

A Comparative Study Between Topical Cyclosporine 0.05% and Topical Fluorometholone 0.1% in the Treatment of Vernal Keratoconjunctivitis

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Abstract:

Introduction: Vernal Keratoconjunctivitis (VKC) is a chronic as well as recurrent, Bilateral, noninfectious disease that generally affects children mostly boys. VKC is seasonal and allergic disease and usually occur in spring and summer season.

Objective: To study the efficacy of topical Cyclosporine (0.05%) and topical Fluorometholone (0.1%) in the treatment of vernal Keratoconjunctivitis.

Methods: A Cross Sectional Study including 100 eyes of 50 Subjects with a mean age of 10.68 ± 3.21 years was undertaken at a tertiary eye care hospital. All the subjects with Vernal Keratoconjunctivitis who were prescribed either Cyclosporine (Group A) or Fluorometholone (Group B) eye drop were studied. Chi-square procedures and unpaired t test procedures were used to find out the significance value.

Results: The mean age of patients was 10.44 ± 3.11 years in Group A & 10.92 ± 3.30 in Group B. The changes in Total Subjective Symptom Score(TSSS) were statistically significant. Treatment & after treatment TSSS were significantly improved to 0.32 ± 0.21 in Group A & 0.30 ± 0.24 in Group B. The changes in Total Objective Sign Score(TOSS) were statistically significant. Treatment & After treatment TOSS were significantly improved to 0.40 ± 0.19 in Group A & 0.36 ± 0.17 in Group B.

Conclusion: Cyclosporine 0.05% may be a first line drug for treatment of vernal Keratoconjunctivitis as it does not causes sight threatening side effects as occur with use of steroid. Cyclosporine eye drops provides quick relief comparable to Fluorometholone with no rise in Intraocular pressure in mild disease. Thus it can be the first line of treatment for vernal Keratoconjunctivitis in mild cases while steroid drops are usually reserved for moderate and severe cases.

Keywords: Vernal Keratoconjunctivitis, Fluorometholone, Cyclosporine, Intraocular Pressure,

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Introduction

Vernal Keratoconjunctivitis (VKC) is a chronic as well as recurrent, Bilateral disease that generally affects children especially boys. It is a seasonal and allergic

disease and more common in spring and summer season although VKC may occur at any time of the year.[1] It is a rare, noninfectious disease which occurs mainly

affect pediatric age and generally resolves spontaneously after puberty. [2]

VKC follows a typical seasonal pattern with onset seen in spring and usually exacerbation occur in summer season and a remission in the winter period.[3] The diagnosis is confirmed by ocular examination findings like conjunctival congestion, papillary hypertrophy and giant papillae in conjunctiva.

Antihistamines and mast cell stabilizers have been proven to be effective for the treatment of mild to moderate forms of VKC. In the most severe cases, topical steroids is used as it reduces conjunctival and corneal inflammation.

Recently VKC treatment also include topical Cyclosporine A and tacrolimus. Topical Cyclosporine 0.05 % is found to be effective in the long-term treatment of VKC. It significantly improving signs and symptoms without causing significant side effects. Topical Corticosteroid such as fluorometholone 0.1 % have been in use for treatment of these cases as they provide relief quickly but there is rapid recurrence of symptoms after their discontinuation. There is also a potential of adverse effect of long term use of corticosteroid, such as Secondary Glaucoma and steroid induced cataract.

Material and Methods

A cross sectional study was conducted at a tertiary eye care hospital on 100 eyes of 50 subjects for the duration of 1 year from Feb 2020 to July 2021 after obtaining ethical committee clearance.

Inclusion Criteria:

Patients with Vernal Keratoconjunctivitis between 5 to 20 years of age.

Exclusion Criteria:

1. Contact lens wearers during the period of study

2. Patient with ocular disorder such as glaucoma, or uveitis
3. history of allergy to corticosteroid
4. history of Ocular trauma or recent surgery in either eyes
5. Patient on oral steroid medications

Data was collected after taking informed consent from the patients or guardians of the patients. A detailed history was taken about onset of symptoms, its duration, progression, any history of recurrences and treatment taken. All the patients who participated in the study are underwent a complete ophthalmological examination such as Uncorrected Visual Acuity (UCVA), Best Corrected Visual Acuity (BCVA), cycloplegic refraction and a detailed slit lamp examination, fundus examination and measurement of Intraocular pressure using Non-contact tonometer.

Patients were then randomized by computer-generated system into 2 groups. Group A was included in Cyclosporine Group & Group B was included in Fluorometholone Group.

