

New Management Of Epidemic Viral Keratoconjunctivitis

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Citation

A Waly. *New Management Of Epidemic Viral Keratoconjunctivitis*. The Internet Journal of Ophthalmology and Visual Science. 2004 Volume 3 Number 2.

Abstract

Epidemic Viral Keratoconjunctivitis (EKC) is a type of adenovirus ocular infection. EPK is highly contagious and has tendency to occur in epidemics.

At least 19 serotypes of adenovirus have been implicated in causing eye infection. The purpose of this study to compare between the usual management and the new management of viral Keratoconjunctivitis.

523 patients of viral conjunctivitis were diagnosed by clinical picture and laboratory investigation. 163 patients (121 males, 42 females, aged from 4 years to 63 years) were treated with usual management (first group).

360 patients (212 males, 148 females, aged from 4 years to 80 years) were treated by the new management (second group).

The study was hold between September 2000 and February 2004 in AL Khafji national hospital (Saudi Arabia). Patients were followed up for 3 months up to 4 years.

13 patients (7.97%) of the first group showed spontaneous recovery, 150 patients (92.02%) showed subepithelial opacities.

312 patients (86.6%) of the second group showed spontaneous recovery, 33 patients (9.1%) of the second group showed recovery after use of topical steroids, 15 patients (4.1%) of the second group showed corneal opacities .

The new management proved to be significantly better than the usual management ($P < 0.0001$).

INTRODUCTION

Epidemic Viral Keratoconjunctivitis (EKC) is a type of adenovirus ocular infection. EKC is highly contagious and has the tendency to occur in epidemics.

More than 50 serotypes of adenovirus have been isolated, and at least 19 documented serotypes cause EKC. ⁽¹⁵⁾

The most commonly associated serotypes include adenovirus 8, 19, and 37; and, less frequently, serotype 2-5, 7, 9, 10, 11, 14, 16, 21, and 29. Because of low, natural immunity against adenovirus in the general population (e.g., adenovirus type 8 antibodies are found in <5% of the general population in the US), every individual is considered susceptible to infection. ⁽²⁾

Adenovirus strains of a new type were isolated from patients with epidemic Keratoconjunctivitis. They were not

completely neutralized by any antiserum against adenovirus prototypes. PCR followed by restriction endonuclease analysis demonstrated that they were type 8. PCR followed by sequencing revealed a high homology rate between them and type 9. ⁽¹⁴⁾

Human adenovirus type 37 (HAdV-37) is a major cause of epidemic Keratoconjunctivitis and has recently been the largest causative agent of Keratoconjunctivitis in Japan. ⁽¹⁷⁾

Adenovirus types 8 and 19 are responsible for epidemic Keratoconjunctivitis and they are highly contagious for up to 2 weeks. ⁽¹⁰⁾

A tandem mass spectrometry-based approach is demonstrated for detecting a receptor for Ad37, one of the causative agents for epidemic Keratoconjunctivitis. Partial purification of membrane glycoproteins was performed by using lectin-affinity chromatography and sodium dodecyl

sulfate- polyacrylamide gel electrophoresis (SDS-PAGE). Gel bands that were shown to bind AD37 by using Viral Overlay Protein Blot Assay (VOPBA) were excised, proteolyzed and analyzed by using liquid chromatography coupled to nano-electrospray tandem mass spectrometry (nanoLC-MS/MS) to identify putative receptors contained in a mixture of proteins. ⁽¹⁹⁾

Four candidate receptors were identified among approximately 50 proteins based on a search against a protein database. Inhibition of gene delivery mediated by an AD37 vector, with antibodies against the glycoproteins identified by tandem mass spectrometry, strongly indicated that Membrane Cofactor Protein (MCP), a member of the complement regulatory family of proteins, is the receptor. This rapid and sensitive mass spectrometry based strategy is perceived to have wide potential applications for the detection of viral receptors. ⁽¹⁹⁾

