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

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

International Journal of Current Pharmaceutical Review and Research 2024; 16(2); 132-136

Original Research Article

A Prospective Single Centre Clinical Trial Assessing Alcaftadine (0.25%) with Olopatadine (0.2%) in Allergic Conjunctivitis

Sujata Kumari[1], Gautam Garg[2], Naveen Kumar[3], Sunil Kumar[4]

[1]Senior Resident, Department of Ophthalmology, Patna Medical College and Hospital, Patna, Bihar, India

[2]Senior Resident, Department of Ophthalmology, Patna Medical College and Hospital, Patna, Bihar, India

[3]Assistant Professor, Department of Ophthalmology, Patna Medical College and Hospital, Patna, Bihar, India

[4]Professor, Department of Ophthalmology, Patna Medical College and Hospital, Patna, Bihar, India

Received: 18-11-2023 Revised: 25-12-2023 Accepted: 20-01-2024
Corresponding author: Dr. Gautam Garg
Conflict of interest: Nil

Abstract

Aim: The aim of the present study was to compare the alcaftadine (0.25%) with olopatadine (0.2%) in allergic conjunctivitis.

Methods: This was a prospective, observer masked, single centre clinical trial conducted in the Department of Ophthalmology for the period of one year.adhered to the principles of the declaration of Helsinki. Informed consent was obtained from all the participants. 200 patients were enrolled in the study.

Results: 100 patients received alcaftadine 0.25 % eye drop and 100 patients received olopatadine 0.2 % eye drop. Mean age of alcaftadine 0.25 % treated group was 26 ± 5.65 years and that of olopatadine 0.2 % treated group was 26.4 ± 6.84 years. Number of males in alcaftadine treated group and olopatadine treated group are 80 and 76 respectively and number of females are 20 and 24 respectively. In alcaftadine 0.25 % treated group, at the time of presentation, mild, moderate, moderately severe and severe cases were 52 (52%), 42 (42%), 6 (6%) and 0 respectively. Similarly, in olopatadine 0.2 % treated group, at the time of presentation, mild, moderate, moderately severe and severe cases were 78 (78%), 15 (15%), 7 (7%) and 0 respectively. Mean severity scores at presentation in both alcaftadine and olopatadine group were comparable with no significant difference (p- value = 0.154, statistically not significant). Both the drugs showed downward shift in mean severity score which was greater in alcaftadine treated group than in olopatadine treated group. Mean reduction in severity score was higher in alcaftadine treated group at both 1 week and 2 weeks post treatment and the difference were statistically significant.

Conclusion: In our study, alcaftadine 0.25 % eye drops showed higher efficacy than olopatadine 0.2 % eye drops in relieving ocular signs and symptoms at both 1 week and 2 weeks follow up. Both drugs were found to be safe and well tolerated. Further research is required to understand the basic factors and reasons responsible for these differences in efficacy between the two treatment arms.

Keywords: Allergic conjunctivitis, Olopatadine, Alcaftadine

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] It is predominantly Ig E-mediated Type I hypersensitivity reaction where allergen binds to specific Ig E molecules, triggers mast cell degranulation and subsequent increase in histamine leading to activation of both H1 and H2 types of histamine receptors. [3] Pharmacological treatment of allergic conjunctivitis includes H1 receptor blockade, mast cell stabilization, and blocking of cytokine production and prostaglandin formation. [4]

Currently, 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. [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. [1,5]

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. [6,7] 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. [8]

Allergic conjunctivitis is mediated by immunoglobulin E-activated degranulation of mast cells and the release of a cascade of inflammatory mediators, including histamine, in response to allergens. [9,10] Histamine release and activation of histamine H1 receptors in the conjunctiva leads to ocular itching, while stimulation of H2 receptors on the ocular surface results in vasodilation and is associated with ocular redness, eyelid swelling, and chemosis. [11,12] Recent evidence suggests that histamine binding to and activation of H4 receptors also play a role in allergic conjunctivitis. [13,14]

The aim of the present study was to compare the alcaftadine (0.25%) with olopatadine (0.2%) in allergic conjunctivitis.

