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Original Research Article

A Comparative Study of Efficacy of Topical Olopatadine (0.1%), Bepotastine (1.5%) and Alcaftadine (0.25%) in Mild to Moderate Allergic Conjunctivitis at Sri Krishna Medical College, Muzaffarpur, Bihar, India

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Abstract

Objectives: This study was to compare the safety and efficacy of topical Olopatadine (0.1%), Bepotastine (1.5%) and Alcaftadine (0.25%) in mild to moderate allergic conjunctivitis at Sri Krishna Medical College, Muzaffarpur, Bihar, India.

Methods: All of the 150 cases were divided into three groups. Each group had 50 cases of allergic conjunctivitis. Group A: Patients were received topical 0.25% Alcaftadine eyedrops OD. Group B: Patients were received topical 0.2% Olopatadine eyedrops OD and Group C: Patients were received topical 1.5% Bepotastine besilate eyedrops BID. All above topical anti-allergic medication was used for 14 days. Total Ocular Symptom Scoring System (TOSS) scoring was used to grade the signs and symptoms. Diagnosis of mild to moderate allergic conjunctivitis was made clinically according to the presence of classical signs and symptoms. Demographic data, ocular and medical histories, concomitant medications, physical examination, clinical examination, including recording of vital signs, Ophthalmological examination and details of drug prescribed by the treating ophthalmologist were recorded in the study pro forma at baseline visit (visit 1). Follow-up visits were done on day 3 (visit 2), day 7 (visit 3) and day 14 (visit 4) after administering the study drugs.

Results: Mean age of group A patients was 28.43 ± 10.43 years, group B patients was 29.56 ± 9.76 years and group C was 28.97 ± 9.65 years. The total ocular symptom score (TOSS) showed a consistent decrease in subsequent visit in all the Groups and it was highly significant, when compared from baseline to 14th day in all the groups ($p = 0.00001$). Conjunctival hyperaemia was highly significantly ($p=0.000001$) reduced in all the treatment groups but there was greatly reduced in Alcaftadine and Bepotastine treatment groups at 14th day compared to olopatadine group.

Conclusions: All three medicines (topical Olopatadine 0.1%, Bepotastine 1.5% and Alcaftadine 0.25%) are effective and safe for the treatment of allergic conjunctivitis. While, Bepotastine besilate and Alcaftadine are more efficacious as compared to Olopatadine for the management of symptoms of allergic conjunctivitis.

Keywords: Allergic conjunctivitis, topical Olopatadine (0.1%), topical Bepotastine (1.5%), topical Alcaftadine (0.25%)

Introduction

Allergic conjunctivitis is a common allergic disorder estimated to affect up to 15-20% of the population worldwide [1]. Various forms of conjunctivitis such as seasonal allergic conjunctivitis, perennial allergic conjunctivitis, vernal kerato conjunctivitis (VKC), atopic kerato conjunctivitis, and giant papillary conjunctivitis are included in ocular allergy, sharing some common markers of allergy [2]. Seasonal and perennial conjunctivitis are in response to exposure to specific allergens and are predominantly mediated by IgE antibodies activating the mast cells [3]. VKC is in response to non-specific allergans and is mediated mainly by Th2 cells, but mast cells and eosinophils also play a major role [4]. Atopic conjunctivitis occurs in patients predisposed to atopy. It is mediated by both Th2 response and mast cells [5]. Avoidance of allergens and lubricants plays a key role in the management of allergic conjunctivitis. Addition of anti-histaminics such as levocarbastine reduce inflammation, whereas mast cell stabilizers prevent mast cell degranulation on exposure to allergans [6].

