Original Research Article

Comparative evaluation of Ketorolac alone and Ketorolac with Olopatadine eye drop for allergic conjunctivitis

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Abstract

Background: Seasonal allergic conjunctivitis is the most common allergic disorder of eyes. **Aim:** to evaluate the efficacy of 0.4% Ketorolac eye drop alone and 0.4% ketorolac with 0.1% Olopatadine eye drop in seasonal allergic conjunctivitis.**Material and Method:** The study was prospective, double blind parallel group comparative. Two hundred cases enrolled in the study. All the subjects were randomly divided in two groups, 100 in each. Group 1 patients received 0.4% ketorolac eye drop in both eyes 2 times a day and group 2 patients received combination of 0.1% olopatadine and 0.4% ketorolac in both eyes 2 times a day. Observations were collected at baseline and on day 3,7,15 and analyzed statistically regarding improvement in sign and symptoms. **Result**: In group 1, 50- 60% patients had no sign and symptoms on day 15 whereas in group 2 more than 95% patients showed improvement in clinical picture. p value was significant ($p<0.0001$) at day 15 in all sign and symptoms and on day 3 in itching and on day 7 in watering. Overall group 2 patients had better and earlier response regarding symptoms of itching at day 3. **Conclusion**: The combination of 0.1% olopatadine and 0.4% ketorolac was more effective than 0.4% ketorolac alone in seasonal allergic conjunctivitis patients.

Key words: Seasonal allergic conjunctivitis, Combination, Ketorolac, Olopatadine, Comparison.

Introduction

Seasonal allergic conjunctivitis affects almost everyone at one or many occasion during their lifetime [1]. Itching, redness, watering and photophobia, are the characteristics of seasonal allergic conjunctivitis, this may also present with chemosis [1- 6]. Severity of allergic conjunctivitis also depends upon allergen and immune system of the patient itself. The causative factor for this is a reaction between allergen and mast cell mediated response [5,7,8,9]. Mast cells plays a key role in mediating pathogenesis of allergic conjunctivitis [10- 14]. The best possible way to reduce its incidence is, identification of allergen and avoid its exposure which is practically impracticable [15]. A wide range of drugs are available in market for allergic conjunctivitis [2,16,17], the mostly used are steroids. The adverse effects and serious complication of steroids has fetched the attention towards non steroidal drugs like ketorolac, ketotifen, sodium chromoglycate, olopatadine etc. In acute emergency cases these non steroidal drugs alone are not efficient in alleviating the problem. Therefore, combination drugs of two or more molecules are made available. Olopatadine poses dual action of mast cell stabilization and antihistaminic effect with safety profile. [18- 22]. Ketorolac inhibits prostaglandins and relieves the symptoms of itching very effectively. The present study aims to evaluate the

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efficacy of 0.4% Ketorolac eye drop alone and 0.4% ketorolac with 0.1% Olopatadine eye drop in seasonal allergic conjunctivitis.

Material and Methods

Study design and Setting: : This Prospective was conducted at Department of Ophthalmology, Sri Krishna Medical College & Hospital, Muzaffarpur. All the samples were randomly selected and the operator was double-blinded for the study. The study was conducted over a period of 6 months time from April 2018 to June 2018 The study was approved by the institutional research committee. A total of 200 subjects were included in the study comprising of equal number of Males and Females in the age range of 18-50 years. An informed and written consent was obtained by all the participating subjects.The subjects reported with complaint of itching, redness, watering eyes with photophobia were diagnosed for seasonal allergic conjunctivitis on the basis of sign (hyperemia) at slit lamp and symptoms (itching, watering, photophobia).

Inclusion criteria:

1. OPD Patients
2. Complaining of itching, redness, watering and photophobia
3. Diagnosed as a case of seasonal allergic conjunctivitis

Exclusion criteria:

1. Uveitis, conjunctivitis and other ocular pathology.
2. Bronchial asthma, eczema.
3. History of dry eye, blepharitis, using contact lens
4. Receiving topical or systemic medication
5. History of sensitivity to any constituents of the eye drops.

Participants- 200 OPD patients diagnosed for allergic conjunctivitis on the basis of sign and symptoms of were included in this study.

Variables- The studied demographic variables included age, sex, rural, urban and occupation. Questionare related to sign and symptoms of allergic conjunctivitis and its severity were asked.

Data Source: Clinical examination of patients and scoring the sign and symptoms.

Bias- No bias.

Study Size- 200 patients with seasonal allergic conjunctivitis.

Quantitative variables: Our study did not studied quantitative variables.

Methodology- After explaining the study and obtaining the informed and written consent the eligible were enlisted in either of the two treatment groups according to a stratified randomization list based on age and sex. Both the study group consisted of equal number of subjects (n=100).

Group 1 (0.4% ketorolac group) – 0.4% ketorolac was administered twice daily in both eyes of the patients.

Group 2 (0.4% ketorolac and 0.1% olopatadine combination group) - A combination of 0.4%ketorolac and 0.1% olopatadine was administered twice daily in both eyes of the patients.

