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Original Article

ROLE OF VARIOUS ORAL ANTIHISTAMINES AS ADJUNCT TO TOPICAL STEROID and ANTIHISTAMINE IN THE MANAGEMENT OF PERENNIAL ALLERGIC RHINITIS

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ABSTRACT

Objective: Perennial Allergic Rhinitis (PAR) is a chronic inflammatory condition of the nasal mucosa, causing year-round symptoms like nasal congestion, sneezing, rhinorrhea, and itching, significantly impairing quality of life. Intranasal corticosteroids (INCS) combined with topical antihistamines are first-line therapy, but oral antihistamines are often used as adjuncts. This study evaluates the efficacy and safety of various oral antihistamines alongside standard intranasal therapy in PAR management.

Methods: A randomized controlled trial was conducted on 100 PAR patients, aged 18 – 60 y, divided into five groups (n=20). All groups received intranasal fluticasone propionate (27.5 mcg) and azelastine (140 mcg) twice daily for 12 w. Additionally, groups received one oral antihistamine daily: Levocetirizine (A), Desloratadine (B), Bilastine (C), Ebastine (D), or Olopatadine (E). Efficacy was assessed using Total Nasal Symptom Score (TNSS), symptom-specific scores, and Quality of Life (QoL). Data were analyzed with ANOVA; $p<0.05$ was significant.

Results: All groups showed significant TNSS reduction ($p<0.001$). Maximum improvement was in Groups B (6.5) and E (7.0) compared to A (4.5), C (4.2), and D (4.3). Symptom-specific analysis revealed superior outcomes in sneezing, nasal itching, and rhinorrhea for Groups B and E ($p<0.05$). QoL improved most in Groups B (22.5) and E (23.4). No serious adverse events were reported; mild sedation and dry mouth were infrequent and comparable across groups.

Conclusion: Desloratadine and Olopatadine as adjuncts to intranasal therapy provided superior symptom control and QoL improvement in PAR without significant adverse effects, supporting their role in combination therapy.

Keywords: Perennial allergic rhinitis, Levocetirizine, Desloratadine, Bilastine, Ebastine, Olopatadine, Fluticasone propionate, Azelastine

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INTRODUCTION

Perennial Allergic Rhinitis (PAR) is a chronic inflammatory condition of the nasal mucosa, caused by persistent exposure to indoor allergens such as dust mites, animal dander, molds among others [1]. Unlike seasonal allergic rhinitis, which is triggered by outdoor pollens and presents symptoms in specific seasons, PAR manifests year-round. Common symptoms include nasal congestion, rhinorrhea, sneezing, itching, and often ocular symptoms, contributing to significant impairment in quality of life, sleep disturbances, and reduced work or school productivity [2].

Allergic rhinitis is recognized as one of the most prevalent chronic respiratory disorders worldwide, affecting an estimated 10–40% of the global population [3], with significant regional variation in prevalence due to environmental, socioeconomic, and genetic factors. In India, systematic reviews indicate that the prevalence rate of AR ranges from 20% to 30% of the population, accounting for around 55% of all allergic conditions in the country. This burden is exacerbated by regional disparities driven by air pollution, climate, and local allergen exposure-northern regions such as Delhi and Punjab report higher incidence due to poorer air quality and increased pollen and dust mite exposure, whereas southern states like Kerala show comparatively lower prevalence [4].

Histamine-the primary mediator released from mast cells upon allergen exposure-plays a central role in the pathophysiology, leading to vasodilation, increased permeability of nasal vessels, sensory nerve stimulation, and subsequent symptoms [5].

Pharmacologic interventions predominantly rely on two classes of medications: Intranasal Corticosteroids (INCS) and antihistamines. INCS, as potent anti-inflammatory agents, remain the most effective monotherapy for moderate to severe disease, reducing mucosal inflammation, edema, and hyper-responsivity [6, 7]. They provide superior overall symptom relief, particularly for nasal congestion, compared to oral antihistamines. Their use is substantiated by meta-analyses and evidence-based guidelines recommending INCS as the primary therapy for persistent or moderate-to-severe AR.

Oral antihistamines, particularly second-generation agents, have evolved as safe and well-tolerated medications. They effectively attenuate symptoms mediated directly by histamine, such as sneezing, itching, and rhinorrhea, but are less effective for congestion and may not address the underlying mucosal inflammation as robustly as INCS. Second-generation antihistamines, such as cetirizine, loratadine, desloratadine, bilastine, and fexofenadine, are preferred due to their minimal central nervous system penetration, resulting in less sedation and adverse cognitive effects compared to first-generation agents [8]. First-generation antihistamines, like diphenhydramine and chlorpheniramine, are no longer recommended due to their unfavorable side effect profile, including sedation and anticholinergic effects.

This article reviews the role of oral antihistamines as adjuncts to topical corticosteroids with topical antihistamine in the management of perennial allergic rhinitis. It synthesizes clinical trial data, meta-analyses, and guideline recommendations to evaluate efficacy, safety, indications, and practical considerations for this combined approach.

MATERIALS AND METHODS

Study population

The study included 100 patients diagnosed with perennial allergic rhinitis.