Patients in the Group A were treated with aqueous ophthalmic solution of topical CYCLOSPORINE 0.05% in either eye with one drop twice a day, and those in the Group B were treated with topical FLUOROMTHOLONE 0.1% in either eye with one drop four times/day. Group B received one drop of topical four times daily initially, and the dose then tapered off from the first followup at day 7 according to the clinical response.

Grading of signs & symptoms was done based on the Bonni et al⁴ scoring systems. The evaluation of Total Subjective Sign Score (TSSS) & Total Objective Symptom Score (TOSS) was done on day 0, 7, 14, 21 & day 28 from the date of enrollment. [Table 1,2]

Table 1: total subjective symptom score = TSSS

| Symptom | Severity Score |
|------------------------|---|
| Itching | 0: Absent, no desire to scratch 1+: Intermittent desire to scratch 2+: Frequent desire to scratch 3+: Constant desire to scratch |
| Watering Redness | 0: Absent, No Redness 1+: Mild 2+: Moderate 3+: Severe |
| Photophobia | 0: Absent, no photophobia 1+: Mild, squints in bright light 2+: Moderate, improves with use of sunglasses 3+: Severe, improves only with total eye occlusion |
| Foreign Body Sensation | 0: Absent, no foreign body sensation 1+: Discrete, similar to dust 2+: Mild, similar to sand 3+: Severe, constant and similar to rock |
| Watering | 0: Absent 1+: Humid, no epiphora 2+: Intermittent epiphora 3+: Constant epiphora |

Table 2: total objective sign score = TOSS

| Sign | Severity Score |
|-------------------------------|--|
| Conjunctival hyperemia | 0: Absent, calm conjunctiva 1+: Mild, increase in vessel diameter, difficult to notice 2+: Moderate, increase in diameter and number of vessels 3+: Diffuse and intense hyperemia |
| Upper tarsal papillae | 0: Absent on the central tarsal conjunctiva 1+: Present on the central tarsal conjunctiva 2+: Some giant papillae 3+: Giant papillae predominance |
| Limbus | 0: No limbal inflammatory activity 1+: Limbal hyperemia 2+: Limbal hyperemia and papillae 3+: Horner-Trantas dots |
| Keratitis | 0: Absent, no epitheliopathy 1+: Superficial punctate keratitis 2+: Confluent punctate keratitis 3+: Shield ulcer |
| Discharge | 0: Absent, no discharge 1+: Little amount in the fornix 2+: Moderate amount in the fornix 3+: Great amount in the fornix, sticky eyes in the morning |

Results

50 Patients with Vernal Keratoconjunctivitis who were prescribed either Cyclosporine or Fluorometholone eye drop were studied. Out of 50 patients, 46% patients were between 8-10 years, 22% were between 11-

13 years 14% between 5-7 years, 14% between 14-16 years & 4% patients between 17-20 years age group. The mean age of patients was 10.44 ± 3.11 years in Group A & 10.92 ± 3.30 in Group B. [Table3]

Table 3: Age wise distribution

| Age Group (Years) | No. of patient in (Cyclosporine) Group | No. of patients in (Fluoromethalone) Group |
|-------------------|--|--|
| 5-7 | 4 | 3 |
| 8-10 | 11 | 12 |
| 11-13 | 6 | 5 |
| 14-16 | 3 | 4 |
| 17-20 | 1 | 1 |
| Total | 25 | 25 |

Out of 50 patients, 34 patients were males & 16 patients were females. The changes in Total Subjective Symptom Score were statistically significant. PreTreatment & after treatment TSSS were significantly improved to 0.32 ± 0.21 in Group A & 0.30 ± 0.24 in Group B. [Fig. 1]

