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Preocular Tear Film Tests in Acute Hemorrhagic Conjunctivitis Caused by Coxsackievirus A24 Variant

Koksaki A24 etkenli Akut Hemorajik Konjonktivitli Hastalarda Preoküler Gözyaşı Film Testleri

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Summary

Purpose: Our aim was to evaluate the preocular tear film in patients who had acute hemorrhagic conjunctivitis (AHC) caused by coxsackievirus A24 variant (CVA24v).

Materials and Method: Seventy-six patients having AHC caused by CVA24v were enrolled in this study. An AHC outbreak was seen in Istanbul during August and September 2010 and lasted for four weeks. All the patients were seen at the first days of their disease period and none of them had received any treatment before. Conjunctival swab specimens were taken from the patients at their first visit. Tear film tests including Schirmer test, tear meniscus height measurement and tear break-up time (TBUT) were done in all patients.

Results: The mean age of the patients was 27.8 years (range: 7-68 years). Forty patients were male (53%) and 36 patients were female (47%). In bilateral conjunctivitis cases, the mean Schirmer test result was 23.7±4.7 mm, mean TBUT was 15.1±2.4 seconds and the mean tear meniscus height was 0.37±0.06 mm. In unilateral conjunctivitis cases, the mean Schirmer test result was 24.4±3.6 mm, mean TBUT was 15.1±2.3 seconds and the mean tear meniscus height was 0.38±0.07 mm in the diseased eyes.

Discussion: The results of the routine preocular tear film tests did not differ in AHC caused by CVA24v when compared with healthy eyes. *(Turk J Ophthalmol 2012; 42: 186-9)*

Key Words: Acute hemorrhagic conjunctivitis, coxsackievirus A24 variant, preocular tear film

Özet

Amaç: Koksaki A24 etkenli akut hemorajik konjonktivitli (AHK) hastalarda preoküler gözyaşı film tabakasının değerlendirilmesi.

Gereç ve Yöntem: Koksaki A24 etkenli AHK saptanan 76 olgu çalışmaya dahil edildi. AHK salgını Ağustos - Eylül 2010 tarihlerinde İstanbul'da ortaya çıkmıştı ve 4 hafta sürmüştü. Çalışmaya alınan bütün hastalar, hastalık evrelerinin ilk günlerinde görüldü ve hiçbiri önceden herhangi bir tedavi almamıştı. İlk vizitte hastalardan konjonktival sürüntü yöntemiyle kültür alındı. Bütün hastalara gözyaşı testleri olarak, Schirmer testi, gözyaşı menisküs yüksekliği ölçümü ve gözyaşı kırılma zamanı ölçümü uygulandı.

Sonuçlar: Hastaların ortalama yaşı 27,8 yıldı (7-68 yaş). Kırk hasta erkek (%53), 36 hasta kadındı (%47). Bilateral konjonktivit olgularında, ortalama Schirmer test değeri 23,7±4,7 mm, ortalama gözyaşı kırılma zamanı 15,1±2,4 saniye ve ortalama gözyaşı menisküs yüksekliği 0,37±0,06 mm idi. Tek taraflı konjonktivit olgularında ise hasta gözde ortalama Schirmer test değeri 24,4±3,6 mm, ortalama gözyaşı kırılma zamanı 15,1±2,3 saniye ve ortalama gözyaşı menisküs yüksekliği 0,38±0,07 mm idi.

Tartışma: Koksaki A24 etkenli AHK olgularında ölçülen gözyaşı film testleri, normal gözlerde ölçülen değerlerle benzerlik göstermiştir. *(Turk J Ophthalmol 2012; 42: 186-9)*

Anahtar Kelimeler: Akut hemorajik konjonktivit, Koksaki A24, preoküler gözyaşı film tabakası

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Introduction

Coxsackievirus A24 variant (CVA24v) and enterovirus 70 are known as the etiologic factors of acute hemorrhagic conjunctivitis (AHC). It was firstly seen as an epidemic in Ghana in 1969. After that, it was reported in some other regions like Southeast Asia and Japan in 1970, Hong Kong in 1988, China in 2002, Singapore in 2005 and India in 2007.1,2 In August-September 2010, an AHC epidemic was seen in Istanbul lasting for about 4 weeks.

