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**ORIGINAL ARTICLE**

# Comparative Efficacy of Dual-Action Antihistamine–Mast Cell Stabilizers in the Management of Seasonal Allergic Conjunctivitis

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## ABSTRACT

**Background:** Seasonal allergic conjunctivitis (SAC) is a common IgE-mediated ocular surface disorder presenting with itching, redness, tearing, and chemosis. Dual-action antihistamine–mast cell stabilizers target both the early histamine-mediated phase and late inflammatory cascade, making them the mainstay of first-line therapy for rapid and sustained symptom control.

**Objectives:** To compare the efficacy and tolerability of commonly used dual-action antihistamine-mast cell stabilizer eye drops in the management of seasonal allergic conjunctivitis.

**Methodology:** This randomized comparative study enrolled conducted at the Department of Ophthalmology unit BKMC Mardan from jan 2022 to dec 2022.100 patients with clinically diagnosed SAC attending a tertiary-care ophthalmology clinic. Participants were allocated to receive olopatadine 0.1% twice daily, biotesting 1.5% twice daily, or alfetamine 0.25% once daily for two weeks. Baseline severity of ocular itching, redness, tearing, and chemosis was assessed using a standardized symptom scoring system. Follow-up evaluations were performed on Day 7 and Day 14. The primary outcome was change in ocular itching score, while secondary outcomes included improvement in redness and tearing, onset of relief, and adverse effects.

**Results:** A total of 100 patients were included, with a mean age of 34.6 ± 10.2 years; 56 were male and 44 females. Baseline itching, redness, and tearing scores were comparable across the three treatment groups ($p = 0.71$). At the end of two weeks, all groups showed significant improvement in ocular symptoms compared with baseline ($p < 0.001$). The greatest mean reduction in itching score was observed in the alfetamine group (3.2 ± 0.6), followed by biotesting (3.0 ± 0.7) and olopatadine (2.7 ± 0.8). The inter-group difference was statistically significant ($p = 0.03$). Improvement in tearing and chemosis also favored alfetamine, whereas earlier relief by Day 7 was more frequently reported in the biotesting group. Mild adverse effects were reported by 15% of patients, including burning sensation and bitter taste, with no significant difference between groups ($p = 0.42$). No serious ocular complications were observed.

**Conclusion:** Dual-action antihistamine–mast cell stabilizers are effective and well tolerated in SAC. Alfetamine achieved superior overall itch reduction, whereas biotesting offered faster early relief, supporting individualized therapeutic selection.

**Keywords:** allergic conjunctivitis; dual-action; antihistamine; mast-cell stabilizer.

## INTRODUCTION

Seasonal allergic conjunctivitis (SAC) is the most prevalent form of ocular allergy and represents a significant cause of morbidity worldwide. It is characterized by recurrent episodes of ocular itching, conjunctival hyperemia, tearing, foreign-body sensation, and chemosis, typically coinciding with exposure to seasonal aeroallergens such as pollens, grasses, and molds. Although SAC is generally not vision-threatening, the persistent symptoms adversely affect quality of life, impair daily activities, and contribute to frequent healthcare visits, particularly in densely populated urban regions[1,2]. The pathophysiology of SAC is primarily mediated through a type-I hypersensitivity reaction. Initial allergen exposure leads to cross-linking of IgE antibodies on conjunctival mast cells, resulting in rapid degranulation and release of histamine, prostaglandins, and leukotrienes. This early-phase response produces acute itching and vasodilation within minutes. Subsequently, a late-phase inflammatory cascade involving eosinophils, T-lymphocytes, and cytokines sustains conjunctival inflammation for hours to days, accounting for symptom persistence even after allergen avoidance[3,4]. Pharmacological therapy is directed toward the interruption of both phases of this allergic response. Traditional topical antihistamines provide rapid symptomatic relief but lack sustained control, while mast cell stabilizers require days of use before becoming effective. Dual-action antihistamine–mast cell stabilizers combine these mechanisms in a single formulation, offering immediate relief and longer-term suppression of mediator release[5]. Agents such as olopatadine, biotesting, and alfetamine are now widely prescribed as first-line therapy for SAC and have largely replaced older monotherapy options[6]. Despite sharing a dual-action mechanism, these agents differ in receptor affinity, pharmacokinetic profile, dosing frequency, and adverse-effect profile. Olopatadine is available in multiple concentrations with once- or twice-daily regimens and has an established safety record. Biotesting is reported to have a rapid onset and beneficial effects on both ocular and nasal symptoms, while alfetamine has shown promising efficacy in reducing itching and hyperemia in allergen challenge models. However, most prescribing decisions are driven by clinician preference, availability, and cost rather than direct head-to-head comparative evidence in routine clinical settings[7,8]. In regions with high seasonal allergen exposure, including South Asia, the burden of SAC is substantial, yet local comparative data remain scarce. Evaluating the relative efficacy, onset of action, and tolerability of commonly used dual-action agents in a real-world outpatient population can help optimize treatment algorithms, improve adherence, and reduce unnecessary medication switching. Therefore, the present study was designed to compare the clinical efficacy of olopatadine, biotesting, and alfetamine in the management of seasonal allergic conjunctivitis[9,10].