Materials and Methods

This was a prospective, observer masked, single centre clinical trial conducted in the Department of Ophthalmology, Patna Medical College and Hospital and Multicentric Hospital, Patna, Bihar, India for the period of one year. adhered to the principles of the declaration of Helsinki. Informed consent was obtained from all the participants. 200 patients were enrolled in the study.

Study Eligibility Criteria

Key inclusion criteria included subjects' age more than 18 years having a positive history of ocular allergies and having a best corrected visual acuity of 6 / 12 or better in each eye. Subjects should have no history of wearing contact lens for at least three days before and during the study period.

Key exclusion criteria included subjects who have undergone any ocular surgical intervention within three months; subjects who have used aspirin, or related products, or H1-antagonist antihistamines within 72 hours; corticosteroids or mast cell stabilising drugs within 14 days, and immunotherapeutic agents; subjects who used any other topical eye drops (including ocular lubricants) other than the drugs under study within 72 hours; or subjects who used any investigational medications or devices within 30 days of the study; or patients with known hypersensitivity to olopatadine and alcaftadine including benzalkonium chloride which is used as preservative in the ophthalmic solutions were excluded. Pregnancy and lactation were also exclusion criteria of the study.

Clinical Grading Systems

Grading system for clinically classifying the patient into different categories, was structured with reference to suggested grading systems by dos Santos et al [15] Uchio et al [16] and Atzin Robles-Contreras et al. [17]

Primary Outcome

Reduction in total severity score at subsequent visits was taken as primary outcome of drug and efficacy was measured as mean difference between severity score at two different visits for all the patients in that treatment group.

Statistic al Analysis

Data analysis was done using Microsoft Excel and GraphPad statistical calculator. Descriptive data were presented as mean and standard deviation for quantitative data and frequency for qualitative data. Tests of significance included independent t-test for quantitative data (age distribution, severity score and reduction in severity score in both treatment groups) and chi-squared test for qualitative data (sex distribution in both treatment groups and number of patients improved by either drug in mild and moderate category). All p-values were two-tailed at a significance level of 0.05. Total severity score was calculated at each visit and categorised as mild: 1 – 9, moderate: 10 – 18, moderately severe: 19 – 27 and severe: 28 - 36.

Results

Table 1: Patient Demographics in Two Treatment Groups

Alcaftadine 0.25 %		Olopatadine 0.2 %	P-Value
Age in Years (Mean ± SD)	26 ± 5.65	26.4 ± 6.84	0.48
Male	80	76	0.72
Female	20	24	

100 patients received alcaftadine 0.25 % eye drop and 100 patients received olopatadine 0.2 % eye drop. Mean age of alcaftadine 0.25 % treated group was 26 ± 5.65 years and that of olopatadine 0.2 % treated group was 26.4 ± 6.84 years. Number of males in alcaftadine treated group and olopatadine treated group are 80 and 76 respectively and number of females are 20 and 24 respectively.

Table 2: Grades of severity score of Alcaftadine 0.25 % Treated Group and Olopatadine 0.2 % Treated Group at the Time of Presentation

Grades At the time of presentation	Alcaftadine 0.25 %	Olopatadine 0.2 %
Mild	52	78
Moderate	42	15
Moderately severe	6	7
Severe	0	0

In alcaftadine 0.25 % treated group, at the time of presentation, mild, moderate, moderately severe and severe cases were 52 (52%), 42 (42%), 6 (6%) and 0 respectively. Similarly, in olopatadine 0.2 % treated group, at the time of presentation, mild, moderate, moderately severe and severe cases were 78 (78%), 15 (15%), 7 (7%) and 0 respectively.

Table 3: Mean Severity Scores of Alcaftadine 0.25 % Treated Group and Olopatadine 0.2 % Treated Group at the Time of Presentation, after 1 Week and after 2 Weeks

Time of Assessment	Alcaftadine 0.25 %	Olopatadine 0.2 %	P-Value
At Time of Presentation	9.31 ± 4.82	8 ± 4.72	0.154
After 1 Week	4.06 ± 3.52	3.82 ± 3.55	
After 2 Weeks	0.86 ± 1.34	1.08 ± 1.54	

Mean severity scores at presentation in both alcaftadine and olopatadine group were comparable with no significant difference (p- value = 0.154, statistically not significant). Both the drugs showed downward shift in mean severity score which was greater in alcaftadine treated group than in olopatadine treated group.

