

To compare efficacy between 0.1% Olopatadine and 4% Cromoglycate in VKC



Ophthalmology

KEYWORDS: Vernal keratoconjunctivitis, Olopatadine, Cromoglycate, Symptomatic scoring

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ABSTRACT

Objective: To compare efficacy and safety of Olopatadine hydrochloride 0.1% ophthalmic solution and Sodium Cromoglycate 4% ophthalmic solution in the treatment of vernal keratoconjunctivitis.

Materials and methods: 100 patients with VKC were included in a prospective randomized double blinded study. Patients were divided into two groups, 50 patients each, Group A received Olopatadine 0.1% and Group B received Sodium Cromoglycate 4%. Subjective symptoms of patients such as itching, discharge, redness, tearing was recorded and scored.

Results: There was no significant difference between the Olopatadine group and Sodium Cromoglycate group regarding subjective symptoms at 28th day of treatment. There was significant improvement in the subjective symptoms of both groups.

Conclusion: In therapy of VKC, similar effects were seen regarding improvement in the subjective symptoms of both groups during the use of topical Olopatadine and Sodium Cromoglycate.

Introduction:
Vernal Keratoconjunctivitis (vernal: Greek, occurring in spring) is a chronic, bilateral conjunctival inflammatory disease that typically affects young individuals with male preponderance(M:F=4:1).It tends to resolve at puberty with male to female ratio nearly equal in older patients.VKC is more frequent in warmer, arid, windy climates, in the Mediterranean area, central Africa, Japan, India, and South America but is also reported in North America, China, Australia, Great Britain, and Sweden. VKC appears mainly seasonally but can be perennial, chronic or with acute exacerbations.A family history of atopy is found in 40-60% of patients. It is mediated via IgE and cell mediated immune mechanism. Cytological, bio humoral, immune-histologic, and molecular biologic studies indicate that VKC is allergic inflammatory disease involving Th2 lymphocyte, mast cells, eosinophils, basophils, macrophages play major roles in the clinical manifestations^{3,8}.

VKC presents in three clinical forms:Tarsal, limbal and mixed forms⁴. Clinically it is characterized by large papillae (fig-1) on the upper tarsal conjunctiva, usually greater than 1 mm in diameter.Tanta's dots (fig 2) and infiltrates on the limbus are typical of the limbal form.Patients with VKC usually present with characteristic ropy, stringy mucous and/or serous discharge, moderate to intense conjunctival hyperemia, intense itching, photophobia, mild to moderate chemosis, foreign-body sensation, and pain which may be very intense upon awakening.

Treatment include topical artificial tears, mast cell stabilizers like Sodium Cromoglycate 4% eye drops, vasoconstrictors, NSAIDs, steroids, dual acting agents like Olopatadine 0.1% eye drops, immunomodulators like Cyclosporine A and Tacrolimus. Combination of drugs usually with steroid agents, are effective when compared to monotherapy. Mast cell stabilizersare the first-line drugs for VKC. Dual acting agents, Olopatadine 0.1% eye drops acts by blocking the H1 receptors as well as act as a mast cell stabilizer, was shown to be effective. Cyclosporine A has immunosuppressive effect^{1,4, and 10}.

PATIENTS AND METHODS:
100 patients with VKC who presented to our tertiary care hospital in south India from December 2014 to September 2016 were included in a prospective randomized double blinded study. Patients were divided into two groups, 50 patients each. Group A received Olopatadine 0.1%twice daily and Group B received Sodium Cromoglycate 4% four times daily by systematic random sampling^{9,10}. 75 patients were boys and 25 patients were girls with mean age of 13.5 years (range 8 to 19).No prior history of usage of systemic antihistamine, steroids or contact lens. Any previous history of personal or

familial allergies was noted. Age of onset of the disease, presenting symptoms, duration of symptoms like itching, discharge, redness, blurring of vision, treatment history were collected.After assessing the best corrected visual acuity (BCVA) a slit lamp bio-microscopic examination of eye was performed this included detailed examination of eye lids and adnexa, conjunctiva, cornea, anterior chamber, iris, pupil and lens. Aguilar Symptom scoringprotocol(table-1) which included hyperemia, discharge, itching and tearing was followed to assess the symptoms.^{5,10}

Table 1

	0 (absent)	1 (mild)	2 (moderate)	3 (severe)
SYMPTOMS				
Itching	None	Mild	Moderate	Severe
Redness	None	Mild	Moderate	Severe
Tearing	Normal	Impression of wet eyes, without tears on the face	Intermittent tears on the face	Constant tears on the face
Discharge	None	Mild	Moderate	Severe

One group received Olopatadine eye drops and the other group received sodium Cromoglycate eye drops. Patients were evaluated based on the scoring system at the time of presentation and at 28 days of treatment¹¹. At the follow-up visit the response to the treatment was assessed by examining the symptoms relief scoring. Outcome variables were Itching score, Redness score, Discharge score,tearing score.