Alcaftadine 0.25%and Olopatadine hydrochloride 0.2% are approved once-daily and Bepotastine besilate 1.5%, twice daily dual-acting antiallergic agents for allergic conjunctivitis which includes inhibition of histamine receptor activation directly and reduction of allergic responses by stabilizing mast cells indirectly [7],[5] Olopatadine hydrochloride is a selective histamine H1 receptor antagonist and mast-cell stabilizer. It also has anti-inflammatory effects which include suppression of interleukins (IL) 6 and 8 production by inhibiting histamine related signalling pathways [8,7]. Objectives of our study was to compared the safety and efficacy of topical Olopatadine (0.1%), Bepotastine (1.5%) and Alcaftadine (0.25%) in mild to moderate allergic conjunctivitis at Sri Krishna Medical College, Muzaffarpur, Bihar, India.

Materials & Methods

This study was conducted in Department of Ophthalmology of SKMCH, Muzaffarpur, Bihar India during a period from June 2020 to January 2021. Entire patients signed an informed consent approved by institutional ethical committee of Sri Krishna Medical College and Hospital (SKMCH), Muzaffarpur, Bihar, India was sought.

A total of 150 allergic conjunctivitis patients with age group 15 to greater than 60 years were enrolled in this study. Total Ocular Symptom Scoring System (TOSS) scoring was used to grade the signs and symptoms. Diagnosis of mild to moderate allergic conjunctivitis was made clinically according to the presence of classical signs and symptoms.

Exclusion Criteria:

Patients with severe allergic conjunctivitis, need for topical steroids or topical immunosuppressive, contact lens wearers, patients with an intra-ocular pressure of more than 21 mm Hg in either eye or any type of glaucoma, history of hypersensitivity to the study medications or their components (including benzalkonium chloride), history of an ocular herpetic infection, an active ocular infection, or any significant illness, taking systemic steroids or antihistamines currently or within 7 days prior to enrolment, pregnant, planning pregnancy, or nursing/lactating and use of any other topical ocular medications were excluded from the study.

All the cases were divided into three groups (Group A, Group B and Group C).

Group A: Patients were received topical 0.25% Alcaftadine eyedrops OD.

Group B: Patients were received topical 0.2% Olopatadine eyedrops OD and

Group C: Patients were received topical 1.5% Bepotastine besilate eyedrops BID.

All above topical anti-allergic medication was used for 14 days.

Complete general, physical, and ophthalmologic examination was done. Patients were examined and their baseline symptoms and signs (TOSS) were recorded. Demographic data, ocular and medical histories, concomitant medications, physical examination, clinical examination, including recording of vital signs, Ophthalmological examination and details of drug prescribed by the treating ophthalmologist were recorded in the study pro forma at baseline visit (visit 1).

Follow-up visits were on day 3 (visit 2), day 7 (visit 3) and day 14 (visit 4) after administering the study drugs.

A deviation of ±1 a day for the first follow-up and ±2 days for subsequent follow-up was accepted. At each follow-up visit data on concomitant medications, ocular symptoms and ocular signs using hyperaemia score graded by slit-lamp examination by the investigator and adverse events (AEs) were collected. In case of relapse, the patient was asked to visit OPD on Day 21. Medication compliance was assessed with the help of a medication compliance card. Safety of study medications was assessed by ADRs.

TOSS score for grading of symptoms (itching, tearing, redness and swelling):

TOSS score: 0 - indicates no symptoms, 1+ = mild symptoms of discomfort, 2+ = moderate discomfort, 3+ = Severe symptoms interfacing in daily life.

Hyperaemia score for grading of signs: 0 – No (Normal), 0.5 – Trace (Inconsistent rose red hyperaemia)., 1 – mild (reddish colour), 2 – moderate (bright red colour), 3 – severe (bright and intense diffuse hyperaemia).

Observations

A total of 150 patients were enrolled in this study. All the cases were divided into three groups (Group A, B and C. Mean age of group A patients was 28.43 ± 10.43 years, group B patients was 29.56 ± 9.76 years and group C was 28.97 ± 9.65 years.

A total of 150 patients with mild or moderate allergic conjunctivitis, who met the required inclusion and exclusion criteria were enrolled in the study. The four major complaints recorded by patients were itching 150(100%), redness 112(74.66%), tearing 128(85.33%), and swelling 48(32%).