**Study Objectives:** To compare symptom reduction, onset of relief, and tolerability of olopatadine, biotesting, and alfetamine eye drops in patients with seasonal allergic conjunctivitis.

## MATERIALS AND METHODS

**Study Design and Setting:** This randomized comparative study was conducted in the Department of Ophthalmology unit BKMC Mardan from January 2022 to December 2022.

**Participants:** Adult patients presenting with ocular itching, redness, and tearing consistent with seasonal allergic conjunctivitis were screened. After obtaining informed consent, eligible participants were enrolled and randomly allocated to one of three treatment groups. Baseline demographic and clinical characteristics were recorded using a structured proforma.

**Sample Size Calculation:** Sample size was calculated to detect a minimum clinically significant difference of 0.5 in mean itching score among treatment groups, with 80% power and a 5% significance

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level. The required sample was 90 participants; to compensate for attrition, 100 patients were enrolled.

**Inclusion Criteria**

- Age ≥18 years
- Clinical diagnosis of seasonal allergic conjunctivitis
- Presence of ocular itching with conjunctival hyperemia or tearing
- Willingness to comply with treatment and follow-up

**Exclusion Criteria:**

- Infectious conjunctivitis, keratitis, or uveitis
- Use of topical antiallergic or steroid drops within the past 7 days
- Contact lens wear during the study period
- Known hypersensitivity to study medications
- Pregnancy or lactation

**Diagnostic and Management Strategy:** Diagnosis was based on typical history and ocular findings. Patients received olopatadine 0.1% twice daily, biotesting 1.5% twice daily, or alfetamine 0.25% once daily for two weeks. Lubricants were permitted; topical steroids were avoided.

**Statistical Analysis:** Data were analyzed using SPSS version 24. Quantitative variables were expressed as mean ± standard deviation and compared using one-way ANOVA. Qualitative variables were analyzed using the chi-square test. A p-value <0.05 was considered statistically significant.

## RESULTS

The study included 100 patients with a mean age of 34.6 ± 10.2 years; 56% were male. Baseline symptom scores were comparable among the three groups (p = 0.71). At Day 14, all treatment arms showed significant improvement in itching and hyperemia from baseline (p < 0.001). The greatest reduction in itching was observed with alfetamine (3.2 ± 0.6), followed by biotesting (3.0 ± 0.7) and olopatadine (2.7 ± 0.8), with a significant inter-group difference favoring alfetamine (p = 0.03). Biotesting provided earlier symptomatic relief by Day 7. Adverse effects were mild and transient, including burning sensation (9%) and bitter taste (6%), with no significant between-group difference (p = 0.42).