The incubation period is 2-14 days and the person may remain infectious for 10-14 days after symptoms develop. ⁽¹⁵⁾

It is characterized by conjunctivitis: acute onset of watering redness, foreign body sensation and discomfort. Both eyes are affected in 60% of cases. ⁽²⁾

Examination show lid oedema, a follicular response which is frequently associated with a preauricular adenopathy, subconjunctival haemorrhages and pseudomembranes may develop ⁽²²⁾

Keratitis occurs in 80 % of cases and divided into 3 stages:

- Stage 1: occurs within 7-10 days of the onset of symptoms. It is characterized by a diffuse punctate epithelial Keratitis which may resolve or may go to stage 2.
- Stage 2: is characterized by focal white subepithelial infiltrates which develop beneath the epithelial lesions. They are thought to represent immune response to adenovirus and may be associated with mild transient anterior uveitis.
- Stage 3: is characterized by anterior stromal infiltrates which may persist for months and even years. ⁽⁹⁾

No gender predilection exists. The infection is more common in adults, but all age groups can be affected. ⁽¹⁵⁾

EKC epidemics tend to occur in closed institutions (e.g., schools, hospitals, camps, nursing homes, workplaces). ⁽⁵⁾

Direct contact with eye secretions is the major mode of transmission. Other possible methods of transmission are through air droplets and possibly swimming pools. Adenovirus can be recovered from the eye and throat for as long as 14 days after onset of clinical symptoms. ⁽¹³⁾

Many epidemics have been initiated in ophthalmology outpatient clinics by direct contact with contaminated diagnostic instruments. ⁽¹⁵⁾

The following explains the infectious transmission in hospitals and clinics: (1) the virus (adenovirus type 19) remains viable for 5 weeks, (2) the virus is resistant against standard disinfectants such as 70% isopropyl alcohol and ammonia, and (3) the virus sheds from the eye 3 days before and 14 days after symptom onset. ⁽⁴⁾

Epidemics of Keratoconjunctivitis are often traced to an eye care facility. Disease is commonly spread by ophthalmologists 'contaminated fingers or contaminated instruments and eye drops. ⁽¹⁾

Virus can be spread by finger to eye contact; it can also be spread to contaminated instruments such as applanation tonometers. ⁽²²⁾

EKC in East Asia and other parts of the world is endemic and does not appear to be transmitted through medical intervention. Viruses were isolated from more than 50% of cases of viral conjunctivitis; adenovirus constituted 94% of the EKC is a self-limiting disease ⁽⁵⁾

It tends to resolve spontaneously within 1-3 weeks without significant complications. In 20-50% of cases, corneal opacities can persist for a few weeks to months (rarely up to 2 y). This phenomenon can decrease visual acuity significantly and cause glare symptoms .In rare cases; conjunctival scarring and symblepharon can occur secondary to membranous conjunctivitis. ⁽¹⁵⁾

The patients recover spontaneously within 2-3 weeks with subepithelial opacities in 80 % of cases which persists for months or years even with the use of topical steroid.⁽²⁾

It is necessary to pay attention to the health education of population as well as to improve hygienic habits. ⁽¹³⁾

AIM OF THE WORK

In this study we compared between the usual management

and the new management of EKC.

PATIENTS AND METHODS

523 patients (333 males, 190 females, aged from 4 years to 80 years) were selected in the study in ophthalmic department in Al-kafji national hospital (Saudi Arabia). The study was started in September 2000 up to February 2004.

They were divided into two main groups.

- First group: 163 patients (121 males, 42 females aged from 4 years to 63 years) were treated by the usual management.
- Second group: 360 patients (212males, 148 females aged from 4 years to 80 years) were treated by the new management.
- All cases were diagnosed by clinical pictures and conjunctival smear.
- The clinical picture is characterized by acute onset of watering, redness, foreign body sensation and discomfort. Both eyes are affected in 60% of cases. (9)
- Examination show lid edema, a follicular response which is frequently associated with a preauricular adenopathy, subconjunctival haemorrhages and pseudo- membranes may develop (3)
- Conjunctival smear showed predominant lymphocytes which is diagnostic for viral infection. (2)
- Close follow up for all cases range from 3 months to 4 years.