No systemic or ocular serious adverse events were reported. Most common adverse events were burning sensation (4) in Alcaftadine group and taste impairment (4) in bepotastine group, followed by headache (1) in Alcaftadine group, dizziness (1) in olopatadine and mild redness (1) in bepotastine group were noted. No significant difference in the number of adverse events was noted among the three groups.

Table 1: Showing the demographic profile of Allergic conjunctivitis.

Demographic profile		Group A (Mean ± S.D)	Group B (Mean ± S.D)	Group C (Mean ± S.D)
Age		28.43 ± 10.43	29.56 ± 9.76	28.97 ± 9.65
Gender	Male	28(56%)	29(58%)	26(52%)
	Female	22(44%)	21(42%)	24(48%)
Total Ocular Symptoms Score (TOSS)		7.43 ± 2.45	7.68 ± 2.18	7.59 ± 2.34

At day 1, TOSS of group A, B and C was 7.43 ± 2.45, 7.68 ± 2.18 and 7.59 ± 2.34 respectively. As compared to 1st visit and last visit (14 days) followed up TOSS was greatly reduced in group A and C than group B cases.

Table 2: Ocular Symptoms score at different visit.

Visits	Group A	Group B	Group C
Day 1 (Base line)	7.43 ± 2.45	7.68 ± 2.18	7.59 ± 2.34
Day 3	4.9 ± 1.98	5.1± 2.01	4.8 ± 1.78
Day 7	2.4 ± 1.16	2.2 ± 1.01	2.1 ± 1.03
Day 14	0.3 ± 0.41	0.4 ± 0.76	0.2 ± 0.27

The total ocular symptom score (TOSS) showed a consistent decrease in subsequent visit in all the Groups and it was statistically significant, when compared from baseline to 14th day in all the groups (p = 0.00001). The difference in mean TOSS between (Group A) Alcaftadine and (Group C) bepotastine treatment groups was observed at the third day of follow-up. This showed early relief of allergic conjunctivitis symptoms by bepotastine (4.8 ± 1.78) compared to Alcaftadine (mean (4.9 ± 1.98) and olopatadine (5.1 ± 2.01) but this was not statistically significant.

Table 3: Conjunctival hyperaemia score at different visits.

Visits	Group A	Group B	Group C
Day 1 (Base line)	1.4 ± 0.76	1.5 ± 0.88	1.5 ± 0.85
Day 3	1.0 ± 0.71	1.0 ± 0.65	1.8 ± 0.59
Day 7	0.2 ± 0.26	0.2 ± 0.26	0.2 ± 0.26
Day 14	0.007 ± 0.05	0.04 ± 0.14	0.007 ± 0.05

Conjunctival hyperaemia had reduced in all the treatment groups but there was a significant reduction in Alcaftadine and Bepotastine treatment groups at 14th day compared to olopatadine group (p = 0.0001).

Table 4: Showing the hyperaemia in different visits.

Degree of hyperaemia	No	Trace	Mild	Moderate	Severe
Visit 1st					
Group A	17	2	4	40	1
Group B	18	2	4	41	1
Group C	16	5	5	39	0
Visit 2nd					
Group A	18	4	20	20	1
Group B	18	4	22	23	1
Group C	19	2	19	19	1
Visit 3rd					
Group A	19	38	4	1	1
Group B	17	38	5	2	2
Group C	18	40	4	1	1
Visit 4th					
Group A	60	2	1	1	1
Group B	55	8	1	1	1
Group C	60	2	1	1	1

In this present study, degree of hyperaemia was highly significantly decrease in 4th visit as compared the 1st visit in all group of patients. Hyperaemia in group A and C patients were greatly reduced as compared to group B patients.

Discussions

Ocular allergy is a commonly encountered pathology in clinical practice, with an increase in number of patients noticed in the last decade [9]. Number of causes have been considered for this increase such as genetics, air pollution, pets, etc [10]. Seasonal and perennial conjunctivitis are in response to exposure to specific allergans and are predominantly mediated by IgE antibodies activating the mast cells [3].

