

Topical Cyclosporine 0.5 Per Cent and Preservative-Free Ketorolac Tromethamine 0.5 Per Cent in Vernal Keratoconjunctivitis

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Abstract

A Prospective, randomized cross-over study was conducted in patients with vernal keratoconjunctivitis, successfully treated with cyclosporine, to evaluate the efficacy of cyclosporine 0.5 per cent compared with preservative-free ketorolac tromethamine 0.5 per cent. Patients received topical cyclosporine in both eyes along with an assessment of the severity of their conjunctivitis. In cyclosporine-treated patients, medication was discontinued 1 week before evaluation, then the medication was started for 1 month, and washed out 1 week before the other drug was started. Symptoms of itching, foreign body sensation, tearing, photophobia, discharge, burning, conjunctival injection, chemosis, giant papilla, keratopathy and intraocular pressure were evaluated weekly. There was a statistically significant decrease in all symptoms of cyclosporine-treated eyes at day 7, 14 and 30 and all signs at day 21 and 30. In ketorolac-treated eyes, there was a significant difference in itching, foreign body sensation, photophobia, tearing, mucous discharge, all symptoms, chemosis, giant papillae and conjunctival injection at day 7, and overall symptoms at day 14. Compared to cyclosporine - treated eyes at day 7, ketorolac-treated eyes had significantly fewer symptoms. Topical cyclosporine 0.5 per cent reduces symptoms and signs slower than preservative-free ketorolac tromethamine 0.5 per cent.

Key word : Vernal Keratoconjunctivitis, Topical Cyclosporine, Ketorolac Tromethamine

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Vernal keratoconjunctivitis (VKC) is a severe type of allergic conjunctivitis which is quite difficult to manage. In addition to ocular itching, foreign body

sensation, red eye, tearing and mucous ropy discharge, there may be personality and behavioral changes including increased blinking and photophobia which

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may reduce the patient's quality of life. Most of the patients have bilateral involvement with various keratopathies, superficial fibrovascular pannus, keratitis and sometimes shield ulcers⁽¹⁾. These symptoms and signs can persist for weeks or months, affecting not only visual function but may also limit the patients' activities. Affected individuals may be unable to attend school or work during the attack, thus adversely affecting education and career performance and possibly leading to financial, social and mental health problems. To the authors' knowledge, VKC results from type I and IV hypersensitivity reactions after exposure to allergens, therefore recurrences are common⁽²⁾. For mild to moderate symptoms, topical mast cell stabilizers such as cromolyn sodium or lodoxamide have a role in treatment and prevention of attacks, but the maximal effect is delayed for a few weeks⁽³⁻¹¹⁾. Initially in severe cases, topical corticosteroids can usually control the inflammatory response, however, in order to avoid their side effects which include glaucoma, cataracts and infection, these should be used only for a short period. The anti-inflammatory agent topical cyclosporine 2 per cent has been reported to reduce the anterior segment inflammation without systemic side effects⁽¹²⁻¹⁷⁾. The intravenous cyclosporine is diluted to 0.5 per cent in castor oil for topical use at Siriraj Hospital in order to control inflammation in uveitis, following penetrating keratoplasty. The cyclosporine is diluted to avoid severe burning that 2 per cent concentration causes. Adult patients can not tolerate this adverse reaction. Children are usually not very co-operative with treatment that involves instilling medication into their eyes. Therefore, the authors chose to use the topical 0.5 per cent instead of 2 per cent because it produce less burning sensation. The authors have been using 0.5 per cent for 5 years to decrease and control symptoms and signs of VKC⁽¹⁸⁾.

Ketorolac tromethamine is a nonsteroidal anti-inflammatory drug (NSAIDs) which can relieve ocular itching associated with seasonal allergic conjunctivitis by blocking prostaglandin synthesis⁽¹⁹⁾. Preservative-free ketorolac tromethamine (ketorolac PF) is an alternative drug ; use of ketorolac PF avoids the epithelial toxicity from preservative agent which may occur with prolonged use. The adverse reactions of ketorolac PF are well tolerated ; including stinging and burning (40%), ocular irritation (3%), allergic reaction to NSAIDs (3%), superficial ocular infection (0.5%) and superficial keratitis (1%) without enhancing the spread of ocular infection induced experimentally.