USUAL MANAGEMENT

Conjunctivitis: non specific antibiotics eye drops and ointments .cold compresses, artificial tears, non steroidal anti inflammatory like voltaren eye drops. (15)

Keratitis: topical steroids in stage 3. Steroids do not shorten the course of the disease but merely suppress the corneal inflammation so that the lesions tend to recur if steroid is discontinued prematurely. (2)

MODIFIED (NEW) MANAGEMENT

- Eye wash with normal saline every day until the patients recovered.

- Manual removal of pseudomembranes with non toothed forceps and cotton tipped applicators during the eye wash.
- Antibiotic eye drops (ciprofloxacin) five times daily, choramphenicol eye ointment once by night.
- Lubricant eye drops (refresh eye drops five times daily).
- Cold compresses.
- Topical steroid (fluorometholone eye drops four times daily) in cases of subepithelial infiltrates.

RESULTS

First group (usual management):

- 150 patients (92.02%) have the usual course of disease and resolve after 3 weeks with anterior stromal infiltrates. The opacities did not resolve even with the use of topical steroids.
- 13 patients (7.97%) have complete recovery without any sequels.

Second group (new management):

- 312 patients (86.6%) recover completely within 9-12 days without subepithelial opacities or stromal infiltrates.
- 33 patients (9.1%) recover with subepithelial infiltrates which resolve with the use of topical steroids (fluorometholone).
- 15 patients (4.1%) recover with subepithelial opacities which persist for years even the use of topical steroids (fluorometholone or prednisolone).

Figure 1

	Number of patients		Complete recovery		Recovery with subepithelial infiltrates		Residual subepithelial opacities		P VALUE
	No.	%	No.	%	No.	%	No.	%	
First group	163	100%	13	7.97%	150	92.02%	150	92.02%	P < 0.0001 highly significant
Second group	360	100%	312	86.6%	33	9.1%	15	4.1%	

DISCUSSION

Epidemic Keratoconjunctivitis is annoying disease producing discomfort and is highly contagious, usual

management did not affect the course of the disease, subepithelial opacities which persist for months or years lead to blurring of vision increase the discomfort of the patient after resolution of infection. (9)

Epidemic Keratoconjunctivitis is a serious ophthalmologic disease that occurs sporadically in families, schools, health units and it can affect the anterior eye segment like turbidities that influence the eyesight sharpness. There is no treatment proved to be curable. (13)

It is necessary to recognize the disease on time, to treat it adequately, to carry out the antiepidemic activities, and to cut the ways of transmission. (14)

It is also necessary to pay attention to the health education of population as well as to improve hygienic habits. The prevention is the best protection from EKC keratoconjunctivitis affection as there is no effective antiviral treatment for the disease. (17)

Patients and health care personnel have acquired and transmitted epidemic Keratoconjunctivitis during the outbreaks. (3)

Viral conjunctivitis is an occupational hazard of eye care physician. Take all precautions possible not to be a victim .The treatment is only supportive. (23) Treatment of Epidemic viral Keratoconjunctivitis is unsatisfactory. (11)

Treatment for adenoviral conjunctivitis is supportive. No evidence exists that demonstrates efficacy of antiviral agents. (1)

The incubation period ranges from 2 to 14 days, and shedding of virus occurs from late in the incubation period to as long as 14 days after onset of disease. (15)

Adenovirus survives for long periods on environmental surfaces; ophthalmologic instruments and equipment can become contaminated and transmit infection. Contaminated hands are also a major source of person-to-person transmission of adenovirus, both from patients to health care personnel and from health care personnel to patients. Hand washing, glove use, and disinfection of instruments can prevent the transmission of adenovirus. (15)

The prevention is the best protection of Keratoconjunctivitis affection. (14)

The new management was a trial to alleviate the patient discomfort and visual disabilities. It is proved now that the

new management is significantly better than the usual management in shortening the course of the disease, decreasing the subepithelial infiltrates ($P < 0.0001$).

