

Study of the Safety and Efficacy of 2% Sodium Cromoglycate Ophthalmic Solution and 0.1% Lodoxamide Ophthalmic Solution in Patients with Spring Catarrh in a Tertiary Care Hospital

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Abstract:

Introduction: Vernal keratoconjunctivitis comprises 0.5% of allergic eye diseases. The study is made to collate the effectiveness of drugs by following the patient to observe the reduction in signs and symptoms.

Objectives: The objective of the study is to compare the effectiveness and safety of 2% sodium cromoglycate ophthalmic solution and 0.1% lodoxamide ophthalmic solution in patients with vernal keratoconjunctivitis (VKC).

Materials and Methods: A randomized, comparative study conducted in patients attending the OPD of Viswabharathi medical college, Penchikalapadu, kurnool, Andhra Pradesh. The study included 50 patients who has attended our OPD diagnosed with VKC, of which odd number to Group A and even numbers to Group B with 25 each were given 2% sodium cromoglycate ophthalmic drops and 0.1% lodoxamide ophthalmic drops, respectively, two times a day for 8 weeks. The reduction in signs and symptoms in both groups was compared. Absolute eosinophil count was evaluated for all the patients before and after. The observations and results were tabulated accordingly, and data were analyzed using the SPSS version. The unpaired t-test is used as the test of significance in between the two groups. P value is statistically significant when it is < 0.05.

Results: Overall, 50 cases were included in the study, 72% of total patients were in the age group of 5–10 years, and 28% were in the age group of 11–15 years. There were 39 males and 11 females. After 8 weeks of follow-up, the mean reduction in making the scores of symptoms and signs provided better and quicker relief of watering, ocular discomfort, and conjunctival hyperemia with 2% sodium cromoglycate eye drops. 0.1% lodoxamide eye drops provided faster improvement in papillary hypertrophy. Both drugs were equally effective in reducing itching. Laboratory findings of absolute eosinophil count had no statistical significance in between the two groups.

Conclusions: In this study, based on the evaluation of therapeutic performance, 0.1% lodoxamide eye drops proved quicker relief to the symptoms and signs compared to 2% sodium chromoglycate eye drops but this was not statistically significant.

Keywords: Sodium Cromoglycate, Lodoxamide, Absolute Eosinophil Count, Allergy, Vernal Keratoconjunctivitis.

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Introduction

Allergies are the fifth leading cause of the world's chronic illnesses, affecting 40% of the population.[1] Globally, in the last 10 years, there has been a drastic increase in allergic diseases. The occurrence of allergic diseases among children is rising moderately in between 0.3% and 20.5%. The incidence of allergic conjunctivitis is more in kurnool district compared to other districts in AP because of the fine dust particles. There are so many causative factors such as genetics, pets, air pollution, and early childhood exposure being the reasons for this increase.[2] Among the causes of

ocular morbidity in India, allergic conjunctivitis is at the second position and involves about 15%–20% of people attending ophthalmology clinic. School absenteeism in children is common because of its distressing symptoms. [3] Allergic conjunctivitis includes persistent allergic conjunctivitis, seasonal allergic conjunctivitis (SAC), vernal keratoconjunctivitis (VKC), and atopic keratoconjunctivitis. SAC is about 25%–50% of cases. [4] VKC constitutes 0.5% of allergic diseases in eye. [5] VKC occurs most frequently in the male population belongs to warm, dry,

subtropical areas such as Japan, India, Thailand, South America, Mediterranean, Central, Middle East, and Western Africa. Most common VKC seen in dark-skinned African and Indian population is limbal form. The prevalence for Western Europe was 3.2 in 10,000, whereas a higher prevalence ranging from 2.4 to 27.8 in 10,000 was seen in Italy, a country with a Mediterranean climate.[6] VKC is a persistent, bilateral, occasionally asymmetric, cyclically worsened, allergic ocular surface inflammation that includes bulbar and/or tarsal conjunctiva. VKC is characterized by giant papillae seen in both upper tarsal conjunctiva or at the limbus. [7] It is an IgE- and T-cell-mediated condition, progressing to a chronic inflammatory conjunctival allergic response involving eosinophil, lymphocyte, and structural cell activation. New antihistamines that combine stabilizing properties of the mast cells with antagonism to histamine receptors such as olopatadine, bepotastine, alcaftadine, azelastine, epinastine, and ketotifen are currently available.

