Original research article

Efficacy of 0.1% Olopatadine Hydrochloride and 0.5% Ketorolac Tromethamine in the Treatment of Seasonal Allergic Conjunctivitis

Dr. Md Idris Akbani

Associate Professor, Department of Ophthalmology, RIMS, Adilabad.

Corresponding Author: Dr. Md Idris Akbani; Email: mohdidrisakbani@yahoo.com

Abstract

Background: Allergic conjunctivitis is a common allergic ocular disorder that leads to itching and discomfort. The current study is aimed to compare the clinical efficacy and therapeutic effects of 0.1% olopatadine hydrochloride to that of 0.5% ketorolac tromethamine ophthalmic solution with different pharmacological mechanisms in the management of seasonal allergic conjunctivitis.

Methods: Based on the inclusion and exclusion criteria a total of n=100 cases were selected by convenient sampling; they were randomly and equally allotted into two groups. Group I (received 0.1% Olopatadine hydrochloride) and group II (received 0.5% Ketorolac tromethamine). All the patients underwent thorough ocular examination that included visual acuity, slit-lamp Bio-microscopy to evaluate conjunctival and corneal involvement. IOP was measured with a non-contact tonometer. Fundus examination was done using indirect ophthalmoscopy.

Results: The comparison of improvement of itching scores at different intervals was done and the p-values were found to be significant at the interval of 30 minutes and 2 days. This shows that rapid improvement of symptoms was found in group I (Olopatadine) as compared to group II (Ketorolac). For improvement of hyperemia scores at different follow-up visits was done and the p-values were found to be significant at the interval of 30 minutes only and the values were not found to be significant at the 2nd day and at the 7th day. Both drugs are equally effective for hyperemia management at follow-up intervals.

Conclusion: The present study found 0.1% Olopatadine eyedrops were more effective and elicited quicker response as compared to 0.1% Ketorolac eye drops. The efficacy of both was similar at the end of 14 days of treatment. Minor side effects were observed in two patients of the Ketorolac group and no side effects were observed in the olopatadine group. Therefore, while choosing treatment for seasonal allergic conjunctivitis due consideration must be given to costs, side effects, and patient compliance.

Keywords: Seasonal Allergic conjunctivitis, Olopatadine eyedrops, Ketorolac eye drops, itching, hyperemia.

Introduction

Allergic conjunctivitis refers to a group of hypersensitivity disorders involving the eyelid, conjunctiva, and cornea having common pathogenesis. [1] The important clinical manifestation of the condition is itching, redness, tearing, swelling, burning, sensation of fullness in the eye leading to rubbing of eye, sometimes blurred vision, mucus discharge, chemosis, and lid edema. [2, 3] It is a type I hypersensitivity reaction mediated by IgE in response to airborne allergens such as pollen, grass, weeds, and animal dander. [4] Mast cells play an important role in the pathophysiology of the condition. [5, 6] The binding of specific allergen to sensitized cells in the conjunctiva leads to degranulation of the mast cells with a release of preformed histamine, eosinophil chemotactic factors, tryptase, prostaglandins, and leukotrienes causing the signs and symptoms of seasonal allergic conjunctivitis. [7] The primary treatment is avoidance of allergens and removal of offending allergen source or changing of occupational areas. Symptomatic relief can be provided by cold compresses especially in ocular pruritis. Artificial lubrication may aid in the removal or dilution of allergen which has come in contact with the ocular surface. Tear substitutes consist of saline combined with a wetting and viscosity agent such as methylcellulose or polyvinyl alcohol may be used. [8] The main aim of the pharmacological intervention is the prevention of degranulation of mast cells in allergy. Topically applied ophthalmic agents are the principal treatment method for allergic conjunctivitis. Frequently used topical drugs include H_1 antihistamines, mast cell stabilizers non-steroidal anti-inflammatory drugs, and steroids. Olopatadine is a novel drug that has been shown clinically to have therapeutic value in the treatment of allergic conjunctivitis. [9, 10] Olopatadine possesses a dual action with limited mast-cell stabilizing effects and H_1 receptor binding. [11, 12] Comparing it with the 1st generation antihistamines, olopatadine was found to inhibit cytokine secretion including the release of tumor necrosis factor-alpha from human conjunctival mast cells. [11-13] Ketorolac tromethamine 0.5% ophthalmic solution is a very potent NSAID that inhibits the enzyme cyclooxygenase and decreases the synthesis of prostaglandins. [14] With this background, we in this study tried to evaluate the Efficacy of 0.1% Olopatadine hydrochloride and 0.5% Ketorolac Tromethamine in the treatment of seasonal allergic conjunctivitis.

