Research Article CODEN: IJPRNK IMPACT FACTOR: 4.278 ISSN: 2277-8713
Udaykumar P, IJPRBS, 2014; Volume 3(4): 801-809 IJPRBS

INTERNATIONAL JOURNAL OF PHARMACEUTICAL RESEARCH AND BIO-SCIENCE

COMPARATIVE STUDY OF EFFICACY AND TOLERABILITY OF ONCE DAILY OLOPATADINE HYDROCHLORIDE 0.2% OPHTHALMIC SOLUTION WITH SODIUM CROMOGLYCATE 2% OPHTHALMIC SOLUTION IN ALLERGIC CONJUNCTIVITIS

SCANDASHREE K[1], PATIL M[2], UDAYKUMAR P[3], MENDONCA N[4]

1. Postgraduate Resident, Department of Pharmacology, Father Muller Medical College, Mangalore 575002, Karnataka.
2. Postgraduate Resident, Department of Ophthalmology, Father Muller Medical College, Mangalore 575002, Karnataka.
3. Professor and Head, Department of Pharmacology, Father Muller Medical College, Mangalore 575002, Karnataka.
4. Professor and Head, Department of Ophthalmology, Father Muller Medical College, Mangalore 575002, Karnataka.

Accepted Date: 11/08/2014; Published Date: 27/08/2014

Abstract: Objective: To compare the efficacy and tolerability of once daily olopatadine hydrochloride 0.2% ophthalmic solution with sodium cromoglycate 2% ophthalmic solution administered QID for six weeks in patients with allergic conjunctivitis. Methods: This randomized, open labeled, parallel group, prospective study enrolled 103 patients aged > 4years attending the ophthalmic OPD with allergic conjunctivitis. The eligible participants were randomized into two groups, one receiving olopatadine hydrochloride 0.2% ophthalmic solution once daily and the other group receiving sodium cromoglycate 2% ophthalmic solution four times a day for six weeks. Patient assessment was done at baseline, week 2 and week 6 for ocular signs and symptoms. Adverse events were recorded. The statistical analysis was done using Mann Whitney U test and Wilcoxon signed rank test. Results: Of the 103 patients enrolled in the study, 98 (49 in olopatadine group and 49 in sodium cromoglycate group) completed the study. At week 6, a significant reduction in the mean scores was seen in both the groups; which means both the drugs were effective in allergic conjunctivitis. The change from baseline (CFB) in the mean scores for both itching and redness showed a significant difference (P=<0.05) between the two groups at week 6 indicating the superior efficacy of olopatadine 0.2% OD compared to sodium cromoglycate. Both the treatments were well tolerated. Conclusion: Once daily olopatadine 0.2% ophthalmic solution was better in relieving the signs and symptoms of allergic conjunctivitis on long term use (for about 6 weeks) when compared to sodium cromoglycate 2% ophthalmic solution administered QID.

Keywords: Olopatadine, allergic conjunctivitis, sodium cromoglycate

PAPER-QR CODE

Corresponding Author: DR PADMAJA UDAYKUMAR

Access Online On:

www.ijprbs.com

How to Cite This Article:

Udaykumar P, Scandashree K, Patil M, Mendonca N; IJPRBS, 2014; Volume 3(4): 801-809

INTRODUCTION

Allergic conjunctivitis is the second most common cause of ocular morbidity in India accounting to almost 15-20% of cases attending ophthalmology clinics. [1] It is also the leading cause of school absenteeism in children because of its distressful symptoms.[2,3]

Ocular allergic diseases can be of acute type or chronic type. [4] Seasonal allergic conjunctivitis (SAC) and perennial allergic conjunctivitis (PAC) are of acute type (IgE mediated) and are the most frequent forms of allergic conjunctival diseases. The exposure of an allergen to a sensitized mast cell is the basis for mast cell degranulation. The subsequent release of many inflammatory mediators give rise to the clinical signs and symptoms of allergic conjunctivitis; of which, conjunctival congestion and ocular itching are mainly due to the action of histamine on H1 receptors. In chronic allergic conditions like vernal keratoconjunctivitis (VKC), atopic keratoconjunctivitis (AKC) and giant papillary conjunctivitis (GPC), the pathophysiology is quite complex as there is a constant inflammatory response due to predominance of eosinophils and cytokine release mediated by Th2 cells. [5,6] The signs and symptoms of allergic conjunctivitis include conjunctival congestion (redness), chemosis, lid edema, ocular itching, discomfort, foreign body sensation, stinging, photophobia and watering of eyes.

