Section: Pharmacology

Original Research Article

COMPARATIVE EFFICACY OF SODIUM CROMOGLYCATE AND OLOPATADINE OPHTHALMIC SOLUTION IN ALLERGIC CONJUNCTIVITIS

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Abstract

Background: Allergic conjunctivitis is one of the most common ocular morbidity. A clear understanding of underlying pathogenesis is utmost important. Olopatadine is dual action and wide spectrum drug with proven efficacy in allergic conjunctivitis. **Aim:** To evaluate the effectiveness, tolerability and safety of olopatadine 0.2% once daily and olopatadine hydrochloride 0.1% twice daily with sodium cromoglycate four times daily as eye drops in cases of allergic conjunctivitis. **Materials and Methods:** This prospective, comparative, single centre study enrolled 300 patients with allergic conjunctivitis attending ophthalmology OPD. Subjects were divided into three groups, receiving different formulations. Subjects were assessed for ocular signs and symptoms using slit lamp at day 0, end of 2nd and 3rd week. The change in mean scores of itching and redness from baseline till end of 3rd week was evaluated. **Results:** All the three groups showed statistically significant reduction in signs and symptoms of allergic conjunctivitis. The olopatadine receiving groups showed better and early relief of ocular symptoms of allergic conjunctivitis compared to sodium cromoglycate. Olopatadine 1% twice daily showed better result statistically compared to Olopatadine 0.2% once daily, though the results were comparable clinically. **Conclusion:** Both the topical ocular therapeutic agents evaluated in the study are effective in improving the signs and symptoms of allergic conjunctivitis. Olopatadine is preferred over sodium cromoglycate.

INTRODUCTION

In India, allergic conjunctivitis is one of the most common ocular morbidity. Approximately 15-20% individuals attending Ophthalmology OPD are affected by this.[1] Allergic conjunctivitis is extremely painful and again is the reason for poor attendance in school during the extreme seasons.[2-3] The condition may vary as acute or chronic type. Seasonal and recurrent allergic conjunctivitis are of acute type mediated by IgE.[4]

Identification and avoidance of allergen is the key of treatment. Various topical pharmac-therapeutic agents are available for the treatment. Antihistaminics provides relief by blocking H1 histaminergic receptors. Mast cell stabilizers maintains stability of mast cells membrane. Dual acting agents provides both antihistaminic and mast cell stabilizing action. Non-steroidal anti-inflammatory drugs (NSAIDs) inhibits prostaglandin release. Corticosteroids are also used occasionally in severe cases. Drugs of choice for the case is dictated by the clinical presentation and severity.[5-8]

Olopatadine hydrochloride is a dual action agents and has broad range of pharmacological action, making it a preferred agent in cases of allergic conjunctivitis. This poses selective role on histaminic receptors. Olopatadine also has very low intrinsic surface activity which causes lesser cell membrane disruption and subsequent inflammatory mediators release, and therefore causes less discomfort on instillation.[9-11] It inhibits inflammatory mediators release very effectively and efficiently.[12-14]

Previous studies have evaluated, 0.1% olopatadine in allergic conjunctivitis, 0.2% Olopatadine as once daily dose, olopatadine 0.1% twice daily Vs olopatadine 0.2% once daily.[15-18]

The synergistic effect of combination drugs is well understood and preferred if available. Therefore,

this comparative study was designed to evaluate the effectiveness, tolerability and safety of olopatadine 0.2% once daily and olopatadine hydrochloride 0.1% twice daily with sodium cromoglycate four times daily as eye drops in cases of allergic conjunctivitis.

MATERIALS AND METHODS

Study Design and Setting : This Prospective comparative study was conducted at department of ophthalmology, at Katihar Medical College, Katihar. All the samples were randomly selected and the operator was double-blinded for the study. The study was conducted over a period of 6 months time from December 2022 to April 2023. The study was approved by the institutional research committee.

Study Sample

The subjects reporting with complaint of itching, redness, watering eyes with photophobia to the ophthalmic OPD of our institute, during the study period and diagnosed for seasonal allergic conjunctivitis on the basis of sign (hyperemia) at slit lamp and symptoms (itching, watering, photophobia) were explained about the study and the willing participants were recruited. A total of 300 randomly selected subjects were included in the study comprising of 208 Males and 92 Females in the age range of 26.98 ±14.72 years. An informed and written consent was obtained by all the participating subjects / parents prior to the commencement of the study. The recruitment was not biased by gender.

Inclusion Criteria

OPD patients aged > 4 years clinically diagnosed for allergic conjunctivitis moderate to severe degree of clinical presentation

Exclusion Criteria

Subjects with ocular surface disorders, drug hypersensitivity already on medications for conjunctivitis, systemic disorders, pregnancy and lactation as well as subjects who were to discontinue contact lens for study.