The present study was conducted on 150 patients of allergic conjunctivitis. All the patients were divided into three groups (group A, group B and group C). Group A: Patients were received topical 0.25% alcaftadine eyedrops OD. Group B: Patients were received topical 0.2% olopatadine eyedrops OD and Group C: Patients were received topical 1.5% bepotastine besilate eyedrops BID. According to result mean age of group A, B and C patients had 28.43 ± 10.43, 29.56 ± 9.76 and 28.97 ± 9.65 years respectively. In all the group most of the were males. TOSS of all the group (A, B & C) had 7.43 ± 2.45, 7.68 ± 2.18 and 7.59 ± 2.34 respectively.

Nagpal H et al., [11] reported that among 150 patients of VKC, 110 (73.33%) were males and 40 (26.67%) were females, the highest incidence occurred in the age group 11-15 years. Leonardi A et al., [12] in one of the largest case series of 406 VKC patients from Italy showed a M: F of 3.3: 1; 83% of patients were under 10 years of age, only 4% were aged 20 years or above. Basic eye care, avoidance of allergens or provocative stimuli, and dual-acting topical drugs with antihistamine and mast cell stabilising properties are corner stones of management of mild to moderate cases of VKC [13,14].

A comparative study done by Dudeja I, et al. [15] concluded alcaftadine 0.25%, olopatadine 0.2%, and bepotastine 1.5% eye drops have been proved to be safe and well-tolerated topical medication for allergic conjunctivitis. This study resounded the same, and the medications were found to be safe, with minimal transient side effects of burning sensation and taste impairment noticed by a few patients (more in group 1 and group 3, respectively). Most patients responded to treatment and were willing to continue the eye drop, if indicated. The efficacy of these anti-allergic medications over placebo has been proven in a study conducted by Donshik et al. [16] All three medications showed significant relief in symptoms of redness and itching, which was proved statistically. This study showed that all three study medications provide significant relief in symptoms from baseline to 14 days. Our study was also found the similar results as above findings. In our study, ocular symptom scores and degree of hyperaemia was greatly reduced in group A and C as compared to group A.

A randomised, observer-masked, single-centre, cross-over study comparing the efficacy of bepotastine besilate 1.5% ophthalmic solution versus olopatadine hydrochloride 0.2% ophthalmic solution evaluated by patient preference showed that bepotastine besilate offered significantly better relief of morning and evening itchy/running nose, evening ocular itch and relief of morning and evening ocular allergy symptoms than olopatadine 0.2%. About 66.7% of patients stated that they would prefer bepotastine besilate 1.5% over olopatadine hydrochloride 0.2% to treat allergic conjunctivitis [17].

A study done by Ackerman S, et al. [18] compared 0.25% alcaftadine and 0.2% olopatadine using conjunctival allergen challenge found alcaftadine superior to

olopatadine at the earliest time point (3 min post-challenge). Alcaftadine showed significant relief in chemosis at 16 and 24 h post instillation. Another study done by McLaurin EB, et al., [7] with 284 subjects found that subjects treated with alcaftadine had a lower overall mean itch score of 3, 5, and 7 min than those treated with olopatadine. This study results also showed alcaftadine is better in reducing the allergic conjunctivitis symptoms compared to Olopatadine at 14th day, which is statistically significant ($p = 0.0007$). A comparative study done by McCabe et al. [19] showed bepotastine provided better relief of ocular allergy symptoms and non-ocular symptoms associated with Allergic conjunctivitis, that is, runny nose compared to olopatadine. [20] The study also found that a higher percentage of patients preferred bepotastine over olopatadine for treatment. The current study indicates a greater significant relief of Allergic conjunctivitis symptoms with bepotastine besilate than olopatadine group at 14th day, which was statistically significant ($p = 0.0007$).

Conclusions

This present study concluded that all three medicines (topical olopatadine 0.1%, bepotastine 1.5% and alcaftadine 0.25%) are effective and safe for the treatment of allergic conjunctivitis. While, Bepotastine besilate and alcaftadine are more efficacious as compared to olopatadine for the management of symptoms of allergic conjunctivitis.

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