Material and Methods

This cross-sectional study was conducted in the Department of Ophthalmology, Rajiv Gandhi Institute of Medical Sciences [RIMS], Adilabad. Institutional Ethical committee permission was obtained for the study. Written consent was obtained from all the participants of the study.

Inclusion Criteria

1. Patients diagnosed with allergic conjunctivitis
2. Patients with palpebral or bulbar conjunctival manifestations or both
3. Aged > 18 years
4. Males and Females

Exclusion criteria

1. Presence of active bacterial or viral conjunctivitis, or any infective etiology.
2. Patients with other co-existing ocular conditions like keratitis, scleritis, and uveitis.
3. Patients with ocular herpes.
4. Pregnant or lactating mothers.
5. Patients with known or suspected immuno-compromised status.

Based on the inclusion and exclusion criteria a total of n=100 cases were selected by convenient sampling; they were randomly and equally allotted into two groups. Group I (received 0.1% Olopatadine hydrochloride) and group II (received 0.5% Ketorolac tromethamine). All the

patients underwent thorough ocular examination that included visual acuity, slit-lamp biomicroscopy to evaluate conjunctival and corneal involvement. IOP was measured with a non-contact tonometer. Fundus examination was done using indirect ophthalmoscopy. Ocular hyperemia was assessed in three-vessel beds: conjunctival, ciliary, and episcleral. They were graded using a scale ranging from 0(none) to 4(maximum). Ocular itching was recorded with 0(none) to 4(severe). Similarly the chemosis scores were analyzed including the lid edema scores. These readings were taken by a single observer at the first visit in 30 minutes after instilling eye drops and follow-up visits at the 2nd day, 7 days, and 14 days. The patients were advised to instill drops twice daily. Response to treatment was evaluated at the end of 14 days. Any adverse reactions were also recorded. Statistical analysis: All the available data was uploaded on an MS Excel spreadsheet and analyzed by SPSS version 19 in windows format. Continuous variables were represented as mean and standard deviations and categorical variables were represented as percentage and p-value of <0.05 was considered as significant.

Results

A total of n=27(54%) males and n=23(46%) females were included in group I (Olopatadine group) and in group II (Ketorolac) n=26(52%) males and n=24(48%) females were included. The overall involvement of males in both groups combined was slightly more 53% as compared to females. The common age group of involvement was 21 – 30 years with 49% of patients of both groups. The mean age group of the population was 24.5 years ± 4.5 years. The demographic profile of the cases and their distribution is given in detail in table 1.

Table 1: Demographic profile of the patients included in the study

Age group	*Group I (N=50)*		*Group II (N=50)*	
	Male	*Female*	*Male*	*Female*
18 – 20	08	06	07	05
21 – 25	07	07	08	08
26 – 30	06	03	04	06
31 – 35	03	04	04	04
36 – 40	03	03	03	01
Total	27	23	26	24

The eye drops were instilled in both groups of patients and itching scores were observed. In group I (Olopatadine group) we found 58% of cases were having improvement in itching symptoms at 30 minutes intervals. For group II (Ketorolac) the improvement in itching scores was found in 36% of patients at the end of 30 minutes. Similarly, the itching scores were obtained at the first follow-up visit at 2 days which showed 70% improvement in scores in group I as compared to 52% in group II. At the next follow-up visit at 7 days and at 14 days the improvement of itching symptoms was found in all the 100% cases of both the groups' details depicted in table 2. The Ocular hyperemia was assessed in three-vessel beds: conjunctival, ciliary, and episcleral. They were graded using a scale ranging from 0(none) to 4(maximum).

The improvement of hyperemia scores in both groups is given in table 2. The mean pre-treatment scores for itching be 1.90 ± 0.34 in group I and 2.01 ± 0.54 in group II cases. Similarly, the mean scores for hyperemia in group I were 1.99 ± 0.72, and group II were 1.95 ± 0.61. A critical examination of table 2 reveals the improvement was comparatively faster in group I (Olopatadine) as compared to group II (Ketorolac) however, the improvement was found in all the 100% cases of both groups at the end of 14 days.

