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A comparative study of efficacy and tolerability of bepotastine besilate (1.5%) and olopatadine hydrochloride (0.1%) eye drops in allergic conjunctivitis in a tertiary care hospital of the southern part of India

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ABSTRACT

Background: Allergic conjunctivitis is increasing with the rise in the levels of allergens. Drug therapy is usually needed in addition to avoidance of general allergens to treat this condition. Both bepotastine besilate and olopatadine hydrochloride ophthalmic solutions are newer additions in the treatment of allergic conjunctivitis having dual properties of second-generation antihistaminics along with mast cell stabilizing activity. **Aims and Objectives:** The aim of the study was to compare the efficacy and tolerability of bepotastine besilate (1.5%) and olopatadine hydrochloride (0.1%) eye drops in patients presenting with allergic conjunctivitis in a tertiary care hospital of Southern part of India. **Materials and Methods:** Sixty patients who were clinically diagnosed to be suffering from allergic conjunctivitis were selected as participants for the study. They were randomly distributed into two groups consisting of 30 patients each. One group received eye drop bepotastine (1.5%) and the other group received eye drop olopatadine (0.1%), with each patient receiving the medication twice daily for a duration of 2 weeks. During the first visit, all the patients were assessed for the signs and symptoms and subsequently re-assessed at weekly intervals for a period of 2 weeks. They were also advised to report occurrence of any unwanted drug reaction during the weekly follow-up visits. **Results:** The above study showed the effectiveness of both bepotastine and olopatadine eye drops in decreasing the signs and symptoms of allergic conjunctivitis. Significant clinical improvement was found in all participants, whereas deterioration was found in none of them. Statistically significant improvement of itching and redness of eyes was observed with use of both the study drugs mentioned beforehand. Both the drugs were well tolerated by the patients. Statistically significant reduction of itching and foreign body sensation was found to be more in patients using bepotastine eye drops compared to those using olopatadine eye drops. Only two patients using bepotastine eye drops complained of having a mild burning sensation in eyes. **Conclusion:** From this study, bepotastine and olopatadine eye drops have been observed to be safe and efficacious in allergic conjunctivitis. Bepotastine eye drop was found to be more efficacious to relieve itching and foreign body sensation compared to that of olopatadine eye drops.

Key words: Allergic conjunctivitis; Antihistaminics; Bepotastine besilate; Olopatadine hydrochloride

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INTRODUCTION

Conjunctival inflammation with an underlying allergic cause, manifesting most commonly as ocular itching and conjunctival hyperemia is termed as allergic conjunctivitis. About 94% of patients with allergic conjunctivitis may also present with symptoms of allergic rhinitis such as nasal itching and rhinorrhea.[1] The term rhinoconjunctivitis can be used to denote both allergic conjunctivitis and rhinitis, as both of these symptoms may present simultaneously.[2] They may create a negative impact on patient's ocular and nasal comfort resulting to hindrance of daily activities, also increasing the socioeconomic burden of the patient and his family.[1] In the Southern part of India, the prevalence of allergic conjunctivitis has been found to be 12.5% among the population belonging to the age group of 18 years and above.[3]

Type I hypersensitivity reaction triggered by exposure to some allergen has been found to be the most common underlying pathogenesis behind the occurrence of allergic conjunctivitis. On repeated exposure of the same allergen to a sensitized subject, cross-linking of the complementary antibody-antigen complex occurs on the surface of the conjunctival mast cells. This causes degranulation of the conjunctival mast cells, leading to the release of histamine.[1]

The above phenomenon is termed as "early-phase response" of allergic conjunctivitis, which manifests as ocular itching, hyperemia, and chemosis. It is followed by a late-phase reaction after 6–12 h, which involves infiltration of inflammatory cells like eosinophils within conjunctiva. Severe allergic inflammation and damage to the conjunctival tissue may occur in this late phase.[1]

With increasing levels of allergens (especially deterioration of air quality), there is a marked upraise of allergic conjunctivitis. Management of this condition involves both non-pharmacological and pharmacological modalities. The non-pharmacological modalities include maintaining general ocular hygiene and avoidance of known allergens.[4,5] Pharmacological management includes both local and systemic therapy with non-steroidal anti-inflammatory drugs, antihistaminics, ocular decongestants, mast cell stabilizers, and corticosteroids.[5]

As there is a progressive increase in the burden of allergic conjunctivitis cases leading to ocular discomfort, there is a need for a highly efficacious, safe, and cost-effective topical medication for the management of the same.[1]

Recent studies show that the newest topical anti-allergy medications for allergic conjunctivitis have good antihistaminic action as well as mast cell-stabilizing activity. Rapid and long-lasting relief from ocular discomfort due to allergic conjunctivitis can be obtained by the application of these drugs. Both bepotastine besilate and olopatadine hydrochloride ophthalmic solutions have dual properties of second-generation antihistaminics along with mast cell stabilizing activity.[1,6] This dual action helps to control signs and symptoms of allergic conjunctivitis both during the early phase (antihistaminic action) and the late phase (long-term mast cell degranulation).[5] The drug controller general of India approved the ophthalmic solutions bepotastine besilate in 2016 and olopatadine hydrochloride in 2006 for the management of ocular itching found in allergic conjunctivitis.

