratitis.

CONCLUSION

However, when they were treated with acyclovir ophthalmic ointment five times a day on the ocular surface with herpetic keratitis showed substantial improvement and in most cases the ocular signs resolved. Topical Acyclovir is as effective in the treatment of herpetic keratitis.

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