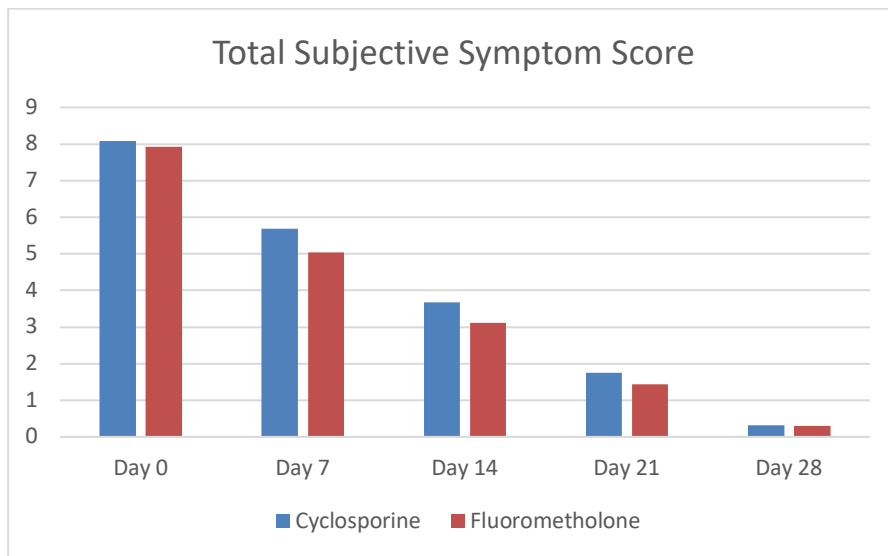


Figure 1: Comparison of Total Subjective Symptom Score between two Groups.

The changes in Total Objective Sign Score were statistically significant. PreTreatment & After treatment TOSS were significantly improved to 0.40 ± 0.19 in Group A & 0.36 ± 0.17 in Group B. [Fig. 2]

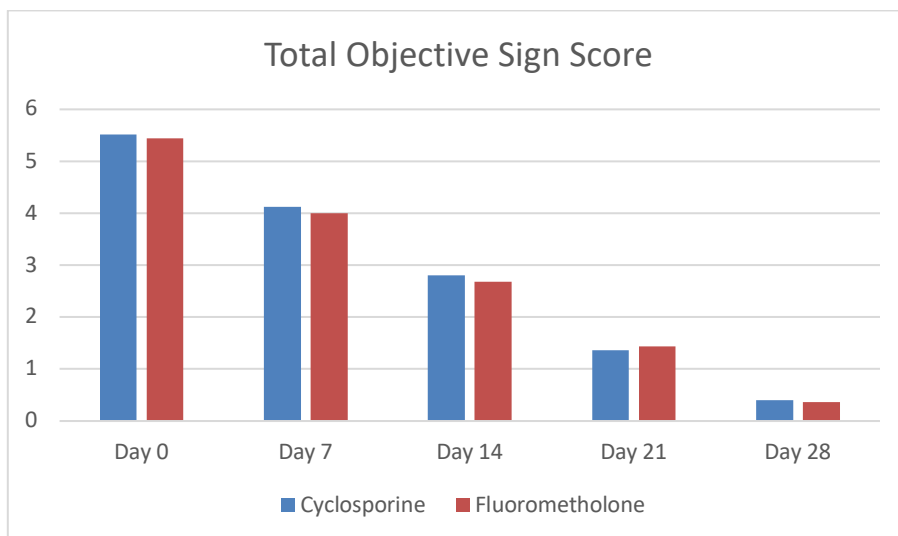


Figure 2: Comparison of Total Objective Sign Score between Two groups

In Comparison to Group A, Group B showing significantly increasing in intra-ocular pressure from 16.22 ± 1.86 to 17.05 ± 2.19 mmHg in Right Eye & 16.14 ± 1.55 to 17.10 ± 1.87 in Left Eye. [Fig. 3]

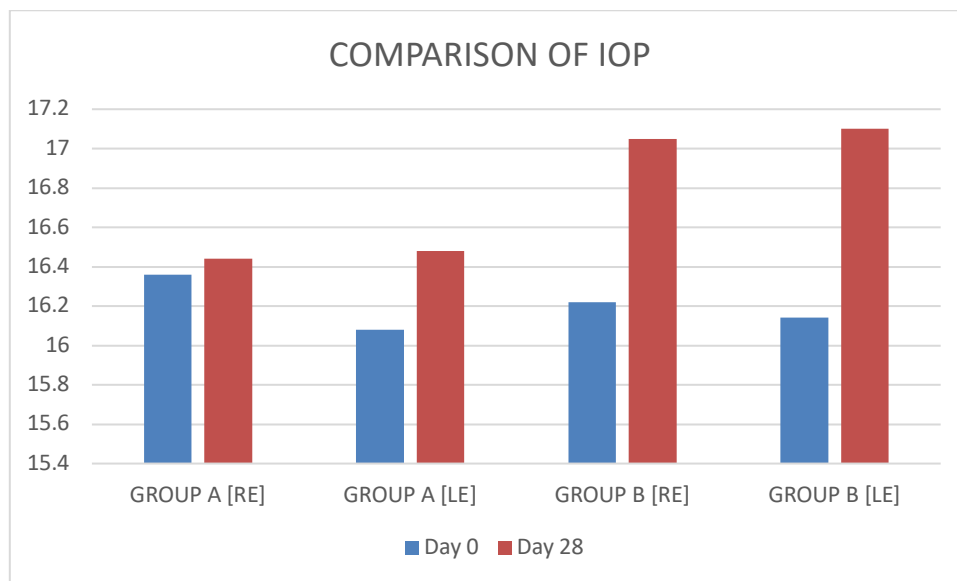


Figure 3: Comparison Of Intraocular Pressure between two Groups.

