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# Comparative Study of Topical Cyclosporine 0.05% and Olopatadine0.1% efficacy in Vernalkeratoconjunctivitis In Children

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***Abstarct***
***Purpose:****Vernal keratoconjunctivitis (VKC) is a chronic, recurrent, bilateral inflammatory disease showing exacerbations during the spring and summer seasons,affecting young children. Boys were commonly affected than girls.Management of VKC is primarily aimed at reducing symptoms and preventing serious vision threatening sequelae.Presentstudywasconductedwiththeaimofcomparing the efficacy of cyclosporine 0.05% with olopatadine0.1% in patients ofVKC.**Materialsandmethods:**Aprospectiverandomized trialwasperformedon54 bilateral casesof VKC upto the age of 15 years having similar symptom score during the period of July 2016to June2017. Patients were randomly assigned to and treated Group Awith olopatadine 0.1%, which has a dual action, i.e., mast cell stabilizer action as well as antihistaminic activity and Group Bwith topical cyclosporine 0.05%, which is a nonsteroidal immunomodulator,twice daily for a period of minimumfour weeks. Grading of signs and symptoms was done at the time of 7th, 14th and 28th day**Results:** When compared with baseline, scores for signs and symptoms at 2 weeks reduced significantly for both cyclosporineandolopatadine.However,atfour weeks,scoresfor signsandsymptomswerefoundtobelowerincyclosporine group as compared with olopatadine group.**Conclusion:** Cyclosporine 0.05% was found to be equally effective in treating signs and symptoms as olopatadine in the early phase of the treatment. But, a significant improvement wasnotedincyclosporineeyesascomparedwitholopatadine eyes in the lateperiod.*

***Keywords:*** *VKC, anti histaminic, Immunomodulator, Nonsteroidal*

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## I. Introduction

Spring catarrh, other name of VKC, bilateral ocular disease commonly involves children during spring and summer months. Incidence is 11-13 years of age.[14,15] It is less common in the girls when compared to boys.The pathogenesis of VKC is considered to be multifocal with the involvement of immune, nervous, and endocrine systems.It is an allergic disease, IgE binds to mast cells surface causing degranulation and releasing mediators of inflammation (Histamine IL-3, IL-4,IL-5, IL-13 and IFN-g).[16] It is a Th2 lymphocyte driven disease and immunologically both a type I and Type IV hypersensitivity reaction.[17]Diagnosis of this allergic condition is done by the presence of characteristic clinical features which consist of itching, tearing, mucous discharge, conjunctival hyperemia, Tarsal papillae seen over upper tarsal conjunctiva, Tranta's spots over the limbus, and superficial keratitis. Severe corneal involvements in the form of shield ulceration and conjunctival cicatrization are sight threatening.Steroids are being used as the mainstay of treatment for VKC. Steroids are very effective in controlling the acute exacerbation, but they may cause intraocular pressure elevation in steroid-responders, risk of corneal infection, and cataract. Therefore, they are used for a short period of time. Antihistaminics (topical and systemic) and Topical mast cell stabilizers are also used to reduce the signs and symptoms of the disease. Olopatadine 0.1% acts as a mast cell stabilizer and H1histamine antogonist in treating patients of VKC. It has rapid onset and long duration of action. On twice daily application it relieves itching, mucous discharge and redness. It hasless action on papillae in tarsal conjunctiva. Cyclosporine 0.05% is a non-steroidal immunomodulator, used as an effective alternative for the control of ocular inflammation. It inhibits eosinophilic infiltration into the conjunctiva without affecting systemic immune responses. It is a specific T-cell inhibitor, causes reduction in T-cells, normalizes CD4 / CD8 ratio, decrease T-cell activation and expression of T-cell cytokines (IL-2,IFN-g).On twice daily application most of the signs and symptoms relieved after 2 weeks and maintained long term.In the present prospective study, we compared the effects of topical olopatadine 0.1% *vs* topical cyclosporine 0.05% on the signs and symptoms of patients with VKC.

