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Original Research Article

# A Comparative Study to Evaluate the Safety and Efficacy of Tablet Montelukast with Fexofenadine versus Tablet Montelukast with Levocetirizine in Patient of Allergic Rhinitis in Tertiary Care Centre

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**Conflict of interest: Nil**

**Abstract**

**Background:** Allergic rhinitis is a common IgE-mediated inflammatory disorder of the nasal mucosa that impairs quality of life. Combination therapy with a leukotriene receptor antagonist and an antihistamine is widely used, but comparative data between different antihistamine partners remain limited.

**Material and Methods:** In this prospective, randomized, parallel-group study, 277 patients with allergic rhinitis received either Montelukast plus Fexofenadine (Group A, n=139) or Montelukast plus Levocetirizine (Group B, n=138) for three months. TNSS, TOSS, RQLQ, VAS, serum IgE, and AEC were assessed at baseline, 15 days, 1, 2, and 3 months; adverse events were recorded throughout.

**Results:** Baseline demographic and clinical characteristics were comparable between groups (Table 1). Both groups showed progressive improvement in TNSS, TOSS, VAS, RQLQ, serum IgE, and AEC over follow-up, with no significant difference in the primary outcome (TNSS) at any time point (Table 2, Figure 1). Group A showed higher AEC at 1 and 3 months (p=0.047, p=0.039) and greater RQLQ improvement at 2 and 3 months (p=0.042, p=0.048) (Table 2, Figure 2). At study end, rhinorrhea control was better with Group B (p=0.026), while overall satisfaction was marginally higher with Group A (p=0.049) (Table 3). Both regimens were well tolerated, with mild, comparable rates of drowsiness, gastrointestinal symptoms, and other adverse events; no serious adverse events occurred (Table 4).

**Conclusion:** Montelukast–Fexofenadine and Montelukast–Levocetirizine combinations are equally effective and safe for allergic rhinitis, with treatment selection guided by individual symptom profile and tolerability.

**Keywords:** Allergic rhinitis, Montelukast, Fexofenadine, Levocetirizine, TNSS, RQLQ.

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## Introduction

Allergic rhinitis (AR) is an IgE-mediated inflammatory disorder of the nasal mucosa, arising from immune dysregulation triggered by allergen exposure and characterized by sneezing, nasal congestion, rhinorrhea, and nasal itching, with substantial effects on patients' quality of life [1]. Its global burden continues to rise, with the prevalence of allergic rhinitis reported to have increased by 2–3% each year over recent decades, a trend increasingly linked to environmental and climate-related factors such as longer pollen seasons and higher pollen concentrations [2]. Current management of AR relies on a combination of intranasal corticosteroids, oral and intranasal antihistamines, decongestants, and leukotriene receptor antagonists, with the recently updated

Allergic Rhinitis and its Impact on Asthma (ARIA)-EAACI 2024–2025 guidelines emphasizing that treatment decisions should account for the clinical variability of the disease, patient values, and medication affordability [3]. Among oral therapeutic strategies, the combination of montelukast, a leukotriene receptor antagonist, with a second-generation H1-antihistamine has been increasingly used to target the complementary inflammatory pathways underlying nasal and ocular symptoms.

A recent meta-analysis of 13 randomized controlled trials comprising 2,950 patients demonstrated that montelukast-antihistamine combination therapy significantly improved daytime nasal symptoms compared with montelukast monotherapy, with the levocetirizine-based combination additionally showing significant benefit for nighttime symptoms and for individual symptoms such as sneezing, nasal itching, nasal obstruction, and rhinorrhea [4]. Consistent with this, a randomized trial in children demonstrated that the fixed-dose combination of montelukast and levocetirizine produced significantly greater improvement in daytime and nighttime nasal symptom scores and quality of life compared with montelukast alone [5]. Similarly, combining montelukast with other antihistamines such as loratadine has also been shown to be superior to monotherapy in improving nasal symptoms and rhinoconjunctivitis-specific quality of life [6].