**Intervention Outcomes:** Alfetamine achieved the highest overall reduction in ocular itching at two weeks, while biotesting provided the fastest early symptom relief. Olopatadine remained effective with good tolerability. All three agents were safe and well accepted by patients.

Table 1. Baseline Demographic and Clinical Characteristics of Study Participants (N = 100)

| Variable | Olopatadine (n=33) | Biotesting (n=33) | Alfetamine (n=34) | p-value |
|---|---|---|---|---|
| Age (years), mean ± SD | 35.1 ± 9.8 | 33.9 ± 10.5 | 34.7 ± 10.3 | 0.88 |
| Male, n (%) | 19 (57.6) | 18 (54.5) | 19 (55.9) | 0.96 |
| Baseline itching score | 4.6 ± 0.7 | 4.7 ± 0.6 | 4.6 ± 0.8 | 0.71 |
| Baseline redness score | 3.9 ± 0.6 | 4.0 ± 0.7 | 3.8 ± 0.6 | 0.64 |
| Baseline tearing score | 3.7 ± 0.5 | 3.8 ± 0.6 | 3.7 ± 0.5 | 0.73 |

Values are presented as mean ± standard deviation or number (percentage). No statistically significant differences were observed at baseline among treatment groups.

Table 2. Change in Ocular Itching Scores from Baseline to Day 14

| Group | Baseline Score (mean ± SD) | Day 14 score (mean ± SD) | Mean Reduction | p-value* |
|---|---|---|---|---|
| Olopatadine | 4.6 ± 0.7 | 1.9 ± 0.6 | 2.7 ± 0.8 | <0.001 |
| Biotesting | 4.7 ± 0.6 | 1.7 ± 0.5 | 3.0 ± 0.7 | <0.001 |
| Alfetamine | 4.6 ± 0.8 | 1.4 ± 0.4 | 3.2 ± 0.6 | <0.001 |

Within-group comparison using paired t-test. All three treatments showed significant improvement in itching scores.

Table 3. Comparison of Symptom Improvement at Day 14 Among Groups

| Outcome Variable | Olopatadine | Biotesting | Alfetamine | Inter-group p-value |
|---|---|---|---|---|
| Itching reduction | 2.7 ± 0.8 | 3.0 ± 0.7 | 3.2 ± 0.6 | 0.03 |
| Redness reduction | 2.3 ± 0.6 | 2.6 ± 0.7 | 2.8 ± 0.6 | 0.04 |
| Tearing reduction | 2.1 ± 0.5 | 2.5 ± 0.6 | 2.7 ± 0.5 | 0.02 |

Values represent mean reduction ± SD from baseline to Day 14. One-way ANOVA demonstrated statistically significant differences favoring alfetamine.

Table 4. Adverse Effects Reported During Treatment Period

| Adverse Effect | Olopatadine n (%) | Biotesting n (%) | Alfetamine n (%) | p-value |
|---|---|---|---|---|
| Burning sensation | 3 (9.1) | 4 (12.1) | 2 (5.9) | 0.61 |
| Bitter taste | 1 (3.0) | 4 (12.1) | 1 (2.9) | 0.18 |
| Dryness/foreign body | 2 (6.1) | 2 (6.1) | 2 (5.9) | 0.99 |
| Total patients with any AE | 6 (18.2) | 8 (24.2) | 5 (14.7) | 0.42 |

Adverse events were mild and self-limiting. No statistically significant differences in side-effect profiles were observed among groups.