The pharmacologic agents that are available as ophthalmic solutions, used in the treatment of allergic conjunctivitis belong to diverse classes: (1) Antihistamines- which block H1 receptors. e.g. levocabastine, azelastine, emedastine, bepostatine, alcaftadine (2) Mast cell stabilizers- which increase the calcium influx to the mast cell and prevent changes in the membrane permeability resulting in the stability of membrane decreasing degranulation of mast cells e.g. sodium cromoglycate, nedocromil sodium, pemirolast, lodoxamide [7] (3) Dual acting agents- they have both antihistaminic and mast cell stabilizing properties e.g. olopatadine, ketotifen, azelastine, epinastine (4) Non-Steroidal Anti-Inflammatory Drugs e.g. ketorolac, diclofenac, flurbiprofen , (5) Corticosteroids- e.g. prednisolone, hydrocortisone, flurometha lone, loteprednol, desonide. In severe cases even immunomodulatory agents are used.[6]

Olopatadine is an antihistamine with high affinity and selectivity for H_1 receptors and a mast cell stabilizer, along with various pharmacological actions like suppressing release of TNF α, IL-6 and IL-8. [8,9] Sodium cromoglycate is a mast cell stabilizer.[7] Olopatadine is being used as 0.1% ophthalmic solution twice daily for prevention of ocular signs and symptoms in allergic conjunctivitis patients. [10] Olopatadine hydrochloride 0.2% ophthalmic solution is recently recommended for OD dosing because of its longer duration of action of up to 24 hours. [11,12] The efficacy and tolerability of olopatadine 0.1% ophthalmic solution BD for 2-4 weeks have been demonstrated in comparative studies on allergic conjunctivitis patients. This study aimed at comparing the efficacy and tolerability of double strength formulation of olopatadine i.e. olopatadine 0.2% ophthalmic solution administered OD with sodium cromoglycate 2% ophthalmic solution administered QID in allergic conjunctivitis patients for 6 weeks.

MATERIALS AND METHODS:

This randomized, prospective, open label, single centre study was conducted in the ophthalmic outpatient department of Father Muller Medical College Hospital, Mangalore from December 2013 to June 2014. The study protocol was approved by the Institutional Ethics Committee. The present study enrolled 103 subjects (34 female and 69 male patients with the mean age (range) of 32- 34 years).

Inclusion and exclusion criteria:

All patients aged > 4 years with clinically diagnosed allergic conjunctivitis attending ophthalmic clinic with moderate to severe degree of clinical presentation were included in the study. Subjects with ocular surface disorders like pterygium, dry eye were excluded from the study. Patients who have known hypersensitivity to the study drugs including benzalkonium chloride which is used as preservative in the ophthalmic solutions were excluded. If the patient has used the study medications from 1 week before the start of the study and patients who were unwilling to discontinue contact lens during study period were excluded. Pregnant and lactating women were also excluded from the study.

