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Original Research Article

The Effectiveness of 0.1% Olopatadine Hydrochloride and 0.5% Ketorolac Tromethamine in Managing Seasonal Allergic Conjunctivitis

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Conflict of interest: Nil

Abstract:

Background: Allergic conjunctivitis, a prevalent allergic ocular condition, often presents with itching and discomfort. This study aims to compare the clinical effectiveness and therapeutic impact of 0.1% olopatadine hydrochloride and 0.5% ketorolac tromethamine ophthalmic solutions—each with distinct pharmacological mechanisms—in managing seasonal allergic conjunctivitis.

Methods: Using specific inclusion and exclusion criteria, a total of n=80 cases were selected through convenient sampling and evenly distributed into two groups: Group I (administered 0.1% Olopatadine hydrochloride) and Group II (administered 0.5% Ketorolac tromethamine). Thorough ocular examinations were conducted, encompassing visual acuity, slit-lamp bio-microscopy to assess conjunctival and corneal involvement, intraocular pressure (IOP) measurement with a non-contact tonometer, and fundus examination using indirect ophthalmoscopy.

Results: The comparison of itching score improvement at various intervals revealed significant p-values at the 30-minute and 2-day marks. Notably, rapid symptom alleviation was observed in Group I (Olopatadine) compared to Group II (Ketorolac). Evaluation of hyperemia score improvement during follow-up visits showed significant p-values at the 30-minute interval only, with no significant values on day 2 and day 7. Both drugs demonstrated equal efficacy in managing hyperemia during follow-up.

Conclusion: This study concluded that 0.1% Olopatadine eyedrops exhibited superior efficacy and a quicker response compared to 0.1% Ketorolac eye drops. However, both were equally effective after a 14-day treatment period. Minor side effects were noted in two patients from the Ketorolac group, while no side effects were observed in the olopatadine group. Therefore, when selecting treatment for seasonal allergic conjunctivitis, careful consideration should be given to factors such as cost, side effects, and patient compliance.

Keywords: Seasonal Allergic Conjunctivitis, Olopatadine Eyedrops, Ketorolac Eye Drops, Itching, Hyperemia.

Introduction

Allergic conjunctivitis encompasses a group of hypersensitivity disorders that affect the eyelid, conjunctiva, and cornea and share a common pathogenesis. [1] The prevalent clinical manifestations of this condition include itching, redness, tearing, swelling, burning sensation, and feeling of fullness in the eye leading to eye rubbing, occasional blurred vision, mucus discharge, chemosis, and lid edema. [2, 3] This allergic response is primarily a type I hypersensitivity reaction mediated by IgE and triggered by airborne allergens such as pollen, grass, weeds, and animal dander. [4] Mast cells contribute significantly to the pathophysiology of this condition. [5, 6] Specific allergen binding to sensitized cells in the conjunctiva prompts mast cell degranulation, releasing preformed histamine, eosinophil chemotactic factors, tryptase, prostaglandins, and leukotrienes, culminating in characteristic signs and symptoms of seasonal allergic conjunctivitis. [7] Fundamental treatment strategies include allergen avoidance, elimination or alteration of the source of offending allergens, and changes in occupational settings if necessary. Symptomatic relief can be achieved through cold compression, particularly in patients with ocular pruritus. Artificial lubrication aids in the removal or dilution of allergens that come in contact with the ocular surface. Tear substitutes, combining saline with a wetting and viscosity agent, such as methylcellulose or polyvinyl alcohol, have proven beneficial. [8] Pharmacological interventions primarily target the prevention of mast cell degranulation during allergies. Topically administered ophthalmic agents are the mainstay of treatment for AC. [9, 10] Commonly used topical medications include H1 antihistamines, mast cell

stabilizers, nonsteroidal anti-inflammatory drugs (NSAIDs), and steroids. Olopatadine, a novel therapeutic agent, has demonstrated clinical efficacy for the treatment of AC. Olopatadine exerts dual action, showing limited mast-cell stabilizing effects and binding to H1 receptors. [11, 12] Compared with first-generation antihistamines, olopatadine displayed inhibitory effects on cytokine secretion, including the release of tumor necrosis factor-alpha from human conjunctival mast cells. [11-13] Ketorolac tromethamine 0.5% ophthalmic solution, a potent NSAID, inhibits cyclooxygenase, subsequently reducing prostaglandin synthesis. [14] Against this backdrop, this study aimed to assess the effectiveness 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 immunocompromised status.