The purpose of the study was to evaluate the efficacy of cyclosporine 0.5 per cent compared to that of ketorolac PF in reducing the symptoms and signs of VKC, including adverse reactions to the drugs themselves.

MATERIAL AND METHOD

The comparison of preservative-free ketorolac tromethamine with cyclosporine 0.5 per cent was conducted from January 2000 to July 2000, in 7 patients who had VKC 5 palpebral type and 2 limbal type, success on using cyclosporine treated eye in 6 patients at the Department of Ophthalmology at Siriraj Hospital. Informed consent was obtained from the patients' parents. Exclusion criteria were bacterial conjunctivitis, viral conjunctivitis, perennial allergic conjunctivitis, and atopic keratoconjunctivitis.

VKC was diagnosed from a history of severe itching, photophobia and : 1) giant papillae size > 1 mm on the upper tarsal conjunctiva was classified as palpebral type, 2) fine papillae size < 1 mm and limbal infiltration with Horner-Trantas dot was classified as limbal type. If all these signs were present it was classified as mixed type.

The history and clinical course were recorded and an eye examination by slit-lamp biomicroscopy was performed ; the severity of the findings was assessed and graded as follows : 0 = none, 1 = mild, 2 = moderate, 3 = severe. See Table 1.

The clinical findings were recorded before starting topical cyclosporine 0.5 per cent or ketorolac PF, and the efficacy of treatment was evaluated using a daily diary card every week. "Success" was evaluated as a marked decrease in symptoms and signs with toleration and compliance at one week. All patients received environmental control and a cold compress to relieve itching, foreign body sensation and redness. Nonpreservative artificial tears were applied every hour till bedtime. This was necessary in order to dilute the allergens.

Treatment was evaluated as "failure" if > 2 weeks of medication or additional drugs or topical corticosteroid were needed to control inflammation. Topical antibiotics were used in patients with blepharitis or a shield ulcer was used to prevent secondary bacterial keratitis.

A randomized crossover study in control patients was conducted by stopping the medication for 1 week as a washout period to create symptoms and signs. A 2 week washout period could not be

Table 1. Grading the severity of symptoms and signs of VKC.

| Symptoms and signs | 1 = mild | 2 = moderate | 3 = severe |
|-------------------------|-----------------------------------|-------------------------------|--|
| Itching | Occasionally | Frequent, tolerable rubs eyes | Rub eye-all day |
| Foreign body sensation | Occasionally | Frequent | All day |
| Tearing | Occasionally | Frequent | All day |
| Photophobia | Occasionally | Sometimes closes eyes | Frequent closes eyes |
| Discharge | Occasionally | Frequent | All day |
| Mucous discharge | Occasionally | Few strands | Easily detectable |
| Burning | Occasionally | Frequent | All day |
| Swollen eyelid | Feels full in morning | Feels full all day | Interpalpebral fissure decreased |
| Chemosis | Conjunctiva separated from sclera | Raised conjunctiva | Ballooning of conjunctiva |
| Conjunctival injection | Minimal | Obvious | Diffuse redness |
| Papillae | Size < 0.2 mm | Size 0.2-1 mm | Size > 1 mm |
| Giant papillae | Size 1.1-1.9 mm | Size 2-5 mm | Size > 5 mm |
| Superficial pannus | Area < 25 per cent | Area 25-50 per cent | Area > 50 per cent |
| Punctate epitheliopathy | 1 quadrant | 2 quadrants | > 3 quadrants |
| | < 1/2 cornea | > 1/2 cornea | Confluent with mucous plaque and ulcer |
| Shield ulcer | Transparent base | White deposit | Elevated plaque |
| Limbal infiltrate | Mild prominent limbal vessel | Moderate area | Severe with pannus 360° |
| Horner trantas dot | 1 quadrant | 2 quadrants | > 3 quadrants |
| Visual acuity | 6/9-6/12 | 6/18-6/36 | < 6/60 |

established as the parents could not tolerate no giving their children treatment, except giving only supportive therapy such as cold compress and preservative-free artificial tears. The test medication was given 4 times daily to both eyes for a month with an eye examination every week. Then the medication was stopped again for 1 week before the other test medication was given for a month with eye check up every week.

Statistical analysis of ordered variables was performed using Wilcoxon's rank sum test for each variable.

