Original Article

Comparison of Treatment Outcome of Ganciclovir Ophthalmic Gel and Moxifloxacin Eye Drop in Acute Adenoviral Keratoconjunctivitis

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ABSTRACT

Adenoviral ophthalmic infection is a self-limiting, highly contagious, very frequent infectious process. It can present in three acute clinical forms: nonspecific acute follicular conjunctivitis, pharyngo-conjunctival fever and epidemic keratoconjunctivitis. This study aims to assess and compare the efficacy of 0.15% ganciclovir gel with Moxifloxacin eye drop in the treatment of acute adenoviral keratoconjunctivitis.This longitudinal prospective study was conducted among 40 patients of acute adenoviral keratoconjuctivitis attending in the cornea clinic of National Institute of Ophthalmology & Hospital (NIOH), Dhaka, Bangladesh. They were randomly divided into two groups: group-I (study group) with 20 patients who used 0.15% ganciclovir gel and group-ii (control group) with 20 patients who used artificial tear and 0.5% moxifloxacin eye drop. Diagnosis was confirmed by expert cornea specialist by methodical ophthalmic examination. They were followed-up on 1,2,4 and 6 weekly. Mean score of symptoms and signs were calculated in every follow-up and compared between two groups. Unpaired t test and chi square test were done in applicable cases with statistical significance p<0.05. This study showed that in study group mean age of the respondents were 36.4±9.59 years and in control group 37±11.02 years. Most of them were male (82.5%). In study group, mean score of symptoms at the beginning of the study was 1.4. It was 1.14, 0.64, 0.20 and 0.04 after1,2,4,6 weeks respectively after starting treatment and in control group mean score of symptoms at the beginning of the study was 1.48. It was 1.46, 1.125,0.59 and 0.23 after1,2,4,6weeks respectively after starting treatment. A trend towards better response was observed in the treatment group and the difference was statically significant. The mean score of signs after starting treatment in group-iwas 1.8.It was 1.35, 0.775, 0.30 and 0.175 after ,2,4,6weeks respectively and in group-ii, mean score of signs at the beginning of the study was 1.675. It was 1.725,1.35,0.725 and 0.300 after 1,2,4,6 weeks respectively after starting treatment. A trend towards improved sings were observed in the study group and the difference was statistically significant at 1 week (p=0.0283), 2 week (p= 0.0003), 4 week (p=0.0016) except 6 week (p=0.1524). At 6th week of treatment improvement of signs occur but not statistically significant because of persistence of some corneal lesion. The significant symptomatic relief and clinical improvement was found in the study group treated with Ganciclovir ophthalmic gel suggesting an effective method for treatment of acute adenoviral keratoconjunctivitis.

Keywords: *Ganciclovir, Adenoviral Keratoconjunctivitis, Moxifloxacin.*

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INTRODUCTION

Adenoviral eye infection is a highly contagious, self-limiting and very frequently occurring infectious disease that can lead to an epidemic outbreak[1,2].The patient has complaints of burning, pain, photophobia, pruritus, irritation and tearing.[1,2] In the acute phase of the disease, follicles in the tarsal conjunctiva, serous or mucous secretion, eyelid edema, chemosis, punctate keratitis, preauricular lymph adenopathy and in the later phase, subepithelial infiltrates in the cornea are observed[1].Onset is acute, with symptoms 6 to 9 days after exposure. The ocular picture is usually bilateral, occurring simultaneously or with a difference of three days between the two eyes.[3,4]

The diagnosis of adenoviral conjunctivitis is generally clinical, based on signs and symptoms, and epidemiology.[1] Laboratory diagnosis of adenoviral infections is rarely indicated and currently is based on cell-culture in combination with immuno-fluorescence staining (CC-IFA), serologic methods, antigen detection, or PCR.[5] Cell culture in combination with immunofluorescence staining (CC-IFA) is the historical gold standard but is not widely used. Since its introduction as a laboratory test for eye disease in 1990, PCR has been used widely in clinical ophthalmology.[6,7] It has demonstrated better sensitivity compared with cell culture.[8,9,10]

Several drugs have been tested for the treatment of viral conjunctivitis, such as cyclosporine, trifluridine, povidone iodine, cidofovir, but none of them proved to be effective.[11] Topical ganciclovir is already available in the market of several countries in Europe, Asia, Africa and South America for treatment of ocular herpes.

Ganciclovir is a more selective and less toxic antiviral compared to other older antivirals[12]. Ganciclovir and aciclovir have similar pharmacological mechanisms. Topical application of gancilovir has been shown to penetrate the corneal stroma and reach the aqueous humor at therapeutic levels.[13,14,15] Ganciclovir has been shown to be a safe and effective topical antiviral, with less toxicity and more convenient in dosage schedule[15] .There are few clinical trials regarding the use of ganciclovir in adenoviral keratoconjunctivitis. Those studies suggested that ganciclovir can help achieving faster resolution of sign and symptoms reducing the contagiousness of the disease and preventing subepithelial opacities.[18,19] Due to the need for effective treatment for this common and highly contagious condition, the present study was conducted.So this study was conducted to campare the efficacy of Ganciclovir ophthalmic gel with Moxifloxacin eye drop in the treatment of acute Adenoviral keratoconjunctivitis.