Table 2: Improvement in itching scores and hyperemia scores in two groups

	Improvement in Itching scores			
Groups	At 30 minutes	2 days	7 days	At 14 days
Group I (Olopatadine)	58%	70%	98%	100%
Group II (Ketorolac)	36%	52%	90%	100%
	Improvement in hyperemia			
Groups	At 30 minutes	2 days	7 days	At 14 days
Group I (Olopatadine)	52%	68%	96%	100%
Group II (Ketorolac)	30%	54%	90%	100%

The comparison of improvement of itching scores at different intervals was done by using a t-test for paired observations. The p-values were found to be significant at the interval of 30 minutes and 2 days. This shows that rapid improvement of symptoms was found in group I (Olopatadine) as compared to group II (Ketorolac). Although, at 14 days the improvement was observed in all cases of both the groups (Table 3). A comparative analysis of the improvement of hyperemia scores at different follow-up visits was done by using a t-test for paired observations. The p-values were found to be significant at the interval of 30 minutes only and the values were not found to be significant on the 2nd day and the 7th day depicted in table 3. This shows that although hyperemia improvement is quick in group I both drugs are equally effective for hyperemia management at follow-up intervals.

Table 3: Comparison of itching scores and hyperemia scores improvement in both groups

Itching Improvement	Group I	Group II	Group I	Group II	Group I	Group II
	58	36	70	52	98	90
Interval	30 minutes		2 days		7 days	
Chi-square	5.012		4.986		1.25	
p-values	0.0121*		0.033*		0.531	
Hyperemia Improvement	Group I	Group II	Group I	Group II	Group I	Group II
	52	30	68	54	96	90
Interval	30 minutes		2 days		7 days	
Chi-square	4.861		1.98		1.02	
p-values	0.023*		0.154		0.867	

The improvement in chemosis and lid edema scores in the two groups has been depicted in table 4. The mean pre-treatment scores of chemosis in group I was 2.01 ± 0.82 and in group II the scores were 2.05 ± 9.02. The mean pre-treatment scores for lid edema were 1.85 ± 0.53 and group II was 1.79 ± 0.42. A critical analysis of the table reveals early improvement in a greater

number of cases with chemosis was seen in group I as compared to group II although the overall improvement at the end of 14 days was the same in both groups.

Table 4: Improvement in chemosis and lid edema scores in two groups

	Improvement in Chemosis			
Groups	At 30 minutes	2 days	7 days	At 14 days
Group I (Olopatadine)	62%	74%	98%	100%
Group II (Ketorolac)	40%	58%	92%	100%
	Improvement in Lid edema			
Groups	At 30 minutes	2 days	7 days	At 14 days
Group I (Olopatadine)	46	68	82	100
Group II (Ketorolac)	38	52	76	100

The comparative analysis of both groups at different time intervals revealed a significant improvement in chemosis scores in group I at the interval of 30 minutes and 2 days similarly the improvement in lid edema was slightly better in group I as compared to group II however the improvement was not found to be significant at any interval of time between both groups depicted in table 5.

Table 5: comparison of Chemosis and lid edema scores improvement in both groups

Chemosis	Group I	Group II	Group I	Group II	Group I	Group II
	62	40	74	58	98	92
Interval	30 minutes		2 days		7 days	
Chi-square	4.023		3.98		1.00	
p-values	0.031*		0.041*		0.912	
Lid edema	Group I	Group II	Group I	Group II	Group I	Group II
	46	38	68	52	82	76
Interval	30 minutes		2 days		7 days	
Chi-square	1.022		1.36		1.86	
p-values	0.236		0.158		0.712	

The safety profile of both drugs was analyzed in both groups by parameters which included Intra Ocular pressure changes, visual acuity changes, fundoscopy changes headache, or any adverse reaction. In this study, we found in group II n=2 patients reporting mild stinging sensation during the first follow-up visit but the symptoms were mild and self-limiting and disappeared after one week.

