ADENOVIRAL KERATITIS: A STUDYR. Anand¹, Deepshikha Solanki², Chahveer Singh Bindra³, Vivek Som⁴**HOW TO CITE THIS ARTICLE:**

R. Anand, Deepshikha Solanki, Chahveer Singh Bindra, Vivek Som. "Adenoviral Keratitis: A Study". Journal of Evolution of Medical and Dental Sciences 2015; Vol. 4, Issue 46, June 08; Page: 7887-7894, DOI: 10.14260/jemds/2015/1150

ABSTRACT: PURPOSE: Assessment of recurrence rate in adenoviral keratitis. **METHOD:** This study includes all patients with clinical features of adenoviral keratitis attending OPD, emergency and special clinic of the RIO. After taking detailed history all the patients included in this study were subjected to detailed examination by torch light & loupe and slit lamp examination. The patients were followed up at 2 weeks, 4 weeks and 8 weeks. Detailed examination was done and degree of relief with the given treatment was evaluated. Also recurrent cases were evaluated. **RESULT:** Most of the cases responded well to treatment given according to the severity of keratitis; however 20% of cases had no significant improvement at the end of 2 weeks and required treatment for longer duration after which they improved. In cases with adenoviral keratitis, 35% showed recurrence of disease after treatment and required steroids with lubricants for longer period of time. **CONCLUSION:** Adenoviral keratitis may limit patient's quality of life- affecting day to day activities and psychosocial relations.

KEYWORDS: Adenovirus, Keratoconjunctivitis, Epidemic.

INTRODUCTION: Adenoviruses are the most common cause of viral conjunctivitis. Fifty-one distinct human adenoviral serotypes have been described,¹ which are classified into 6 sub-genera (A-F). More than half of all adenoviral serotypes belong to subgenus D.²

Classically ocular adenoviral infection is divided into following 4 different clinical presentations:

1. Pharyngoconjunctival fever.
2. Epidemic Keratoconjunctivitis.
3. Acute nonspecific follicular conjunctivitis.
4. Chronic conjunctivitis.

Epidemic keratoconjunctivitis is the severest ocular disease caused by adenoviruses³ Ad 8, 9 and 37 are the serotypes most commonly associated with EKC. Ad 8 is the classic cause of EKC and its clinical picture in the prototype of ocular changes induced by adenoviral disease.⁴ The incubation period of the disease is about one week. Persons with EKC suffer from an intense foreign body sensation, pain, pre-auricular lymphadenopathy, oedema of the eyelids, subconjunctival haemorrhage, reduced visual acuity, and often a general feeling of being unwell. Tarsal pseudomembranes, which consist of necrotic tissue and fibrin on an intact epithelial surface, can be seen in acute fulminant disease. EKC is sometimes followed by the development of corneal sub-epithelial opacities, called nummuli, which may persist for months and are difficult to treat.⁵ Transmissibility is high during the first day of symptoms, and hospital breakdown are not uncommon.

The initial corneal alteration in EKC, can be detected 2 days after the onset of the disease as the epithelial vesicle like elevations of about 25-30 µm in diameter, hardly perceptible on the slit

ORIGINAL ARTICLE

lamp. On day 5, these elevations are easily visible both with and without fluorescein,⁶ these findings are classified as stage 0 and stage 1 respectively.

The stage 2 persists for 2 to 5 days and is characterized by a coalescence of the lesion and involvement of the deep epithelium. The incidence of stage 0-2 keratitis range from as low as 13% to as frequent as 70% of patients with EKC.⁶

The superficial keratitis can resolve or progress to sub epithelial infiltrates (SEIs) in 43% of patients of EKC.⁷ In stage 3 besides the deep epithelial punctuate keratitis, faint SEIs just beneath the compromised areas of epithelium are present. Stage 3 is typically detected during the 2nd week.