Method of data collection

A written informed consent was obtained from the patients who fulfilled the inclusion and exclusion criteria. Participant's demographic data and relevant medical and ocular history was taken at baseline. Enrolled subjects were randomized into 2 groups; one receiving olopatadine hydrochloride 0.2% ophthalmic solution OD and the other receiving sodium cromoglycate 2% ophthalmic solution QID and were followed up for 6 weeks. Patient assessment was done at Visit 1(at baseline), Visit 2 (at week 2) and Visit 3 (at week 3) during which they were examined for ocular signs and symptoms; ocular signs assessed were conjunctival congestion, chemosis, lid edema using slit lamp biomicroscope that was graded according to the severity (grade 0-absent, grade1-mild, grade 2-moderate, grade 3 severe) by the ophthalmologist; and ocular symptoms assessed were itching, discomfort, foreign body sensation, stinging, photophobia, and watering (grade 0-absent, grade1-mild, grade 2-moderate, grade 3 severe) by interviewing the patients. Adverse events were noted if any during visit 2 and visit 3.

Outcome measures:

The primary outcome measure was Change from baseline (CFB) in the mean scores of itching and redness at visit 3. The secondary outcome measures included CFB in mean scores of itching and redness at visit 2 and treatment related adverse events.

Statistical analysis:

Statistical analyses were performed using SPSS version 13.0. Data was tabulated, analyzed, reviewed and evaluated. Statistical tests used were Mann Whitney U test and Wilcoxon signed rank test. P-values < 0.05 were considered statistically significant.

RESULTS:

The study enrolled 103 patients where 53 subjects received olopatadine hydrochloride 0.2% ophthalmic solution OD and 50 subjects received sodium cromoglycate 2% ophthalmic solution QID. Of them, five patients were lost to follow up and 98 patients (49 in olopatadine group and 49 in sodium cromoglycate group) completed the study.

Table 1 shows the baseline characteristics of subjects in the study.

Table 2 shows the mean scores for ocular signs and symptoms in allergic conjunctivitis at each examination. There was no significant difference among the groups regarding baseline scores of conjunctival congestion, ocular itching, ocular discomfort, stinging and photophobia. The mean scores of all the parameters significantly reduced at visit 2 and visit 3 ($P < 0.001$) in both the groups. Thus both the treatments were effective in alleviating the clinical signs and symptoms of allergic conjunctivitis.

Table 3 shows change from baseline (CFB) in the mean scores of ocular itching and conjunctival congestion at week 2 and week 6. The difference in the CFB in the mean scores of itching and redness between two groups was statistically significant at week 6 showing that once daily olopatadine 0.2% was better than sodium cromoglycate 2% in allergic conjunctivitis. There was no statistically significant difference in the CFB in mean scores of itching and redness between the two groups at week 2. Scoring of zero at week 6 in terms of itching and redness was considered as complete resolution, and

Graph 3 shows the proportion of patients with complete resolution in both the groups. The proportion of patients with complete resolution of itching and redness were higher in olopatadine group in terms of both ocular itching and conjunctival congestion.

(Graph 1, 2, 3)

There were no treatment related adverse events reported during the study.

DISCUSSION:

Various pharmacological agents have been used to prevent ocular signs and symptoms in allergic conjunctivitis which include antihistamines, mast cell stabilizers and corticosteroids. The choice of a specific antiallergic drug to treat the symptoms and signs of allergic conjunctivitis often depends on the clinical severity. [13] New antiallergic ophthalmic solutions like olopatadine, ketotifen, epinastine, which have various pharmacological actions are available now, where as sodium cromoglycate is an old drug.

The efficacy of olopatadine 0.1% BD in allergic conjunctivitis has been demonstrated in multiple studies including the conjunctival allergen challenge (CAC) model. [14, 15, 16] According to Aguilar et al olopatadine 0.1% shows superior efficacy in the rapid resolution of the signs and symptoms of allergic conjunctivitis. [17] Patient preference for olopatadine is also better compared to ketotifen. [18] In the CAC studies, olopatadine 0.1% twice daily was found to be more efficient than epinastine and loteprednol etabonate 0.2% in decreasing the signs and symptoms of allergic conjunctivitis such as itching, redness and chemosis. [15, 19] The efficacy of two doses of olopatadine 0.1% has been

