Topical Piroxicam and Conjunctivitis†

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Abstract

The study of comparison of the clinical responses of acute hemorrhagic conjunctivitis to antibiotic eye drops alone and combined with topical piroxicam was analyzed. Seventy-five patients (146 eyes) with viral conjunctivitis were randomly assigned to receive topical antibiotic (35 cases) or antibiotic combined with piroxicam eye drops (40 cases). The patients were examined under slit lamp biomicroscope every other day for the first week, then twice a week until recovery. There was no statistically significant difference between groups in mean age, sex, bilaterality, history of contact, systemic involvement, mean incubation period, mean onset and mean follow-up time. Mean recovery time in the piroxicam group (4.9 days) was less than for the control group (P=0.003). Foreign body sensation, pain and tearing in the piroxicam group recovered significantly faster than in the control group. Complete recovery of all symptoms and signs in piroxicam treated eyes (61%) was significantly more common than with antibiotic only (29%) in spite of more drug induced burning. Piroxicam eye drops may have beneficial effects for acute hemorrhagic conjunctivitis to relieve discomfort, pain, and accelerate recovery.

Acute viral conjunctivitis, one of the most common ocular diseases, is a major public health problem all over the world; prevention and control of spreading are required to reduce the costs of these epidemics to communities. At present, there is no effective antiviral treatment to reduce the symptoms and shorten the duration of the illness. Viral conjunctivitis includes a variety of diseases such as epidemic keratoconjunctivitis (EKC) and pharyngoconjunctival fever, (associated with adenovirus) and acute hemorrhagic conjunctivitis (AHC) (associated with picornaviruses). Its clinical manifestation is characterized by sudden onset of lacrimation, foreign body sensation, redness, pain, edema, and production of mucus, epithelial cells, and inflammatory cells especially monocytes. Secondary

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bacterial infection sometimes develops in this suppurative conjunctivitis which requires topical antibiotics. Ward et al recommended the prompt isolation of patients, identification of viruses, and symptomatic treatment without antibiotics, antiviral or steroid medication, because they found no statistically significant differences among EKC patients treated with these agents[1]. Sklar et al found that the treatment of AHC with artificial tears, topical decongestants, or topical 1 per cent prednisolone acetate had no advantage over a cold compress[2]. Prophylactic treatment with interferon or other endogenously produced substances in patients exposed to conjunctivitis had some effect, although the clinical course of AHC was not different[3,4].

Viral corneal opacity can be mediated by deposition of immune complexes with precipitation, cellular infiltration, localized tissue damage of the supporting cellular lysis, and induction of an autoimmune response. However, application of topical corticosteroid is debatable in viral epithelial keratitis because it prolonged the course and the keratitis rebound on attempted withdrawal[5]. Complications caused by corticosteroids include posterior subcapsular cataract and steroid-induced glaucoma. They are sometimes applied in patients with severe inflammation or subepithelial opacity with reduced vision. To avoid the side effects, nonsteroidal anti-inflammatory drugs (NSAIDs) are currently used in topical eye drops but no clinical trial of their use in acute viral conjuntivitis has been done. NSAIDs can inhibit thromboxane A2, prostaglandins (PGE2, PGF2α, PGD2) and prostacyclin (PGI2) by inhibiting cyclooxygenase enzyme in the transformation of arachidonic acid from liberated membrane phospholipids after trauma[6]. They effectively prevent the increase of intraocular pressure, inflammation after paracentesis, lens extraction and implantation, neovascularization of the cornea, and cystoid macular edema [7-14]. Their applications in decreasing pain have been used for episcleritis and scleritis, radial keratotomy and excimer laser photorefractive keratectomy, immunosuppression and iridocyclitis, as well[15-18].

The purpose of this prospective, randomized study was to evaluate the analgesic and anti-inflammatory properties of topical NSAIDs eye drops combined with antibiotic eye drops in patients with AHC.