RESULTS

The mean age of patients with VKC was 11.2 ± 6.1 years, range 4.5-24 years, males accounted for 71.4 per cent. All patients had allergic rhinitis, except 2 patients with additional associated disease (asthma and atopic dermatitis). Five patients (71.4%) had a family history of atopy, and allergic rhinitis (85.7%). The average age at onset of VKC was 5.4 ± 3.2 years (2-12 years). These patients experienced symptoms of VKC everyday with a duration less than 5 years in 5 patients. Most symptoms were moderate (57.1%) and severe (42.9%), they frequently occurred in the morning (57.1%) and at night 28.6 per cent, especially in the summer (42.9%) and all year round (57%). Only 5 patients with VKC showed positive

results on a skin prick test of allergens, house-dust mite (71.4%), house-dust (57.1%), grass (42.9%), cockroach (42.9%), weed pollen (28.6%), food (28.6%) and mold (28.6%).

Symptoms included itching (85.7%), photophobia (64.3%), foreign body sensation (57.1%), tearing (42.8%) and mucous discharge (42.8%). The signs of VKC consisted of chemosis, giant papillae, fine papilla, mild lid swelling, and minimal conjunctival injection. Corneal epitheliopathy was found in only 42.8 per cent. There was a statistically significant difference between groups in itching, foreign body sensation and overall symptoms at day 0, and mucous discharge at day 7. There was an insignificant decrease from baseline in itching, foreign body sensation, photophobia, tearing, mucous, burning, chemosis, punctate epitheliopathy, Horner Trantas dot and overall signs in cyclosporine-treated eyes at each interval, but overall symptoms statistically decreased at day 7; at day 14, mucous, lid-swelling, conjunctival injection decreased; overall signs decreased at day 21; photophobia, mucous, overall symptoms, chemosis and overall signs decreased at day 30 (Table 2, 3). There was a significant decrease from day 7 in lid swelling, conjunctival injection and overall signs in cyclosporine-treated eyes at day 21 ($p = 0.014, 0.046$).

Table 2. Comparison of symptoms between cyclosporine treated eyes and ketorolac treated eyes.