AHC caused by CVA24v has a short incubation period (18-48 hours). Usually, it starts in one eye and transmits to the fellow eye in a short period. It is a very contagious disease and is transmitted mainly by eye-hand-eye contact. It affects all age groups and causes significant work force loss socially. Crowded places, low socio-economic status and poor hygiene cause faster infestation.[1,2]

The common features of AHC are follicular conjunctivitis, subconjunctival hemorrhage, purulent discharge, lid swelling, pre-auricular lymphadenopathy and punctuate epithelial keratitis.[3] Respiratory and gastrointestinal disturbances, headache and myalgia may also accompany some AHC cases.[4,5] Also, rare cases of neurological complications including radiculomyelitis and Bell's palsy may be seen.6 Usually, biomicroscopical inspection and patient history can help us to diagnose the disease, but viral culture must be done, if possible. The treatment of AHC is mainly symptomatic.[2]

Although AHC is a self-limiting disease, in order to fasten the recovery period, to prevent secondary bacterial infection and some possible complications, to provide patient comfort and to decrease virus load in the eye, various topical medications including antibiotics, steroids and artificial tear drops may be used.

In this study, our aim was to present the clinical findings of AHC epidemic caused by CVA24v which occurred in Istanbul and lasted for 4 weeks. We also evaluated the effect of the disease on tear secretion and function as well as the effect of topical artificial tear drops on the disease progress.

Methods

Seventy-six patients having AHC caused by CVA24v were enrolled in this study. The AHC epidemic was seen in Istanbul during August and September 2010 and lasted for 4 weeks. About 310 patients were admitted and treated in our hospital due to AHC, but in this report, we included only 76 patients in whom tear tests and conjunctival swab specimen were obtained.

The age of the patients ranged from 7 to 68 years. All patients were seen at the first days of their disease period and none of them had received any treatment. Contact lens users, cases with allergic conjunctivitis and chronic topical agent users were excluded from the study. Firstly, we diagnosed the disease clinically and then the cell culture results confirmed our diagnosis. Conjunctival swab specimens were taken from the patients at their first visit. The specimens were inoculated in specific cell cultures and viral isolation was confirmed by performing indirect immunofluorescence assay in Istanbul University Microbiology Department.

All patients were examined under biomicroscope and the data were documented at that time by one doctor (GP). The tear tests that we used were Schirmer test (with anesthesia), tear break-up time (TBUT) and tear meniscus height measurement. Also, we asked and documented the symptoms of the patients like burning, foreign body sensation and itching.

The Schirmer test was done by using a strip of filter paper 35 mm long and 5 mm wide which was bent at one end and placed in the lower conjunctival sac about one-third of the palpebral width from the temporal canthus, after one drop of topical anesthetic. The observation of the tear meniscus height was done under biomicroscope using a slit lamp equipped with a micrometer.[7] TBUT measurement was done by applying a moistened fluorescein strip to the bulbar conjunctiva and after a few blinks to spread the fluorescein evenly, the tear film was viewed with the help of a blue filter in front of the biomicroscope. When a dark area appeared, it represented the rupture of the tear film and the time elapsed since the last blink was recorded as TBUT.

The statistical analysis used in this study was done by the help of SPSS 14.0 software. Mann-Whitney U test and t test were used. A p-value lower than 0.05 was accepted as statistically significant.

Results

The mean age of the patients was 27.8 years (range: 7-68 years). Forty patients were male (53%) and 36 patients were female (47%). Sixty-nine patients (91%) told that they had close contact with an AHC patient.

Bilateral conjunctivitis was present in 48 (63%) patients, lid swelling in 73 (59%), chemosis in 14 (11%), subconjunctival hemorrhage was seen in 114 (92%) eyes. Punctuate corneal epitheliopathy was seen in 8 eyes (6%). Three cases had the disease twice in a two-month period. Only one patient had glaucoma as

Table 1. The mean values and ranges of eye tear function test results of the patients who had bilateral AHC

	Mean	Range
Schirmer test (mm)	23.7±4.7	8-30
TBUT (seconds)	15.1±2.4	10-20
Meniscus height (mm)	0.37±0.6	0.3-0.5

Table 2. The mean values of eye tear function test results of the patients who had unilateral AHC

	Diseased eye	Fellow eye	p-value
Schirmer test (mm)	24.4±3.6	24.1±3.7	0.73
TBUT (seconds)	15.1±2.3	15.2±2.4	0.88
Meniscus height (mm)	0.38±0.07	0.38±0.07	0.66

a chronic eye disease. Table 1 shows the tear test results in cases that had bilateral AHC and Table 2 shows the tear test results in patients who had unilateral AHC.