However, there are only a few studies that have compared the efficacy and tolerability of bepotastine and olopatadine in allergic conjunctivitis in the India population. Hence, the following study has been undertaken to compare both efficacy and tolerability of bepotastine and olopatadine in patients suffering from allergic conjunctivitis in a tertiary care hospital of southern part of India.

Aims and objectives

This study is undertaken to compare the efficacy and safety of Bepotastine besilate 1.5% and Olopatadine hydrochloride 0.1% eye drops in patients of allergic conjunctivitis.

MATERIALS AND METHODS

Approval was obtained from the Institutional Ethics Committee before starting the study (Ref No: KIMS/IEC/D-01/2017dated November 16, 2017). It was a prospective, open-labeled study, where the subjects were randomized by a simple randomization method using random number table into two groups for comparison between them. Participants were allergic conjunctivitis patients attending the ophthalmology outdoor of Kempegowda Institute of Medical Sciences Hospital and Research Centre. A case record form was prepared for recording the patients' data in this study. Witten informed consent form, patient information sheet, and drug reminder chart were created for distribution among the participants. Participants presenting with the pathognomonic symptom of ocular itching accompanied with other features of allergic conjunctivitis were diagnosed clinically.[7] The participants were randomly divided into two groups (30 in each group) using a random number table. One group received bepotastine besilate (1.5%) eye drops, whereas the other group received olopatadine hydrochloride (0.1%) eye drops twice a day for 2 weeks. Rescue medications included topical corticosteroids (dexamethasone, fluorometholone, prednisolone acetate, or loteprednol).[8] However, none of the study participants required rescue medications.

Inclusion criteria

Participants of both sexes belonging to age groups more than 18 years suffering from seasonal allergic conjunctivitis or perennial allergic conjunctivitis, available for regular follow-up visits.

Exclusion criteria

Patients suffering from infective conjunctivitis (bacterial/viral/fungal) and severe allergic conjunctivitis (vernal/atopic keratoconjunctivitis/giant papillary conjunctivitis), with a history of severe dry eye or ocular herpes. Furthermore, patients having allergy to the drugs under study or already on them were excluded from the study. Pregnant women and lactating mothers were similarly not included in the study.

On the first visit, a clinical assessment of signs and symptoms of the patients was done. Follow-up visits were done on weekly intervals which included the study of improvement/deterioration of clinical features of the patients for a duration of 2 weeks. The assessment of the clinical parameters was done by a grading scale having four points (no signs and symptoms=0; mild=1; moderate=2; severe=3) with respect to hyperemia/redness, tearing/watering, itching, photophobia, chemosis, lid edema, and foreign body sensation/stinging.[5,9-12]

The tolerability of the study drugs was assessed by adverse events/reactions reported and whether adverse events/reactions resulted in either decreasing the dose of the study drugs, discontinuation of the study drugs, or using any other medications/treatment to either treat or overcome the adverse events/reactions due to the study drugs.

The adverse event(s) reported were subsequently analyzed for causality assessment using the World Health Organization-Uppsala Monitoring Centre (WHO-UMC) causality scale. The response to the adverse event/reaction was recorded in terms of whether it required any dose reduction or discontinuation of the study drug or any other measures were required for the management of the adverse event/reaction.

Patients' data collection was initiated in December 2017, which continued up to October 2019. Then, the data collected from the study participants were analyzed statistically by the help of SPSS software. Since the study involved two groups, Student's "t" test was used for comparing their parameters.[13]

RESULTS

In this study, a total of 60 patients suffering from allergic conjunctivitis were selected as participants, who were divided into two groups randomly (each group containing 30 participants) irrespective of age and sex. One group received eye drop bepotastine besilate whereas the other one received olopatadine hydrochloride eye drop.

The mean age of the participants receiving bepotastine was 31.2±9.17 years, whereas it was 35.6±12.24 years in those receiving olopatadine. There was no statistical significance in the differences in the mean age and gender distribution of both study groups (Table 1).

The assessment of the clinical parameters was done by a grading scale having four points (no signs and symptoms=0; mild=1; moderate=2; severe=3) with respect to signs and symptoms such as hyperemia/redness, tearing/watering, itching, photophobia, chemosis, lid edema, and foreign body sensation/stinging. The scoring was assessed in the beginning of the study, and then, they were re-assessed on 7th and 14th day of the treatment by both drugs. The mean score of effects on each sign and symptom due to both the drugs under study was tabulated individually.