For statistical analysis, mean discharge score, mean redness score, mean itching score, mean tearing score of both the groups were used. Variables including discharge, redness, itching, tearing has been expressed in mean +/- standard deviation. All variables in each group were tested for normality (Kolmogorov – Smirnov one sample test) and homogeneity of variances (Levene test) for parametric test. Quantitative variables were compared in each group before and after treatment using the paired 't' test. Quantitative variables were compared between the study groups using the independent sample 't' test. Statistical analysis was performed using SPSS 20.0 software (SPSS Inc., Chicago, IL, USA), and P-values 0.05 or less were considered to indicate a significant difference.



Results:

At the end of study difference between two groups was not statistically significant regarding subjective symptoms such as itching, discharge, redness, tearing ($p>0.05$).

A significant difference was observed between the levels of itching, discharge, redness, tearing of two groups after treatment ($p<0.01$)^{9,10}.

Baseline mean discharge score was 2.24 $\pm$ 0.43(SD) in Group-A and 2.26 $\pm$ 0.44 (SD) in Group-B. Meandischarge score after 28 days was 0.42 $\pm$ 0.49(SD) in Group-A and 0.50 $\pm$ 0.50(SD) in Group-B. Symptom relief was more in Group A cases but the differences was not statistically significant ($p=0.25$). (Table – 2, fig 4).

Table -2: Mean discharge score before and after treatment in both groups

	Group A				Group B			
Discharge	Sampl e	Mean	SD	P value	Sampl e	Mean	SD	P value
Before treatment	50	2.24	0.43	<0.01	50	2.26	0.44	<0.01
After treatment	50	0.42	0.49		50	0.5	0.5	

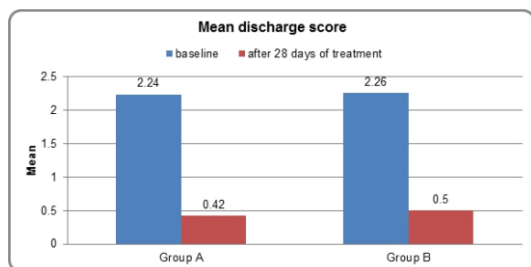


Figure - 1: Distribution of mean discharge score of the study subjects

Baseline mean redness score was 2.32 $\pm$ 0.47(SD) in Group-A and 2.24 $\pm$ 0.43 (SD) in Group-B. Mean redness score after 28 days was 0.44 $\pm$ 0.50(SD) in Group-A and 0.38 $\pm$ 0.53 (SD) in Group-B. Symptom relief was more in Group A cases but the differences was not statistically significant ($p=0.8$) (table – 3, fig-5).

Table -3: Mean redness score before and after treatment in both groups

	Group A				Group B			
Redness	Sampl e	Mean	SD	P value	Sampl e	Mean	SD	P value
Before treatment	50	2.32	0.47	<0.01	50	2.24	0.43	<0.01
After treatment	50	0.44	0.50		50	0.38	0.53	

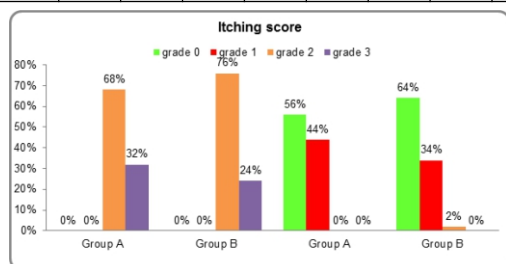


Figure 2: Comparison of percentage of itching score in two groups.

Baseline mean itching score was 2.26 $\pm$ 0.44 (SD) in Group-A and 2.2 $\pm$ 0.40 (SD) in Group-B. Mean itchingscore after 28 days was 0.40 $\pm$ 0.49 (SD) in Group-A and 0.50 $\pm$ 0.50 (SD) in Group-B. Symptom relief was more in Group A cases but the differences was not statistically significant ($p=0.8$). (Table -4, fig- 6).

Table -4 Mean itching score before and after treatment in both groups

	Group A				Group B			
Itching	Sampl e	Mean	SD	P value	Sampl e	Mean	SD	P value
Before treatment	50	2.26	0.44	<0.01	50	2.2	0.4	<0.01
After treatment	50	0.4	0.49		50	0.5	0.5	

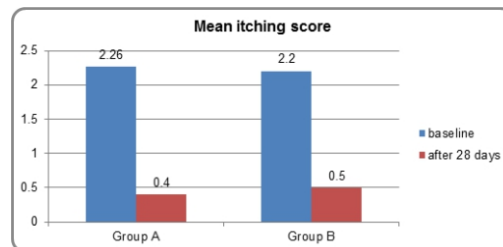


Figure 3: Distribution of mean itching score of the study subjects⁷

Baseline mean tearing score was 2.10 $\pm$ 0.30 (SD) in Group-A and 2.14 $\pm$ 0.35 (SD) in Group-B. Mean tearing score after 28 days was 0.30 $\pm$ 0.46 (SD) in Group-A and 0.32 $\pm$ 0.4 (SD) in Group-B. Symptom relief was more in Group A cases but the differences was not statistically significant ($p=0.67$). (table-5, fig- 7).