MATERIAL AND METHOD

From October through December 1992, 100 patients with AHC caused by coxsackievirus A24 variant in Thailand were enrolled in this study at the outpatient department of ophthalmology at Siriraj Hospital, Bangkok[19]. These patients, who gave informed consent after interview, represented approximately one third of the total cases with suspected AHC during that time. Symptoms had started within the previous 14 days. The patients were randomized to two equal groups. Patients in the control group received antibiotic eye drops every hour during the day. Patients in the piroxicam group received antibiotic eye drops every hour and NSAIDs eye drops (Piroxicam) four times daily.

Each patient's history was recorded, including onset, incubation period, contact persons, systemic symptoms (upper respiratory tract infection, pharyngitis, gastrointestinal disturbances) and ocular symptoms such as discharge, foreign body sensation, tearing, ocular pain, itching, burning, lid swelling and decreased vision. All eyes were examined with a slit lamp biomicroscope for ocular signs which consisted of swollen eyelids, ciliary injection, subconjunctival hemorrhage, chemosis and anterior chamber reaction with grading of severity as mild, moderate or severe. Superficial punctate epithelial keratitis and subepithelial opacity were graded as few spots, focal area or diffuse. Exclusion criteria included chemical or allergic conjunctivitis, intolerance of the eye drops (2 cases in control group, one case in the piroxicam group). The author was unable to follow-up 13 cases in the control group and 9 cases in the piroxicam group. The remaining patients were examined and followed-up every other day in the first week and twice a week until improved or complete resolution.

All statistical analysis was two-sided, using the 0.05 level of significance with SPSS version 4.0 and Epi info version 6.0. Quantitative data were analysed using pair Student's *t*-test and Mann-Whitney U-Wilcoxon Rank Sum W test. Demographic characteristics and qualitative data were compared using two-sided chi-square test or Fisher exact test for small expected distributions.

RESULTS

A total of 75 patients (146 eyes) in AHC, sampled randomly 35 cases (69 eyes) in the control

Table 1. Comparison of age, sex, bilaterality, history of contact, systemic symptoms, recovery days, ocular symptoms, and signs between treatment groups of patients with acute hemorrhagic conjunctivitis.

	Control group	Piroxicam group	Total (%)	P-value
Age (mean ± SD) (years)	31.8 ± 16.1	30.9 ± 14.8	31.4 ± 15.3	0.800
Sex female	17	22	39 (52.0)	0.750
Bilaterality				
first visit	28	31	59 (78.7)	0.980
last visit	34	37	71 (94.7)	0.620
History of contact	28	24	52 (69.3)	0.100
Systemic symptoms	16	18	34 (45.3)	0.860
Recovery days (mean ± SD)	5.2 ± 3.8	4.9 ± 4.4	5.0 ± 4.2	0.003*
(min ; max)	(1 ; 30)	(1 ; 24)	(1 ; 30)	
Presenting symptoms (%)				
mucopurulent discharge	84.1	77.5	80.6	0.451
foreign body sensation	74.6	85.9	80.6	0.152
tearing	69.8	80.3	75.4	0.230
pain	60.3	36.6	47.8	0.010*
itching	34.9	38.0	36.6	0.847
burning	30.2	15.5	22.4	0.068
blurred vision	15.9	14.1	14.9	0.962
Ocular findings (%)				
lid swelling	69.8	83.1	76.9	0.107
ciliary injection	30.2	32.4	31.3	0.927
superficial punctate keratitis	15.9	16.9	16.4	0.942
subconjunctival hemorrhage	11.1	12.7	11.9	0.990
preauricular node	4.8	14.1	9.7	0.127
chemosis	4.8	5.6	5.2	0.871
subepithelial opacities	0	2.8	1.5	0.498

* P-value < 0.05 significant

group and 40 cases (77 eyes) in the piroxicam group. Table 1 shows that the ages of patients in the study ranged from 1 to 74 years (mean 31 ± 15); approximately equal numbers of each sex were included. Nearly 80 per cent of patients had bilateral ocular involvement at the first examination; this rose to 95 per cent later. The majority of cases (69.3%) had a history of contact from family members, friends or others. Systemic involvement including upper respiratory tract infection and viral infection (fever, headache, cough) was observed in nearly half the patients. The mean incubation period and time from onset to presentation of this AHC outbreak were not significantly different between the two groups. Mean follow-up time was about one week for both groups. The mean recovery time for the piroxicam group is significantly less than for the control group (P = 0.003).