compared to one dose of olopatadine 0.2% in the prevention of ocular itching associated with allergic conjunctivitis over 24 hours in a conjunctival allergen challenge study which did not show any significant difference between the two groups. [20] Olopatadine has greater economic benefit over sodium cromoglycate in treating allergic conjunctivitis. [21] A randomized controlled trial by International Olopatadine Study Group has shown that olopatadine 0.1% BD has a better efficacy compared to sodium cromoglycate 2% QID in reducing itching and redness. [10] Most of the studies have compared 0.1% olopatadine administered twice daily; but in our study, we used recently recommended 0.2% ophthalmic solution of olopatadine which can be administered once daily as it can improve the patient compliance and compared with sodium cromoglycate 2% administered four times daily in allergic conjunctivitis.

According to the study results, both the treatments were effective in reducing the scores of signs and symptoms of allergic conjunctivitis. During the early phase of study (at week 2), there was no significant difference between the two groups which imply that both treatment was equally effective in the early phase. However, olopatadine 0.2% OD was better than sodium cromoglycate 2% QID in reducing itching and redness on long term use (at week 6) in allergic conjunctivitis patients.

Table 1: Baseline characteristics of allergic conjunctivitis patients in the study

Parameters		Olopatadine 0.2% OD N= 53	Sodium cromoglycate 2% QID N= 50
Age	Mean	33.89	32.32
	>15yrs	45	41
	<15yrs	8	9
Sex	Male	36	33
	Female	16	18
Allergic conjunctivitis		53	50
Associated allergic rhinitis		4	2

Table 2: Mean scores of ocular signs and symptoms

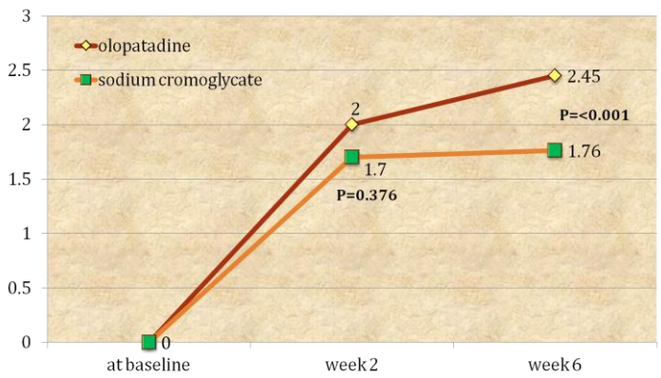
	Olopatadine 0.2% OD			Sodium cromoglycate 2% QID		
VARIABLE	Visit 1	Visit 2	Visit 3 †	Visit 1	Visit 2	Visit 3†
Redness	2.57	0.84	0.51	2.29	0.85	0.69
Chemosis	0.33	0.06	0.04	0.19	0.04	0.04
Lid edema	0.29	0.04	0.00	0.19	0.02	0.00
Itching	2.71	0.71	0.27	2.4	0.69	0.63
Discomfort	1.98	0.14	0.06	1.6	0.13	0.04
Stinging	2.16	0.02	0.00	1.73	0.04	0.04
Photophobia	0.65	0.02	0.00	0.44	0.02	0.00
FB sensation	2.31	0.08	0.02	2.04	0.13	0.08

† P value was < 0.001

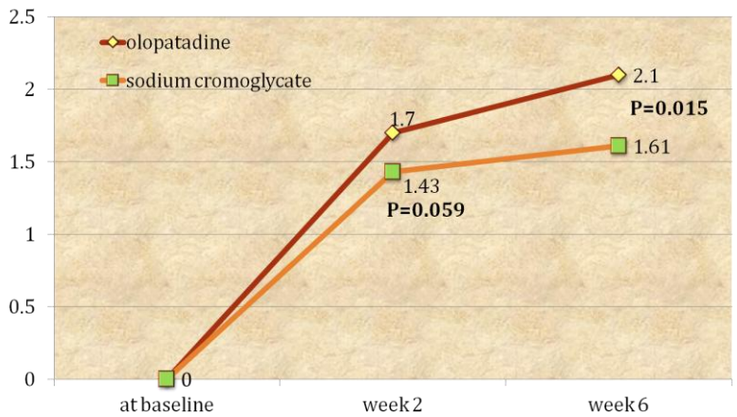
Table 3: Change from baseline in the mean scores of ocular itching and conjunctival congestion.