METHODS

This prospective longitudinal study was conducted in the Department of Cornea, NIOH, Dhaka since June 2020 to July 2021,comprising of 40 cases of adenoviral keratoconjunctivitis who attended the cornea clinic, selecting them by non-random purposive sampling technique.

Inclusion Criteria: Patient with acute viral keratoconjunctivitis with onset of symptoms 5 days or less, over 18 years old were included in the study

Exclusion Criteria: Patients with central or para central corneal opacities, Pregnant or nursing mother immunodeficiency, corneal dystrophy, degeneration and corneal ectatic condition , previous ocular surgery (previous keratoplasty), kerato-uveitis, patient with corticosteroid or antibiotic use by any route within 30 days prior to the study and one eyed patients were excluded.

This 40 patients of viral keratoconjunctivitis with symptoms onset 5 days or less non randomly divided into two groups:group-i (Study group) with 20 patients who used 0.15%ganciclovir and group-ii (control group) with 20 patients who used artificial tear and 0.5% moxifloxacineye drop for 6 weeks. Data was collected from both groups. All patients with viral keratoconjunctivitis had gone ophthalmic examination. A data sheet was filled by interviewer by face to face interview.

They were followed-up on 1, 2, 4, 6 weekly. Mean score of symptoms and signs were calculated in every follow-up and compared between two groups. Statistical analyses were done to assess the level of significance. All the relevant data was recorded in a pre-designed data collection sheet.

The Statistical analysis was performed using the SPSS program, version 13.0. Unpaired t test and Chi square test were done in applicable cases. At 95% CI, p-value <0.05 will be considered as significant.

RESULTS

Mean age of the respondents were 36.4±9.59 years and in control group37±11.02 years. Most of them were male (82.5%). In study group, mean score of symptoms at the beginning of the study was 1.4. It

was1.14, 0.64, 0.20 and 0.04 after1,2,4,6 weeks respectively after starting treatment and in control group mean score of symptoms at the beginning of the study was 1.48. It was 1.46, 1.125,0.59 and 0.23 after1,2,4,6weeks respectively after starting treatment. A trend towards better response was observed in the treatment group and the difference was statically significant. The mean score of signs after starting treatment in group-iwas 1.8.It was 1.35 ,0.775 ,0.30 and 0.175 after ,2,4,6weeks respectively and in group-ii, mean score of signs at the beginning of the study was 1.675. It was 1.725,1.35,0.725 and 0.300 after 1,2,4,6 weeks respectively after starting treatment. A trend towards improved sings were observed in the study group and the difference was statistically significant at 1 week (p=0.0283), 2 week (p= 0.0003), 4 week (p=0.0016) except 6 week (p=0.1524). At 6th week of treatment improvement of signs occur but not statistically significant because of persistence of some corneal lesion.

Table I : *Distribution of frequency of symptoms*

Symptoms	Group-i (n=20)	Group-ii (n=20)
Foreign body sensation	19	17
Watering	18	20
Photophobia	18	18
Discharge	10	9
Eye ache	12	18
Reduced vision	6	4

Table II: *Distribution of frequency of signs*

Symptoms	Group-i (n=20)	Group-ii (n=20)
Intact corneal sensation	20	20
Punctate epithelial keratitis	20	20
Reduced visual acuity	18	20
Conjunctival congestion	18	16

Table III: *Distribution of mean score of symptoms*

Assessment periods	Group-I	Group-II	p value
Baseline	1.4±0.45 (SD)	1.48±0.26(SD)	0.6^{ns}
1 week after treatment	1.14±0.49(SD)	1.46±0.28(SD)	0.02^{s}
2 weeks after treatment	0.64±0.29(SD)	1.13±0.25(SD)	0.0001^{s}
4 weeks after treatment	0.20±0.25(SD)	0.59±0.18(SD)	0.0001^{s}
6 weeks after treatment	0.04±0.14(SD)	0.23±0.21(SD)	0.0016^{s}

ns= non-significant, s= significant, p value obtained by unpaired t test

Table IV: *Distribution of mean score of signs*

Assessment periods	Group-I	Group-II	p value
Baseline	1.8±0.41 (SD)	1.68±0.47(SD)	0.37^{ns}
1 week after treatment	1.35±0.56(SD)	1.73±0.47(SD)	0.0283^{s}
2 weeks after treatment	0.78±0.50(SD)	1.35±0.40(SD)	0.0003^{s}
4 weeks after treatment	0.30±0.47(SD)	0.73±0.30(SD)	0.0016^{s}
6 weeks after treatment	0.18±0.24(SD)	0.30±0.30(SD)	0.1524^{ns}