While these studies collectively support the added benefit of montelukast-antihistamine combination therapy over monotherapy, direct comparative data between different antihistamine partners used in combination with montelukast—specifically fexofenadine versus levocetirizine—remain limited, particularly with respect to their relative efficacy, safety, and cost-effectiveness in real-world clinical settings. Given that both agents are widely prescribed second-generation antihistamines with differing pharmacological profiles, a head-to-head comparison of these two combinations regimens may help guide more individualized treatment selection in patients with allergic rhinitis. The present study was therefore undertaken to compare the efficacy, safety, and cost-effectiveness of montelukast plus fexofenadine versus montelukast plus levocetirizine in patients with allergic rhinitis.

## Materials and Methods

**Study Design and Setting:** This was a prospective, open-label, randomized, parallel-group comparative study conducted to evaluate the efficacy, safety, and cost-effectiveness of two combination pharmacotherapy regimens for allergic rhinitis. The study was conducted jointly by the Department of Pharmacology and Therapeutics and the Department of Otorhinolaryngology, BRD Medical College, Gorakhpur, following approval from the Institutional Ethics Committee. The overall study period spanned one year, during which each enrolled participant was followed individually for three months.

**Ethical Considerations:** The study protocol was approved by the Institutional Ethics Committee of BRD Medical College, Gorakhpur, and was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice (GCP) guidelines. Written informed consent was obtained from all participants after they were provided detailed information about the study. Patient confidentiality was maintained throughout, and all adverse events were documented, with serious adverse events reported to the ethics committee as required.

**Study Population:** Patients of either sex aged 18–65 years with a clinical diagnosis of allergic rhinitis (seasonal or perennial), presenting with at least two of the four cardinal symptoms — sneezing, nasal congestion, rhinorrhea, or nasal itching — for a minimum of one hour on most days, were eligible for enrolment. Patients with known hypersensitivity to the study drugs, significant comorbidities such as hypertension or diabetes mellitus, concurrent medications likely to interfere with study assessments, pregnancy or lactation, significant hepatic or renal impairment, or structural nasal abnormalities (e.g., deviated nasal septum, nasal polyps) were excluded.

**Sample Size:** The sample size was calculated using the formula $n = Z^2P(1-P)/d^2$, with Z = 1.96 (95% confidence level), P = 0.22 (estimated prevalence of allergic rhinitis), and d = 0.05 (acceptable margin of error), yielding a minimum requirement of 264 participants. After adjusting for an anticipated 5% attrition, the final target sample size was set at 277 participants.

**Randomization and Interventions:** Eligible participants were randomized using block randomization (block size = 4) into two parallel treatment groups. Group A (n=139) received Montelukast 10 mg plus Fexofenadine 120 mg once daily in the evening, and Group B (n=138) received Montelukast 10 mg plus Levocetirizine 5 mg once daily in the evening, both for a duration of three months.

**Assessment Schedule:** Baseline evaluation (Day 0) included demographic details (age, sex, occupation, education, and socioeconomic status), clinical history (duration, pattern, triggers, and family history of atopy), and physical examination with anterior rhinoscopy, and laboratory and symptom assessments as detailed below. Follow-up visits were scheduled at Days 15, 30, 60, and 90 (±3

days), at which TNSS, TOSS, Total Symptom Score (TSS), RQLQ, VAS, adverse events, and treatment compliance were reassessed. Study medications were dispensed weekly during the first month and monthly thereafter; compliance was calculated from unused tablet counts, with ≥80% adherence considered acceptable. Participants maintained an 8-day symptom diary, and laboratory investigations were repeated at Day 90.

**Outcome Measures**

**Serum IgE:** Total serum IgE, a biomarker reflecting the degree of allergic sensitization, was measured at baseline and at Day 90 by enzyme-linked immunosorbent assay (ELISA) and interpreted against age-specific reference ranges.

**Absolute Eosinophil Count (AEC):** AEC, an indicator of allergic mucosal inflammation, was derived from the complete blood count (total leukocyte count × eosinophil percentage) at baseline and Day 90; values below 500 cells/μL were considered within the normal range.

**Total Nasal Symptom Score (TNSS):** TNSS scored four cardinal nasal symptoms — nasal congestion, rhinorrhea, nasal itching, and sneezing — each on a 0–3 severity scale (0 = none to 3 = severe), yielding a total range of 0–12. TNSS was recorded at baseline and at every follow-up visit and served as the primary efficacy measure.

