e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2023; 15(8); 363-367

Original Research Article

Comparative Study of Efficacy of Topical Olopatadine (0.1%), Bepotastine (1.5%) and Alcaftadine (0.25%) in Mild to Moderate Allergic Conjunctivitis

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Received: 15-05-2023 Revised: 19-06-2023 / Accepted: 11-07-2023

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Conflict of interest: Nil

Abstract

Aim: The aim of the present study was to compare the efficacy and safety of Alcaftadine 0.25%, Olopatadine hydrochloride 0.1%, and Bepotastine besilate 1.5% ophthalmic solutions in the treatment of allergic conjunctivitis.

Methods: A prospective study was conducted on 210 patients of allergic conjunctivitis visiting Department of Ophthalmology of a tertiary care hospital in south Bihar after random selection. Randomly generated treatment regimens were sealed within opaque envelopes and were allocated to the patients after obtaining their informed consent. A total of 210 patients were enrolled in this study. All the cases were divided into three groups (Group A, B and C).

Results: Mean age of group A patients was 27.33 ± 10.30 years, group B patients was 29.61 ± 9.31 years and group C was 28.82 ± 9.81 years. There was male predominance in all the three groups. At day 1, Total ocular symptom score (TOSS) of group A, B and C was 7.49 ± 2.48, 7.63 ± 2.28 and 7.56 ± 2.36 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. 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 ($p = 0.0001$). In this present study, degree of hyperaemia was highly significantly decreases 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.

Conclusion: All three topical ophthalmic medications used in the study are safe and effective in the treatment of allergic conjunctivitis. However, Bepotastine and Alcaftadine appear to outweigh Olopatadine in resolving the symptoms of allergic conjunctivitis.

Keywords: Alcaftadine, allergic conjunctivitis, Bepotastine besilate, hyperaemia scale, olopatadine, Total ocular symptom score (TOSS).

Introduction

The conjunctiva of the eye is continually exposed to a variety of airborne antigens that can lead to inflammation, termed allergic conjunctivitis, [1] which is an ocular surface inflammatory disease that affects approximately 40% of the global population. [2] Allergic conjunctivitis is a common allergic disorder estimated to affect up to 15-20% of the population worldwide. [3] Various forms of conjunctivitis such as seasonal allergic conjunctivitis (SAC), perennial allergic conjunctivitis (PAC), vernal kerato conjunctivitis (VKC), atopic kerato conjunctivitis (AKC), and giant papillary conjunctivitis are included in ocular allergy, sharing some common markers of allergy. [4] Allergic response in SAC and PAC results from interaction of allergens with IgE bound to sensitized mast cells. [5] VKC is a chronic allergic inflammation of the ocular surface mediated mainly by Th2- lymphocytes with overexpression of mast cells, eosinophils, neutrophils, Th2 derived cytokines, chemokines, adhesion molecules, growth factors, fibroblasts and lymphocytes. [6]

AKC is the ocular manifestation of systemic altered immune response, often associated with atopic dermatitis and with other allergic disorders such as rhinitis and asthma.

Symptoms of allergic conjunctivitis include itching, redness, watering, foreign body sensation, photophobia and discharge. Patients often present with a papillary reaction of the upper tarsal conjunctiva and limbus ranging in size from 1 mm to giant cobblestone papillae. Pharmacological treatment of allergic conjunctivitis includes H1 receptor blockade, mast cell stabilization, and blocking of cytokine production and prostaglandin formation. [7] Currently, Alcaftadine 0.25% approved once-daily and Bepotastine besilate 1.5% and Olopatadine hydrochloride 0.1% are 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. [8] 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. [1,8]