Stage 4 and 5 are detected in or after the 3rd week. No staining is seen. Stage 4 is characterized by the classic SEIs that may be present weeks or months after the infection. Stage 5 is characterized by punctuate epithelial granularity, often overlying sub-epithelial opacities.

Keratitis is usually central, but the periphery can also be affected. Visual acuity is often diminished without any pain, watering or foreign body sensation, especially when there is coalescence of the SEIs located in the visual axis which can persist for long duration in spite of treatment and can flare up or recur later on indicating the virus may lie dormant in cornea as with herpes simplex virus.

MATERIALS AND METHOD: This is a retrospective study conducted in the regional institute of Ophthalmology, Gandhi Medical College and Hamidia Hospital Bhopal from January 2012 to December 2013. It is a non-randomized retrospective hospital based study.

This study includes all patients with clinical features of adenoviral keratitis attending OPD, emergency and special clinic of the department. Patients with mixed microbial or other viral keratitis and already diagnosed to have adenoviral keratitis were excluded.

EXCLUSION CRITERIA:

1. Cases of mixed microbial or other viral keratitis.
2. Old diagnosed cases of adenoviral keratitis.

EXAMINATION: A thorough examination of the patient is done at the time of presentation to obtain a baseline data against which further follow up examination will be compared with:

1. HISTORY: Details regarding demographic characters including:

- Name, age, sex, residence, occupation and socio-economic status.
- A detailed history of the chief complaints like watering, redness, photophobia, type of discharge, swelling of lid, pain and foreign body sensation along with duration was recorded.
- The presenting complaints were recorded with special reference to onset of symptoms, progression, seasonal variation, aggravating and relieving factors.
- Significant past history of similar complaints was taken.
- Any systemic illness, if present, was noted.
- History in relation to trigger factors for reactivation including fever, UV light exposure, intraocular surgery, Ocular trauma, laser treatment of eye and use of topical steroids was taken.

ORIGINAL ARTICLE

2. GENERAL EXAMINATION: To rule out systemic diseases e.g. HIV, diabetes mellitus and other immunosuppressive disease.

3. OCULAR EXAMINATION:

- All the patients included in this study were subjected to detailed examination by torch light & loupe and slit lamp examination.

Examination was done under the following headings:

- Visual acuity: visual acuity for distance and near unaided and with glasses.
- Lid: swelling of the lids, and discharge was noted.
- Conjunctiva:

The following observations were made:

1. Any conjunctival or ciliary congestion.
 2. Type of discharge.
 3. Papillae or follicles if present.
 4. Ulcers- any evidence of ulcer was recorded after staining with fluorescent dye.
 - Cornea: following points were noted-
- a) Site of corneal involvement- corneal involvement was divided into 3 layers:
- Epithelium: corneal epithelium was examined for any epithelial defect or ulcer, being confirmed
 - By fluorescein staining, Characteristic superficial and deep punctuate keratitis pattern was noted down if present. Sub epithelial opacities were also looked for which were fluorescein stain negative. Also superficial vascularization was looked for.
 - Stromal: corneal stroma was looked for any signs of inflammation and opacity. Also deep vascularization if present was noted.
 - Endothelium: corneal endothelium was examined for any signs of inflammation, keratic precipitates and iris pigments.
- b) Corneal sensation: To document and loss in corneal sensation.
- c) Schimer test: To see the level of wetting of Schirmers strip.
- d) Fluorescein staining: to confirm superficial or deep punctuate keratitis.

FOLLOW UP: The patients were followed up at 2 weeks, 4 weeks and 8 weeks. Detailed examination was done and degree of relief with the given treatment was evaluated. Also recurrent cases were evaluated.

OBSERVATION:

Types of viral keratitis	0-10 yrs	11-20 yrs	21-30 yrs	31-40 yrs	40-50 yrs	>50 yrs	Total
Adenovirus	3	8	18	14	9	8	60

Table 1: Distribution of patients of adenoviral keratitis in relation to age group

ORIGINAL ARTICLE

When the cases of adenoviral keratitis were evaluated, most of the cases were found to be in age group of 20-50 years of age (68.33%) of total adenoviral cases.