Change from baseline		Ocular itching			Conjunctival congestion		
		Olopatadine 0.2% OD	Sodium cromoglycate 2% QID	P value	Olopatadine 0.2% OD	Sodium cromoglycate 2% QID	P value
		Mean ±SD	Mean ±SD		Mean ±SD	Mean ±SD	
At 2	Week	2.00(0.76)	1.71(1.27)	0.376	1.73(0.76)	1.44(1.03)	0.059
At 6	Week	2.45(0.82)	1.75(0.81)}	<0.001	2.06(0.89)	1.61(0.87)	0.015

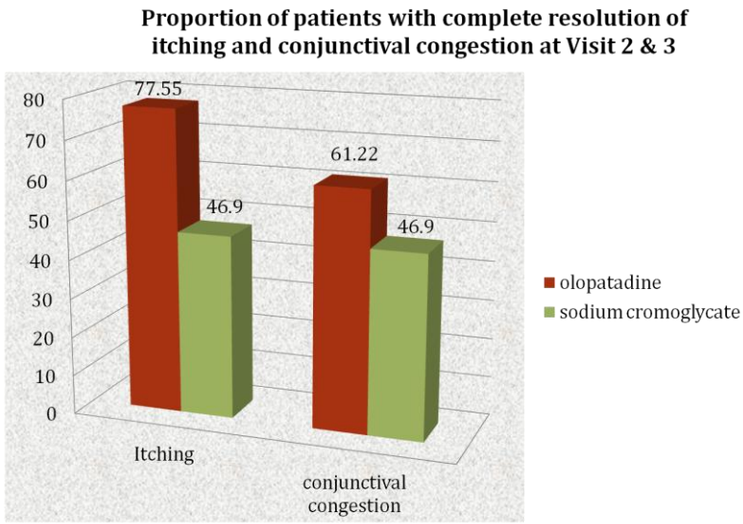
Graph 1: Change from baseline in the mean scores of ocular itching.



Graph 2: Change from baseline in the mean scores of conjunctival congestion



Graph 3: Proportion of patients with complete resolution of itching and redness



CONCLUSION:

Olopatadine hydrochloride 0.2% ophthalmic solution administered once daily and sodium cromoglycate 2% ophthalmic solution administered four times were equally effective in providing relief from the ocular signs and symptoms of allergic conjunctivitis during the early phase of the study but once daily 0.2% olopatadine hydrochloride was more efficacious in reducing itching and redness on long term use.

REFERENCES:

1. Biswas J, Saha I, Das D, Bandyopadhyay S, Ray B, Biswas G. Ocular morbidity among children at a tertiary eye care hospital in Kolkata, West Bengal. Indian Journal of Public Health. 2012;56(4):293.

2. Chakraborti C, Mallik S, Choudhury KP, Das J.Childhood ocular morbidity in Eastern India: a tertiary hospital study. SUDANESE JOURNAL OF PUBLIC HEALTH. 2012 Oct;7(4):126-30

3. Prasanna Kamath BT, Guru Prasad BS, Deepthi R, Muninrayana C. Prevalence of ocular morbidity among school going children (6-15years) in rural area of Karnataka, South India.Int J Pharm Biomed Res. 2012;3(4):209-12.

4. McGill JI, Holgate ST, Church MK, Anderson DF, Bacon A. Allergic eye disease mechanisms. Br J Ophthalmol. 1998 Oct;82(10):1203-14. Review. PubMed MID: 9924312; PubMed Central PMCID: PMC1722368.

5. Leonardi A, De Dominicis C, Motterle L. Immunopathogenesis of ocular allergy: a schematic approach to different clinical entities. Curr Opin Allergy Clin Immunol. 2007 Oct;7(5):429-35. Review. PubMed PMID: 17873584.