Discussion

Allergic conjunctivitis is often a bilateral self-limiting inflammatory process characterized by IgE mediated immune response to immediate hypersensitivity from direct exposure to the allergen with the conjunctival sac in sensitized patients leading to activation of mast cells and release of different mediators of allergy. [15, 16] The important symptoms of allergic conjunctivitis include tearing, photophobia, blurry vision, foreign body sensation, redness, and itching. The presence of itching is a distinctive indicator of allergic conjunctivitis. [16] The initial treatment approach for allergic conjunctivitis is to irrigate dilute and remove allergens from the ocular surface. [17, 18] The pharmacological treatment of allergic conjunctivitis are topical decongestants, antihistamines, mast cell stabilizers, and Non-steroidal anti-inflammatory agents. [17-19] In the current study we estimated the topical eye drop application of Olopatadine and Ketorolac in the group of patients diagnosed with allergic conjunctivitis. The mean age of our cohort was 24.5 years ± 4.5 years. Yaylali et al., [7] in a similar study

found the mean age of the population with allergic conjunctivitis was 19 years. This indicates the young population is commonly affected by this condition. Sarker et al., [20] studying allergic conjunctivitis in n=92 patients found 42-45% were male patients and the mean age was 28 ± 12 and 28 ± 11 years agreeing with observations of the current study. The mean scores of the clinical parameters were computed for each examination, like in our study it was itching, hyperemia, chemosis, and lid edema. In this study, we found the mean pre-treatment scores for itching to be 1.90 ± 0.34 in group I and 2.01 ± 0.54 in group II cases. Similarly, the mean scores for hyperemia in group I were 1.99 ± 0.72, and group II were 1.95 ± 0.61. The mean pre-treatment scores of chemosis in group I was 2.01 ± 0.82 and in group II the scores were 2.05 ± 9.02. The mean pre-treatment scores for lid edema were 1.85 ± 0.53 and group II was 1.79 ± 0.42. The baseline parameters were comparable in both groups. Sarker et al., [20] have similarly shown the mean pre-treatment scores for hyperemia, tearing, itching and photophobia were similar in both the Ketotifen group and Olopatadine group. Table 3 of this study shows significant improvement in itching symptoms at 30 minutes and 2 days in the olopatadine group. Hyperemia improvement was significant at 30 minutes in the olopatadine group. AJ Aguilar et al., [21] found a 42.5% to 62.5% improvement of symptoms in the olopatadine group at 0 minutes and 30 minutes. And 57.5% to 75% of patients showed improvement at 2 days and the end of 7 days, the improvement was seen in 80% to 87.5% cases. Deschenes et al., [22] Studying the efficacy of olopatadine and ketorolac using a provocative antigen challenge model with olopatadine in one eye and placebo in the contralateral eye or ketorolac in one eye with placebo in another found olopatadine was significantly more effective than ketorolac in the alleviation of the clinical parameters studied. The mean scores for hyperemia were found to be lower in the olopatadine group than in the ketorolac group in our study (Table 3). The ocular itching difference was statistically different indicating olopatadine was superior to ketorolac in inhibiting ocular pruritus. This could be due to the dual action of olopatadine. Ketorolac unlike olopatadine does not inhibit mast cell degranulation hence does not possess antihistamine activity. Although it is found to inhibit pruritogenic prostaglandin synthesis thus has anti-pruritogenic effectiveness in seasonal allergic conjunctivitis. However, the resultant anti-itching effect is lesser as compared to olopatadine. [7] The limitations of the current study include smaller sample size and a convenient sampling method was employed which may not indicate the true representation of seasonal allergic conjunctivitis. The estimation of improvement was done by a single observer however, there are chances of interobserver differences in grading the parameters.

Conclusion

The present study found 0.1% Olopatadine eyedrops were more effective and elicited quicker response as compared to 0.1% Ketorolac eye drops. The efficacy of both was similar at the end of 14 days of treatment. Minor side effects were observed in two patients of the Ketorolac group and no side effects were observed in the olopatadine group. Therefore, while choosing treatment for seasonal allergic conjunctivitis due consideration must be given to costs, side effects, and patient compliance.

References

1. Figus M, Fogagnolo P, Lazzeri S, Capizzi F, Romagnoli M, Canovetti A, et al. Treatment of allergic conjunctivitis: results of a 1-month, single-masked randomized study. Eur J Ophthalmol. 2010; 20(5):811-18.
2. Uchio E. Treatment of allergic conjunctivitis with olopatadine hydrochloride eye drops. Clin Ophthalmol Auckl NZ. 2008; 2(3):525-31.
3. Abokyi S, Koffuor G, Ntodie M, Kyei S, Gyanfosu L. Epidemiological profile and

