

## Comparative evaluation of the efficacy and safety of olopatadine and sodium cromoglycate eye drops

Arun Kumar Sinha<sup>1\*</sup>, Sunil Kumar<sup>2</sup>

<sup>1</sup>Professor and Head, Department of Eye, V.I.M.S., Pawapuri, Nalanda, India

<sup>2</sup>Associate Professor, Department of Eye, P.M.C.H., Patna, Bihar, India

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### Abstract

**Background:** Allergic conjunctivitis is the commonest ocular morbidity worldwide. Understanding of underlying mechanisms is important to choose the best therapy. Olopatadine with a wide spectrum has proven to be very effective in allergic conjunctivitis. **Aim:** To compare the efficacy and tolerability of olopatadine 0.2% eye drops once daily and olopatadine hydrochloride 0.1% eye drops twice daily along with sodium cromoglycate in allergic conjunctivitis. **Methods:** This was a prospective, single centre study enrolling 304 patients with allergic conjunctivitis attending ophthalmology clinics. Subjects were assessed for ocular signs and symptoms at 3 visits-baseline, week 2, week 3. The change from baseline in the mean scores of itching and redness at 3 weeks was primary outcome variable. **Results:** The reduction in signs and symptoms were statistically significant in all the three groups ( $p < 0.001$ ). Both the olopatadine receiving groups were better than sodium cromoglycate receiving group in reducing ocular signs and symptoms by pairwise comparison by wilcoxon signed rank test. **Conclusion:** Olopatadine ophthalmic solution is better than sodium cromoglycate ophthalmic solution in reducing the ocular signs and symptoms in allergic conjunctivitis.

**Keywords:** Olopatadine, Allergic conjunctivitis, Sodium cromoglycate.

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### Introduction

The second most common ocular morbidity in India affecting the life style is allergic conjunctivitis, which encompasses approximately 15-20% cases attending Ophthalmology Department[1]. This may also be an explanation for school non-attendance in children because of its distressful symptoms[2,3]. Allergic ocular diseases may be of acute or chronic type[4]. Of which, seasonal and perennial allergic conjunctivitis are of acute type. This acute conjunctival illness is IgE mediated [4]. The interaction of sensitized mast cell to an allergen with subsequent release of inflammatory mediators is the key explanation for the signs and symptoms of conjunctivitis which includes mainly of these approaches have improved considerably over.

\*Correspondence

**Dr. Arun Kumar Sinha**

Professor and Head, Department of Eye, V.I.M.S.,  
Pawapuri, Nalanda, India.

E-mail: [arun.ak.kumar8@gmail.com](mailto:arun.ak.kumar8@gmail.com)

ocular itching and conjunctival congestion. Identification and keep away from allergen may be the most suitable treatment, which again is near impossible in majority of cases. Numerous pharmacologic therapeutic agents that are available as eye drops for the treatment of allergic conjunctivitis. Antihistaminics(e.g. levocabastine, azelastine, bepotastine, alcaftadine.) block H1 histaminergic receptors. Mast cell stabilizers (e.g. sodium cromoglycate, nedocromil sodium, lodoxamide.)[7] maintains the membrane stability of mast cells by increased calcium influx and thus preventing degranulation. Dual acting agents (e.g. olopatadine, ketotifen, azelastine, epinastine.) has both antihistaminic as well as mast cell stabilizing action. Non-steroidal anti-inflammatory drugs (e.g. ketorolac, diclofenac, flurbiprofen.) inhibits prostaglandin release.

Corticosteroids (e.g. prednisolone, hydrocortisone, flumethalone, loteprednol, desonide.) are used in

severe cases[5]. Clinical the severity of allergic conjunctivitis decides the drugs of choice[8].The broad range of pharmacological action makes Olopatadine hydrochloride a preferred agent. This poses a high affinity towards H1 receptor and comparatively low to H2 and H3 receptors[9]. It inhibits the release of histamine, PGD<sub>2</sub> and tryptase[10]. Olopatadine also is cell membrane friendly because of its very low intrinsic surface activity and less interaction with membrane phospholipids. As a result, Olopatadine causes less cell membrane disruption and subsequent release of inflammatory mediators and thus causes less discomfort on instillation[11]. This also inhibits TNF alfa release, and restrains phosphatidylinositol turnover stimulated by histamine as well as IL-6 and IL-8 secretion[12-14]. The effectiveness and tolerability of olopatadine 0.1% in allergic conjunctivitis was found to be satisfactory in several comparative studies [15,16]. Recently, 0.2% Olopatadine is also reported to be a safe and effective in reducing ocular itching with the advantage of once-a-day dosing [17]. The effectiveness of twice daily dosing of olopatadine 0.1% has also been compared with once daily dosing of olopatadine 0.2%[18]. The synergistic effect combination drugs of two or more molecules are well known and are available. Therefore, this study was conducted to compare the efficacy and tolerability of olopatadine 0.2% eye drops once daily and olopatadine hydrochloride 0.1% eye drops twice daily along with sodium cromoglycate in allergic conjunctivitis.

