

Comparative Analysis of the Efficacy and Side Effects of Topical Cyclosporine 0.05% with Fluorometholone 0.1% in Vernal Keratoconjunctivitis

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Abstract

Vernal conjunctivitis is a bilateral, recurrent inflammation of conjunctiva that tends to occur in children. The prominent features are itching, photophobia, redness, tearing, mild ptosis and thick ropy yellow mucoid discharge. The main clinical signs are cobblestone papillary hypertrophy, hyperemia of upper tarsal conjunctiva localized edema and Trantas dots. The three forms of vernal conjunctivitis are palpebral, limbal and mixed. Wide range of treatment modalities are now available for vernal keratoconjunctivitis. This study included 80 patients of both sex in the age group 5-25 years with any form and severity of vernal keratoconjunctivitis. Patients were randomly divided into two groups A and B. Group A patients were given cyclosporine (0.05%) eye drops and group B patients were given fluorometholone (0.1%) eye drops. The results were statistically analyzed by Mann Whitney Test and p value of <0.05 was taken as statistically significant. Maximum numbers of patients were below 15 years of age in both the groups and, in both groups; males were more than females. Most of the eyes presented with palpebral type of disease in both groups. Patients had maximum symptomatic relief at the end of fourth week in both the groups. Response to fluorometholone (0.1%) was significantly better than cyclosporine (0.05%).

Keywords: Vernal keratoconjunctivitis, Cyclosporine, Fluorometholone, Ocular allergy, Conjunctivitis, Anti-allergic treatment.

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INTRODUCTION

Constant exposure of ocular surface to airborne particles from atmosphere, in patients predisposed to allergy often results in signs and symptoms of ocular allergy [1]. The principal ocular allergies are hay fever conjunctivitis, vernal keratoconjunctivitis, atopic keratoconjunctivitis and giant papillary conjunctivitis [2].

Vernal conjunctivitis is a bilateral, recurrent inflammation of conjunctiva that tends to occur in children. The higher incidence of disease is in warm, temperate regions of Middle East, Mediterranean and Mexico. It occurs mainly in children and young adults in the age of 5 to 20 years with peak incidence between 11 and 13 years. In young age, boys are affected twice as frequently as girls [3].

The prominent features are itching, photophobia, redness, tearing, mild ptosis and thick ropy yellow mucoid discharge. The three forms of

vernal conjunctivitis are palpebral, limbal and mixed [4]. The clinical signs in palpebral form of disease are cobblestone papillary hypertrophy and hyperemia of upper tarsal conjunctiva [5]. Bulbar form of disease mainly affects the limbus. Limbal changes include localized edema, thickening, hyperemia and Trantas dots. Corneal changes include punctate keratopathy, epithelial erosions, ulcers and plaques [6].

There are variable numbers of views as far as etiology of the disease is concerned like atopic response to pollens, low blood calcium levels, deficiency of vitamin B-complex and purely endocrine imbalance. However, most widely accepted hypothesis is "Vernal keratoconjunctivitis is a form of physical allergy, that is ocular reaction to warm season in specially predisposed atopic individuals" [7]. Atopic response results from reaction of allergen with IgE on surface of mast cells in conjunctival stroma. This leads to release of inflammatory mediators [8]. The tears of patients with vernal conjunctivitis contain increased levels of

histamine [9], eosinophilic cationic proteins [10] and prostaglandins [11]. Wide range of treatment modalities is now available for vernal keratoconjunctivitis. Milder cases are treated with cold compresses, tear substitutes [12] topical vasoconstrictors and antihistamines [13]. Apart from topical steroids and 2% sodium cromoglycate, several other therapeutic agents including topical mast cell stabilizer, Iodoxamide [14] topical NSAID [15] and even oral aspirin [16] have been used with varying success. However in patients with advanced vernal keratoconjunctivitis with large cobblestone papillae or severe limbal involvement or shield ulcers, these modalities are minimally effective. Supratarsal injection of corticosteroids has been used for treating refractive vernal keratoconjunctivitis [17]. Topical cyclosporine 2% is also safe and effective treatment in vernal keratoconjunctivitis. So the present study was conducted to study the efficacy and side effects of 0.05% cyclosporine eye drops and to compare its efficacy with 0.1% fluorometholone [18].