Upper respiratory tract infections (URTIs) were seen in 9 (12%) cases and gastroenteritis was seen in 6 (9%) patients. Systemic disease history of the patients revealed that 2 patients had diabetes mellitus, 4 patients had systemic hypertension and 1 patient had asthma.

In none of the patients, corneal edema, anterior chamber fibrin reactions and posterior segment disturbances were seen. As a systemic disorder, we did not encounter radiculomyelitis and Bell's palsy which are the rare complications of AHC.

Thirty-one patients came to their follow-up visit. Eighteen of them (group 1) had been prescribed only topical antibiotics and the other 13 patients (group 2) used both topical antibiotics and preservative-free artificial tear drops. Patients' history and biomicroscopical examinations revealed that there was no statistical difference between these groups in the aspect of recovery period (p=0.54). The recovery period ranged from 7 to 13 days. However, symptomatic relief was better in group 2 according to patients' subjective evaluation.

Discussion

Ocular surface disorders can disturb ocular tear film. As an ocular surface disorder, AHC produces abnormalities both in cornea and conjunctiva, and so tear film stability may be affected. Also, it is possible that the components of tear may change due to secretions and mediators formed in AHC. Although we did not have the opportunity to investigate the biochemical properties of the tears in the diseased patients, we think that the routine tear film tests that we applied may also give some clues about the status of tear film in AHC.

It is obvious that the ocular secretions, and so the tear amount, increase in AHC. But the tear meniscus height is not directly related with the amount of tear secretions. The formation of the tear meniscus depends on the balance between the negative pressure induced by its concave surface and the hydrostatic pressure due to the height of the fluid column in the meniscus.8 Also, the abnormalities occurring on the corneal surface may affect the meniscus height in AHC. Tear meniscus height lower than 0.3 mm is accepted as an indication of dry eye.[9] In our study, we found that the mean tear meniscus height ranged between 0.3 and 0.5 mm, thus, AHC did not decrease the tear meniscus height.

Observation of the rupture of the preocular tear film before a subsequent blink is one of the most commonly used tests of tear film stability and it is known as TBUT. TBUT in AHC might be abnormal due to both ocular surface disease and biochemical alterations in tear ingredients due to addition of inflammatory mediators. A TBUT of <10 seconds usually reveals an abnormality of preocular tear film.[10,11] In this study, the mean TBUT was 15.1±2.4 seconds (range: 10-20 seconds) in bilateral AHC cases, and so it might be said that TBUT was not adversely affected in AHC.

Schirmer test with topical anesthetics shows the amount of basal tear secretion. In our study, almost all of the patients had >10 mm test results. In spite of the usage of topical anesthetic drops, this result might be expected due to increased irritation of the eye in AHC. Also, we observed corneal epithelial changes in 6% of eyes, which may cause additional reflex tear secretion. Therefore, it is obvious that tear secretion function did not decrease in AHC.

Many viral agents may cause AHC. Commonly used diagnostic tests for these virus infection are based on virus isolation in cell culture, followed by identification of serotypes with neutralizing antisera, or on serological tests. Uchio et al. reported that the cause of AHC epidemic in Japan in 1994 was enterovirus type 70 and the subconjunctival hemorrhage was seen in 24% patients.[12] In our study, the cause of AHC was CVA24v and subconjunctival hemorrhage was seen in 92% eyes. We observed that the disease transmission was very rapid and the incubation period was very short in this AHC epidemic. It has been reported that CVA24v AHC tends to cause more explosive and extensive outbreaks than enterovirus type 70.[5,13]

Moura et al. reported that AHC epidemic occurred in Brazil in 2003, the symptoms lasted for 5-14 days, and punctuate epithelial keratitis was seen in 3%.[14] In our study, the symptoms of the patients lasted for 7-13 days and punctate epithelial keratitis was seen in 6%.