CONCLUSION

We conclude from our study that the new management of epidemic viral Keratoconjunctivitis: alleviate the patient's symptoms (redness, swelling, discomfort, photophobia, pain, and tearing), decrease the course of the disease, decrease the occurrence of subepithelial opacities and help topical steroids to vanish residual opacities.

Figure 2

ملخص بحث

"علاج جديد للإنتهاب الفيروسي الوبائي لملتحمة و قرنية العين ."

د. عادل والي - أخصائي العيون

مستشفى الخفجي الأهلي

الإنتهاب الفيروسي الوبائي لملتحمة و قرنية العين هو نوع من التهاب العيون بالآدينوفيروس. و هو مرض سريع العدوى و قد يحدث على شكل وبائي. و قد ثبت أن هناك تسعة عشر نوعاً من الآدينوفيروس من أصل خمسين نوعاً مسؤولون عن حدوث هذا الإنتهاب.

و الإنتهاب الفيروسي لملتحمة و قرنية العين يحدث على شكل إحصار و تورم بالعين و دموع و إحساس بوجود جسم غريب داخل العين ، و قد ينتقل هذا الإنتهاب إلى العين الأخرى.

و الفحص الإكلينيكي يبين حدوث تورم بالقرن و احتقان بالعين و نزيف لقطبي تحت الملتحمة، و في حالات كثيرة تتكون أغشية مخاطية كثيفة. و كذلك يمكن تحسس الغدد الدمعية الموجودة أمام صوان الأذن. أيضاً يمكن حدوث عتامات بالقرنية و قد تمتد لسنوات طويلة تؤثر على حدة الإبصار.

أما الفحص المخبري فيتم بأخذ عينة أو مسحة من ملتحمة العين و فحصها بالمجهز (الميكروسكوب) بعد صبغها بصبغة ليثمان. و في حالات الإنتهاب الفيروسي تكثر كرات الدم البيضاء من نوع الخلايا اللمفاوية.

يهدف هذا البحث إلى مقارنة العلاج التقليدي لهذا المرض مع علاج جديد له. و أجري هذا البحث في مستشفى الخفجي الأهلي بالمملكة العربية السعودية. و امتد هذا البحث من (سبتمبر ٢٠٠٠م) حتى (فبراير ٢٠٠٤م) ، و تراوحت مدة متابعة الحالات المرضية ما بين ثلاثة شهور و أربع سنوات.

تم إجراء هذا البحث على ٥٢٣ مريضاً تم تقسيمهم إلى مجموعتين :

- المجموعة الأولى: ١٢٣ مريضاً (١٢١ ذكر و ٢ أنثى). تراوحت أعمارهم بين ٤ سنوات و ٦٣ سنة. تم علاجهم جميعاً بالعلاج التقليدي.

العلاج التقليدي: عبارة عن قطرة و مرهم مضاد حيوي ، مع قطرة كورتيزون في حالات التهاب القرنية، بجانب قطرة مرطبة للعين.

- المجموعة الثانية: ٣٦٠ مريضاً (٣١٢ ذكر و ٤٨ أنثى). تراوحت أعمارهم بين ٤ سنوات و ٨٠ سنة. تم علاجهم جميعاً بالعلاج الجديد.