## II. Materials and Methods

This was a double blind randomized controlled trial performedon54diagnosed bilateral cases of VKC upto 15 years of age having similar symptom score were randomly assigned to and treated with Group A (Olopatadine 0.1%) and Group B (Cyclosporine 0.05%) by independent Ophthalmologist during the period from July 2016 to June 2017.On each follow up patients compliance and comfort were assured.Exclusion Criteria are patients who did not giveconsent,patients with other active ocular inflammatory disorders apart fromVKC, patients lost to follow up, patients on steroids, patients with corneal ulcers, patients on systemic medication or having any other ocular disease.Aninformedconsent was taken from them after which each patient was subjected to a detailed slit lamp examination.Symptoms like itching, tearing,redness, lid edema, discharge,tarsal papillae and keratopathy were graded on a scale of 0 to 3 on the basis of grading system.Grading systemis shown in Table1.Aftergradingofsignsandsymptoms,treatmentwas initiated. The patients were given drops after removing the labels instructed to put drops twice a day for a minimum of four weeks. The patients were assessed on $7^{th}$, $14^{th}$ and $28^{th}$ day.The pretreatment and post treatment average symptom score was noted on each follow up using a grading scale (Grade 0-3) based on subjective assessment of severity of symptoms and objective assessment of signs. Scores were given to each patient for their grades of symptoms or signs and by adding up the total score of each patient were found out. The score of all the patients in the group were added up to find out the total symptom score of each group. The average symptom score was then calculated by dividing the total score with the number of patients in each group. Recurrence rates were assessed in the both groups after 8 weeks of treatment.Statistical analysis of data was done using Statistical Package for the Social Sciences software version 22.0 and unpaired t-test was applied. A p-value of $<0.05$ was considered statistically significant.

## III. Results

The present study was done on 54 patients of VKC in whom male (60%) are more when compared to females (40%).[1,5,13]The symptomatic relief attained with topical Olopatadine and topical Cyclosporine was comparable at the end of $1^{st}$ week.There is a significant difference in the efficacy of both the drugs. By comparing proportion of symptomatic relief of both drugs, Group B is more effective in relieving the Tarsal papillae(85% vs 58%), Redness (100% vs 96%),Discharge(100% vs 97%) and Itching (100% vs. 97%) as compared to Group A after 4 weeks of treatment. Cyclosporine had 44% and 64% of patients relieved from symptoms $1^{st}$ and $2^{nd}$ week respectively as compared to Olopatadine, having 51.72% in $1^{st}$ week and 58.62% in the $2^{nd}$ week respectively. On $4^{th}$ week follow up Cyclosporine showed significant improvement in symptoms score with 80% patients relieved as compared to 68.96% patients with Olopatadine.[18-21] (In accordance with study of Aloy Majumdar et al 2006). Side effects of both drugs consisted of mild ocular stinging after initial application but were relieved by $4^{th}$ or $5^{th}$ day of treatment. Recurrence rates were lower with Cyclosporine as compared to Olopatadine.

## IV. Discussion

Topical cyclosporine is powerful immunomodulator acting at an early stage of antigenic sensitization. High corneal level of cyclosporine remains long after it has eleminated from ocular tissue. Cyclosporine with low recurrence rates is effective for long term control of VKC. Both the drugs are well tolerated and have similar clinical effects in the first week after therapy but considering cost effectiveness, Olopatadine is preferred for initial therapy of VKC cases**.** Cyclosporine is more effective in recurrent cases when compared to Olopatadine. To conclude topical Cyclosporine 0.05% is more effective than topical Olopatadine in the management of VKC patients.

Grading / Scoring of Ocular Signs and Symptoms of VKC in the Study
**Grading Score**

| S.No | Clinical Features | Grade (0) | Grade (1) | Grade (2) | Grade (3) |
|---|---|---|---|---|---|
| 1 | Itching | Absent | Mild | Moderate | Severe |
| 2 | Lacrimation | Absent | Mild | Moderate | Severe |
| 3 | Redness | Absent | Mild | Moderate | Severe |
| 4 | Lid Oedema | Absent | Mild | Moderate | Severe |
| 5 | Discharge | Nil | Present no mucus strands | Few mucus strands | Many mucus strands |
| 6 | Tarsal Papillae | Absent | Few small size (<0.3mm) | Papillae (0.4 - 1.0 mm) | Gaint Papillae (>1mm ) |
| 7 | Keratopathy | Absent | one quadrant | Two quadrants | Three quadrants |