Following the predefined inclusion and exclusion criteria, a total of 80 cases were selected through a convenient sampling method, and then randomly and evenly distributed into two groups: Group I, administered 0.1% olopatadine hydrochloride; and Group II, administered 0.5% ketorolac tromethamine. A comprehensive ocular examination was conducted in all patients, encompassing assessments of visual acuity, slit-lamp biomicroscopy to assess conjunctival and corneal involvement, and intraocular pressure (IOP) measurements using a non-contact tonometer. Fundus examinations were performed using an indirect ophthalmoscope. Ocular hyperemia was evaluated across three vessel beds, conjunctival, ciliary, and episcleral, and graded on a scale from 0 (absent) to 4 (severe). Ocular itching was documented on a scale of 0 (none) to 4 (severe). Likewise, the scores for chemosis and lid edema were also noted. These assessments were conducted by a single observer during the initial visit, at 30 min post eye drop instillation, and during follow-up visits on the 2nd day, 7th day, and 14th day. The patients were advised to instill drops twice daily. The treatment response was assessed at the end of the 14 days, and no adverse reactions were recorded. Statistical analysis involved organizing the data in an MS Excel spreadsheet and utilizing SPSS version 19 for analysis in Windows format. Continuous variables are presented as means and standard deviations, while categorical variables are expressed as percentages. Statistical significance was set at $P < 0.05$.

Results

A total of n=22(55%) males and n=18(45%) females were included in group I (Olopatadine group) and in group II (Ketorolac) n=21(52.5%) males and n=19(47.5%) females were included. The overall involvement of males in both groups combined was slightly more than 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 26.5 years ± 3.5 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=40)		Total	Group II (N=40)		Total
	Male	Female	(%)	Male	Female	(%)
18 – 20	07	05	13	06	04	10
21 – 25	06	06	12	07	07	14
26 – 30	05	02	07	03	05	08
31 – 35	02	03	05	03	02	05
36 – 40	02	02	04	02	01	03
Total	22	18	40	21	19	40

The eye drops were instilled in both groups of patients and itching scores were observed. In group I (Olopatadine group) we found 57.5% of cases were having improvement in itching symptoms at 30-minute intervals. For group II (Ketorolac) the improvement in itching scores was found in 35% 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 72.5% improvement in scores in group I as compared to 52.5% in group II.

At the next follow-up visit at 7 days and 14 days, the improvement of itching symptoms was found in 100% of cases of both the groups' details depicted in Table 2.

Ocular hyperemia was evaluated in three vascular areas: conjunctival, ciliary, and episcleral, and graded on a scale ranging from 0 (absent) to 4 (maximum). The enhancements in hyperemia scores for both groups are detailed in Table 2. The initial mean scores for itching were 1.90 ± 0.34 for group I and 2.01 ± 0.54 for group II. Similarly, the mean scores for hyperemia were 1.99 ± 0.72 for group I and 1.95 ± 0.61 for group II. A thorough review of Table 2 demonstrates a relatively quicker improvement in group I (Olopatadine) compared to group II (Ketorolac). Nonetheless, noteworthy improvement was observed in all 100% of cases in both groups by the conclusion of the 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)	57.5%	72.5%	95%	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)	52.5%	67.5%	95%	100%
Group II (Ketorolac)	30%	55%	87.5%	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). However, at 14 days the improvement was observed in all cases of both 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	**Group I**	**Group II**	**Group I**	**Group II**	**Group I**	**Group II**
Improvement	57.5	35	60	52.5	97.5	87.5
Interval	30 minutes		2 days		7 days	
Chi-square	5.020		4.785		1.23	
p-values	0.01*		0.021*		0.533	
Hyperemia	**Group I**	**Group II**	**Group I**	**Group II**	**Group I**	**Group II**
Improvement	52.5	30	67.5	52.5	95	87.5
Interval	30 minutes		2 days		7 days	
Chi-square	4.50		1.90		1.12	
p-values	0.030*		0.135		0.772	

*Significant

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 2.02 ± 0.83 and in group II the scores were 2.04 ± 9.01. 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)	62.5%	75%	97.5%	100%
Group II (Ketorolac)	40%	57.5%	92.5%	100%
	Improvement in Lid edema			
Groups	At 30 minutes	2 days	7 days	At 14 days
Group I (Olopatadine)	45%	67.5%	82.5%	100%
Group II (Ketorolac)	37.5%	52.5%	75%	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**
	62.5	40	75	57.5	97.5	92.5
Interval	30 minutes		2 days		7 days	
Chi-square	4.102		3.99		1.00	
p-values	0.031*		0.041*		0.731	
Lid edema	**Group I**	**Group II**	**Group I**	**Group II**	**Group I**	**Group II**
	45	37.5	67.5	52.5	82.5	75
Interval	30 minutes		2 days		7 days	
Chi-square	1.022		1.36		1.86	
p-values	0.354		0.182		0.632	

*Significant

The safety assessment of both medications was conducted in both groups, considering parameters such as changes in intraocular pressure, alterations in visual acuity, fundoscopy findings, occurrences of headaches, or any adverse reactions. In this investigation, we observed that in group II, two patients reported experiencing a mild stinging sensation during the initial follow-up visit. However, these symptoms were mild, self-limiting, and resolved within one week.