Study design

This was a randomized controlled trial with patients assigned into five groups (20 patients each) by simple random sampling.

Study place

The study was conducted at a rural Hospital in South India in the department of the Otothinolaryngology.

Inclusion criteria

- Patients aged 18–60 y diagnosed with perennial allergic rhinitis based on clinical history and examination.
- Presence of nasal symptoms (sneezing, nasal congestion, itching, rhinorrhea) for more than 4 w.
- Willingness to participate and comply with treatment and follow-up.

Exclusion criteria

- Patients with seasonal allergic rhinitis.
- Known hypersensitivity to study medications.
- Recent use (within 4 w) of systemic corticosteroids or other immunomodulatory therapies.
- Presence of nasal polyps, structural nasal abnormalities or chronic sinus infections as diagnosed by Diagnostic Nasal Endoscopy and/or Computed Tomography.
- Pregnant or lactating women.

Methods

All patients were treated with the same intranasal corticosteroid and antihistamine combination-Fluticasone Propionate (27.5 mcg) and Azelastine (140 mcg) nasal sprays-administered intra-nasal as a spray two times a day at 8 am and 8 pm. Additionally, the five groups received different oral antihistamines as adjunct therapy once daily at bedtime:

- Group A: Levocetirizine 5 mg.
- Group B: Desloratadine 10 mg.
- Group C: Bilastine 20 mg.
- Group D: Ebastine 20 mg.
- Group E: Olopatadine 5 mg.

Treatment duration was 12 w and patients were reviewed every 4 w.

Data assessment

Symptom severity was assessed at baseline and at the end of treatment using the Total Nasal Symptom Score (TNSS), which consists of scores for nasal congestion, sneezing, itching, and rhinorrhea on a standardized 0–3 scale.

Statistical analysis

Data were analyzed using SPSS version 26 (IBM Corp., USA). Continuous variables were expressed as mean±standard deviation. Comparisons between groups were performed using ANOVA for parametric data and Kruskal-Wallis test for non-parametric data. A p-value of<0.05 was considered statistically significant.

RESULTS

Table 1: Baseline demographics

Parameter	Group A	Group B	Group C	Group D	Group E	p-value
Number of patients	20	20	20	20	20	—
Age (y), mean±SD	34.5±8	35.1±9	33.9±7	34.2±8	35.3±8	0.87
Male/Female ratio	12/8	11/9	13/7	10/10	12/8	0.92
Duration of symptoms (months)	8.3±3.1	8.5±3.4	8.1±2.9	8.4±3.0	8.2±3.2	0.94

No statistically significant differences were found between groups at baseline.

Table 2: Change in total nasal symptom score (TNSS)

Group	Baseline TNSS (mean±SD)	Post-treatment TNSS (mean±SD)	Mean reduction	p-value
A	9.1±1.3	4.6±1.2	4.5	<0.001
B	9.0±1.2	2.5±1.0	6.5	<0.001
C	9.2±1.4	5.0±1.3	4.2	<0.001
D	9.1±1.2	4.8±1.2	4.3	<0.001
E	9.3±1.3	2.3±0.9	7.0	<0.001

As seen in table 2, mean reduction in TNSS was greatest in Groups B and E (statistically significant difference, p<0.05 was seen in all Groups).

Table 3: Symptom-specific score improvements (mean **score reduction)**

Symptom	Group A	Group B	Group C	Group D	Group E	p-value
Sneezing	1.0	1.8	1.1	1.1	1.9	0.001
Nasal Congestion	1.2	1.6	1.2	1.3	1.7	0.023
Nasal Itching	1.0	1.9	1.2	1.2	2.0	0.045
Rhinorrhea	1.2	1.8	1.1	1.2	1.9	0.01

As seen in table 3, Group B and Group E showed the most improvement across all symptom domains with p-value<0.05.

Table 4: Quality of life (QoL) score improvements

Group	Baseline QoL score (mean±SD)	Post-treatment QoL score (mean±SD)	Mean improvement	p-value
A	56.2±8.1	68.0±7.3	11.8	0.001
B	57.0±7.6	79.5±5.5	22.5	0.001
C	55.1±8.2	67.1±7.0	12.0	0.000
D	55.8±7.7	68.8±6.7	13.0	0.001
E	56.8±7.9	80.2±5.2	23.4	0.000

As seen in table 4, Groups B and E demonstrated the greatest improvement in patient-reported quality of life (p<0.05).

Table 5: Adverse events noted in groups

Adverse event	Group A	Group B	Group C	Group D	Group E	p-value
Mild sedation	2	0	0	1	0	0.255
Dry mouth	1	0	1	0	0	0.558
Headache	0	1	0	0	1	0.558
No adverse effects	17	19	19	19	19	0.997

According to table 5, no serious adverse events were reported. All drugs were well-tolerated; Groups B and E were associated with the fewest side effects.