MATERIALS AND METHODS

This study included 80 patients of both sex in the age group 5-25 years with any form and severity of vernal keratoconjunctivitis.

Patients presenting for the first time, patients refractory to ongoing treatment and patients with perennial form of disease were included in the study. Patients with active ocular infection, patients with raised IOP and patients already on topical corticosteroids, non-steroidal anti-inflammatory drugs or mast cell stabilizers were excluded.

Patients were randomly divided into two groups A and B. Group A patients were given

Cyclosporine (0.05%) eye drops and group B patients were given Fluorometholone (0.1%) eye drops.

Detailed history was taken. Frequency of instillation was four times a day for four weeks followed by three times a day up to three months and on each followup visit itching, tearing, photophobia, redness, lid edema, tarsal papillae, conjunctival chemosis, conjunctival discharge, Trantas dots and keratopathy were assessed and graded.

The results were statistically analyzed by Mann Whitney Test and p value of <0.05 was taken as statistically significant.

RESULTS

The present study included 80 patients of vernal keratoconjunctivitis of any form and severity attending the OPD of Regional Institute of Ophthalmology, Pt. B. D. Sharma PGIMS, Rohtak.

After the washout period of 1 week, group-A patients were given Cyclosporine (0.05%) eye drops and group-B patients were given Fluorometholone (0.1%) eye drops. Frequency of instillation was four times a day for four weeks followed by three times a day for next 2 months.

The following observations were made.

Age Distribution

Maximum number of patients were below 15 years of age in both the groups. Mean age in group A was 10.2 ± 4.2 and in group B was 10.15 ± 3.5 (Table-1).

Table-1: Age Distribution

Age in Years	No. of patients	
	Group-A	Group-B
5-10	22(55%)	23(57.5%)
11-15	13(32.5%)	14(35%)
16-20	5(12.5%)	3(7.5%)

Sex distribution

In both groups, males were more than females. Ratio of male to female was 9:1 (Table-2).

Type of Disease

Most of the eyes presented with palpebral type of disease in both groups. None of the eyes had purely bulbar type of disease (Table-3).

Table-2: Sex Distribution

Sex	No. of patients	
	Group-A	Group-B
Male	37	35
Female	3	5

Table-3: Type of Disease

Type of disease	No. of patients	
	Group-A	Group-B
Palpebral	62(77.5%)	64(80%)
Bulbar	0	0
Mixed	18(22.5%)	16(20%)

Response to Treatment

Response to treatment was evaluated at the end of first week, second week, third week, fourth week, second month and at third month.

Response with treatment with Cyclosporine Table-4, Fig 1 & 2.

Table-4: Showing response to treatment with cyclosporine (0.05%) eye drops

Type of response	Number of eyes					
	1 st week	2 nd week	3 rd week	4 th week	2 nd month	3 rd month
Better	70	54	63	64	12	10
Static	10	25	15	16	14	10
Recurrence	0	1	2	0	54	60

**Fig-1: Tarsal papilla grade 2 before start of Cyclosporine****Fig-2: Tarsal papilla grade 2 relieved to grade 0 after treatment with Cyclosporine**

Number of eyes which responded within first week with cyclosporine (0.05%) eye drops were 70 out of 80. At the end of second week out of those 10 eyes which did not respond at first week, 8 eyes responded. Out of above 70 eyes 46 eyes showed further improvement, 23 eyes showed no further improvement and 1 eye had worsening of symptoms, thus overall 54 eyes showed better response.

At the end of 3rd week those 2 eyes which did not respond at 2nd week now showed improvement. Out of above 23 eyes 18 eyes showed further improvement (2 eyes totally improved), 5 eyes showed no further improvement. Out of 54 eyes 42 eyes showed further improvement, 10 eyes showed no further improvement and 2 eyes showed worsening of total score. Eyes with worsening of total score at 2nd week also showed

improvement. Overall at the end of 3rd week all 80 eyes responded.