Alcaftadine is an anti-allergic agent that provides relief from ocular itching by inverse agonistic effects on H1, H2 and H4 receptors in early phase and also stabilizes mast cells by inhibiting release of mediators such as cytokines and lipid mediators in the late phase of an ocular allergic response and decreases chemotaxis, eosinophil activation thereby exerts anti-inflammatory property. [9,10] Bepotastine besilate 1.5% ophthalmic solution is the dual-action agent, which combines strong antihistaminic activity with mast cell-stabilizing properties to provide both rapid and long-lasting relief in allergic conjunctivitis. [11] Considering the paucity of comparative studies between long-acting anti-histamines, efficacy of topical olopatadine (0.1%), bepotastine (1.5%) and alcaftadine (0.25%) in mild to moderate allergic conjunctivitis with regard to efficacy and safety amongst Indian patients, this study was undertaken.

Material & Methods

A prospective study was conducted on 210 patients of allergic conjunctivitis visiting Department of Ophthalmology of a tertiary care hospital in south Bihar. Randomly generated treatment regimens were sealed within opaque envelopes and were allocated to the patients after obtaining their informed consent. This study was conducted after obtaining approval from Institutional Review Board in accordance with the Declaration of Helsinki. A total of 210 patients were enrolled in this study. All the cases were divided into three groups (Group A, B and C).

Exclusion Criteria

Patients with a history of recent ocular surgery or retinal disease, signs of active ocular infection, hypersensitivity to any of the study drugs or its components and pregnant or lactating women were excluded from our study.

Methodology

Patients presenting with symptoms of allergic conjunctivitis with history suggestive of the same were examined with the help of a slit-lamp to look for conjunctival hyperemia, papillary reaction, chemosis, lid edema and corneal epithelial signs. Symptoms such as itching, lacrimation, redness, foreign body sensation and discharge were graded on a 4-point scale wherein 0 denoted no symptoms and 3 denoted severe symptoms.

Signs such as eyelid edema, bulbar conjunctival edema, palpebral hyperemia, papillary reaction and corneal epithelial signs were graded in a similar manner from 0 – 3 wherein 0 denoted absence of signs and 3 denoted severe signs.

Patients of group A were given **olopatadine 0.1%** ophthalmic solution (Winolap DS®, Sun Pharmaceutical Industries Ltd, Mumbai, India) twice daily in the morning and evening.

Patients of group B were given **bepotastine 1.5%** ophthalmic solution (Bepofree®, Mankind Pharma, New Delhi, India) twice daily in the morning and evening.

Patients of group C were given **alcaftadine 0.25%** ophthalmic solution (Alcarex®, Ajanta Pharma, Mumbai, India) once daily in the morning.

First dose was instilled under direct supervision at the time of presentation to note the average time for beginning of itch relief in each patient. Follow-up was done on day 1, day 3, 1 week and at 2 week. Patients who showed minimal or no improvement at the end of one week were prescribed fluorometholone 0.1% thrice daily, tapered gradually over a period of 15 days and were excluded from the study.

Statistical Analysis

All data was analyzed by IBM® SPSS® Statistics ver. 26 (Armonk, NY, USA). Chi square test was applied to compare gender and rural/ urban distribution data between the three groups. Age distribution between the groups was analysed using one-way ANOVA test. Wilcoxon signed rank test was used to do paired analysis of median itch scores at each follow-up visit in each group. Inter-group comparison of median symptom scores and sign scores was done using Kruskal Wallis test. p value less than 0.05 was considered as statistically significant.

Results

Table 1: Demographic profile of Allergic conjunctivitis

Demographic profile		Group A (Mean ± S.D)	Group B (Mean ± S.D)	Group C (Mean ± S.D)
Age		27.33 ± 10.30	29.61 ± 9.31	28.82 ± 9.81
Gender	Male	40 (58.14%)	42 (60%)	36 (51.42%)
	Female	30 (42.86%)	28 (40%)	34 (48.58%)
Total Ocular SymptomsScore (TOSS)		7.43 ± 2.48	7.63 ± 2.22	7.64 ± 2.36

Mean age of group A patients was 27.33 ± 10.30 years, group B patients was 29.61 ± 9.31 years and group C was 28.82 ± 9.81 years. There was male predominance in all the three groups.