[8]Sodium cromoglycate stabilises mast cell membranes and prevents the release of histamines and other biochemical mediators. Ocular sodium cromoglycate prevents many of the signs and symptoms associated with type I allergic reactions which include allergic conjunctivitis, vernal keratoconjunctivitis, giant papillary conjunctivitis and hay fever. In clinical trials of open and controlled studies sodium cromoglycate have shown effective relief in symptoms and signs. It also decreases the need for supplementary oral antihistamines and need for ocular corticosteroids. In severe cases combined ocular application of sodium cromoglycate and corticosteroids may be very effective. No systemic and severe adverse reactions, since systemic absorption is minimal. Local burning and stinging, it is clear that the safety and efficacy of the drug in allergic eye diseases and considered as first line agent.

Lodoxamide is an antiallergic drug. It is under the trade name Alomide, like cromoglycic acid it acts as a mast cell stabiliser.[9]Lodoxamide 0.1% is approximately 2500 times more potent than cromolyn in prevention of the histamine release. It is effective in reducing try-take and histamine levels and recruitment of inflammatory cells in tear fluid after allergen challenge as well as tear eosinophilic cationic proteins and leukotrienes (BLT and CysLT1) when compared to cromolyn. In clinical trials lodoxamide was shown to deliver greater and earlier relief in patients of VKC including upper tarsal papillae, limbal signs, and conjunctival discharge and to improve epithelial defects seen in chronic forms of conjunctivitis than cromolyn. In VKC patients it's approved for 0.1% four times a day. Lodoxamide may be used

continuously for 3months in children older than 2years of age.

Materials and Methods

The study was done in the Outpatient Department of Ophthalmology in Viswabharathi Medical College, Penchikalapadu, Andhra Pradesh for duration of 3 months from February 2023 to April 2023. Institutional ethics committee approved the study. For participants above 18 years of age, written informed consent was taken in an authorized format in local language after describing all study procedures and course of action. For participants less than 18 years of age, their parents or guardians were explained the procedures, and written informed consent was attained. For illiterate people, left thumb mark was taken. After acquiring informed consent from all participants, the analytical details of 59 patients including past and present history and clinical and slit-lamp examination of eyes performed were entered. Following the screening of 59 patients, 50 patients were enlisted in the study who fit into inclusion and exclusion criteria by dividing odd numbers into Group A and even numbers Group B with 25 patients each. Absolute Eosinophil Count was evaluated for all the patients before and after the study.

Inclusion criteria

1. Patients with the age group of 5–25 years attending our OPD.
2. Patients who can adhere to follow-up schedule.

Exclusion criteria

1. Age less than 5 years
2. Contact lens wearer during the period of study
3. Patients with active ocular infections and pathological conditions
4. Patients with ocular disorders such as pterygium, dry eyes, and ophthalmic conditions such as uveitis or glaucoma
5. History of ocular surgery in 3 months.

By simple randomization (odd/even number) method, registered patients were grouped into A and B. Group A and Group B were given 2% sodium cromoglycate ophthalmic drops and 0.1% lodoxamide ophthalmic drops, respectively, administered one drop in the affected eye twice daily for 8 weeks. The ocular signs such as conjunctival hyperemia and papillary hypertrophy were evaluated. The gradings were given according to the severity of signs (absence of signs as grade 0, mild signs as grade 1, moderate signs as grade 2, and severe signs as grade 3).

Ocular symptoms such as itching, discomfort, and watering were estimated by discussing with the patients, and grading was given depending on

severity (absence of signs as grade 0, mild signs as grade 1, moderate signs as grade 2, and severe signs as grade 3). During the study, none of the patients were lost to follow-up.

Statistical analysis

The observations and results were tabulated accordingly and data were analyzed using the SPSS Version 16. The unpaired t-test is used as the test of significance in between two groups. P value is statistically significant when it is less than 0.05.