Table – 5: Mean tearing score before and after treatment in both groups

	Group A				Group B			
Tearing	Sampl e	Mean	SD	P value	Sampl e	Mean	SD	P value
Before treatment	50	2.10	0.30	<0.01	50	2.14	0.35	<0.01
After treatment	50	0.30	0.46		50	0.32	0.47	

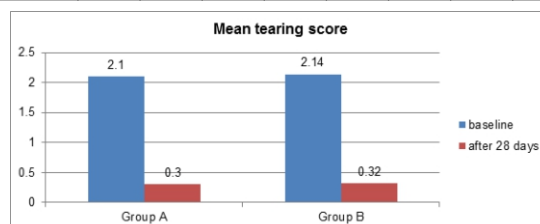


Figure 4: Distribution of mean tearing score of the study subjects

Discussion: VKC is a severe chronic allergic inflammatory disease characterized by recurrent, bilateral, occasionally asymmetrical, seasonally exacerbating ocular inflammation. It may also be seen in severe chronic forms that can inflict irreversible corneal changes, profoundly impairing vision. Previous studies for the management of allergic eye disease are aimed at blocking the release of allergic mediators in order to control the allergic inflammatory cascade and to prevent ocular surface damage secondary to the allergic response. In addition, we also need to minimize the impact of the allergic reaction on the quality of life of the individual.

There are studies showing that Olopatadine and Sodium Cromoglycate are effective in the treatment of VKC, it is reported that they are inadequate to control severe cases and to prevent recurrence. In our prospective study, comparison of the efficacy between Olopatadine and Sodium Cromoglycate ophthalmic solutions for patients who are having VKC is done. In this study patient of both gender equally approached for treatment because of discomfort caused due to the disease. All the patients were followed-up till the end of study. The parameters assessed were itching score, redness score, discharge score, tearing score. The assessment was done at the time of presentation and on 28th day of treatment.

On comparing itching score, discharge score, redness score, tearing score in both groups, there was no significant difference observed between Patanol and Cromal Forte in grading of itching, discharge, redness, tearing at 28th day of treatment. A clinically and statistically significant decrease in itching, discharge, redness, tearing at follow-up was present in each group respectively ($p < 0.05$)

In a study conducted by Uddin Aima et al¹⁰, to find out an effective drug for the treatment of allergic conjunctivitis and to compare the efficacy of Sodium Cromoglycate 2% ophthalmic solution and Olopatadine Hydrochloride 0.1% ophthalmic solution in the treatment of allergic conjunctivitis. This study took itching score, redness score, and discharge score for evaluation. This clinical study concludes that the relieving of symptoms and signs Olopatadine was found to be superior over Sodium Cromoglycate 2% but the difference was not statistically significant.

Similar study conducted by Katelaris et al^{2,10} in their study comparison of the efficacy and tolerability of Olopatadine hydrochloride 0.1% ophthalmic solution and Cromolyn sodium 2% ophthalmic solution in seasonal allergic conjunctivitis. After 6 weeks' instillation of Olopatadine 0.1% ophthalmic solution BID had a significantly greater effect on the ocular signs and symptoms of allergic conjunctivitis compared with 6 weeks' instillation of Cromolyn 2% ophthalmic solution QID. Both treatments were well tolerated by patients in all age groups. However, Olopatadine appeared to have better local tolerability in children aged <11 year. This study concluded that subjects had significantly reduction in signs and symptoms of allergic conjunctivitis in Olopatadine and Cromoglycate groups and they are well tolerated.

Study conducted by B. Mortemousque et al^{6,12}, comparison of preservative free Ketotifen 0.025% ophthalmic solution to Olopatadine 0.1% ophthalmic solution in with the treatment of seasonal allergic conjunctivitis (SAC) in clinical practice. This study concluded that both Ketotifen and Olopatadine are equally effective in treatment of seasonal allergic conjunctivitis (SAC). Conjunctival impression cytology was performed at each visit to assess the evolution of ICAM-1 expression (day 0, 7, 28). At day 28, the composite score for primary criteria (itching, tearing, and conjunctival hyperemia) improved from 6.8 ± 1.2 to 0.9 ± 1.0 in the Ketotifen group, without statistically significant difference between treatment groups ($P = 0.67$).

Results of present study correlate with the above studies.

In the present study, the efficacy of Olopatadine and cromolyn sodium drops was found to be similar in reducing the symptoms of the patients at the end of 28 days of therapy^{9,10}. Availability of conjunctival impression cytology for further analyzing the control of the disease by the treatment may be preferred. Palpebral and bulbar forms of VKC responded better with the treatment when compared to mixed form which required usage of steroid drops in some cases.

Limitations:

Availability of conjunctival impression cytology for further analyzing the control of the disease by the treatment may be preferred.

For mixed forms and recurrent cases steroids are better when compared to Olopatadine and Cromoglycate.

Conclusion : results of present study concluded that palpebral and bulbar forms of VKC responded better with the treatment when compared to mixed form which required usage of steroid drops in some cases.

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