The above-mentioned ocular inflammatory parameters showed marked improvement at the end of the study with application of both drugs. The symptoms such as tearing, photophobia, and lid edema completely resolved at the end of 14th day in both groups. The improvement pattern of ocular itching in both the study groups was found to be almost similar. However, improvement of other parameters such as hyperemia, chemosis, and foreign body sensation was more marked in the group receiving olopatadine compared to that receiving bepotastine eye drops (Tables 2 and 3). In the group receiving bepotastine eye drops, the reduction of the scores from baseline to day 14 was statistically significant for the parameters of itching (P<0.001), hyperemia/redness (P<0.001), and foreign body (P=0.043) (Table 2). In contrast, the group receiving olopatadine eye drops, the reduction of the scores from baseline to day 14 was statistically significant for the parameters of itching (P<0.001) and foreign body/itching sensation (P<0.001) (Table 3).

There was improvement in symptoms without any worsening in all the subjects.

Table 1: Mean age comparison and gender distribution of the patients

Gender	Bepotastine		Olopatadine	
	n	Mean±SD	n	Mean±SD
Male	18	31.4±9.376	13	34.0±11.979
Female	12	30.8±9.236	17	36.9±12.658
Total	30	31.2±9.165	30	35.6±12.243
P-value*		0.843		0.532

SD: Standard deviation.*Student "t" test

Table 2: Mean score and change from baseline score in bepotastine group

Parameters	Mean score			Change from baseline		P-value*
	Day 0	Day 7	Day 14	Day 7	Day 14	
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	
Itching	1.37±0.758	0.57±0.500	0.03±0.181	−0.80±0.514	−1.33±0.774	<0.001
Hyperemia	0.95±0.872	0.32±0.469	0.02±0.129	−0.63±0.551	−0.93±0.861	<0.001
Tearing	0.55±0.769	0.15±0.360	0.00±0.000	−0.40±0.527	−0.55±0.769	0.215
Photophobia	0.22±0.585	0.07±0.252	0.00±0.000	−0.15±0.404	−0.22±0.585	0.469
Chemosis	0.03±0.181	0.03±0.181	0.02±0.129	0.00±0.000	−0.02±0.129	0.319
Lid Edema	0.10±0.303	0.00±0.000	0.00±0.000	−0.10±0.303	−0.10±0.303	1.000
FB sensation	0.95±0.891	0.33±0.542	0.08±0.381	−0.62±0.524	−0.87±0.791	0.043

SD: Standard deviation.*Student "t" test

Table 3: Mean score and change from baseline score in olopatadine group

Parameters	Mean score			Change from baseline		P-value*
	Day 0	Day 7	Day 14	Day 7	Day 14	
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	
Itching	0.95±0.723	0.18±0.469	0.03±0.181	−0.77±0.533	−0.92±0.645	<0.001
Hyperemia	0.77±0.745	0.18±0.390	0.00±0.000	−0.58±0.530	−0.77±0.745	<0.001
Tearing	0.47±0.700	0.07±0.252	0.00±0.000	−0.40±0.588	−0.47±0.700	0.573
Photophobia	0.05±0.287	0.00±0.000	0.00±0.000	−0.05±0.287	−0.05±0.287	1.000
Chemosis	0.07±0.312	0.00±0.000	0.00±0.000	−0.07±0.312	−0.07±0.312	1.000
Lid edema	0.13±0.503	0.05±0.220	0.00±0.000	−0.08±0.334	−0.13±0.503	0.523
FB sensation	0.45±0.675	0.08±0.279	0.00±0.000	−0.37±0.520	−0.45±0.675	0.450

SD: Standard deviation. *Student "t" test, *All subjects had improvement in symptoms and no subject had worsening of symptoms

Table 4: Comparison of changes from baseline score at day 14

Parameters	Bepotastine	Olopatadine	P-value*
	Mean±SD	Mean±SD	
Itching	−1.33±0.774	−0.92±0.645	0.002
Hyperemia/redness score	−0.93±0.861	−0.77±0.745	0.259
Tearing/watering score	−0.55±0.769	−0.47±0.700	0.536
Photophobia score	−0.22±0.585	−0.05±0.287	0.050
Chemosis score	−0.02±0.129	−0.07±0.312	0.253
Lid edema score	−0.10±0.303	−0.13±0.503	0.661
FB sensation/stinging score	−0.87±0.791	−0.45±0.675	0.002

*Student "t" test

The above results show that there is a considerable decrease in the mean scores of all the parameters assessed, that is, itching, hyperemia/redness, tearing/watering, photophobia, chemosis, lid edema, and foreign body/stinging sensation, in both the bepotastine and the olopatadine groups. The mean reduction of scores of itching, hyperemia/redness, tearing, photophobia, and foreign body/stinging sensation on 14th day was greater in the bepotastine group when compared with the olopatadine group, among which the reduction in the mean scores in the parameters of itching and foreign body/stinging sensation was statistically significant (P=0.002 for both parameters) (Figure 1 and Table 4). Olopatadine showed greater decrease in the mean reduction scores of chemosis and lid edema when compared to the bepotastine group, but there was no statistical significance of this difference.