## Methods

### Study design and setting

This Prospective was conducted at department of ophthalmology, at Vardhman Institute of Medical Sciences, Pawapuri . 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 2019 to April 2019. The study was approved by the institutional research committee. A total of 304 subjects were included in the study comprising of 212 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. The subjects reported with complaint of itching, redness, watering eyes with photophobia were diagnosed for seasonal allergic conjunctivitis on the basis of sign (hyperemia) at slit lamp and symptoms (itching, watering, photophobia).

### 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 like pterygium, dry eye etc.

Known case of hypersensitivity to the study drugs. Patient already on medications for conjunctivitis.

Patients who were to discontinue contact lens for study.

Pregnancy and lactation.

### Method of data collection

After fulfilling the inclusion and exclusion criteria an informed and written consent was taken from all the participants. The demographic details and ocular details was noted at baseline. The subjects were divided into 3 groups by stratified randomization and were given different topical ophthalmic solutions-

Group 1 - Olopatadine hydrochloride 0.2% ophthalmic solution once daily (OD)

Group 2- Olopatadine hydrochloride 0.1% ophthalmic solution twice daily (BD), and

Group 3- Sodium cromoglycate 2% ophthalmic solution four times daily (QID), and were followed for 6 weeks.

Ophthalmic assessment was done by trained ophthalmologist for ocular signs and symptoms at baseline, 2weeks and 3 weeks. The ocular signs was assessed using slit lamp biomicroscope 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 contact the principal investigator immediately if adverse events noticed.

### Statistical analysis

The data was tabulated in Microsoft excel and was subjected to statistical analysis using SPSS software version 11. Friedman test, wilcoxon signed rank tests was performed and 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.

Group 1 (n=105) subjects received olopatadine hydrochloride 0.2% ophthalmic solution in a dose of once daily, Group 2 (n=98) subjects received olopatadine hydrochloride 0.1% ophthalmic solution in a dose of twice daily and Group 3 (n=101) subjects received sodium cromoglycate 2% ophthalmic solution

in a dose of four times daily. The study sample consisted of 92 females and 212 males. Table 1 shows the baseline characteristics of subjects in the study. The mean scores for ocular itching and conjunctival congestion in allergic conjunctivitis at each

examination is shown in Table 2. There was no significant difference among the groups regarding baseline scores of conjunctival congestion, ocular itching, ocular discomfort, stinging and photophobia.

**Table 1: Baseline characteristics of allergic conjunctivitis patients in the study**

| Parameters              |          | Olopatadine 0.2% OD | Olopatadine 0.1% BD | Sodium cromoglycate 2% QID |
|-------------------------|----------|---------------------|---------------------|----------------------------|
| Age                     | Mean(SD) | 33.51(15.49)        | 25.1(13.4)          | 22.01(12.6)                |
|                         | <16yrs   | 16                  | 26                  | 32                         |
|                         | >16yrs   | 89                  | 72                  | 69                         |
| Sex                     | Male     | 73                  | 66                  | 73                         |
|                         | Female   | 32                  | 32                  | 28                         |
| Allergic conjunctivitis |          | 105                 | 98                  | 101                        |

**Table 2: Mean scores of ocular signs and symptoms**

| Variable                | Olopatadine 0.2% OD |         |          |                     | Olopatadine 0.1% BD |         |          |                     | Sodium cromoglycate 2% QID |         |          |                     |
|-------------------------|---------------------|---------|----------|---------------------|---------------------|---------|----------|---------------------|----------------------------|---------|----------|---------------------|
|                         | Visit 1             | Visit 2 | Visit 3† | Friedman test value | Visit 1             | Visit 2 | Visit 3† | Friedman test value | Visit 1                    | Visit 2 | Visit 3† | Friedman test value |
| Itching                 | 3.67                | 1.65    | 0.50     | 208                 | 3.66                | 1.42    | 0.35     | 195.5               | 3.51                       | 2.62    | 1.46     | 183                 |
| Conjunctival congestion | 3.67                | 2.3     | 1.18     | 207.5               | 3.73                | 2.18    | 1.14     | 195                 | 3.63                       | 3.00    | 2.28     | 145.079             |