Results

The age and gender distribution of the study population is shown in Figure 1.

Among 50 patients, 36 patients (72%) are in the range of 5-10 years, and 14 patients (28%) are in the range of 11-15 years. Of 50 patients included in the study, 39 (78%) patients were male and 11 (22%) patients were female.

Table 1 shows mean itching scores during each visit. The itching scores among the treatment

groups with all follow-ups compared with baseline are not statistically significant ($P > 0.05$). Table 2 shows the mean ocular discomfort scores during each visit. At the 1st, 2nd, and 3rd follow-up, there is statistical significance in ocular discomfort scores with Group B ($P < 0.05$). Table 3 shows the mean watering scores during each visit. In Group B, during the 2nd, 3rd, and 4th follow-ups, there is statistical significance in watering scores ($P < 0.05$).

Table 4 shows the mean conjunctival hyperemia scores during each visit. During 1st, 2nd, and 3rd follow-ups, there is statistical significance in conjunctival hyperemia scores with Group B ($P < 0.05$).

Table 5 shows the mean papillary hypertrophy scores during each visit. During the 2nd, 3rd, and 4th visits, there is statistical significance in papillary hypertrophy scores with Group A ($P < 0.05$).

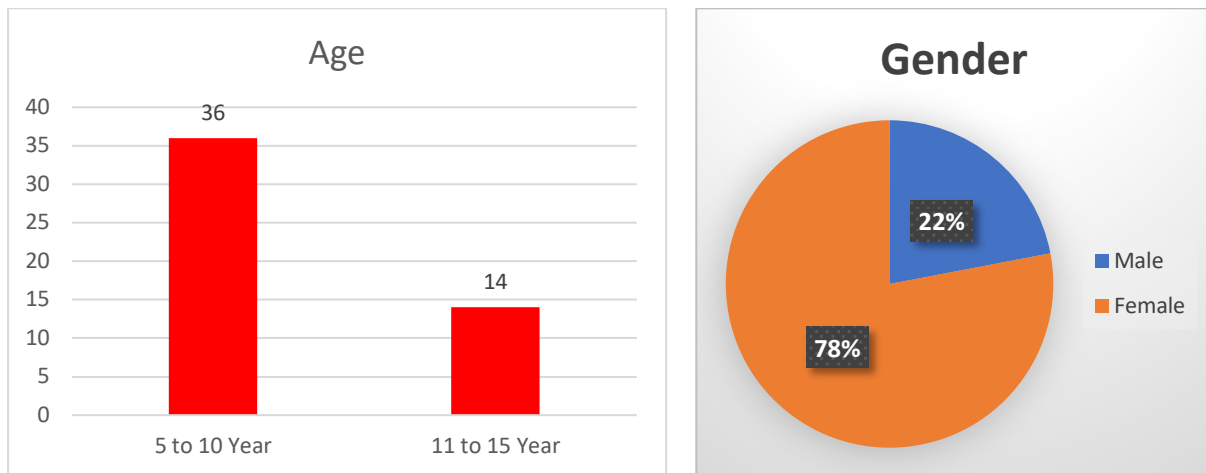


Figure 1: Age and gender distribution

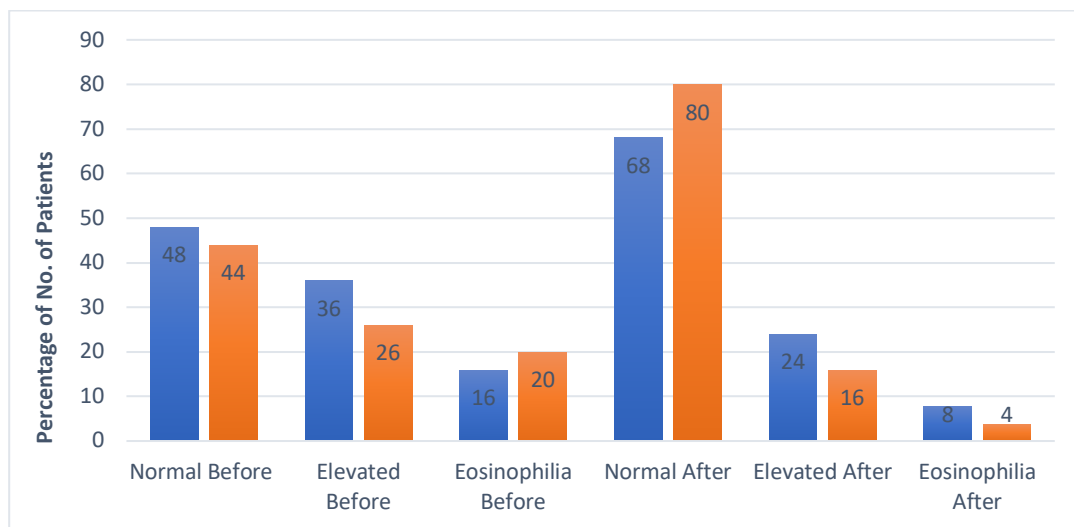


Figure 2: Changes in the levels of absolute eosinophil count between treatment groups

Figure 2 shows the absolute eosinophil count (AEC) levels between treatment groups. Before and after the treatment, there is no statistical significance in reduction of AEC levels. Very minimal patients complained of adverse events during the study. In Group A, two patients had headache, and in Group B, three patients encountered headache and one had sinusitis.

Table 1: Mean itching scores during each visit Itching scores

Itching scores	Group A Cromoglycate		Group B Lodoxamide		Unpaired t-test significance level
	μ	SD	μ	SD	
Preintervention	2.88	0.332	2.88	0.332	1.000