The most common symptoms and signs included mucopurulent discharge, foreign body sensation, swollen eyelids, and tearing. Superficial punctate keratitis was found in only 16.4 per cent of eyes. Surprisingly, subconjunctival hemorrhage and preauricular lymphadenopathy were seen in only 11.9 per cent and 9.7 per cent of eyes, respectively. In general, the differences in ocular symptoms and signs between the groups were not significant except for pain which was more frequent in the control group than in the piroxicam group (P=0.01).

Foreign body sensation, pain and tearing were relieved more quickly in the piroxicam group (P<0.05) (Table 2). Other ocular findings, including itching, superficial punctate keratitis, anterior chamber reaction, and subepithelial opacity in the piroxicam group were resolved insignificantly faster than in the control group.

Complete resolution of all complaints and findings was found in only 12 patients in the control group (20 eyes, 29%) less than 25 patients in the piroxicam group (47 eyes, 61%), (P=0.0002) (Table 3). However, patients with keratitis after treatment were more frequent in the piroxicam group but with less severity than in the control

Table 2. Comparison of mean recovery time of symptoms and signs in patients with acute hemorrhagic conjunctivitis treated with antibiotics and piroxicam.

	Days (Mean ± SD)		
	Control group	Piroxicam group	P-value
Symptoms			
discharge	4.0 ± 2.7	4.0 ± 4.4	0.208
foreign body sensation	4.4 ± 3.3	3.2 ± 3.3	0.006*
pain	5.0 ± 3.1	3.4 ± 2.9	0.026*
blurred vision	5.0 ± 3.1	5.8 ± 4.5	0.534
tearing	5.1 ± 2.8	4.3 ± 4.5	0.022*
burning	5.0 ± 2.6	4.8 ± 4.0	0.840
itching	7.7 ± 4.7	4.5 ± 4.5	0.160
Signs			
lid swelling	3.7 ± 2.1	4.1 ± 3.3	0.531
chemosis	4.3 ± 3.7	9.3 ± 5.2	0.078
conjunctival injection	5.3 ± 2.2	5.2 ± 2.7	0.899
ciliary injection	5.4 ± 4.3	5.7 ± 5.9	0.851
superficial punctate keratitis	9.9 ± 7.7	7.4 ± 4.6	0.215
anterior chamber reaction	14.5 ± 3.5	7.5 ± 3.5	0.186
subepithelial opacities	18.0 ± 0	9.4 ± 9.0	0.237

* P-value < 0.05 significant

Table 3. Clinical responses after treatment without and with piroxicam eye drop in patient with acute hemorrhagic conjunctivitis.

	%		
Clinical response	Control group	Piroxicam group	P-value
Complete recovery of all symptoms and signs	29.0	61.0	0.0002*
Keratitis after treatment	34.8	50.6	0.077
Burning			
before treatment	32.4	23.7	0.578
after treatment	41.2	89.5	<0.0001

* P<0.05 significant

group. Topical piroxicam caused a burning sensation in 34 patients more frequently than 14 patients in the control group with statistical significance.

DISCUSSION

Several currently available nonsteroidal anti-inflammatory agents inhibited arachidonic acid cascade in ocular inflammation have been widely used in many applications[20]. The NSAIDs eye drop, piroxicam can prevent postoperative inflammation after argon laser trabeculoplasty with equal effect to prednisolone acetate 0.5 per cent without influence on postoperative intraocular pressure [21,22]. In addition, it was the only available drug in Thailand at the time the present study was initiated.

In this study, the author found topical piroxicam combined with antibiotic eye drops to be an effective treatment for AHC. Mucopurulent discharge was frequently found in over 80 per cent of cases associated with late presentation for treatment. Therefore, antibiotic eye drops should be

appropriate to prevent superimposed bacterial infection. In contrast, in an epidemic of coxsackie virus type A24 variant AHC in Singapore, purulent discharge was present in only 18 per cent of patients because the time between onset and treatment was shorter.[23]. The mean recovery time of the piroxicam group was significantly less than that of patients receiving antibiotic alone. Pain and foreign body sensation were relieved in 3 days, and tearing in 4 days. In addition, complete recovery occurred in more eyes in the piroxicam group than in the control group. Although ocular pain is subjective and difficult to measure, pain relief with faster improvement in the piroxicam group was more frequent than in the control group.