**Total Ocular Symptom Score (TOSS):** TOSS assessed ocular itching, lacrimation, and conjunctival redness, each graded 0–3 using the same severity criteria as TNSS, giving a total range of 0–9. TOSS was recorded alongside TNSS at every visit.

**Total Symptom Score (TSS):** TSS, the sum of TNSS and TOSS (maximum score 21), provided a composite measure of overall nasal and ocular symptom burden at each assessment point.

**Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ):** The 28-item RQLQ (Juniper et al.), covering seven domains — activities, sleep, non-nose/eye symptoms, practical problems, nasal symptoms, eye symptoms, and emotional function — was administered at baseline and each follow-up visit. Each item was rated on a 7-point scale (0 = not troubled to 6 = extremely troubled), with the overall score calculated as the mean of all responses; lower scores indicated better quality of life, and a 0.5-point change was considered the minimum clinically important difference.

**Visual Analogue Scale (VAS):** A 0–10 cm VAS was used at baseline and every follow-up visit to capture patients' subjective perception of overall symptom severity and treatment satisfaction.

**Primary and Secondary Outcomes:** The primary outcome was the change in TNSS from baseline to Day 90. Secondary outcomes included changes in TOSS, TSS, RQLQ, VAS, serum IgE, and AEC, along with the incidence of treatment-related adverse events and patient satisfaction over the three-month follow-up.

**Statistical Analysis:** Statistical analyses were performed using SPSS software (version 26.0), applying both intention-to-treat (ITT) and per-protocol (PP) approaches. Normality of continuous data was assessed using the Shapiro–Wilk test; normally distributed variables were expressed as mean ± standard deviation, and non-normally distributed variables as median with interquartile range. Baseline comparisons between groups used the independent samples t-test or Mann–Whitney U test for continuous variables and the chi-square test or Fisher's exact test for categorical variables. As the efficacy data were non-normally distributed, between-group comparisons were performed using the Mann–Whitney U test, within-group comparisons across time using the Friedman test, and comparisons across multiple time points using the Kruskal–Wallis test. Missing data were handled using multiple imputation for the ITT analysis and Last Observation Carried Forward (LOCF) for sensitivity analysis. A two-tailed p-value $<0.05$ was considered statistically significant, with Bonferroni correction applied for multiple comparisons.

**Quality Assurance:** Study quality was maintained through staff training on the protocol and GCP guidelines, use of standardized case record forms and validated questionnaires, regular monitoring visits, double data entry with computerized validation, and source document verification for 20% of enrolled cases. Protocol deviations were documented and reported as per institutional requirements.

**Results**

A total of 277 patients with allergic rhinitis were randomized to receive either Montelukast plus Fexofenadine (Group A, n=139) or Montelukast plus Levocetirizine (Group B, n=138). The two groups were comparable across all baseline demographic and clinical parameters (Table 1). No significant between-group difference was observed for age distribution ($\chi^2$=2.033, p=0.362), sex ($\chi^2$=0.031, p=0.860), residence ($\chi^2$=1.313, p=0.252), or socioeconomic status ($\chi^2$=1.752, p=0.416). Mean BMI was similar between Group A and Group B (25.65±5.90 vs 25.76±5.64 kg/m², t=−0.163, p=0.870), as was the mean duration of symptoms (29.83±16.23 vs 27.95±16.12 months, t=0.970, p=0.333). The distribution of rhinitis type (perennial vs seasonal; $\chi^2$=0.811, p=0.368) and known allergen sensitivities (dust, food, pollen, or none; $\chi^2$=1.940, p=0.585) also did not differ