Method of Data Collection

The demographic data and baseline ocular details was noted. The subjects were randomly divided into 3 study groups (n=100 in each group) and were prescribed different eye drops, and were followed for 6 weeks.

Group 1 (n=100)	0.2% Olopatadine eye drops hydrochloride as once daily (OD)
Group II (n=100)	0.1% Olopatadine hydrochloride eye drops as twice daily (BD)
Group III (n=100)	2% Sodium cromoglycate eye drops four times daily (QID),

Detailed Ophthalmic examination was done using slit lamp biomicroscope by trained ophthalmologist for ocular signs and symptoms at 0 day, 2 weeks and 3 weeks. The eyes were assessed for conjunctival congestion, chemosis and lid edema. This was graded according to the severity (grade 0-absent, grade1-mild, grade 2-moderate, grade 3 severe). The ocular symptoms was assessed by interviewing the subjects for- itching, discomfort, foreign body sensation, stinging, photophobia, and watering (grade 0-absent, grade1-mild, grade 2-moderate, grade 3 severe). The participating subjects were advised to discontinue the drug and contact principal investigator immediately in case of discomfort or any adverse events noticed.

Statistical Analysis

The data was tabulated in Microsoft excel and was subjected to statistical analysis using SPSS software version 11. p-value <0.05 was considered statistically significant

RESULTS

This study was conducted on 304 subjects divided into 3 groups. The total duration of study was 3 weeks. The study sample consisted of 92 females and 208 males. [Figure 1]

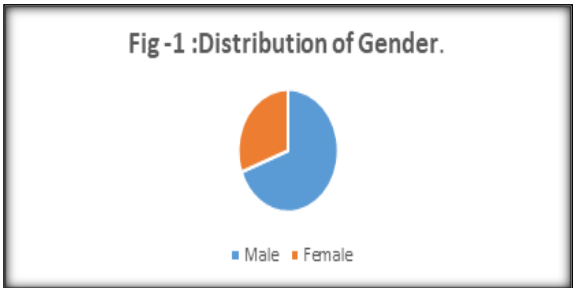

Figure 1: Distribution of Gender

Table 1 shows the baseline characteristics of the participating subjects. The number of subjects in Group 1, Group II and Group III were equally distributed (n=100). The mean age of the 26.98 ±14.72 years, the same in Group-I, Group II and Group III was 33.51±15.49, 25.1±13.4, and 22.01±12.6 years respectively. The number of subjects less than age 16 years of age was 16, 28 and 31 in Group-I, Group II and Group III respectively. And the number of subject age more than 16 years of age was 84, 72 and 69 in Group-I, Group II and Group III respectively. The gender wise distribution of subjects in Group-I was 70 male and 30 female, in Group II -68 male and 32 female, while in Group III it was 73 male and 27 female, respectively.

Table 1: Demography and Baseline characteristics of subjects

Parameters		Olopatadine 0.2% OD (n=100)	Olopatadine 0.1% BD (n=100)	Sodium cromoglycate 2% QID (n=100)
Age	Mean (SD)	33.51(15.49)	25.1(13.4)	22.01(12.6)
	<16yrs	16	28	31

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	>16yrs	84	72	69
Sex	Male	70	68	73
	Female	30	32	27
Allergic conjunctivitis		100	100	100

The mean scores for ocular itching and conjunctival congestion in allergic conjunctivitis at each examination is shown in Table 2. All the three groups had almost similar and clinically comparable score at the time of recruitment and initial examination. There was no significant difference among the groups regarding baseline scores of conjunctival congestion, ocular itching, ocular discomfort, stinging and photophobia. At 2nd week examination the ocular symptom score shad reduced significantly in all the three groups with least severity of symptom in Group II and highest severity score in Group III. The trend of reduction in ocular symptom was similar at 3rd week examination.

Table 2: Mean scores of ocular signs and symptoms at Baseline, 2nd week and 3rd week

Group I				
Variable	Visit 1	Visit 2	Visit 3	Friedman test value
Itching	3.67	1.65	0.50	208
Conjunctival congestion	3.67	2.3	1.18	207.5
Group II				
Variable	Visit 1	Visit 2	Visit 3	Friedman test value
Itching	3.66	1.42	0.35	195.5
Conjunctival congestion	3.73	2.18	1.14	195
Group III				
Variable	Visit 1	Visit 2	Visit 3	Friedman test value
Itching	3.51	2.62	1.46	183
Conjunctival congestion	3.63	3.00	2.28	145.079

The mean difference of ocular itching and conjunctival congestion scores between 1st visit and 3rd visit is shown in table 3. Group II had 90 % improvement in the ocular itching score and 69.4 % improvement in ocular congestion score between 1st visit and 3rd visit. This score was the highest, showing maximum improvement of ocular symptoms in group II compared to Group I and Group III. This was least in Group III.