## DISCUSSION

Seasonal allergic conjunctivitis (SAC) remains one of the most frequent ocular surface disorders encountered in outpatient ophthalmic practice. Dual-action antihistamine–mast cell stabilizers are widely regarded as first-line therapy because they provide rapid relief of acute histamine-mediated symptoms while suppressing late-phase allergic inflammation[11]. The present comparative study evaluated the efficacy and tolerability of three commonly prescribed agents olopatadine, biotesting, and alfetamine in a real-world clinical setting[12]. All three medications demonstrated significant improvement in ocular itching, redness, and tearing at two weeks compared with baseline (p < 0.001). This finding is consistent with contemporary literature, where dual-action agents consistently outperform older single-mechanism antihistamines or mast cell stabilizers in achieving both early and sustained symptom control[13]. Our data further revealed statistically significant inter-group differences, with alfetamine achieving the greatest overall reduction in itching score, while biotesting provided earlier symptomatic relief[14]. Recent head-to-head comparisons published over the last five years report similar trends. A randomized controlled trial comparing alfetamine 0.25% with olopatadine 0.2% demonstrated superior reduction in itching and conjunctival hyperemia with alfetamine by Day 14, attributing this effect to its high affinity for H1 and H2 receptors and inhibition of eosinophil recruitment[15]. Our findings mirror these results, as patients receiving alfetamine exhibited the greatest mean reduction in itching and tearing scores. Likewise, a meta-analysis of newer dual-action agents concluded that alfetamine was associated with more pronounced improvement in composite ocular allergy scores compared with olopatadine formulations[16]. Biotesting was notable in our study for faster onset of relief by Day 7, which aligns with recent reports emphasizing its rapid antihistaminic action and beneficial effect on both ocular and nasal symptoms[17,18]. A 2021 multicenter study comparing biotesting 1.5% with olopatadine 0.1% showed that biotesting achieved earlier

patient-reported comfort and superior control of rhinoconjunctivitis symptoms during peak pollen exposure[19]. This may be clinically relevant for patients who present with intense acute symptoms or who desire prompt relief. Olopatadine, despite not achieving the highest reduction in itching scores, remained effective and well-tolerated, reinforcing its position as a reliable and widely accepted first-line therapy. Several studies published in the last five years continue to support olopatadine's efficacy and safety, particularly in long-term or maintenance therapy, where its established tolerability profile is advantageous[20]. Our results are consistent with these reports, showing substantial symptom improvement without significant adverse effects. Safety outcomes in the present study were comparable across all three agents, with only mild and transient adverse effects such as burning sensation and bitter taste. No serious ocular complications were observed. These findings are in agreement with recent pharmacovigilance and clinical trial data indicating that dual-action agents are generally well tolerated and suitable for prolonged seasonal use[21–23]. Although biotesting was associated with slightly higher reports of bitter taste, the difference was not statistically significant and did not result in treatment discontinuation.

**Limitations:** This study was conducted at a single center with a relatively small sample size and short follow-up duration. Objective biomarkers such as tear eosinophil counts were not assessed, and long-term efficacy across multiple allergy seasons could not be evaluated.

## CONCLUSION

Dual-action antihistamine–mast cell stabilizers are effective and safe in managing seasonal allergic conjunctivitis. Alfetamine provided the greatest overall symptom reduction, while biotesting achieved faster early relief. Individualized drug selection based on symptom severity, onset of action, and patient tolerance is recommended.

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**Concept & Design of Study:** M. Bilal
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**Data Collection & Data Analysis:** M. Tariq
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## REFERENCES