6. Mishra GP, Tamboli V, Jwala J, Mitra AK. Recent patents and emerging therapeutics in the treatment of allergic conjunctivitis. Recent Pat Inflamm Allergy Drug Discov. 2011 Jan;5(1):26-36.

7. La Rosa M, Lionetti E, Reibaldi M, Russo A, Longo A, Leonardi S, et al. Allergic conjunctivitis: a comprehensive review of the literature. Ital J Pediatr. 2013;39:18.

8. 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;278:1252-61.

9. Lippert U, Moller A, Welker P, Artuc M, Henz BM. Inhibition of cytokine secretion from human leukemic mast cells and basophils by H1and H2 receptor antagonists. Exp Dermatol. 2000;9:118-24.

10. Katelaris CH, Ciprandi G, Missotten L, Turner FD, Bertin D, Berdeaux G; International Olopatadine Study Group. A comparison of the efficacy and tolerability of olopatadine hydrochloride 0.1% ophthalmic solution and cromolyn sodium 2% ophthalmic solution in seasonal allergic conjunctivitis. Clin Ther. 2002 Oct;24(10):1561-75.

11. Uchio E. Treatment of allergic conjunctivitis with olopatadine hydrochloride eye drops. Clin Ophthalmol. 2008;2(3):525-31

12. Abelson MB, Gomes PJ. Olopatadine 0.2% ophthalmic solution: the first ophthalmic antiallergy agent with once-daily dosing. Expert Opin Drug Metab Toxicol. 2008 Apr;4(4):453-61

13. Friedlaender MH. Epinastine in the management of ocular allergic disease. Int Ophthalmol Clin. 2006;46(4):85-6

14. Avunduk AM, Tekelioglu Y, Turk A & Akyol N (2005): Comparison of effects of ketotifen fumarate 0.025% and olopatadine HCI 0.1% ophthalmic solutions in seasonal allergic conjunctivitis: a 30-day, randomized, double-masked, artificial tear substitute-controlled trial. Clin Ther 27: 1392–1402.

15. Berdy GJ, Stoppel JO & Ebstein AB : Comparison of the clinical efficacy and tolerability of olopatadine hydrochloride 0.1% ophthalmic solution and loteprednol etabonate 0.2% ophthalmic suspension in the conjunctival allergen challenge model. Clin Ther. 2002 (24): 918–29.

16. Kamis U, Ozturk BT, Ozkagnici A & Gunduz K : Comparison of the efficacy of olopatadine hydrochloride 0.1% ophthalmic solution and artificial tears in seasonal allergic conjunctivitis. Acta Ophthalmol Scand. 2006(84): 148–9.

17. 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. 2000 (78): 52–55.

18. Leonardi A & Zafirakis P : Efficacy and comfort of olopatadine versus ketotifen ophthalmic solutions: a double-masked, environmental study of patient preference. Curr Med Res Opin. 2004 (20): 1167–73.

19. Lainer B, Finegold I, D'Arienzo P, Granet D, Ebstein AB & Ledgerwood GL: Clinical efficacy of olopatadine versus epinastine ophthalmic solution in the conjunctival allergen challenge model. Curr Med Res Opin. 2004 (20): 1227–33.

20. Abelson MB, Spangler DL, Epstein AB, Mah FS, Crampton HJ. Efficacy of once-daily olopatadine 0.2% ophthalmic solution compared to twice-daily olopatadine 0.1% ophthalmic solution for the treatment of ocular itching induced by conjunctival allergen challenge. Curr Eye Res. 2007 Dec; 32(12): 1017-22.

21. Guest JF, Clegg JP, Smith AF. Health economic impact of olopatadine compared to branded and generic sodium cromoglycate in the treatment of seasonal allergic conjunctivitis in the UK. Curr Med Res Opin. 2006 Sep;22(9):1777-85