Types of viral keratits	Male	Female	Ratio (M: F)
Adenovirus	25	35	1: 1.4

Table 2: Distribution of patients of viral keratitis in reference to sex

Female preponderance was seen in adenoviral keratitis (M: F= 1: 1.4).

Symptoms on presentation	No. of cases	Percentage (%)
Redness	48	80%
Watering	52	86.67%
Dimintion of vision	40	66.67%
Photophobia	28	46.67%
Pain	28	46.67%
Foreign body sensation	26	43.33%
Fever	3	5%

Table 3: Distribution of cases based on symptomatology

On evaluation of the symptomatology the commonest presentation was watering (86.67%) and redness (80%). Diminution of vision (66.67%) was the next common symptom while photophobia and pain were also present in half of the cases (46.67%), while foreign body sensation was seen in 43.33% cases.

Signs on presentation	No. of cases	Percentage (%)
Superficial punctate keratits (stage 1)	5	8.33%
Tarsal plate thickig with SPK	3	5%
Deep epithelial punctate keratitis (stage 2)	13	21.67%
Deep epithelial punctate keratitis with SEIs (stage 3)	17	28.33%
Sub epithelial infiltrates (SEIs) (stage 4)	20	33.33%
Corneal Nummular opacities (stage 5)	2	3.33%
Total	60	100

Table 4: Distribution of cases with reference to signs

The commonest sign seen in cases of adenoviral keratitis on presentation was found to be sub epithelial infiltrates (33.33%) , followed by deep epithelial punctate opacities with SEIs (28.33%). Superficial punctate keratitis was found in 8.33% cases on presentation however, tarsal plate thickening was along with SPKs was observed in 5% of cases. In only 3.33% cases, corneal nummular opacities were seen. Thus, most of the cases of adenoviral keratitis presented in stage 3 or stage 4.

ORIGINAL ARTICLE

Treatment Modality	No. of Cases	Percentage (%)
Group A- Lubricants	20	33.33%
Group B- Lubricants+ steroids (Prednisolone acetate 1%)	29	48.33%
Group B- Lubricants+ steroids (Prednisolone acetate 1%)+ systemic anti-inflammatory (NSAID)	11	18.33%
Total	60	100%

Table 5: Treatment modality in adenoviral keratitis

In patients with adenoviral keratitis, 3 groups were made in accordance to degree of corneal involvement and treatment given. In GROUP A only Lubricants were used (in 33.33%) while in GROUP B Lubricants along with steroids (prednisolone acetate 1%) were used (in 48.33% of cases), In GROUP C Lubricants, steroids (prednisolone acetate 1%) and systemic anti-inflammatory (NSAID) were used (in 18.33% of cases).

RESULTS: Prognosis was accessed on basis of symptomatic relief and clearing of vision.

Treatment Given	Responders (Clearing of vision and Symptomatic relief)	Persisting Blurring of vision
GROUP A Lubricants	20	-
GROUP B- Lubricants+ steroids (prednisolone acetate 1%)	20	9
GROUP B- Lubricants+ steroids (prednisolone acetate 1%) + systemic anti inflammatory (NSAID)	8	3
Total	48	12

Table 6: Adenoviral keratitis- prognosis (after 2 weeks)

Most of the cases responded well to treatment given according to the severity of keratitis, however 20% of cases had no significant improvement at the end of 2 weeks and required treatment for longer duration after which they improved.

Viral keratitis	Recurrence (No. of patients)	Percentage
Adenoviral keratitis	21/60	35%

Table 7: Recurrence rate

In cases with adenoviral keratitis, 35% showed recurrence of disease after treatment and required steroids with lubricants for longer period of time.