Figure 3



References

1. Azar MJ; and Dhaliwal DK, and Bower KS .Possible Consequences of Shaking Hands with Your Patients with Epidemic Keratoconjunctivitis. Pa Am J Ophthalmol 121:711-712, 1996.
2. Barnard DL, Hart JCD, Marmion VJ, and Clarke SKR. Outbreak in Bristol of conjunctivitis caused by adenovirus type 8, and its epidemiology and control. Br Med J 1973;2:165-9.
3. Boerner CF, Lee FK, and Wickliffe CL. Electron microscopy for the diagnosis of ocular viral infections. Ophthalmology 1981 Dec; 88(12): 1377-81.
4. Buehler JW , Finton RJ and Goodman RA. Epidemic keratoconjunctivitis: report of an outbreak in an ophthalmology practice and recommendations for prevention. Infect Control 1984;5:390-4.
5. D'Angelo LJ, Hierholzer JC, Holman RC , and Smith JD. Epidemic keratoconjunctivitis caused by adenovirus type 8: epidemiologic and laboratory aspects of a large outbreak. Am J Epidemiol 1981;113:44-9.)
6. Evans A and Kaslow R. Viral Infections in Humans: epidemiology and control.(Text book) 4th ed. New York: Plenum; 1997:119-138
7. Ford E, Nelson KE, and Warren D. Epidemiology of epidemic keratoconjunctivitis. Epidemiol. Rev 1987;9:244-61.
8. Garner JS and Simmons BP. Guideline for isolation precautions in hospitals. Atlanta: US Department of Health and Human Services, Public Health Service, CDC, 1985; DHHS publication no. 83-8314.
9. Jack J. Kanski . Adenoviral Epidemic keratoconjunctivitis. Clinical Ophthalmology. (Text book) 3rd ed. 1998; 86-70.
10. Jackson WB: Differentiating conjunctivitis of diverse origins. Surv. Ophthalmol 1993 Jul-Aug; 38 Suppl: 91-104.
11. Kaufman HE, Barron BA, and McDonald MB: Non herpetic Viral Infections. Cornea (Text book) 2nd ed.1998; 303-6.
12. Leibowitz HM, and Waring GO: Superficial Punctate Keratopathy. In: Clinical Disorders: Clinical Diagnosis and Management. (Text book) 2nd ed. 1998; 445-7.
13. Nagington J , Stehall GM, and Whipp P. Tonometer disinfection and viruses. Br J Ophthalmol 1983;67:674-6.
14. Papetropoulou M and Vantarakis AC. Detection of adenovirus outbreak at a municipal swimming pool by nested PCR amplification. J Infect 1998; 36:101-103
15. Tasman W and Jaeger EA: Epidemic Keratoconjunctivitis. Duane's Clinical Ophthalmology (Text book) 8th ed. 2001; 4(7): 5-8.
16. Peter G,. Adenovirus Infections: Report of the Committee on Infectious Diseases. American Academy of Pediatrics; 131. 1997.
17. Satoshi Takeuchi, Adenovirus Strains of Subgenus D Associated with Nosocomial Infection as New Etiological Agents of Epidemic Keratoconjunctivitis in Japan Journal of Clinical Microbiology, October 1999, p. 3392-3394, Vol. 37.
18. Toshihide Ariga. Epidemic Keratoconjunctivitis. Journal of Clinical Microbiology, February 2005, p. 726- 732, Vol. 43, No. 2).
19. Trauger, S.A. , Wu, E., Bark, S.J., Nemerow, G.R., and Siuzdak, G. The identification of an adenovirus receptor by using affinity capture and mass spectrometry. Chembiochem 5:1095, 2004.
20. Warren D, Nelson KE and Farrar JA. A large outbreak of epidemic keratoconjunctivitis: problems in controlling nosocomial spread. J Infect Dis 1989;160:938-43.
21. Wegman DH , Guinee VF, and Millian SJ. Epidemic Keratoconjunctivitis. Am J Public Health 1970;60:1250-7.
22. Weiss AH, Brinser JH, and Nazar-Stewart V. Acute conjunctivitis in childhood. J Pediatr. 1993;122(1):10-14.
23. Yanoff M, and Duker JS: Disorders of the Conjunctiva and Limbus. Ophthalmology 1998; 514-515.

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