During the study a thorough history and clinical examination were performed and noted in a prescribed data collection form.An identical containers were used for the study medications so that both participating subjects and the operator remained blinded. Follow up was done at day 0,3,7,15 regarding improvement, and the subjects were evaluated for Itching, Hyperemia, watering and photophobia by using four point scale method. The participating subjects were advised to contact the principal investigator immediately in case of any complaint or any side effect of eye drop.

Statistical Methods: The data was tabulated in Microsoft excel and was subjected to statistical analysis using SPSS software version 11. Chi-square test was performed and p-value <0.0001 was considered statistically significant.

Results

A total of 200 subjects participated in this study. Data were collected and arranged in tables. The demographic profile of patients, age, sex and occupation is shown in Table - 1. All the participating subjects were in the age range of 18-50 years. Mean age of group1 subjects was 30.24 years and that in group 2 was 33.52 years. A majority of the subjects in both groups were male and field workers by occupation, the affected females were housewives. All these data showed no significant difference in between two groups.

Table 1: Distribution of cases according to age and sex

	Group 1	Group 2
Mean age	30.24	33.52
Male	58	68
Female	42	32
Total	100	100

Table 2: Scoring of sign and symptom of allergic conjunctivitis

Sign and symptoms	Scoring of Sign and symptoms of allergic conjunctivitis			
	Score 0 (absent)	Score 1(mild)	Score 2(moderate)	Score 3 (severe)
Itching	Absent	occasionally	frequently	continuously
Hyperemia	Absent	Slightly dilated blood vessels	Moderate vasodilatation	Obviously dilated blood vessels deep red in colour
Watering	Absent	occasionally	frequently	Persistent
Photophobia	Absent	occasionally	continuous	Eye responds to lepharospasm on exposure to light

Table 3: Scoring of itching on different day

		0 (none)	1 (mild)	2 (moderate)	3(severe)	Total	Chi square	P value
Baseline	Group1	00	20	40	40	100	2.667	0.2635
	Group2	00	30	35	35	100		
Day3	Group1	30	40	20	10	100	18.333	0.0003
	Group 2	50	20	10	20	100		
Day 7	Group 1	40	45	10	05	100	12.00	0.0074
	Group2	60	30	10	00	100		
Day 15	Group1	50	40	05	05	100	51.188	<0.0001*
	Group 2	95	05	00	00	100		

Table 4: Scoring of hyperemia on different day

		0 (none)	1 (mild)	2 (moderate)	3(severe)	Total	Chi square	P value
Baseline	Group 1	00	15	45	40	100	5.794	0.0552
	Group 2	00	25	30	45	100		
Day 3	Group 1	25	45	20	10	100	26.408	<0.0001*
	Group 2	60	20	15	05	100		
Day 7	Group 1	50	37	10	03	100	9.559	0.02271
	Group 2	68	22	10	00	100		
Day 15	Group 1	60	30	08	02	100	35.76	<0.0001*
	Group 2	95	05	00	00	100		

Table 5: Scoring of Watering on different day

		0(none)	1 (mild)	2 (moderate)	3(severe)	Total	Chi square	P value
Baseline	Group1	00	40	40	20	100	5.853	0.0536
	Group 2	00	30	35	35	100		
Day 3	Group1	30	40	15	15	100	13.262	<0.0041
	Group2	53	32	10	05	100		
Day 7	Group1	38	42	08	12	100	21.77	<0.0001*
	Group2	65	30	05	00	100		
Day 15	Group1	50	42	05	03	100	59.391	<0.0001*
	Group2	98	02	00	00	100		

Table 6: Scoring of photophobia on different day

		0(none)	1(mild)	2 (moderate)	3(severe)	Total	Chi square	P value
Baseline	Group1	00	58	32	10	100	0.098	0.9522
	Group2	00	60	30	10	100		
Day3	Group1	38	43	15	04	100	10.78	0.0129
	Group2	58	32	10	00	100		
Day 7	Group1	42	47	10	01	100	11.364	0.0099
	Group2	65	30	05	00	100		
Day 15	Group1	53	44	01	02	100	58.01	<0.0001*
	Group2	99	01	00	00	100		

Table 3 showed that in group 1 patients had improvement in itching on day 3 and 7 which is not so significant (p >0.0001) whereas group 2 patients had significant improvement at day 15(p<0.0001). Table 4 has data of hyperemia which reflect that group 1 patients also have good response in this sign although not significant. Table 5 depict that group 2 patients had better response in symptom of watering (p<0.0001) Table 5 & 6 also depict that group 2 patients had good results in comparison of group 1 if considering watering of eye and photophobia. (p<0.0001)