| Symptoms | Mean ± SD | | | | | | | |
|------------------------|---|---------------------------------------|--------------------------------------|--|--|--------------------------------------|--|--------------------------------------|
| | Day 0 | | Days 7 | | Days 14 | | Days 21 | |
| | Cyclosporine | Ketorolac | Cyclosporine | Ketorolac | Cyclosporine | Ketorolac | Cyclosporine | Ketorolac |
| Itching | 0.8 ± 0.9 1 (0 : 3) p = 0.041† | 1.8 ± 1.0 2 (0 : 3) p = 0.041† | 0.6 ± 0.5 1 (0 : 1) | 0.3 ± 0.5 0 (0 : 1) p = 0.005* | 0.5 ± 0.5 0.5 (0 : 1) | 0.3 ± 0.5 0 (0 : 1) | 0.8 ± 0.4 0 (0 : 1) | 0 ± 0 0 (0 : 0) |
| Foreign body sensation | 0.6 ± 0.9 0 (0 : 3) p = 0.039† | 1.4 ± 1.0 1 (0 : 3) p = 0.039† | 0.4 ± 0.5 0 (0 : 1) | 0.3 ± 0.5 0 (0 : 1) p = 0.004* | 0.5 ± 0.5 0.5 (0 : 1) p = 0.025* | 0.3 ± 0.5 0 (0 : 1) p = 0.025* | 0.5 ± 0.5 0.5 (0 : 1) | 0 ± 0 0 (0 : 0) |
| Photophobia | 0.4 ± 0.6 0 (0 : 2) | 0.7 ± 0.8 0.5 (0 : 2) | 0.1 ± 0.3 0 (0 : 1) | 0.1 ± 0.4 0 (0 : 1) p = 0.023* | 0.1 ± 0.3 0 (0 : 1) | 0.3 ± 0.5 0 (0 : 1) | 0 ± 0 0 (0 : 0) | 0.2 ± 0.4 0 (0 : 1) p = 0.046* |
| Tearing | 0.4 ± 0.8 0 (0 : 2) | 0.9 ± 0.9 1 (0 : 3) | 0.2 ± 0.0 (0 : 1) | 0.4 ± 0.5 0 (0 : 1) p = 0.038* | 0.2 ± 0.5 0 (0 : 1) | 0.2 ± 0.4 0 (0 : 1) | 0.8 ± 0.4 0 (0 : 1) | 0.2 ± 0.4 0 (0 : 1) |
| Mucous | 1.1 ± 0.7 1 (0 : 2) | 1.4 ± 1.0 1.50 (0 : 3) | 0.9 ± 0.9 1 (0 : 2) p = 0.038† | 0.3 ± 0.5 0 (0 : 1) p = 0.007* | 1.1 ± 1.0 1.5 (0 : 2) | 0.7 ± 0.5 1 (0 : 1) | 0.5 ± 0.5 0.5 (0 : 1) p = 0.046* | 0.3 ± 0.5 0 (0 : 1) p = 0.025* |
| Discharge | 0.1 ± 0.4 0 (0 : 1) | 0.4 ± 0.6 0 (0 : 2) | 0.2 ± 0.4 0 (0 : 1) | 0.1 ± 0.4 0 (0 : 1) | 0.2 ± 0.5 0 (0 : 1) | 0 ± 0 0 (0 : 0) | 0 ± 0 0 (0 : 0) | 0 ± 0 0 (0 : 0) |
| Burning | 0.6 ± 0.8 0 (0 : 2) | 0.2 ± 0.6 0 (0 : 2) | 0.2 ± 0.6 0 (0 : 2) | 0.2 ± 0.4 0 (0 : 1) | 0.6 ± 0.9 0 (0 : 2) | 0.2 ± 0.4 0 (0 : 1) | 0.2 ± 0.4 0 (0 : 1) | 0 ± 0 0 (0 : 0) |
| Nasal congestion | 0.6 ± 1.1 0 (0 : 3) | 0.4 ± 0.5 0 (0 : 1) | 0.6 ± 1.0 0 (0 : 3) | 0.1 ± 0.4 0 (0 : 1) | 0 ± 0 0 (0 : 0) | 0.3 ± 0.5 0 (0 : 1) | 0.5 ± 0.5 0.5 (0 : 1) | 0.5 ± 0.5 0.5 (0 : 1) |
| Overall symptoms | 3.9 ± 3.2 2.5 (0 : 10) p = 0.037† | 7.0 ± 4.4 7 (0 : 13) p = 0.037† | 2.9 ± 3.1 2 (0 : 7) p = 0.046* | 1.9 ± 2.1 0.5 (0 : 5) p = 0.002* | 3.5 ± 2.8 3.5 (0 : 7) p = 0.034* | 2.0 ± 0.6 2 (1 : 3) p = 0.027* | 3.0 ± 1.7 3 (0 : 5) | 0.7 ± 1.2 0 (0 : 3) p = 0.039* |

* statistical significant (p < 0.05) in day 7-0, day 14-0, day 21-0 and day 30-0.

† statistical significant (p < 0.05) cyclosporine compared with ketorolac.

Table 3. Comparison of signs between cyclosporine treated eyes and ketorolac treated eyes.