Discussion

Allergic conjunctivitis is a bilateral inflammatory condition, often self-limiting, characterized by an IgE-mediated immune response triggered upon direct exposure to allergens in the conjunctival sac of sensitized individuals. This immune response leads to the activation of mast cells and subsequent release of various allergic mediators [15, 16]. Key symptoms of allergic conjunctivitis include tearing, photophobia, blurred vision, foreign body sensation, redness, and itching, with itching being a distinct indicator of this condition [16]. The initial approach for managing allergic conjunctivitis involves irrigating and diluting allergens on the ocular surface [17, 18]. Pharmacological treatments include topical decongestants, antihistamines, mast cell stabilizers, and non-steroidal anti-inflammatory agents [17-19]. In our study, we evaluated the application of topical eye drops containing Olopatadine and Ketorolac in patients diagnosed with allergic conjunctivitis. The mean age of the participants in our cohort was 24.5 years ± 4.5 years. In a similar study by Yaylali et al. [7], the mean age of individuals with allergic conjunctivitis was 19 years, suggesting a higher prevalence in younger populations. Sarker et al. [20], in their study on allergic conjunctivitis in 92 patients, found that 42-45% were male, with a mean age of 28 ± 12 and 28 ± 11 years, aligning with our study's observations. Clinical parameters such as itching, hyperemia, chemosis, and lid edema were assessed by computing the mean pre-treatment scores for each group. In our study, the mean pre-treatment itching scores were 1.90 ± 0.34 in group I and 2.01 ± 0.54 in group II cases. Similarly, the mean scores for hyperemia were 1.99 ± 0.72 in group I and 1.95 ± 0.61 in group II. The mean pre-treatment chemosis scores were 2.01 ± 0.82 in group I and 2.05 ± 9.02 in group II. Lastly, the mean pre-treatment lid edema scores were 1.85 ± 0.53 in group I and 1.79 ± 0.42 in group II. These baseline parameters were comparable in both groups.

Sarker et al. [20] also found similar mean pre-treatment scores for hyperemia, tearing, itching, and photophobia in both the Ketotifen and Olopatadine groups, corroborating our study's findings. Our study revealed significant improvements in itching symptoms at 30 minutes and 2 days in the Olopatadine group. Moreover, hyperemia improvement was significant at 30 minutes in the Olopatadine group. In a study by AJ Aguilar et al. [21], olopatadine demonstrated 42.5% to 62.5% improvement in symptoms at 0 minutes and 30 minutes. At 2 days and the end of 7 days, 57.5% to 75% of patients showed improvement, further supporting our findings. In a study by Deschenes et al. [22], olopatadine was significantly more effective than ketorolac in alleviating the clinical parameters studied. The mean scores for hyperemia were lower in the olopatadine group than in the ketorolac group, as seen in our study (Table 3). The difference in ocular itching was statistically significant, indicating that olopatadine was superior to ketorolac in inhibiting ocular pruritus. This superiority could be attributed to the dual action of olopatadine. Unlike olopatadine, ketorolac does not inhibit mast cell degranulation and therefore does not possess antihistamine activity. Although ketorolac is found to inhibit pruritogenic prostaglandin synthesis, resulting in anti-pruritic effectiveness in seasonal allergic conjunctivitis, the resultant anti-itching effect is lesser compared to olopatadine [7]. However, our study had certain limitations, including a smaller sample size and the use of a

convenient sampling method, which may not accurately represent the true nature of seasonal allergic conjunctivitis. Additionally, the estimation of improvement was performed by a single observer, and interobserver differences in grading the parameters might exist.

Conclusion

The current investigation demonstrated that 0.1% Olopatadine eye drops exhibited superior and faster results compared to 0.1% Ketorolac eye drops. However, both were equally effective after the 14-day treatment period. Minor side effects were reported by two patients in the Ketorolac group, while no side effects were noted in the Olopatadine group. Thus, when selecting a treatment for seasonal allergic conjunctivitis, factors such as cost, side effects, and patient compliance should be taken into careful consideration.

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