Discussion

We performed study to compare the efficacy of topical Cyclosporine (0.05%) & fluorometholone (0.1%) in treatment of vernal Keratoconjunctivitis. The efficacy of drugs used in this study were assessed by comparing the TSSS & TOSS Score on each follow up. In Our study demographic data like mean age, sex and severity of the disease were comparable in two groups. There were 34 boys and 16 girls in the study. Majority of the patients in Group A (96%) and Group B (92%) were below 16 years of age. Mean age in group A was 10.44 ± 3.11 years and in group B 10.92 ± 3.30 years. This finding is consistent with Dr. Mita Saha et al who found that disease occurs usually below the age of 16 years[5].

VKC is predominantly a disease of males. In the present study 34(68%) patients were males and 16(32%) patients were females. Similar were the findings of Bielory BP et al[6], Daniell M et al[7], and Mishra GP et al.² 60% of patients had palpebral, 10% of patients had Bulbar and 30% patients had mixed form of disease. This finding is similar to Alimuddin et al. [8] study.

We have compared the efficacy and safety of Cyclosporine (Group A), and Fluorometholone (Group B). We found that during initiation of therapy the symptomatic relief was found in both groups. Symptomatic relief attained at the end of first week was comparable in the two groups i.e. 70.29% (Group A), 63.63% (Group B). [9,10,11] While on further follow up in group A (Cyclosporine) patients there is fast onset of action observable at 1 week and increasing relief in signs and symptoms (itching, watering, discharge, punctate keratitis, reduce size of papillae, redness) is seen till 4 week time, when there is maximum effect. After 4 weeks the effect seems to plateau off (but does not dip) as seen in Dr. Deepa et al.[9] study.

In group B (Fluorometholone) patients also have maximum effect on symptoms and signs is seen in at 4 week time, except redness and photophobia on which maximum effect was earlier (at day 14) and no recurrences found as seen in Baisakhiya et al. [10] study.

Akpek et al [12] found that cyclosporine 0.05% has been found to be useful in the treatment of VKC. It is also an effective steroid sparing agent and Altan A et al[13] observed that Cyclosporine 0.05% is more effective and safe in the treatment of patients with VKC in steroid resistant patients.

In our study analysis on the basis of total signs and symptoms score (excluding the IOP) showed that eyes treated with Fluorometholone eye drops did better at all the observation points when compared to Cyclosporine and this difference was much more pronounced and statistically significant on day 30. Before that there was no statically significant difference between these two study groups.

In both the groups patients having mild disease (total subjective symptom score & total objective sign score at enrollment, range 0-15) showed equal response. Cyclosporine eye drops does not lead to any rise of Intraocular pressure. It is well tolerated and does not cause any increase in punctate keratitis on cornea. One of the important observation noted with Cyclosporine eye drops is that its neutrality on Intraocular pressure as it does not cause any rise in intraocular pressure. With the use of steroid eye drops in VKC patients there is tendency to increase Intraocular pressure, this is observed in the Fluorometholone group in our study. This IOP rise had a positive linear trend with maximum IOP seen at the end of study duration at day 30. Average increase in IOP was 0.90 mm Hg as seen in Gupta et al. [11] study.

Possibility of further rise in IOP if patients are on continuous use of steroids, cannot be ruled out. In long term use of steroids there is possibility of development of vision threatening steroid induced glaucoma may be there. Other adverse effects are development of cataract and local infective lesions due to use of steroid drops, which we did not see in any of our patients during

study due to short study period. There were no serious side effects of the two drugs except mild burning and stinging after initial application.

Conclusion

Thus, according to our study Cyclosporine may be a first line drug for treatment of vernal Keratoconjunctivitis. It does not lead to rise in intraocular pressure and other sight threatening side effects of steroid. Cyclosporine provides prompt and adequate relief comparable to Fluorometholone with no rise in Intraocular pressure in mild disease, which constitutes the majority of patients. Thus it can be the first line of treatment for vernal Keratoconjunctivitis especially in mild cases and steroid drops to be reserved for moderate and severe cases.

Limitations

Our study has a small sample size and 1 month follow up period. Large sample size and longer follow up period would have helped in better evaluation.

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