| Signs | Mean \pm SD Median (min : max) | | | | | | | |
|-------------------------|-------------------------------------|-------------------------------|-----------------------------------|---------------------------------|-------------------------------|-------------------------------|-------------------------------|-----------------------------|
| | Day 0 | | Days 7 | | Days 14 | | Days 21 | |
| | Cyclosporine | Ketorolac | Cyclosporine | Ketorolac | Cyclosporine | Ketorolac | Cyclosporine | Ketorolac |
| Chemosis | 1.7 \pm 0.5 2 (1 : 2) | 1.7 \pm 0.5 2 (1 : 2) | 1.4 \pm 0.5 1 (1 : 2) | 1.4 \pm 0.5 1 (1 : 2) | 1.4 \pm 0.7 1.5 (0 : 2) | 1.4 \pm 0.5 1 (1 : 2) | 1.3 \pm 0.5 1 (1 : 2) | 1.0 \pm 0 1 (1 : 1) |
| Giant papillae | 1.1 \pm 1.2 1 (0 : 3) | 1.3 \pm 1.3 1 (0 : 3) | 1.2 \pm 1.4 1 (0 : 3) | 1.1 \pm 1.2 1 (0 : 3) | 1.5 \pm 1.3 2 (0 : 3) | 1.8 \pm 1.6 3 (0 : 3) | 1.6 \pm 1.5 2 (0 : 3) | 0.8 \pm 1.3 0 (0 : 3) |
| Papillae | 2.4 \pm 0.8 3 (1 : 3) | 2.3 \pm 0.8 2.5 (1 : 3) | 2.3 \pm 0.8 2.5 (1 : 3) | 2.3 \pm 0.8 2.5 (1 : 3) | 2.5 \pm 0.8 3 (1 : 3) | 2.4 \pm 0.9 3 (1 : 3) | 2.4 \pm 0.8 3 (1 : 3) | 1.7 \pm 1.0 1 (1 : 3) |
| Punctate epitheliopathy | 0.9 \pm 1.1 0.5 (0 : 3) | 0.7 \pm 1.6 0 (0 : 3) | 0.7 \pm 1.1 0 (0 : 3) | 0.3 \pm 0.6 0 (0 : 2) | 0.6 \pm 0.9 0 (0 : 2) | 0.4 \pm 0.9 0 (0 : 2) | 0.9 \pm 1.2 0 (0 : 3) | 0.5 \pm 0.8 0 (0 : 2) |
| Lid swelling | 0.6 \pm 0.6 0.5 (0 : 2) | 0.7 \pm 0.5 1 (0 : 1) | 0.8 \pm 0.6 1 (0 : 2) | 0.5 \pm 0.5 0.5 (0 : 1) | 0.7 \pm 0.5 1 (0 : 1) | 0.4 \pm 0.5 0 (0 : 1) | 0.3 \pm 0.5 0 (0 : 1) | 0.2 \pm 0.4 0 (0 : 1) |
| Conjunctival injection | 0.6 \pm 0.6 0.5 (0 : 2) | 0.6 \pm 0.7 0.5 (0 : 2) | 0.6 \pm 0.5 1 (0 : 1) | 0.4 \pm 0.7 0 (0 : 2) | 0.6 \pm 0.5 1 (0 : 1) | 0.2 \pm 0.4 0 (0 : 1) | 0.1 \pm 0.4 0 (0 : 1) | 0 \pm 0 0 (0 : 0) |
| Pannus | 0.9 \pm 1.2 0 (0 : 3) | 0.9 \pm 1.2 0 (0 : 3) | 1.0 \pm 1.2 0.5 (0 : 3) | 0.9 \pm 1.2 0 (0 : 3) | 1.2 \pm 1.4 1 (0 : 3) | 1.2 \pm 1.6 0 (0 : 3) | 0.9 \pm 1.5 0 (0 : 3) | 0 \pm 0 0 (0 : 0) |
| Epitheliopathy | 0 \pm 0 0 (0 : 0) | 0.1 \pm 0.3 0 (0 : 1) | 0 \pm 0 0 (0 : 0) | 0 \pm 0 0 (0 : 0) | 0 \pm 0 0 (0 : 0) | 0 \pm 0 0 (0 : 0) | 0 \pm 0 0 (0 : 0) | 0 \pm 0 0 (0 : 0) |
| Blepharitis | 0.1 \pm 0.3 0 (0 : 1) | 0 \pm 0 0 (0 : 0) | 0 \pm 0 0 (0 : 0) | 0 \pm 0 0 (0 : 0) | 0 \pm 0 0 (0 : 0) | 0 \pm 0 0 (0 : 0) | 0 \pm 0 0 (0 : 0) | 0 \pm 0 0 (0 : 0) |
| Trantas dot | 0.2 \pm 0.8 0 (0 : 3) | 0.1 \pm 0.4 0 (0 : 1) | 0 \pm 0 0 (0 : 0) | 0.1 \pm 0.4 0 (0 : 1) | 0 \pm 0 0 (0 : 0) | 0 \pm 0 0 (0 : 0) | 0 \pm 0 0 (0 : 0) | 0 \pm 0 0 (0 : 0) |
| Overall signs | 8.8 \pm 4.7 7.5 (3 : 17) | 8.4 \pm 3.5 9 (3 : 13) | 8.2 \pm 4.4 7.5 (2 : 14) | 6.9 \pm 3.0 8 (3 : 11) | 8.6 \pm 4.7 9.5 (1 : 14) | 7.8 \pm 3.8 10 (2 : 11) | 7.4 \pm 3.7 7 (2 : 12) | 4.2 \pm 3.5 2 (2 : 10) |
| Visual acuity | 0.9 \pm 0.9 1 (0 : 3) | 0.9 \pm 1.0 0 (0 : 3) | 0.7 \pm 1.1 0 (0 : 3) | 0.9 \pm 1.0 1 (0 : 3) | 0.7 \pm 1.2 0 (0 : 3) | 1.4 \pm 1.1 1 (0 : 3) | 0.9 \pm 1.2 0 (0 : 3) | 0.3 \pm 0.5 0 (0 : 1) |
| Intraocular pressure | 11.6 \pm 3.2 12.2 (6 : 16) | 12.7 \pm 3.2 14 (6 : 17) | 12.5 \pm 4.6 12.2 (8.5 : 17) | 13.3 \pm 4.1 13.4 (5 : 19) | 13 \pm 1.4 13 (12 : 14) | 10.0 \pm 3.6 11 (6 : 13) | 9.5 \pm 4.9 9.5 (6 : 13) | 15 \pm 0 15 (15 : 15) |