Compared to the control group, superficial punctate keratitis, anterior chamber reaction, and subepithelial opacity in the piroxicam group resolved quickly in 7-9 days but without statistical significance. A larger sample should be studied to investigate this trend. Although, topical piroxicam did not prevent epithelial keratitis this was less severe than in the antibiotic only group. However, in this study it did not prolong the course of keratitis, in contrast to the action of corticosteroids in another study[5]. Topical piroxicam might not be as involved in delayed healing process as steroids are; further research on delayed healing is required. A burning sensation was experienced more often by patients in the piroxicam group than by those using antibiotic alone. Less acidity, improved vehicle, and decreased concentration of the drug might lessen this adverse effect.

In conclusion, this study showed that topical piroxicam may have a beneficial effect in decreasing pain, foreign body sensation and tearing in AHC patients with faster complete recovery than in patients using antibiotic alone. Further research is needed to clarify its mode of action and to reduce the side effects.

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REFERENCES

1. Ward JB, Jiojo LG, Waller SG. A prospective, masked clinical trial of trifluridine, dexamethasone, and artificial tears in the treatment of epidemic keratoconjunctivitis. Cornea 1993; 12: 216-21.
2. Sklar VEF, Patriarca PA, Onorato IM, et al. Clinical findings and results of treatment in an outbreak of acute hemorrhagic conjunctivitis in Southern Florida. Am J Ophthalmol 1983; 95: 45-54.
3. Stansfield SK, de la Pena W, Koenig S, et al. Human leukocyte interferon in the treatment and prophylaxis of acute hemorrhagic conjunctivitis. J Infect Dis 1984; 149: 822-3.
4. Langford MP, Barber JC, Sklar VEF, et al. Virus-specific, early appearing neutralizing activity and interferon in tears of patients with acute hemorrhagic conjunctivitis. Curr Eye Res 1985; 4: 233-9.
5. Laibson PR, Dhiri S, Oconer J, Ortolan G. Corneal infiltrates in epidemic keratoconjunctivitis. Response to double-blind corticosteroid therapy. Arch Ophthalmol 1970; 84: 36-40.
6. Bhattacherjee P. Prostaglandins and inflammatory reactions in the eye. Methods Find Exp Clin Pharmacol 1980; 2: 17-31.
7. Strelow SA, Sherwood MB, Broncato LJB, et al. The effect of diclofenac sodium ophthalmic solution on intraocular pressure following cataract extraction. Ophthalmic Surg. 1992; 23: 170-5.
8. Kulkarni PS, Srinivasan BD. The effect of intravitreal and topical prostaglandins on intraocular inflammation. Invest Ophthalmol Vis Sci 1982; 23: 383-92.
9. Ertürk H, Özcetin H, Avci R. Diclofenac sodium for the prevention of surgically induced miosis. Eur J Implant Ref Surg 1991; 3: 55-7.
10. Ronen S, Rozenman Y, Zylbermann R, Berson D. Treatment of ocular inflammation with diclofenac sodium : double-blind trial following cataract surgery. Ann Ophthalmol 1985; 17: 577-81.
11. Blaydes JE, Kelley EP, Walt JG, DeGryse RE, Harper DG, Novack GD. Flurbiprofen 0.03% for the control of inflammation following cataract extraction by phacoemulsification. J Cataract Refract Surg 1993; 19: 481-7.
12. Cooper CA, Bergamini M, Leopold I. Use of flurbiprofen to inhibit corneal neovascularization. Arch Ophthalmol 1980; 98: 1102-5.
13. Miyake K. Prevention of cystoid macular edema after lens extraction by topical indomethacin. II. A controlled study in bilateral extractions. Jap J Ophthalmol 1978; 22: 80-94.