Table 4: Mean Reduction in Severity Score of Alcaftadine 0.25 % Treated Group and Olopatadine 0.2 % Treated Group after 1 Week and after 2 weeks

Treatment Groups	At 1 Week Mean Reduction± SD	At 2 Weeks Mean Reduction± SD
Alcaftadine 0.25 %	5.255 ± 2.428	8.382 ± 4.176
Olopatadine 0.2 %	4.156 ± 2.936	6.954 ± 4.386
P Value	0.0220	0.0482

Mean reduction in severity score was higher in alcaftadine treated group at both 1 week and 2 weeks post treatment and the difference were statistically significant.

Discussion

Ocular allergy is a commonly encountered pathology in clinical practice, with an increase in the number of patients noticed in the last decade with a prevalence of approximately 40% of the population globally. Avoidance of allergens plays a key role in the prevention of allergic conjunctivitis. Addition of anti-histamine reduces inflammation, whereas mast cell stabilizers prevent mast cell degranulation on an exposure to allergens. Topical corticosteroids are the most potent agents to control inflammatory symptoms of allergic conjunctivitis but there is a risk of many side-effects. Mast cells release histamine which is responsible for early acute phase of allergies and pro-inflammatory mediators like prostaglandins, leukotrienes etc. which are responsible for the late phase. [18] Activation of H1 receptors on conjunctival neurons causes itching [19] while that of H1 and H2 receptors on vascular endothelium is responsible for vasodilation (appearing as redness) and endothelial swelling. [20,21] Itching and inflammation is caused by response of H4 receptors on immune and inflammatory cells. [22-24]

100 patients received alcaftadine 0.25 % eye drop and 100 patients received olopatadine 0.2 % eye drop. Mean age of alcaftadine 0.25 % treated group was 26 ± 5.65 years and that of olopatadine 0.2 % treated group was 26.4 ± 6.84 years. Number of males in alcaftadine treated group and olopatadine treated group are 80 and 76 respectively and number of females are 20 and 24 respectively. In alcaftadine 0.25 % treated group, at the time of presentation, mild, moderate, moderately severe and severe cases were 52 (52%), 42 (42%), 6 (6%) and 0 respectively. Similarly, in olopatadine 0.2 % treated group, at the time of presentation, mild, moderate, moderately severe and severe cases were 78 (78%), 15 (15%), 7 (7%) and 0 respectively. Ackerman et al [25] showed better results with alcaftadine 0.25 % than olopatadine 0.2 % in relief of itching in ocular

allergy. In a previous study, Greiner et al [26] showed that alcaftadine had earlier onset of action than olopatadine, and also its effects were more sustained compared to olopatadine. Ono SJ et al [27] in his study on murine model of allergic conjunctivitis demonstrated greater reduction of eosinophilic recruitment and higher zonula occludens stability for alcaftadine than olopatadine. Contreras-Ruiz L et al[28] in his study on corneal epithelial barriers, suggested the cause of these observed clinical differences to be greater efficacy of alcaftadine in preventing allergen-activated disruption of the epithelial barriers.

Mean severity scores at presentation in both alcaftadine and olopatadine group were comparable with no significant difference (p- value = 0.154, statistically not significant). Both the drugs showed downward shift in mean severity score which was greater in alcaftadine treated group than in olopatadine treated group. Mean reduction in severity score was higher in alcaftadine treated group at both 1 week and 2 weeks post treatment and the difference were statistically significant. A study by Nakatani et al [29] revealed that alcaftadine 0.25% dosed 8 h before allergen challenge was found to be effective or superior in preventing ocular signs and symptoms of Japanese cedar pollen-induced allergic conjunctivitis, compared to olopatadine 0.2% ophthalmic solution (challenged 4 h post dose). The results of the study showed statistical significance in reduction of ocular itching score and conjunctival hyperemia scale in alcaftadine 0.25% group compared to olopatadine 0.2% group. In pooled analysis of two multicenter, randomized clinical trials, done by McLaurin et al [30] revealed that alcaftadine and olopatadine hydrochloride was superior to placebo at relieving ocular itching alcaftadine 0.25% ophthalmic solution provided greater relief at 16 h post administration and significantly lower mean itch score at 3 min post CAC with similar safety profile, compared to olopatadine hydrochloride 0.2%

Conclusion

In our study, alcaftadine 0.25 % eye drops showed higher efficacy than olopatadine 0.2 % eye drops in relieving ocular signs and symptoms at both 1 week and 2 weeks follow up. Both drugs were found to be safe and well tolerated. Further research is required to understand the basic factors and reasons responsible for these differences in efficacy between the two treatment arms.