† P value was < 0.001

**Table 3: Change from baseline in the mean scores of ocular itching and conjunctival congestion at week 3**

|  | Ocular itching      |                     |                            | Conjunctival congestion |                     |                            |
|--|---------------------|---------------------|----------------------------|-------------------------|---------------------|----------------------------|
|  | Olopatadine 0.2% OD | Olopatadine 0.1% BD | Sodium cromoglycate 2% QID | Olopatadine 0.2% OD     | Olopatadine 0.1% BD | Sodium cromoglycate 2% QID |
| Change from baseline (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                      |

**Table 4: Between group comparisons using wilcoxon signed rank test**

|         | Ocular itching        |                       |                       | Conjunctival congestion |                       |                       |
|---------|-----------------------|-----------------------|-----------------------|-------------------------|-----------------------|-----------------------|
|         | Between group 1 and 2 | Between group 1 and 3 | Between group 2 and 3 | Between group 1 and 2   | Between group 1 and 3 | Between group 2 and 3 |
| P value | 0.085                 | 0.000                 | 0.000                 | 0.137                   | 0.000                 | 0.000                 |

In all the 3 groups and for all the parameters, the mean scores reduced significantly at visit 2 and visit 3 ( $P < 0.001$ ). Therefore both olopatadine and sodium cromoglycate pphthamic solutions were effective in alleviating signs and symptoms of allergic conjunctivitis. Table 3 shows change from baseline in the mean scores and percent change in ocular itching and conjunctival congestion at week 3. The difference

in the CFB in the mean scores of itching and redness between the three groups was statistically significant at week 3. Wilcoxon signed rank test was done to know exactly between which groups results were statistically significant. Thus group A and group B showed statistically significant difference from group C, whereas there was no statistically significant difference between group A and group B. Therefore

olopatadine receiving groups showed better efficacy than sodium cromoglycate receiving group showing that once daily olopatadine 0.2% or twice daily olopatadine 0.1% was better than sodium cromoglycate 2% QID in allergic conjunctivitis. There was no statistically significant difference in the CFB in mean scores of itching and redness between once daily olopatadine 0.2% or twice daily olopatadine 0.1% at week 3. There were no treatment related adverse events reported during the study.

### Discussion

A wide range of pharmacological ophthalmological solutions are offered today to prevent and treat allergic conjunctivitis. These includes antihistaminics, mast cell stabilizers, non-steroidal anti-inflammatory drugs and corticosteroids. A thorough clinical examination and judgment of severity determines the drug of choice[19]. Newer pharmacological agents are available today with dual action and wide spectrum of action e.g; olopatadine, epinastine, ketotifen. Whereas, sodium cromoglycate is an old drug. Previously, a number of studies have proven the efficacy of 0.1% olopatadine solution twice daily in allergic conjunctivitis [20-22]. Olopatadine 0.1% has also shown to have superior efficacy in rapidly alleviating the signs and symptoms of allergic conjunctivitis (Aguilar et al) [23]. olopatadine also is better preferred compared to ketotifen[24]. Studies have also reported the better efficacy olopatadine 0.1% twice daily compared to epinastine and loteprednol etabonate 0.2% in decreasing allergic conjunctivitis related itching, redness and chemosis[21,25]. In the *in-vivo* studies, olopatadine has shown to reduced tear levels of histamine and allergic inflammatory response [26,27]. A comparative study of 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 is an cost effective option 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]. In our study, we compared 0.2% olopatadine once daily with 0.1% olopatadine twice daily and sodium cromoglycate 2% administered four times daily in allergic conjunctivitis patients. Our study results found, both the treatment modalities were effective in reducing the signs and symptoms of allergic conjunctivitis. Olopatadine also was found to be superior than sodium cromoglycate. Thus, olopatadine

0.1% or 0.2% is better compared to sodium cromoglycate 2% in alleviating allergic conjunctivitis related ocular itching and redness in patients.

### Conclusion

The understanding of underlying pathogenesis triggering the allergy is utmost important in selecting the best therapy for allergic conjunctivitis. The dual action and wide spectrum of Olopatadine has proven to be very effective in allergic conjunctivitis. Thus, Olopatadine 0.2% once daily and/or olopatadine 0.1% twice daily are a better preferred compared to sodium cromoglycate 2% four times a day for allergic conjunctivitis.

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