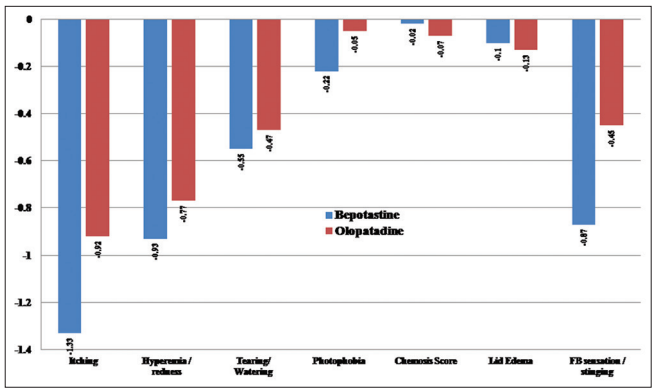

Figure 1: Comparison of mean change from baseline score at the 14th day between the study groups

Only 2 adverse events (burning sensation of the eyes) were reported from the bepotastine group and no adverse events were reported from the olopatadine group. The WHO-

UMC causality assessment revealed association of both the adverse events to be possible in nature.

DISCUSSION

One of the most common ocular-allergic conditions prevalent in the present world is allergic conjunctivitis. It may present either in acute or chronic form. For the management of this condition, different classes of drugs are available for topical application. Few drugs having both mast cell stabilizing and histamine receptor (H_1) blocking action are used widely for managing this condition. In our study, the effect two such drugs, that is, bepotastine besylate (1.5%) and olopatadine hydrochloride (0.1%) on study groups of patients have been evaluated.

Bepotastine's efficacy for managing allergic conjunctivitis has been documented in many earlier studies, for example, McCabe and McCabe, Parida and Mallik.[1,14] Similarly, the efficacy of olopatadine for managing allergic conjunctivitis has been also proven in many earlier studies by Sarker et al., and Mah et al.[5,15]

The efficacy of bepotastine has been reported to be better than olopatadine in earlier reported studies by McCabe and McCabe, Parida and Mallik, Ayyappanavar et al., and Marini et al.[1,14,16,17]

This study reveals that the efficacy of bepotastine is greater when compared to olopatadine in relieving the symptoms of allergic conjunctivitis such as itching, hyperemia/redness of the eyes, watering/tearing which is similar to the study done by McCabe and McCabe.[1]

However, in this study, it was found that olopatadine was better in relieving the symptoms of chemosis and lid edema when compared to bepotastine, although not statistically significant, which is in variance with other reported studies by McCabe and McCabe, Parida and Mallik.[1,14]

This study also reported that both the study drugs were safe and had very good tolerability among the study participants. Only two participants reported burning sensation in the eyes which were mild in nature. None of the study participants required rescue medications and none of the study participants had to discontinue the study medications. Other studies have reported similar tolerability (McCabe and McCabe, Sarker et al., and Dudeja et al.)[1,5,18]

Limitations of the study

This study was an open-labeled study and included a relatively small sample size and short duration of study (2 weeks), which are the major limitations of the study. Studies with larger sample sizes can be conducted to generalize the results of this study.

CONCLUSION

Both bepotastine besilate (1.5%) and olopatadine hydrochloride (0.1%) eye drops were found to be effective in decreasing signs and symptoms of allergic conjunctivitis in this study. Both the eye drops resulted in a statistically significant reduction in ocular itching and hyperemia. Bepotastine besilate (1.5%) eye drops led to a greater reduction in ocular itching when compared to olopatadine hydrochloride (0.1% eye drops which were statistically significant). Both the eye drops were well tolerated with only two participants reporting mild adverse drug reactions to the bepotastine eye drops. None of the participants were required to either discontinue the study medications or reduce the dosage/frequency of drug administration and no rescue medication(s) were needed. To conclude, both the eye drops bepotastine besilate and olopatadine hydrochloride were found to be safe and effective in the management of allergic conjunctivitis.

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SC - Concept, design, clinical protocol, collection of data, preparing the whole study, manuscript preparation, statistical analysis, and interpretation; **VR -** Concept, design, clinical protocol, manuscript preparation, statistical analysis, and interpretation; **SM -** Manuscript editing, and revision, statistical interpretation; **KKL-** Preparing the whole study, concept, design

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