## V. Results

**Table-1**. Baseline Charecteristics

| S No | Baseline Charecteristics | No of Patients | | Total |
|---|---|---|---|---|
| | | Group A (Olopatadine ) | Group B (Cyclosporine) | |
| 1 | No. of patients(%) | N=29(53.70%) | N=25(46.30%) | N=54 |
| 2 | Sex Male | 17 (58.62%) | 15 (60.00%) | 32 (59.25%) |
| | Female | 12 (41.38%) | 10 (40.00%) | 22 (40.75%) |
| 3 | Age groups(Yrs) 0-5 | 1 | 1 | 2 (3.70%) |
| | 6-10 | 5 | 7 | 12 (22.22%) |
| | 11-15 | 23 | 17 | 40 (74.08%) |

**Table-2** Frequency of signs and symptoms

| S No | Clinical Features | No of Patients | | Total |
|---|---|---|---|---|
| | | Group A (Olopatadine ) | Group B (Cyclosporine) | |
| 1 | Itching | 27(93.10%) | 23(92.00%) | 50(92.59%) |
| 2 | Lacrimation | 18(62.06%) | 15(60.00%) | 33(61.11%) |
| 3 | Redness | 21(72.41%) | 18(72.00%) | 39(72.22%) |
| 4 | Lid Oedema | 12(41.37%) | 8(32.00%) | 20(37.03%) |
| 5 | Discharge | 22(75.86%) | 19(76.00%) | 41(75.92%) |
| 6 | Tarsal Papillae | 21(72.41%) | 17(68.00%) | 38(70.37%) |
| 7 | Keratopathy | 5(17.24%) | 4(16.00%) | 9(16.66%) |

**Table3:**Treatment effects: No of patients (%) Relieved of symptoms and signs/Recurrence rate

| Day | Signs / Symptoms | No of Patients | | Total |
|---|---|---|---|---|
| | | Group A (Olopatadine ) | Group B (Cyclosporine) | |
| 0 | With Symptoms | 29 | 25 | 54 |
| 7 | Relieved Symptoms | 15(51.72%) | 11(44.00%) | 26(48.14%) |
| 14 | Relieved Symptoms | 17(58.62%) | 16(64.00%) | 33(61.11%) |
| 28 | Relieved Symptoms | 20(68.96%) | 20(80.00%) | 40(74.07%) |
| 60 | Recurrence | 5(17.24%) | 2(8.00%) | 7(12.96%) |

**Table-4**: Sore of each symptom/sign in agroup and their (%)improvement Pre and Post Treatment

Group A (Olopatadine) Group B (Cyclosporine)

Day Symptom score (% improvement) Symptoms Score (% improvement)

| 3 | I | La | R | Ld | D | T | K | I | La | R | Ld | D | T | K |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 0 | 79 | 53 | 62 | 34 | 65 | 60 | 7 | 72 | 50 | 59 | 30 | 61 | 58 | 6 |
| 7 | 40 (49) | 38 (29) | 36 (42) | 25 (25) | 39 (40) | 58 (3.5) | 6 (11) | 34 (53) | 32 (37) | 32 (46) | 22 (27) | 37 (40) | 55 (6) | 5 (15) |
| 14 | 12 (85.37) | 14 (74.5) | 9 (86) | 15 (55) | 15 (77) | 46 (23) | 6 (11) | 10 (86) | 12 (75) | 7 (88) | 13 (55) | 13 (78) | 13 (75) | 4 (29) |
| 28 | 2 (97.35) | 2 (96) | 2 (96) | 3 (91) | 2 (97) | 25 (58) | 3 (50) | 0 (100) | 1 (99) | 0 (100) | 2 (96) | 0 (100) | 9 (85) | 2 (58) |

Abv: I- Itching, La- Lacrimation, R-Redness, Ld- Lid edema, D- Discharge, T-Tarsal Papillae, K- Keratopathy

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