References

1. Gong L, Sun X, Qu J, Wang L, Zhang M, Zhang H, Wang L, Gu Y, Elion-Mboussa A, Roy L, Zhu B. Loteprednol etabonate suspension 0.2% administered QID compared with olopatadine solution 0.1% administered BID in the treatment of seasonal allergic conjunctivitis: a multicenter, randomized, investigator-masked, parallel group study in Chinese patients. Clin Ther. 2012 Jun;34(6): 1259-1272.e1.
2. Chigbu DI, Coyne AM. Update and clinical utility of alcaftadine ophthalmic solution 0.25% in the treatment of allergic conjunctivitis. Clin Ophthalmol. 2015 Jul 8;9: 1215-25.
3. Ackerman S, D'Ambrosio F Jr, Greiner JV, Villanueva L, Ciolino JB, Hollander DA. A multicenter evaluation of the efficacy and duration of action of alcaftadine 0.25% and olopatadine 0.2% in the conjunctival allergen challenge model. J Asthma Allergy. 2013 Apr 8;6:43-52.
4. Borazan M, Karalezli A, Akova YA, Akman A, Kiyici H, Erbek SS. Efficacy of olopatadine HCI 0.1%, ketotifen fumarate 0.025%, epinastine HCI 0.05%, emedastine 0.05% and fluorometholone acetate 0.1% ophthalmic solutions for seasonal allergic conjunctivitis: a placebo-controlled environmental trial. Acta Ophthalmol. 2009 Aug;87(5):549-54.
5. McLaurin EB, Marsico NP, Ackerman SL, Ciolino JB, Williams JM, Villanueva L, Hollander DA. Ocular itch relief with alcaftadine 0.25% versus olopatadine 0.2% in allergic conjunctivitis: pooled analysis of two multicenter randomized clinical trials. Adv Ther. 2014 Oct;31(10):1059-71.
6. Gallois-Bernos AC, Thurmond RL. Alcaftadine, a new antihistamine with combined antagonist activity at histamine H1, H2, and H4 receptors. Journal of Receptor, Ligand and Channel Research. 2012 Dec 20:9-20.
7. Meena MK, Gupta VA. 0.25% versus olopatadine 0.2% in allergic conjunctivitis. Int J Sci Res. 2018;7:53.
8. McCabe CF, McCabe SE. Comparative efficacy of bepotastine besilate 1.5% ophthalmic solution versus olopatadine hydrochloride 0.2% ophthalmic solution evaluated by patient preference. Clin Ophthalmol. 2012; 6:1731-8.
9. Leonardi A, De Dominicis C, Motterle L. Immunopathogenesis of ocular allergy: a schematic approach to different clinical entities. Current opinion in allergy and clinical immunology. 2007 Oct 1;7(5):429-35.
10. Ono SJ, Abelson MB. Allergic conjunctivitis: update on pathophysiology and prospects for future treatment. Journal of Allergy and Clinical Immunology. 2005 Jan 1;115(1):118-22.
11. Abelson MB, Udell IJ. H2-receptors in the human ocular surface. Archives of Ophthalmology. 1981 Feb 1;99(2):302-4.
12. Bielory L, Ghafoor S. Histamine receptors and the conjunctiva. Current opinion in allergy and clinical immunology. 2005 Oct 1;5(5):437-40.
13. Nakano Y, Takahashi Y, Ono R, Kurata Y, Kagawa Y, Kamei C. Role of histamine H4