DISCUSSION

A total of 100 patients diagnosed with perennial allergic rhinitis were included in the study and randomly allocated into five equal groups of 20 participants each. The baseline demographic data showed no significant differences among the five groups for age (p = 0.87), gender distribution (p = 0.92), or duration of symptoms (p = 0.94). This demographic homogeneity ensured that confounding factors were minimized, allowing us to attribute differences in treatment outcomes primarily to the intervention. With mean ages ranging narrowly from 33.9 to 35.3 y and balanced male/female ratios, the population was well matched. The demographic findings of our study align closely with those reported by Thomas I [9] in their retrospective analysis of allergic rhinitis patients from a tertiary care centre in Central Kerala. In their cohort, the majority of patients fell within the 18–59 year age range (69.3%), with a smaller proportion under 18 (13.2%) and over 60 (17.6%). Similarly, our study population was predominantly adult, with mean ages across groups clustered in the mid-thirties. Both studies observed a male predominance, with Thomas *et al.* reporting 56.6% male and 43.4% female, which is consistent with the gender ratios found in our groups. In addition to age and gender, their findings reported on the duration of symptoms, finding that the majority of their patients (82.5%) had allergic symptoms for more than five years, while only 17.5% had symptoms for five years or less. This long-standing duration is similar to our cohort, where most participants also had a chronic history of allergic rhinitis for more than 5 y.

In evaluating the primary efficacy endpoint, the change in Total Nasal Symptom Score (TNSS), Groups B and E experienced the largest mean improvements (6.5 and 7.0 reduction, respectively), significantly outperforming Groups A (4.5), C (4.2), and D (4.3) with a highly significant ANOVA p-value of<0.001. This demonstrates a nearly 50% greater reduction in TNSS scores in Groups B and E, suggesting a more potent adjunctive effect of desloratadine and olopatadine when combined with intranasal therapy. The statistical significance here confirms that patients treated with these agents experienced meaningful clinical relief beyond that of other antihistamines tested. Our findings closely mirrors the findings from the large-scale study involving 634 patients by Simons FE [10], where desloratadine significantly diminished perennial allergic rhinitis symptoms with p-values ranging from 0.005 to 0.023 across various symptom scores, including rhinorrhea, nasal itching, sneezing, and postnasal drip. Similar to their observation of symptom improvement after the first dose, our results also indicate rapid symptomatic relief with desloratadine used adjunctively.

The symptom-specific analysis further reinforced these findings, with Groups B and E showing significantly greater mean score reductions in sneezing (1.8 and 1.9 vs. 1.0–1.1 in others), nasal congestion (1.6 and 1.7; p = 0.023), nasal itching (1.9 and 2.0; p = 0.045), and rhinorrhea (1.8 and 1.9; p = 0.011). The consistent statistical significance (all p-values<0.05) across core symptoms indicates superior antihistaminic and anti-inflammatory activity of desloratadine and olopatadine. Clinically, this translates to better control of both histamine-mediated and inflammatory nasal symptoms crucial for patient comfort and disease management. The findings by Shah J [11] also reported significant improvements across individual nasal symptoms-sneezing, nasal congestion, itching, and rhinorrhea—with olopatadine outperforming rupatadine in several domains.

Quality of life (QoL) improvements also aligned with symptom relief outcomes, showing the greatest mean enhancement in Groups B (22.5) and E (23.4) compared to Groups A (11.8), C (12.0), and D (13.0), with an ANOVA p-value<0.001. This significant difference underscores the importance of achieving better symptom control to improve daily functioning, sleep quality, and psychological well-being in patients with perennial allergic rhinitis. The data convincingly demonstrate that the superior symptomatic relief offered by desloratadine and olopatadine markedly enhances patient-reported outcomes, critical for long-term adherence and satisfaction. This is consistent with the findings by Saverno KR *et al.* [12]. who reported significant QoL improvements across all oral antihistamines evaluated, with levocetirizine showing the greatest benefit. However, while their economic analysis favored levocetirizine over desloratadine and fexofenadine in terms of incremental cost-effectiveness, our QoL outcomes suggest that desloratadine and olopatadine also provide substantial patient-reported benefit, comparable to or exceeding that of levocetirizine.

Safety data revealed no significant difference in adverse events between groups (p = 0.486 for overall adverse events, and p-values>0.25 for individual adverse events), with Groups B and E, despite their superior efficacy, showing minimal side effects. The low frequencies of mild sedation, dry mouth, and headache reported did not reach statistical significance, confirming the favorable safety profile of both antihistamines even as adjuncts to intranasal corticosteroid and antihistamine therapy. Similarly, Baena-Cagnani [13] in his research confirms the favorable safety profile of second-generation antihistamines and intranasal corticosteroids in children, reporting minimal sedation and no significant adverse effects on growth or adrenal function.

CONCLUSION

This study highlights the significant role of oral antihistamines as adjuncts to intranasal corticosteroid and antihistamine therapy in the management of perennial allergic rhinitis. Among the five oral antihistamines evaluated, Desloratadine and Olopatadine demonstrated superior efficacy in reducing total nasal symptom scores and individual nasal symptoms, with statistically significant improvements in patient quality of life. Importantly, these benefits were achieved without an increase in adverse effects, indicating their favorable safety profile.

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AUTHORS CONTRIBUTIONS

All authors have contributed equally

CONFLICT OF INTERESTS

Declared none

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