pharmacological management of allergic conjunctivitis: A study in Ghana. Int J Pharm Biomed Res 2012; 34: 195-200.
4. Abelson MB, Schaefer K. Conjunctivitis of allergic origin: Immunological mechanisms and current approaches to therapy. Surv Ophthalmol 1993; 38: 115–132.
5. Udell IJ, Abelson MB. Animal and human ocular surface response to a topical nonimmune mast-cell degranulating agent (compound 48/80). Am J Ophthalmol. 1981; 91(2):226 30.
6. Allansmith MR, Ross RN. Ocular allergy and mast cell stabilizers. Surv Ophthalmol. 1986; 30(4):229 44.
7. V Yaylali, I Demirlenk, S Tatlipinar, Davut O¨ zbay, et al. Comparative study of 0.1% olopatadine hydrochloride and 0.5% ketorolac tromethamine in the treatment of seasonal allergic conjunctivitis. Acta Ophthalmol. Scand. 2003: 81: 378–382.
8. Bielory L. Update on ocular allergy treatment. Expert Opin Pharmacother. 2002; 3(5):541 53.
9. McGill JI. A review of the use of olopatadine in allergic conjunctivitis. Int Ophthalmol. 2004 May;25(3):171 9.
10. Yanni JM, Stephens DJ, Miller ST, Weimer LK, Graff G, Parnell D, et al. The in vitro and in vivo ocular pharmacology of olopatadine (AL-4943A), an effective anti-allergic/antihistaminic agent. J Ocul Pharmacol Ther Off J Assoc Ocul Pharmacol Ther. 1996;12(4):389 400.
11. Yanni JM, Weimer LK, Sharif NA, Xu SX, Gamache DA, Spellman JM. Inhibition of histamine-induced human conjunctival epithelial cell responses by ocular allergy drugs. Arch Ophthalmol Chic Ill 1960. 1999 May;117(5):643 7.
12. Sharif NA, Xu SX, Miller ST, Gamache DA, Yanni JM. Characterization of the ocular antiallergic and antihistaminic effects of olopatadine (AL-4943A), a novel drug for treating ocular allergic diseases. J Pharmacol Exp Ther. 1996; 278(3):1252 61.
13. Lippert U, Möller A, Welker P, Artuc M, Henz BM. Inhibition of cytokine secretion from human leukemic mast cells and basophils by H1- and H2-receptor antagonists. Exp Dermatol. 2000; 9(2):118 24.
14. Woodward DF, Nieves AL, Hawley SB, Joseph R, Merlino GF, Spada CS. The pruritogenic and inflammatory effects of prostanoids in the conjunctiva. J Ocul Pharmacol Ther Off J Assoc Ocul Pharmacol Ther. 1995;11(3):339 47.
15. Sanchez M, Parra B, Matheu V, Navarro A, Ibáñez M, Dávila I, et al. Allergic Conjunctivitis. J Investig Allergol Clin Immunol Off Organ Int Assoc Asthmology INTERASMA Soc Latinoam Alerg E Inmunol. 2011; 21:1 16.
16. Aguilar AJ. Comparative study of clinical efficacy and tolerance in seasonal allergic conjunctivitis management with 0.1% olopatadine hydrochloride versus 0.05% ketotifen fumarate. Acta Ophthalmol Scand Suppl. 2000;(230):52-55.
17. Bielory L. Update on ocular allergy treatment. Expert Opin Pharmacother. 2002; 3(5):541-53.
18. Bielory L. Ocular Allergy Guidelines: A Practical Treatment Algorithm. Drugs. 2002; 62(11):1611-34.
19. Wallace DV, Dykewicz MS, Bernstein DI, Blessing-Moore J, Cox L, Khan DA, et al. The diagnosis and management of rhinitis: an updated practice parameter. J Allergy Clin Immunol. 2008; 122(2 Suppl): S1-84.
20. Sarker S-J, Chowdhury AN, Hussain Z, Hossain AM, Chowdhury H. Comparison of the therapeutic efficacy of 0.1% olopatadine hydrochloride and 0.025% ketotifen fumarate in allergic conjunctivitis. Therapy 2011; 8(5): 545-53.
21. Aguilar AJ. Comparative study of clinical efficacy and tolerance in seasonal

allergic conjunctivitis management with 0.1% olopatadine hydrochloride versus 0.05% ketotifen fumarate. Acta Ophthalmol Scand Suppl. 2000;(230):52-55.
22. Deschenes J, Discepola M, Abelson M. Comparative evaluation of olopatadine ophthalmic solution (0.1%) versus ketorolac ophthalmic solution (0.5%) using the provocative antigen challenge model. Acta Ophthalmol Scand 1999; 77: 47–52.