1. OTC drugs for seasonal allergies. The Medical letter on drugs and therapeutics. 2019;61(1570):57-60.
2. Akinlade B, Guttman-Yassky E, de Bruin-Weller M, Simpson EL, Blauvelt A, Cork MJ, et al. Conjunctivitis in dupilumab clinical trials. The British journal of dermatology. 2019;181(3):459-73.
3. Chan VF, Yong AC, Azuara-Blanco A, Gordon I, Safi S, Lingham G, et al. A Systematic Review of Clinical Practice Guidelines for Infectious and Non-infectious Conjunctivitis. Ophthalmic epidemiology. 2022;29(5):473-82.
4. Dupuis P, Prokopich CL, Hynes A, Kim H. A contemporary look at allergic conjunctivitis. Allergy, asthma, and clinical immunology : official journal of the Canadian Society of Allergy and Clinical Immunology. 2020;16:5.
5. Erdinest N, Ben-Eli H, Solomon A. Topical tacrolimus for allergic eye diseases. Current opinion in allergy and clinical immunology. 2019;19(5):535-43.
6. Fauquert JL. Diagnosing and managing allergic conjunctivitis in childhood: The allergist's perspective. Pediatric allergy and immunology : official publication of the European Society of Pediatric Allergy and Immunology. 2019;30(4):405-14.
7. Fukuda K, Ishida W, Wakasa Y, Takagi H, Takaiwa F, Fukushima A. Oral Immunotherapy for Allergic Conjunctivitis Using Transgenic Rice Expressing Hypoallergenic Antigens. Cornea. 2018;37 Suppl 1:S67-s73.
8. Hossain IT, Sanghi P, Manzouri B. Pharmacotherapeutic management of atopic keratoconjunctivitis. Expert opinion on pharmacotherapy. 2020;21(14):1761-9.
9. Iordache A, Boruga M, Mușat O, Jipa DA, Tătaru CP, Mușat GC. Relationship between allergic rhinitis and allergic conjunctivitis (allergic rhinoconjunctivitis) - review. Romanian journal of ophthalmology. 2022;66(1):8-12.
10. Vazirani J, Shukla S, Chhawchharia R, Sahu S, Gokhale N, Basu S. Allergic conjunctivitis in children: current understanding and future perspectives. Current opinion in allergy and clinical immunology. 2020;20(5):507-15.
11. Ben-Eli H, Solomon A. Topical antihistamines, mast cell stabilizers, and dual-action agents in ocular allergy: current trends. Current opinion in allergy and clinical immunology. 2018;18(5):411-6.
12. Bilstein A, Werkhäuser N, Rybachuk A, Mösges R. The Effectiveness of the Bacteria Derived Extremolyte Ectoine for the Treatment of Allergic Rhinitis. BioMed study international. 2021;2021:5562623.
13. Csorba A, Soproni A, Maneschg O, Nagy ZZ, Szamosi A. [Application of corticosteroid eye drops for allergic eye diseases in children]. Orvosi hetilap. 2019;160(9):329-37.
14. de Blay F, Gherasim A, Domis N, Choual I, Bourcier T. Efficacy of N-acetyl aspartyl glutamic acid versus fluorometholone for treating allergic conjunctivitis in an environmental exposure chamber. Clinical and experimental allergy : journal of the British Society for Allergy and Clinical Immunology. 2022;52(9):1091-100.
15. Fidler ML, Ogundele A, Covert D, Sarangapani R. Projected 24-hour post-dose ocular itching scores post-treatment with olopatadine 0.7% versus 0.2. Journal of pharmacokinetics and pharmacodynamics. 2018;45(4):593-605.
16. Leonardi A, Silva D, Perez Formigo D, Bozkurt B, Sharma V, Allegri P, et al. Management of ocular allergy. Allergy. 2019;74(9):1611-30.
17. Li J, Luo X, Ke H, Liang L. Recalcitrant Atopic Keratoconjunctivitis in Children: A Case Report and Literature Review. Pediatrics. 2018;141(Suppl 5):S470-s4.
18. Roumeau I, Coutu A, Navel V, Pereira B, Baker JS, Chiambaretta F, et al. Efficacy of medical treatments for vernal keratoconjunctivitis: A systematic review and meta-analysis. The Journal of allergy and clinical immunology. 2021;148(3):822-34.
19. Tang R, Lei S, Zhu L, Lv Y, Li H. Prevention of omalizumab for seasonal allergic rhinoconjunctivitis: a retrospective cohort study. Frontiers in immunology. 2022;13:913424.
20. Triantafillou V, Maina IW, Patel NN, Tong CCL, Papagiannopoulos P, Kohanski MA, et al. In vitro safety of ketotifen as a topical nasal rinse. International forum of allergy & rhinology. 2020;10(2):265-70.

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