As it is known, some systemic diseases accompany AHC.5 In our study, we detected URTIs in 12% patients and gastroenteritis in 9% patients. Yin-Murphy reported those values as URTI in 86% of patients, gastroenteritis in 11% of patients and headache in 34% of patients.[5] Rare cases of neurological complications including radiculomyelitis, palatal paresis, and Bell's palsy accompanying or following AHC especially caused by enterovirus 70 were reported in the literature.[6,15] But, in our study, we did not encounter any of these complications.

The classical treatment option for AHC is topical antibiotics in order to prevent secondary bacterial infections. Because of this, we prescribed topical antibiotics to all patients. Also, we prescribed artificial tear drops to some of the patients randomly in order to see the effects on symptomatic relief and recovery period. We thought that the amount of inflammatory mediators and virus load might be diminished by washing out effect of the artificial tear drops. We observed that patients had some symptomatic relief by using artificial tear drops, but the recovery period and possible complication rates did not differ statistically when compared with the patients not using artificial tear drops.

As a conclusion, AHC is an important public health problem. It disseminates very fast unless the patients are informed about the prevention. Although it is an ocular surface disorder, tear film stability is not disturbed in most of the patients. Although we did not have enough data to achieve an exact conclusion, artificial tear drops might be prescribed to the patients beside topical antibiotics, in order to gain symptomatic relief.

References

1. Wairagkar NS. Acute Hemorrhagic Conjunctivitis. Current Ocular Therapy, 6th edition. Saunders Elsevier; 2008:10-11.
2. Seal D, Pleyer U. Ocular Infection, 2nd edition. Informa Healthcare, 2007:142-143.
3. American Academy of Ophthalmology. External disease and cornea. San Francisco: 2007-2008:162-3.
4. Lim KH, Yin-Murphy M. Epidemic conjunctivitis in Singapore in 1971. Singapore Med J. 1973;14:86-9.
5. Yin-Murphy M, Ishak B, Phoon MC, Chow VTK. A recent epidemic of Coxsackie virus type A24 acute haemorrhagic conjunctivitis in Singapore. Br J Ophthalmol.1986;70:869-73.
6. Kono, R, Miyamura K, Tajiri E, Sasagawa A, Phuapradit P. Virological and serological studies of neurological complications of acute haemorrhagic conjunctivitis in Thailand. J Infect Dis. 1977;135:706-13.
7. Oguz H, Yokoi N, Kinoshita S. The height and radius of the tear meniscus and methods for examining these parameters. Cornea. 2000;19:497-500.
8. Holly FJ. Tear film physiology. Am J Optom Physiol Opt. 1980;57:252-7.
9. Terry JE. Eye disease of the elderly. J Am Optom Assoc. 1984;55:23-9.
10. Norn MS. Desiccation of the pre corneal film. Corneal wetting time. Acta Ophthalmol (Copenh). 1969;47:865-80.
11. Lemp MA, Dohlman CH and Holly FJ. Corneal desiccation despite normal tear volume. Ann Ophthalmol. 1970;2:258-61.
12. Uchio E, Yamazaki K, Ishikawa H, et al. An epidemic of acute haemorrhagic conjunctivitis caused by enterovirus 70 in Okinawa, Japan, in 1994. Graefes Arch Clin Exp Ophthalmol. 1999;237:568-72.
13. Park K, Lee K, Lee J, et al. Acute Hemorrhagic Conjunctivitis Epidemic Caused by Coxsackievirus A24 Variants in Korea During 2002-2003. J Med Virol. 2006;78:91-7.
14. Moura FEA, Ribeiro DCS, Gurgel N, et al. Acute haemorrhagic conjunctivitis outbreak in the city of Fortaleza, northeast Brazil. Br J Ophthalmol. 2006;90:1091-3.
15. Chaopra JS, Sawhney IMS, Dhand UK, Prabhakar S, Naik S, Sehgal S. Neurological complications of acute haemorrhagic conjunctivities. J Neurol Sci. 1986;73:177-91.