Table 3: Difference in the mean ocular itching and conjunctival congestion scores (from visit 1 to visit 3)

	OCULAR ITCHING			**CONJUNCTIVAL CONGESTION**		
	Group I	Group II	Group III	Group I	Group II	Group III
Mean difference	3.163	3.316	2.059	2.486	2.592	1.356
% Change	86.36	90.53	58.59	67.79	69.4	37.33

Therefore overall olopatadine showed better efficacy than sodium cromoglycate. Though there was not much of difference clinically between 0.2% Olopatadine OD and 0.1% Olopatadine BD, but 0.1% Olopatadine BD could be referred as a preferred choice over 0.2% Olopatadine OD.

Table 4: Comparison of groups using wilcoxon signed rank test

	Ocular itching			**Conjunctival congestion**		
	Group I Vs Group II	Group I Vs Group III	Group II Vs Group III	Group I Vs Group II	Group I Vs Group III	Group II Vs Group III
p- value	0.085	0.000	0.000	0.137	0.000	0.000

The comparison of groups for improvement of ocular symptoms is shown in Table 4. All the 3 groups showed a significantly reduced mean scores for all the parameters at visit 2 and visit 3 ($p < 0.001$). This signifies that both the topical ocular therapeutic agents evaluated in the study are effective in improving the signs and symptoms of allergic conjunctivitis.

DISCUSSION

The ever dynamic world of pharmacology has offered a wide array of ophthalmological pharmacological solutions, for the prevention and treatment of allergic conjunctivitis. This cart provides us the options with antihistaminics, mast cell stabilizers, non-steroidal anti- inflammatory drugs and corticosteroids, or a combination of drugs. The drug of choice is dictated by clinical presentation, severity of symptoms, and overall clinician's judgment.[19]

Sodium cromoglycate is an old drug with proven efficacy in treating allergic conjunctivitis for number of years. Currently, dual action and wide spectrum pharmacological agents (e.g; olopatadine, epinastine, ketotifen) are available. Previous studies in the series have highlighted the advantages of using olopatadine for the treatment of allergic conjunctivitis and have also proven the efficacy of

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0.1% olopatadine solution twice daily in allergic conjunctivitis.[20-22]

Aguilar et al reported, Olopatadine 0.1% ophthalmic solution to have superior efficacy in speedily alleviating the signs and symptoms of allergic conjunctivitis.[23] Olopatadine also to have better efficacy and tolerability and also as a preferred molecule compared to ketotifen.[24] Olopatadine 0.1% twice daily is also proven to have better efficacy, provide quick relief and early decrease in allergic conjunctivitis related itching, redness and chemosis, compared to other molecules like epinastine and loteprednol etabonate 0.2%.[25] Olopatadine is reported to control histamine release effectively, which is evident by reduced tear levels of histamine and subsequent little allergic inflammatory response, in in-vivo studies.[26-27] Study comparing 0.1% olopatadine twice daily with 0.2% olopatadine once daily did not show any statistically significant difference in the prevention of allergic conjunctivitis associated itching.[18] Olopatadine has overcome the limitations of sodium cromoglycate by its dual action and better efficacy and is also a cost effective alternative of sodium cromoglycate in treatment of allergic conjunctivitis.[28]

A randomized controlled trial has reported better efficacy of 0.1% olopatadine twice daily compared to sodium cromoglycate 2% quarterly in a day in reducing conjunctival congestion and itching.[16]

The present study, evaluated the effecicacy, tolerability and safety of olopatadine 0.2% once daily and olopatadine hydrochloride 0.1% twice daily with sodium cromoglycate four times daily as eye drops in cases of allergic conjunctivitis.

Our study results found, both the treatment modalities were effective in reducing the signs and symptoms of allergic conjunctivitis. Olopatadine was found to be superior to sodium cromoglycate. Thus, olopatadine 1% or 0.2% has better efficacy and tolerability compared to sodium cromoglycate 2% in relieving the signs and symptoms of allergic conjunctivitis. Olopatadine 1% twice daily showed better result statistically compared to Olopatadine 0.2% once daily, though the results were comparable clinically.

CONCLUSION

A clear understanding of primary triggering allergen and its pathogenesis causing allergy is the best option in selecting the modality of therapy for allergic conjunctivitis. The dual action and wide spectrum of Olopatadine makes it quite effective in early relieving the signs and symptoms of allergic conjunctivitis. Olopatadine are a better preferred compared to sodium cromoglycate for allergic conjunctivitis.

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