Discussion

Allergic conjunctivitis is a very common illness of eye. It impedes the quality of life due to its recurrent nature. This rarely is associated with vision-threatening complication. An immediate symptomatic relief is urgent to restore the quality of life. Allergic conjunctivitis is of three types - acute, seasonal and perennial. Allergic conjunctivitis affects 10% to 30% of population in general [23]. In majority younger age group are affected more frequently than elderly [24, 25]. The pathogenesis of allergic conjunctivitis being IgE-mediated hypersensitivity, where IgE bound sensitized mast cells is interacted by allergens, causing increased levels of histamine, tryptase, prostaglandins and leukotrienes in tear [26,27].The diagnosis confirmed clinically by detailed history and clinical examination. A wide array of treatment options are available for allergic conjunctivitis, starting from patients education to artificial tear and frequent cool compresses. After ineffectiveness of preventive measures, the pharmacologic agents are applied topically to diminish the allergic responseThe basic management of ocular allergy requires therapeutic anti-allergic agents such as antihistaminic, vasoconstrictor, and mast cell stabilizer. Topical antihistaminics are comparatively short acting, therefore requires frequent application of up to 6 hourly per day [28]. A combination of antihistamines with decongestants is proven to be more effective. [29]. Hyperemia is reduced effectively by decongestants but the side

effects persists with chronic use [29]. Therefore these agents are preferred for shorter duration. The mechanism for mast cell stabilizer's is not obvious. Mast cell stabilizers can only be used for prophylaxis. Recently many therapeutic agents are available with manifold anti-allergic action. Olopatadine, ketotifen, azelastine and epinastine provides multiple actions, including histamine receptor antagonist, stabilization of mast-cell degranulation and suppression of eosinophilic activation and infiltration [30].Olopatadine is a topical ocular dibenzoxepin derivative and acts by inhibiting the release of inflammatory mediators from mast cells and also poses antihistaminic properties. This dual activity makes it suitable for both therapeutic and prophylactic action. This dual action makes it superior by rapid onset, better clinical efficacy, and increased duration of action [19,20,22]. Ketorolac (NSAIDs) acts by inhibiting of cyclooxygenase pathway, inhibiting inflammatory mediator production. This causes a decrease in signs and symptoms of allergic conjunctivitis. These are used as additive drugs to reduce itching and conjunctival hyperemia[31]. Corticosteroids are having immunosuppressive and anti-proliferative properties and therefore, are used in severe variants of ocular allergy [32-36]. A possibility of increased intraocular pressure, and formation of cataract restricts its use only for short duration. However, a regular ocular examination including assessment for cataracts and intraocular pressure should be carried if used for longer durations. [37,38]. Olopatadine hydrochloride is shown to be significantly more efficacious than NSAIDs, mast cell stabilizers, and placebo. [48,39,13]. The present single centric, double blinded, randomized trial, was done to evaluate the efficacy of 0.4% Ketorolac eye drop alone and 0.4% ketorolac with 0.1% Olopatadine eye drop in seasonal allergic conjunctivitis.Yaylali et al compared the effect of olopatadine and ketorolac on 40 patients (m=21, f=19) of allergic conjunctivitis, in the age range of 15–25 , mean age19 years, and found the mean scores of hyperemia being lower in the olopatadine group, demonstrating better therapeutic efficacy, though the difference was not statistically significancant. [39] Our study reports was in consonance with this study. The present study reports also showed, the mean score of itching, hyperemia watering and photophobia in group 2 subjects were 95,95,98,99% respectively which strongly supports the combination of olopatadine with ketorolac being better effective and safe. A similar result was reported by Chaudhary et al [44] Our study report of higher prevalence of allergic conjunctivitis was similar to the results of Pallasaho et al[40] who reported that, males were at higher risks for presenting allergic symptoms than females. Raukas-Kivioja et al [41] in their study showed prevalence of allergic conjunctivitis being inversely related with the age. Most of the patients in our study were outdoor worker which shows gives allergic conjunctivitis is more in field worker especially young patients although could not prove statistically. In our study, the mean itching scores was lower in the olopatadine with ketorolac group compared to ketorolac group. At day 15, 95% 0f patients had no complain of itching in group 2 (p value<0.0001), indicating that combination of olopatadine with ketorolac is superior to ketorolac alone in inhibiting ocular itching. The better clinical effectiveness in improvement of signs and symptoms allergic conjunctivitis, particularly of pruritis may be due to dual action of olopatadine. [3,19, 47-51]. Group-2 in our study also showed reduced eye watering and photophobia, both the result are consistent with Deschenes et al. 1999 [47]. Castilo M et al [1] proved, olopatadine has cumulative role when administered in combination with 0.4% ketorolac. Our overall study result is also in favor of combined olopatadine and ketorolac eye drop for allergic conjunctivitis[48-51].

Conclusion

Understanding the underlying mechanisms of allergy and choosing the best therapy for allergic conjunctivitis, is very crucial . The dual action of Olopatadine with an added effect of Ketorolac makes the combination better accepted than Ketorolac alone in the management of seasonal allergic conjunctivitis. The combination drug provided better and faster recovery thus offering a promising result.

Benefit of study in future- This is the one of unique study in terms of that we used combination of olopatadine and ketorolac in treatment of allergic conjunctivitis which have better efficacy and results rather than single drug so it will be beneficial in future for patients as well as doctor.

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