1st week (1st visit)	2.84	0.374	2.84	0.374	1.000
3rd week (2nd visit)	2.08	0.4	2.00	0.289	0.421
5th week (3rd visit)	1.16	0.374	1.08	0.277	0.394
8th week (4th visit)	0.32	0.690	0.12	0.332	0.198

SD=Standard deviation

Table 2: Mean ocular discomfort scores during each visit

Ocular discomfort scores	Group A Cromoglycate		Group B Lodoxamide		Unpaired t-test significance
	μ	SD	μ	SD	
Preintervention	2.88	0.332	2.92	0.277	0.646
1st week (1st visit)	2.76	0.436	2.08	0.277	0.000*
3rd week (2nd visit)	2.00	0.408	1.20	0.408	0.000*
5th week (3rd visit)	1.20	0.408	0.40	0.500	0.000*
8th week (4th visit)	0.32	0.476	0.12	0.332	0.091 *

Significant if P<0.05, SD=Standard deviation.

Table 3: Mean watering scores during each visit

Watering scores	Group A Cromoglycate		Group B Lodoxamide		Unpaired t-test significance
	μ	SD	μ	SD	
Preintervention	2.92	0.277	2.92	0.277	1.000
1st week (1st visit)	2.80	0.408	2.00	0.000	0.000*
3rd week (2nd visit)	2.00	0.000	1.04	0.200	0.000*
5th week (3rd visit)	1.08	0.277	0.28	0.458	0.000*
8th week (4th visit)	0.36	0.490	0.08	0.277	0.016*

Significant if P<0.05, SD=Standard deviation.

Table 4: Mean conjunctival hyperaemia scores during each visit

Conjunctival hyperaemia scores	Group A Cromoglycate		Group B Lodoxamide		Unpaired t-test significance
	μ	SD	μ	SD	
Preintervention	2.96	0.200	2.96	0.200	1.000
1st week (1st visit)	2.76	0.436	1.96	0.200	0.000*
3rd week (2nd visit)	2.00	0.500	1.08	0.277	0.000*
5th week (3rd visit)	1.04	0.539	0.28	0.542	0.000*
8th week (4th visit)	0.24	0.436	0.16	0.374	0.490 *

Significant if P<0.05, SD=Standard deviation.

Table 5: Mean papillary hypertrophy scores during each visit

Papillary hypertrophy scores	Group A Cromoglycate		Group B Lodoxamide		Unpaired t-test significance
	μ	SD	μ	SD	
Preintervention	2.68	0.476	2.60	0.500	0.565
1st week (1st visit)	2.44	0.507	2.60	0.500	0.267
3rd week (2nd visit)	1.08	0.277	1.64	0.490	0.000*
5th week (3rd visit)	0.08	0.277	1.08	0.277	0.000*
8th week (4th visit)	0.00	0.000	0.40	0.500	0.000*

*Significant if P<0.05. SD=Standard deviation.