receptor in allergic conjunctivitis in mice. European journal of pharmacology. 2009 Apr 17;608(1-3):71-5.
14. Zampeli E, Thurmond RL, Tiligada E. The histamine H 4 receptor antagonist JNJ7777120 induces increases in the histamine content of the rat conjunctiva. Inflammation Research. 2009 Jun;58:285-91.
15. Dos Santos MS, Alves MR, de Freitas D, et al. Ocular allergy Latin American consensus. Arq Bras Oftalmol 2011;74(6):452-456.
16. Uchio E, Kimura R, Migita H, et al. Demographic aspects of allergic ocular diseases and evaluation of new criteria for clinical assessment of ocular allergy. Graefes Arch Clin Exp Ophthalmol 2008;246(2):291- 296.
17. Robles-Contreras A, Santacruz C, Ayala J, Bracamontes E, Godinez V, Estrada-García I, Estrada-Parra S, Chávez R, Perez-Tapia M, Bautista-De Lucio VM, Jiménez-Martínez MC. Allergic conjunctivitis: an immunological point of view. Conjunctivitis-A Complex and Multifaceted Disorder. Zdenek Pelikan (Ed.) Intech Open Access Publisher (Rijeka–Croatia). 2011 Nov 23:33-56.
18. Church MK, McGill JI. Human ocular mast cells. Curr Opin Allergy Clin Immunol 2002; 2(5):419-422.
19. Abelson MB, Udell IJ. H2-receptors in the human ocular surface. Arch Ophthalmol 1981;99(2):302-304.
20. Abelson MB, Loffler O. Conjunctival allergen challenge: models in the investigation of ocular allergy. Curr Allergy Asthma Rep 2003;3(4): 363-368.
21. Nakano Y, Takahashi Y, Ono R, et al. Role of histamine H(4) receptor in allergic conjunctivitis in mice. Eur J Pharmacol 2009; 608(1-3):71-75.
22. Thurmond RL, Gelfand EW, Dunford PJ. The role of histamine H1 and H4 receptors in allergic inflammation: The search for new antihistamines. Nat Rev Drug Discov 2008; 7(1):41-53.
23. Zampeli E, Thurmond RL, Tiligada E. The histamine H4 receptor antagonist JNJ7777120 induces increases in the histamine content of the rat conjunctiva. Inflamm Res 2009;58(6):285-291.
24. Kenji O Ken-Ichi H, Toshihiko K, et al. Pharmacological, pharmacokinetic and clinical properties of olopatadine hydrochloride, a new antiallergic drug. Jpn J Pharmacol 2002; 88(4):379-397.
25. Ackerman S, D'Ambrosio Jr F, Greiner JV, Villanueva L, Ciolino JB, Hollander DA. A multicenter evaluation of the efficacy and duration of action of alcaftadine 0.25% and olopatadine 0.2% in the conjunctival allergen challenge model. Journal of asthma and allergy. 2013 Apr 8:43-52.
26. Greiner JV, Edwards-Swanson K, Ingerman A. Evaluation of alcaftadine 0.25% ophthalmic solution in acute allergic conjunctivitis at 15 minutes and 16 hours after instillation versus placebo and olopatadine 0.1%. Clinical Ophthalmology. 2011 Jan 13:87-93.
27. Ono SJ, Lane K. Comparison of effects of alcaftadine and olopatadine on conjunctival epithelium and eosinophil recruitment in a murine model of allergic conjunctivitis. Drug Design, Development and Therapy. 2011 Feb 8:77-84.
28. Contreras-Ruiz L, Schulze U, García-Posadas L, Arranz-Valsero I, López-García A, Paulsen F, Diebold Y. Structural and functional alteration of corneal epithelial barrier under inflammatory conditions. Current eye research. 2012 Nov 1;37(11):971-81.
29. Nakatani H, Gomes P, Bradford R, Guo Q, Safyan E, Hollander DA. Alcaftadine 0.25% versus Olopatadine 0.1% in preventing cedar pollen allergic conjunctivitis in Japan: a randomized study. Ocular Immunology and Inflammation. 2019 May 19;27(4):622-31.
30. McLaurin EB, Marsico NP, Ackerman SL, Ciolino JB, Williams JM, Villanueva L, Hollander DA. Ocular itch relief with alcaftadine 0.25% versus olopatadine 0.2% in allergic conjunctivitis: pooled analysis of two multicenter randomized clinical trials. Advances in therapy. 2014 Oct;31:1059-71.