* statistical significant ($p < 0.05$) in day 7-0, day 14 -0, day 21-0 and day 30-0.

Table 4. Comparison of changes in all symptoms and intraocular pressure on different occasions following treatment.

| Change | Mean \pm SD | | | | | |
|----------------------|---------------|----------------|---------|---------------|---------------|---------|
| | Day 0-7 | | | Day 0-14 | | |
| | Cyclosporine | Ketorolac | P-value | Cyclosporine | Ketorolac | P-value |
| All symptoms | 1.3 \pm 2.0 | 5.4 \pm 3.7 | 0.021 | 0.6 \pm 1.1 | 4.2 \pm 2.9 | 0.066 |
| Intraocular pressure | 1.1 \pm 3.8 | -0.7 \pm 2.4 | 0.299 | 1.5 \pm 0.7 | 2.3 \pm 3.2 | 0.754 |

and 0.024, respectively). In Ketorolac-treated eyes, there was a significant difference in symptoms from baseline at day 7 and 14, except for discharge, burning on both occasions and itching, photophobia, tearing, mucous, burning at day 14. However, chemosis, giant papillae and conjunctival injection in ketorolac-treated eyes were also significantly decreased at day 7. There was an insignificant difference from baseline in visual acuity and intraocular pressure at each interval for both drug treatments. Compared to ketorolac-treated eyes at day 7, cyclosporine-treated eyes had significantly fewer changes in symptoms (Table 4). By day 14 the intraocular pressure in ketorolac-treated eye had increased less significantly than in the cyclosporine-treated eyes. The additional drugs were applied in ketorolac-treated eyes after two weeks.

All patients undergoing treatment with cyclosporine experienced a burning sensation lasting a minute or more; compared with ketorolac-treated eyes that had burning for less than 1 minute.

DISCUSSION

Various methods of managing VKC can be applied in an appropriate manner to improve the ocular surface and promote a rapid recovery. Topical cyclosporine 2 per cent has an anti-inflammatory effect that enables the physicians to avoid using a corticosteroid in the treatment of VKC for long periods (12-16). However, its adverse reactions include burning which reduces compliance in some patients and requires careful explanation in order to obtain the patient's full co-operation. In this study both drugs relieved symptoms of VKC within a week with tolerable mild burning following application, despite more initial symptoms in ketorolac-treated eyes (Table 2). This reveals that preservative-free ketorolac tromethamine can relieve symptoms of VKC within a week by anti-inflammatory action of both pathways, similar to the effect of a corticosteroid. However, the intraocular pressure after applying each drug increases insignificantly at each interval. Compared to cyclosporine,

the response to ketorolac tromethamine is faster, with signs of VKC taking 1 week to resolve; with cyclosporine the response time is about 3 weeks (Table 2, 3). Despite efforts at environmental control, there are still a lot of factors affecting the disease and its responses to treatment. Therefore, additional drugs may be used and adjusted appropriately. Because the number of patients in the present study is very small it is very difficult to make a comparison of the drugs with different time intervals and can compromise the clinical significance of the results. The study design is before and after, therefore a smaller sample size can be enrolled, though the authors would like to have more patients to study. Not only did few of the children co-operate with the drug regimen, but the requirement of weekly follow-up made it difficult to find more subjects to enroll.