ns= non-significant, s= significant, p value obtained by unpaired t test

Table V: Distribution of complications of the study

Complications	Group-i(n=20)	Group-ii(n=20)	p value
Pseudo-membrane	5	6	1.12^{ns}
Sub-epithelial infiltrate	4	5	

ns= non-significant, p value obtained by a''^{2} test

Table V: Distribution of days of improvement and recovery after treatment

	Group-I	Group-II	p value
Improved	8.40±2.6 (SD)	18.70±3.6 (SD)	<0.001[s]
Recovered	34.20±8.3 (SD)	42.85±6.14 (SD)	<0.001[s]

s= significant, p value obtained by a"[2] test

DISCUSSION

Adenoviral eye infection is a serious public health problem.It is extremely contagious and can easily lead to epidemics. The cost of this disease to the citizens is high. It is needed to explore effective drugs for treatment of adenoviral keratoconjunctivitis which will provide faster recovery and should prevent any squelae and complications. Keeping all these aspects in consideration this study was conducted to evaluate the efficacy of 0.15% ganciclovir in treatment of adenoviral keratoconjunctivitis patients and showed that the drug is effective in controlling signs and symptoms of diseases.

In this study, patients were within 18-60 years of age. This age range represents the people working outside in crowd with the chance of more adenoviral infection.

Maximum number of participants were male 33 (82.5%),female were 7(17.5%).Most of the patients (70%) were service holder and middle class, most of them were engaged in outdoor activities.

Most of the patients (95%) of both groups presented with watering at the beginning of the study, which was followed by reduced vision (50%), discharge (47.5%), eye ache (75%), FB sensation (90%) and photophobia (90%). Study done by Tabbara K et al showed that patients with adenoviral kerato-conjunctivitis presented with tearing, photophobia, FB sensation and discharge was consistent with this study findings.[18] In this study corneal lesion was found in all the patients (100%) on examination at the beginning of the study. This was followed by congestion (85%) and reduced visual acuity (95%) in our study. Study done by Yabiku ST et al showed that the patients of severe adenoviral keratitis had congestion, hyperemia, corneal lesion and sub epithelial infiltration. They did not find reduced corneal sensation in adenoviral keratoconjunctivitis patients which also correlates with this study.[19]

By comparing proportion of symptomatic relief of both groups it appears that topical gancyclovir 0.15% eye gel is more effective in relieving symptoms compared to topical artificial tear and moxifloxacin after 6 weeks of treatment.

By comparing proportion of substitution of signs of both groups it appears that topical gancyclovir0.15% eye gel is more effective in relieving signs as compared to artificial tear and moxifloxacin after 6 weeks of treatment. Study done by Yabiku ST et al showed that topical gancyclovir 0.15% eye gel is more effective in relieving symptoms and signs of tearing, congestion, corneal lesion, sub epithelial opacitiesas compared to artificial tear and moxifloxacin 0.5% eye drop after 2 weeks of treatment.[19]

Study done by Yabiku ST et al showed that there is faster improvement of symptoms in study group compared to control group which supports this study findings.[19] There is statistically significant ($p<0.05$) difference in efficacy of topical gancyclovir eye gel in relieving symptoms of patients with adenoviral keratoconjunctivitis.

Study done by Jeng BH et al showed that mean score of signs after 2 weeks and 3 weeks of starting treatment with topical gancyclovir eye gel were 1.7 and 0.2 respectively which support this study findings[20]. There is statistically significant ($p<0.05$) difference in efficacy of topical gancyclovir eye gel and artificial tear and moxifloxacineye drop in relieving signs of patients with adenoviral keratoconjunctivitis.

At the end of the study, in group-i, 5 patients had pseudomembrane and 4 patients had sub-epithelial infiltrate. In group-ii, 6 patients had pseudomembrane and 5 patients had sub-epithelial infiltrate. In our study, there was corneal sub epithelial infiltrates, conjuctival pseudo membranes were higher in group-ii compared to group-i. So, study showed fewer complications in the ganciclovir group.

Tabbara K, et al found that ganciclovir significantly reduced both the duration of disease and the incidence of subepithelial infiltrates. They found mean time of adenovirus recovery was significantly shorter for ganciclovir-treated patients at 7.7 days in contrast to 18.5 days for those who received artificial tears ($P < 0.05$). In addition subepithelial opacities less developed in patients treated with ganciclovir 2

(22%) compared to 7 (77%) patients in treated with artificial tear and moxifloxacin.[18] Shiota H et al showed ganciclovir ophthalmic gel treatment shortens the recovery time and prevent complications in the keratoconjunctivitis which correlate with this study.[15]

CONCLUSION

The present study showed a tendency of faster improvement of signs and symptoms treated with 0.15% ganciclovir gel compared to the group treated with artificial tear and moxifloxacin eye drop. Which demonstrates this therapeutic modality to be an effective method of treatment for acute adenoviral keratoconjuctivitis.

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