Table 2: Ocular Symptoms score at different visit

Visits	Group A	Group B	Group C
Day 1 (Base line)	7.49 ± 2.48	7.63 ± 2.28	7.56 ± 2.36
Day 3	4.8 ± 1.96	5.4± 2.03	4.6 ± 1.82
Day 7	2.5 ± 1.16	2.3 ± 1.01	2.2 ± 1.03
Day 14	0.4 ± 0.43	0.5 ± 0.75	0.3 ± 0.28

At day 1, TOSS of group A, B and C was 7.49 ± 2.48, 7.63 ± 2.28 and 7.56 ± 2.36 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 3: Conjunctival hyperaemia score at different visits

Visits	Group A	Group B	Group C
Day 1 (Base line)	1.5 ± 0.75	1.6 ± 0.86	1.4 ± 0.84
Day 3	1.0 ± 0.73	1.0 ± 0.68	1.8 ± 0.58
Day 7	0.2 ± 0.28	0.2 ± 0.28	0.2 ± 0.29
Day 14	0.007 ± 0.06	0.04 ± 0.16	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	20	3	5	45	1
Group B	22	3	5	44	1
Group C	21	7	6	42	0
Visit 2nd					
Group A	20	5	21	21	1
Group B	23	5	23	24	1
Group C	22	3	20	20	1
Visit 3rd					
Group A	20	39	5	1	1
Group B	18	38	6	3	2
Group C	19	42	5	1	1
Visit 4th					
Group A	62	3	1	1	1
Group B	57	8	1	1	1
Group C	63	3	1	1	1

In this present study, degree of hyperaemia was highly significantly decreases 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.

Discussion

Allergic conjunctivitis represents one of the most common ocular conditions encountered in clinical practice. It is an ocular manifestation of IgE immune responses to allergen exposure in sensitized individuals. [12] It can be classified as seasonal allergic conjunctivitis (SAC), perennial allergic conjunctivitis(PAC), vernal keratoconjunctivitis (VKC), atopic keratoconjunctivitis (AKC) and giant papillary conjunctivitis. Allergic response in SAC and PAC results from interaction of allergens with IgE bound to sensitized mast cells. [13] AKC is the ocular manifestation of systemic altered immune response, often associated with atopic dermatitis and with other allergic disorders such as rhinitis and asthma.

Mean age of group A patients was 27.33 ± 10.30 years, group B patients was 29.61 ± 9.31 years and

group C was 28.82 ± 9.81 years. There was male predominance in all the three groups. At day 1, TOSS of group A, B and C was 7.49 ± 2.48, 7.63 ± 2.28 and 7.56 ± 2.36 respectively. Nagpal H et al [14] reported that among, most patients responded to treatment and were willing to continue the eye drop, if indicated. 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 [15] 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. [16,17]

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. 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 ($p = 0.0001$). A comparative study done by Dudeja I, et al. concluded Alcaftadine 0.25%, olopatadine 0.1%, and bepotastine 1.5% eye drops have been proved to be safe and well-tolerated topical medication for allergic conjunctivitis. [18] 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). A study done by Ackerman S, et al. compared 0.25% Alcaftadine and 0.1% 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. [19] Another study done by McLaurin EB, et al., 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. [8]

A randomised, observer-masked, single Centre, cross-over study comparing the efficacy of bepotastine besilate 1.5% ophthalmic solution versus olopatadine hydrochloride 0.1% 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 0.1%. About 66.7% of patients stated that they would prefer bepotastine besilate 1.5% over olopatadine hydrochloride 0.1% to treat allergic conjunctivitis. [20] In this present study, degree of hyperaemia was highly significantly decreases 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.

Conclusion

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. Bepotastine besilate and alcaftadine are more efficacious as compared to olopatadine for the management of symptoms of allergic conjunctivitis.

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