ORIGINAL ARTICLE

Aggravating Factor	Number of Cases	Percentage
Fever. Systemic illness	8/21	38.09
UV light exposure	-	-
Intra ocular surgery	1/21	4.7
Ocular trauma	2/21	9.52
Laser treatment o the eye	1/21	4.7
Topical steroids, etc.	1/21	4.7

Table 8: Recurrence rate in relation to aggravation factor

Fever and other systemic illness was found to be most common association with recurrence of adenoviral keratitis (38.09%) followed by ocular trauma (9.52%).

DISCUSSION: In the present study, the patients attending eye OPD from 1st January 2012 to 31st December 2013, 60 patients were clinically diagnosed to have adenoviral keratitis that is 0.39% of the total ophthalmic patients. In a similar study done by Khurana AK, Gutain HR, Parmar, in 1984⁸; it was noticed that 0.53% of the total ophthalmic patients who visited us, during this year, were suffering from viral involvement of cornea.

In the present study, adenoviral keratitis was seen in 68.33% of cases in age group of 20-50 years. On evaluation of cases of adenoviral keratitis female preponderance was seen (M: F= 1: 1.4).

On evaluation of the symptomatology the commonest presentation was watering (86.67%) and redness (80%).

Diminution of vision (66.67%) was the next common symptoms while photophobia and pain and were also present in half of the cases (46.67%), while foreign body sensation was seen in 43.33% cases.

The commonest sign seen in cases of adenoviral keratitis on presentation was found to be sub epithelial infiltrates (33.33%) , followed by deep epithelial punctate with SEIs (28.33%). Thus, most of the cases of adenoviral keratitis presented in stage 5 or stage 4.

In a similar study done by Chang C, 2000,⁶ the incidence of stage 0-2 keratitis range from as low as frequent as 70% of patients with EKC.

According to study done by Darougar S, 1983,⁷ the superficial keratitis can resolve or progress to sub epithelial infiltrates (SEIs) in 43% of patients of EKC.

In patients with adenoviral keratitis, 3 groups were made in accordance to degree of corneal involvement and treatment given. In Group A, only Lubricants were used (in 33.33%) while in Group B- Lubricants along with steroids (prednisolone acetate 1%) were used (in 48.33% of cases). In Group C- Lubricants, steroids (prednisolone acetate 1%) and systemic anti-inflammatory (NSAID) were used (in 18.33% of cases).

Most of the cases responded well to treatment given according to the severity of keratitis, however 20% of cases had no significant improvement at the end of 2 weeks and required treatment for longer duration after which they improved.

Local steroids were found to be useful in providing symptomatic relief to the patient, improving diminution of vision and also reverting back the recurrent infection to normal.

ORIGINAL ARTICLE

In a study done by Romanowski EG, 2001,⁹ Corticosteroids enhance viral replication and increase the duration of viral shedding. These effects have been demonstrated for both potent (1% prednisolone acetate) and limited potency (0.2% prednisolone acetate 0.1% fluorometholone) topical corticosteroids, even when used for the short period.

In cases with adenoviral keratitis, 53% showed recurrence of disease after treatment, out of which 21 cases were associated with some aggravating factor.

Fever and other systemic illness was found to be most common association with recurrence of adenoviral keratitis (38.09%) followed by ocular trauma (9.52%).

SUMMARY AND CONCLUSIONS: Viral keratitis has become a special concern for clinical and basic research on its impact on quality of life among individuals; it annually represents an important issue to find better treatments, particularly to control the effects of chronic disease which could threaten vision and influence on daily life activities. Following conclusions were drawn from study:

- All age groups were affected with higher incidence in females (1: 1.4).
- Watery discharge was present in maximum number of cases (86.67%) followed by redness (80%).
- Various presentations of adenoviral keratoconjunctivitis are reported. Most patients presented in stage 3-4 with epithelial punctate keratitis and sub epithelial infiltrates (Together forming 61.66% cases). Also seasonal variation was noted with peak between February to May (62.22%).
- On presentation, 6.67% of patients had severe keratitis which was visually disturbing, which responded well to steroids, however 23.33% of cases had no significant improvement at the end of 2 weeks and required treatment for longer duration after which keratitis was relieved.
- One patient aged 3 years had pseudomembranous conjunctivitis, with typical adenoviral keratitis and was started on lubricants and steroids (prednisolone acetate 1%) for 1 week.
- 35 % cases had episodes of recurrence of subepithelial keratitis which was visually disturbing and affected their profession. They responded well to topical prednisolone acetate given for at least 2 weeks followed by fluorometholone eye drops for 1 week. Their intra ocular pressure was monitored.
- Patients needed a regular follow up and counselling regarding prevention of spread of infection.

Adenoviral keratitis may limit patient's quality of life- affecting daily life activities and psychosocial relations. Increasing the awareness amongst general population, more so in underdeveloped class may help in reducing the incidence of viral keratitis. This can be achieved by increased literacy rate increasing the awareness about the impact of trauma to eye, preventing the availability of over the counter medicines can be increased through the medium of television & radio talks, organizing awareness and screening camps in areas of risks can also help in lowering the incidence. All local infections should be treated with appropriate therapy, to prevent unavoidable corneal complication.

ORIGINAL ARTICLE

REFERENCES:

1. Shenk T (1996). Adenoviridae: the viruses and their replication. In Fields BN, Knipe DM, Howley PM, eds. Fields virology, 5th ed. Philadelphia: Lippincott- Raven: 2111–2148.
2. Kemp MC, Hierholzer JC (1983). The changing etiology of epidemic keratoconjunctivitis: antigenic and restriction enzyme analyses of adenovirus types 19 and 37 isolated over a 10-year period. J Infect Dis; 148: 24–33.
3. Pavan Langston D, Dunkel E: major ocular infections-antiviral agents and viral diseases of man, Lippincott raven, 1977 pp 1887-228.
4. Tabery H: Corneal epithelial changes due to adenovirus type 8 infection, Acta Ophthalmologica Scandinavica Volume 78, Issue 1, pages 45–48, February 2000.
5. Sundmacher R, Hillenkamp J, Reinhard T (2001). Prospects for therapy and prevention of adenovirus keratoconjunctivitis. Ophthalmology; 98: 991–1007.
6. Chang C, Chern C: epidemic keratoconjunctivitis caused by a new genotype of adenovirus type 8, Jpn J ophthalmol 45-160-166, 2001.
7. Darougar S, clinical and epidemiological features of adenovirus keratoconjunctivitis in London, Br J ophthalmol 67: 1-7, 1983.
8. Khurana A K, Gutain H R, Parmar I. Regional hospital prevalence of viral keratitis. Indian J Ophthalmol 1984.
9. Romanowski EG, Yates et al. Short-term Treatment with a Potent Topical Corticosteroid of an Acute Ocular Adenoviral Infection in the New Zealand White Rabbit; Cornea: August 2001 - Volume 20 - Issue 6-pp 657-660, 2001.

AUTHORS:

1. R. Anand
2. Deepshikha Solanki
3. Chahveer Singh Bindra
4. Vivek Som

PARTICULARS OF CONTRIBUTORS:

1. Director, Regional Institute of Ophthalmology, Bhopal, M.P.
2. Senior Resident, Regional Institute of Ophthalmology, Bhopal, M.P.
3. Junior Resident, Regional Institute of Ophthalmology, Bhopal, M.P.

FINANCIAL OR OTHER

COMPETING INTERESTS: None

4. Assistant Professor, Regional Institute of Ophthalmology, Bhopal, M.P.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Deepshikha Solanki,
C/o. Mr. Chandrashekhar Solanki,
D/21, Char Imli,
Bhopal-462016, M. P.
E-mail: drdeepshikha.eyes@gmail.com

Date of Submission: 15/05/2015.
Date of Peer Review: 16/05/2015.
Date of Acceptance: 30/05/2015.
Date of Publishing: 05/06/2015.