At the end of 4th week 60 eyes showed further improvement, 4 eyes totally cured and 16 eyes showed no further improvement.

At the end of 2nd month 54 eyes showed recurrence, 12 eyes showed further improvement and 14 eyes showed static response.

At the end of 3rd month 60 eyes showed recurrence, 10 eyes showed further improvement and 10 eyes showed static response.

Response to treatment with Fluorometholone
Table-5, Fig 3 & 4.

Table-5: Showing response to treatment with fluorometholone (0.1%) eye drops

Type of response	Number of eyes					
	1 st week	2 nd week	3 rd week	4 th week	2 nd month	3 rd month
Better	76	64	63	58	16	17
Static	4	14	17	22	52	44
Recurrence	0	2	0	0	12	19



Fig-3: Tarsal Papilla grade 1 before start of treatment with Fluorometholone



Fig-4: Tarsal Papilla grade 1 relieved to grade 0 after treatment with Fluorometholone

At the end of first week out of 80 eyes 76 showed improvement. At the end of second week other 4 eyes also showed improvement. Out of 76 eyes, 60 eyes showed further improvement. 14 eyes showed no further improvement and 2 eyes showed recurrence. Thus in all there were 64 eyes with better response.

At the end of third week out of 64 eyes, 49 showed further improvement, 15 had static response, 14 eyes which were not showing improvement at the end

of second week did not show any improvement. 2 eyes which were showing recurrence at the end of second week remained the same. Thus in all there were 63 eyes which showed better response at the end of third week.

At the end of fourth week 58 eyes showed further improvement (2 eyes totally improved), 22 eyes showed the static response.

At the end of second month recurrence occurred in 12 eyes, 16 eyes showed further improvement (2 eyes totally improved) and 52 eyes showed static response.

At the end of third month recurrence occurred in 7 more eyes thus increasing it to 19. 17 eyes showed further improvement and 44 eyes remained static.

On applying Mann Whitney Test to the mean ranks of total scores there was no significant difference in the baseline score but significant difference ($p < 0.05\%$) was present at every follow up. Response to fluorometholone (0.1%) was significantly better than cyclosporine (0.05%).

DISCUSSION

Vernal keratoconjunctivitis is a recurrent, bilateral, interstitial inflammation of conjunctiva. It may involve the palpebral conjunctiva, limbal conjunctiva or both. It is predominantly the disease of the young male with self limiting character. It has a complex immunological etiology and a chronic inflammatory component. Both humoral and cell mediated reaction play role in pathogenesis of VKC. It can also be associated with other atopic conditions. Symptoms include itching, tearing, photophobia and redness. Diagnosis includes a thick, stingy mucous discharge, a giant 'cobblestone' papillary reaction of the upper tarsal conjunctiva, papillary changes of bulbar conjunctiva especially at upper limbus and corneal pathology ranging from superficial punctate keratitis to ulceration and plaque formation. Conventional treatment modalities include antihistamines, mast cell stabilizers, vasoconstrictors, NSAIDS and topical steroids. Prolonged treatment with topical steroids leads to serious ocular complications. There remains a great need for other treatment modalities. More recently topical cyclosporine have been used.

With these considerations in mind, the present study was conducted on 80 patients of any form and severity of VKC. In the present study, majority of the patients 87.5% in group A and 92.5% in group B were below 15 years of age. Mean age in group A was 10.2 ± 4.2 years and in group B 10.15 ± 3.5 years. This finding is consistent with other investigations [2, 18, 19]. Who found that disease occurs usually below the age of 16 years.

VKC is predominantly a disease of males. In the present study 90% patients were males and 10% patients were females. Similar were the findings of other investigators [3, 18].

In the present study the disease has seasonal variation. 70% of the patients had exaggeration of symptoms during summer season. These findings are similar to those of other investigators [19] who

observed exaggeration of symptoms during summers and relief during winters.

In the present study 78.7% of patients had palpebral and 21.3% patients had mixed form of disease. This observation was similar to that by M. Alimuddin [19].

CONCLUSION

On comparing Cyclosporine and Fluorometholone in cases of Vernal keratoconjunctivitis the response was found to be better with Fluorometholone.