Discussion

VKC is a bilateral, long-term, cyclical allergic ocular inflammation which affects bulbar or tarsal conjunctiva. Children and young adults with an atopic history are more prone to VKC. It

commonly affects people with history of allergic conditions such as seasonal allergy, bronchial asthma, or eczema. VKC has a wide geographic distribution. Young males are primarily affected in the dry and hot climates.[10] It is prevailing in Mediterranean temperate zones, Western Africa,

Middle East, Japan, Indian subcontinent, and South America.[11] 49% of VKC patients show familial history of allergic conditions such as asthma, rhinitis, eczema, urticaria, and multiple atopic diseases.[12] Among them, asthma is the most frequently seen allergic disorder in VKC.[13] Other inflammatory diseases, such as psoriasis and thyroiditis, may be associated with a family history.[14,15] It has a major impact on day-to-day life and performance in school-going children. The present research was conducted in an attempt to determine which agent would help regulate the symptoms of VKC in our patient population. It is very important to understand the fundamental mechanisms in allergy and selection of the right medication. Olopatadine found to be effective in VKC.[16,17] Lodoxamide is a less commonly used drug.[18]

In this review, we seek to assess the two medications and evaluate their effectiveness in treating Spring Catarrh. For this study, different signs and symptoms of VKC were used as criteria for assessment.[19] This is a randomized study in which the patients diagnosed with VKC who attended ophthalmic outpatient department divided into Group A and Group B. Group A patients were given 2% sodium cromoglycate twice a day for 8 weeks, and Group B patients were given 0.1% lodoxamide twice a day for 8 weeks. Sodium cromoglycate which is commonly used compared with lodoxamide for efficacy, safety, and tolerability. In the present study, out of 59 patients who were screened, 50 patients were included in the study, randomized to Group A and Group B, each including 25. During the study period, none of the patients have not missed their follow-ups. A study between 2% sodium cromoglycate and 0.1% lodoxamide worked similarly in relief of mild-to-moderate allergic conjunctivitis symptoms, after 1 week of treatment.

For allergic conjunctivitis, 2% sodium cromoglycate and 0.1% lodoxamide eye drops are safe and well-tolerated topical medications. In a study done by Dr. Caldwell et al., a comparison between 2% sodium cromoglycate and 0.1% lodoxamide eye drops in VKC between the baseline and the 2nd visit, cromolyn treatment resulted in decreased burning, but lodoxamide was slightly better after 4th visit. In response to treatment showed lodoxamide 0.1% effected a greater and earlier improvement than cromolyn sodium 4% Papillae and Horner-trans dots in both classes were not significantly different. In our study, during initial follow-ups on days 7, 21, and 35. Lodoxamide showed significant reduction in symptoms such as ocular discomfort, watering, and capillary hyperemia, suggesting the faster onset of action. Sodium chromoglycate showed marked reduction in papillary hypertrophy. After 8 weeks

of treatment, both drugs were uniformly efficacious in reducing signs and symptoms of VKC. Studies with different attributes such as larger sample size, double masking, and patient preference and studies at different geographical locations and during different seasons of the year are needed for better definition of therapy in VKC.

Conclusions

In this study, although lodoxamide altered the natural course with quicker onset of action at the end of the 8th week, both drugs are equally effective in reducing the signs and symptoms. Lodoxamide proved quicker to relieve watering, ocular discomfort, and conjunctival hyperemia. Sodium cromoglycate provided faster improvement in papillary hypertrophy.

Laboratory findings had no statistical significance between 2% sodium cromoglycate and 0.1% lodoxamide in improving the AEC of the VKC patients. Being more commonly prescribed of the two drugs, Sodium chromoglycate is readily available at the pharmacy store. Lodoxamide, on the other hand, was available at a few selected retail stores and comparatively as it is a cheaper drug it can be prescribed for poor people often. Researches with above-mentioned attributes can be done in the future.

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