14. Kraff MC, Sanders DR, Jampol LM, Peyman GA, Lieberman HL. Prophylaxis of pseudophakic cystoid macular edema with topical indomethacin. Ophthalmology 1982; 89: 885-90.
15. Watson PG. Disease of the sclera and episclera. In : Tasman W and Jaeger EA eds. Duane's clinical ophthalmology. Vol. 4 Philadelphia : Lippincott ; 1991: 1-43.
16. Gwon A, Vaughan ER, Cheetham JK, De Gryse R. Ocufen (Flurbiprofen) in the treatment of ocular pain after radial keratectomy. CLAO J 1994; 20: 131-8.
17. Steinert RF. Refractive surgery. Surgical correction of myopia : radial keratectomy and excimer laser photorefractive keratectomy. In : Smolin G and Thoft RA eds. The cornea 3 rd ed. Boston : Little, Brown and Co; 1994: 687.
18. Olson NY, Lindsley CB, Godfrey WA. Nonsteroidal anti-inflammatory drug therapy in chronic childhood iridocyclitis. Am J Dis Child 1988; 142: 1289-92.
19. Kosrirukvongs P, Kanyok R, Siritantikorn S, Wasi C. Acute hemorrhagic conjunctivitis outbreak in Thailand, 1992. Southeast Asian J Trop Med Public Health 1996; 27: 244-9.
20. Srinivasan BD, Kulkarni PS. Inhibitors of the arachidonic acid cascade in the management of ocular inflammation. Prog Clin Biol Res 1989; 312: 229-49.
21. Dorigo MT, Doro D, Cecchinato A. Aqueous prostaglandin E2 and intraocular pressure after argon laser trabeculoplasty in glaucoma patients pretreated with topical piroxicam. Int J Tiss Reac 1987; 9: 73-5.
22. Rolando M, Sanfelici G, Calabria G, Ciurlo G, Costa EB, Contos S. Piroxicam eye drops for the control of inflammation after argon laser trabeculoplasty. Glaucoma 1985; 7: 195-7.
23. Yin-Murphy M, Ishak B, Phoon MC, Chow VTK. A recent epidemic of coxsackievirus type A 24 acute haemorrhagic conjunctivitis in Singapore. Br J Ophthalmol 1986; 70: 869-73.

ยาหยอดตาไพโรซิแคมช่วยลดอาการของโรคตาแดงระบาด†

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ได้ทำการศึกษาเปรียบเทียบอาการของโรคตาแดงระบาดในผู้ป่วย 75 ราย (146 ตา) โดยสุ่มตัวอย่างแบ่งเป็น 2 กลุ่ม กลุ่มแรกได้รับยาหยอดปฏิชีวนะอย่างเดียวมี 35 ราย กลุ่มที่สองได้รับยาหยอดไพโรซิแคมเพิ่มเติมมี 40 ราย โดยการใช้กล้องตรวจตาผู้ป่วยทุกราย วันเว้นวัน ในสัปดาห์แรก หลังจากนั้นสัปดาห์ละ 2 วัน จนกว่าจะหาย พบว่าไม่มีความแตกต่างอย่างมีนัยสำคัญทางสถิติ ในอายุเฉลี่ย เพศ จำนวนตา ประวัติการติดต่อ อาการโรคทั่วไป ระยะเวลาฟักตัว ระยะเวลาที่เริ่มเป็น และระยะเวลาที่ติดตามผู้ป่วยทั้งสองกลุ่ม ในกลุ่มที่หยอดไพโรซิแคม ใช้เวลาหายเฉลี่ย (4.9 วัน) เร็วกว่ากลุ่มที่ได้รับยาหยอดตาปฏิชีวนะอย่างเดียว (ค่าพี 0.003) โดยเฉพาะอาการเคืองตา ปวดตา และน้ำตาไหล นอกจากนั้นจำนวนตาที่หายในกลุ่มไพโรซิแคม (ร้อยละ 61) มีมากกว่า กลุ่มที่ได้ยาหยอดตาปฏิชีวนะ (ร้อยละ 29) อย่างมีนัยสำคัญทางสถิติ ถึงแม้ว่าจะมีอาการแสบตามากกว่าก็ตาม ดังนั้นยาหยอดตาไพโรซิแคมในผู้ป่วยโรคตาแดงระบาดมีประโยชน์ช่วยลดอาการไม่สบายตา ปวดตา และทำให้หายเร็วขึ้น

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