REFERENCES

1. Tinkelman, D. G., Rupp, G., Kaufman, H., Pugely, J., & Schultz, N. (1993). Double-masked, paired-comparison clinical study of ketorolac tromethamine 0.5% ophthalmic solution compared with placebo eyedrops in the treatment of seasonal allergic conjunctivitis. *Survey of ophthalmology*, 38, 133-140.
2. Allansmith, M. R., & Ross, R. N. (1986). Ocular allergy and mast cell stabilizers. *Survey of ophthalmology*, 30(4), 229-244.
3. Neumann, E., Gutmann, M. J., Blumenkrantz, N., & Michaelson, I. C. (1959). A review of four hundred cases of vernal conjunctivitis. *American journal of ophthalmology*, 47(2), 166-172.
4. Stock, E. L., & Meisler, D. M. (1995). Vernal conjunctivitis. In: Tasman W, Jaeger EA, eds. *Duanes's clinical ophthalmology*, vol. 4. Philadelphia: JB Lippincott, 9: 1-5.
5. Friedlaender, M. H. (1993). Conjunctivitis of allergic origin: clinical presentation and differential diagnosis. *Survey of ophthalmology*, 38, 105-114.
6. Friedlaender, M. H. (1991). Current concepts in ocular allergy. *Annals of allergy*, 67(1), 5-10.
7. Theodore, F. H., & Schlossman, A. (1958). Vernal conjunctivitis. In: Baltimore, eds. *Ocular allergy*. Waverly Press Inc., 98-137.
8. Allansmith, M. R., Greiner, J. V., & Baird, R. S. (1978). Number of inflammatory cells in the normal conjunctiva. *American journal of ophthalmology*, 86(2), 250-259.
9. Abelson, M. B., Soter, N. A., Simon, M. A., Dohlman, J., & Allansmith, M. R. (1977). Histamine in human tears. *American journal of ophthalmology*, 83(3), 417-418.
10. Leonardi, A., Borghesan, F., Faggian, D., Secchi, A., & Plebani, M. (1995). Eosinophil cationic protein in tears of normal subjects and patients affected by vernal keratoconjunctivitis. *Allergy*, 50(7), 610-613.
11. Dhir, S. P., Garg, S. K., Sharma, Y. R., & Lath, N. K. (1979). Prostaglandins in human tears. *American journal of ophthalmology*, 87(3), 403-404.

12. Abelson, M. B., & Schaefer, K. (1993). Conjunctivitis of allergic origin: immunologic mechanisms and current approaches to therapy. *Survey of ophthalmology*, 38, 115-132.
13. Abelson, M. B., Allansmith, M. R., & Friedlaender, M. H. (1980). Effects of topically applied ocular decongestant and antihistamine. *American journal of ophthalmology*, 90(2), 254-257.
14. Caldwell, D. R., Verin, P., Hartwich-Young, R., Meyer, S. M., & Drake, M. M. (1992). Efficacy and safety of lodoxamide 0.1% vs cromolyn sodium 4% in patients with vernal keratoconjunctivitis. *American journal of ophthalmology*, 113(6), 632-637.
15. Buckley, D. C., Caldwell, D. R., & Reaves, T. A. (1986). Treatment of vernal keratoconjunctivitis with suprofan, a topical non-steroidal anti-inflammatory agent. *Invest Ophthalmol Vis Sci*, 27: 29-37.
16. Abelson, M. B., Butrus, S. I., & Weston, J. H. (1983). Aspirin therapy in vernal conjunctivitis. *American journal of ophthalmology*, 95(4), 502-505.
17. Singh, S., Pal, V., & Dhull, C. S. (2001). Supratarsal injection of corticosteroids in the treatment of refractory vernal keratoconjunctivitis. *Indian journal of ophthalmology*, 49(4), 241-245.
18. Gupta, V., & Sahu, P. K. (2001). Topical cyclosporin A in the management of vernal keratoconjunctivitis. *Eye (London, England)*, 15(Pt 1), 39-41.
19. Alimuddin, M. (1955). Vernal conjunctivitis. *The British journal of ophthalmology*, 39(3), 160.