Table 4 shows that cyclosporine-treated eyes showed less change in overall symptoms than did ketorolac tromethamine-treated eyes in the first week, probably due to baseline differences and irritation from some ingredients or the drug itself. The mean change of intraocular pressure in cyclosporine-treated eyes at day 14 was less than in ketorolac-treated eyes, probably due to the effect of greater anti-inflammatory action. Although topical cyclosporine 0.5 per cent might be the appropriate drug for patients with VKC, a commercial preparation is not available in Thailand. All other symptoms and signs of both groups were not significantly different. Ketorolac tromethamine and corticosteroids have similar pharmacological anti-inflammatory actions: (blocking of cyclooxygenase and lipoxygenase pathway); the maximum response occurs late. However, a mast cell stabilizer has a maximized effect after a few weeks as well. Other additional drugs should be initially considered to relieve symptoms and signs in severe cases.

Regarding comfort, some patients preferred preservative-free ketorolac tromethamine to 0.5 per cent cyclosporine as there was less burning for a

shorter period. Therefore, ketorolac PF can be applied in the initial period followed by topical cyclosporine 0.5 per cent. Overall, ketorolac tromethamine ameliorated symptoms and signs better than topical 0.5 per

cent cyclosporine did at each interval visit compared to the baseline. If the patient can not tolerate cyclosporine, preservative-free ketorolac tromethamine is an alternative choice for the treatment of VKC.

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ผลการรักษาโรคภูมิแพ้ที่มีเยื่อตากระจกตาอักเสบชนิดเวอร์นัลด้วยยาหยอดตาไซโคล- สปอริน ร้อยละ 0.5 เปรียบเทียบกับคีโตรอลแอครอมเมธามีนที่ไม่มีสารกันเสียร้อยละ 0.5

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คณะผู้วิจัยทำการศึกษาใช้ยาสองชนิดในคนกลุ่มเดียวกันคนละช่วงเวลาแบบสุ่มตัวอย่างศึกษาแบบไปข้างหน้าในผู้ป่วยโรคภูมิแพ้ที่มีเยื่อตากระจกตาอักเสบชนิดเวอร์นัลที่เคยรักษาหายด้วยยาหยอดตาไซโคลสปอริน ทำการเปรียบเทียบยานี้กับยาหยอดตาคีโตรอลแอครอมเมธามีนที่ไม่มีสารกันเสียร้อยละ 0.5 โดยหยดยาที่เคยใช้อยู่ก่อน 1 สัปดาห์ แล้วให้ยาหยอดตาทั้ง 2 ยาหยอดวันละ 4 ครั้งนาน 1 เดือนหลังจากนั้นหยดยาที่ใช้อยู่ 1 สัปดาห์ ก่อนสลับใช้ยาอีกชนิดหยอดตาวันละ 4 ครั้งนาน 1 เดือน ทำการประเมินสภาพอาการทางตาและความรุนแรง ได้แก่ อาการคันตา เคืองตา น้ำตาไหล สู้แสงไม่ได้ มีขี้ตา แสบตา ตาแดง เยื่อตาบวม เยื่อตาโตขนาดใหญ่และผิวกระจกตาหลุดลอก ตรวจตาด้วยกล้องขยายและวัดความดันตาก่อนและหลังใช้ยาทุกสัปดาห์นาน 1 เดือน อาการรวมและอาการแสดงรวมในกลุ่มที่หยอดยาไซโคลสปอรินลดลงทุกช่วงเวลา ยกเว้นอาการรวมในวันที่ 21 และอาการแสดงรวมในวันที่ 7 และ 14 สำหรับอาการเคืองตาและอาการรวมในวันที่ 7 และ 14 ลดลง ยกเว้นอาการแสดงรวมในกลุ่มที่รักษาด้วยยาคีโตรอลแอคร เมื่อเปรียบเทียบในสองกลุ่มพบว่าในกลุ่มคีโตรอลแอครมีอาการน้อยกว่ากลุ่มไซโคลสปอรินในวันที่ 7 ยาหยอดตาไซโคลสปอรินลดอาการและอาการแสดงซ้ำกว่ายาคีโตรอลแอคร

คำสำคัญ : เยื่อตากระจกตาอักเสบชนิดเวอร์นัล, ยาหยอดตาไซโคลสปอริน, ยาหยอดตาคีโตรอลแอครอมเมธามีน

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