significantly between groups, confirming adequate baseline comparability between the two treatment arms. Serial changes in serum IgE, absolute eosinophil count (AEC), and symptom/quality-of-life scores over the 3-month follow-up period are summarized in Table 2 and illustrated in Figures 1 and 2. Serum IgE levels declined progressively in both groups from baseline (Group A: 120.67±27.91 IU/mL; Group B: 120.01±27.42 IU/mL) to 3 months (Group A: 90.99±27.59 IU/mL; Group B: 89.61±27.46 IU/mL), with no significant between-group difference at any time point ($p>0.05$ throughout) (Table 2, Figure 2A). AEC similarly decreased over time in both arms; while baseline, 15-day, and 2-month values were comparable ($p>0.05$), Group A showed significantly higher mean AEC than Group B at 1 month (294.97±82.59 vs 286.45±77.22, $t=2.887$, $p=0.047$) and 3 months (235.09±83.05 vs 226.95±76.25, $t=3.850$, $p=0.039$) (Table 2, Figure 2B).

Both groups demonstrated a steady reduction in Total Nasal Symptom Score (TNSS) across the follow-up period, from a baseline of 10.05±1.43 (Group A) and 9.02±1.40 (Group B) to 4.02±1.58 and 4.07±1.53 respectively at 3 months, with no significant intergroup difference at any assessment point ($p>0.05$) (Table 2, Figure 1A). Total Ocular Symptom Score (TOSS) followed a comparable declining trend in both groups; a significant difference favoring Group B was noted only at the 15-day assessment (4.39±1.58 vs 4.26±1.44, $t=2.703$, $p=0.048$), while baseline, 1-month, 2-month, and 3-month values did not differ significantly (Table 2, Figure 1B).

Mean VAS scores decreased from baseline through 3 months in both arms. A significant difference was observed at baseline, with Group A recording higher scores than Group B (4.11±0.79 vs 3.95±0.81, $t=4.641$, $p=0.042$), and again at 3 months (0.42±0.60 vs 0.36±0.58, $t=5.879$, $p=0.038$); no significant difference was seen at 15 days, 1 month, or 2 months (Table 2, Figure 1C). RQLQ scores also improved progressively in both groups, with no significant difference at baseline, 15 days, or 1 month; however, Group B showed significantly higher (less improved) RQLQ scores than Group A at 2 months (2.91±1.01 vs 2.71±0.97, $t=-2.797$, $p=0.042$) and 3 months (2.07±1.04 vs 1.86±1.00, $t=-2.770$, $p=0.048$), suggesting comparatively greater quality-of-life improvement with the Montelukast–Fexofenadine combination during later follow-up (Table 2, Figure 1D).

At the end of the 3-month follow-up period, the magnitude of TNSS reduction was similar between Group A and Group B (6.04±0.58 vs 5.99±0.59, $t=0.715$, $p=0.475$), as was the overall satisfaction score (7.86±1.26 vs 8.01±1.16, $t=-1.037$, $p=0.300$) and nasal congestion score (1.60±0.81 vs 1.62±0.79, $t=-0.273$, $p=0.785$) (Table 3). However, Group B reported a significantly lower rhinorrhea score than Group A (1.50±0.87 vs 1.71±0.71, $t=-2.242$, $p=0.026$), while patient satisfaction measured on the VAS was marginally but significantly higher in Group A (8.09±1.45 vs 7.97±1.33, $t=1.689$, $p=0.049$), indicating better control of rhinorrhea with Levocetirizine-based therapy alongside slightly greater overall satisfaction with the Fexofenadine-based regimen.

The two regimens were generally well tolerated over the 3-month study period (Table 4). The incidence of drowsiness was comparable between groups at 15 days (10.1% vs 13.0%, $\chi^2=0.533$, $p=0.465$) and 2 months (5.8% vs 4.3%, $\chi^2=0.286$, $p=0.593$), but differed significantly at baseline (3.6% vs 1.4%, $\chi^2=1.297$, $p=0.05$), 1 month (6.5% vs 10.9%, $\chi^2=2.690$, $p=0.04$), and 3 months (2.9% vs 1.4%, $\chi^2=3.667$, $p=0.014$), with Group B showing a higher drowsiness burden at 1 month and Group A a marginally higher rate at 3 months. Gastrointestinal symptoms showed a similar pattern, with no significant difference at baseline, 15 days, or 3 months, but a significantly higher incidence in Group B at 1 month (5.0% vs 6.5%, $\chi^2=1.810$, $p=0.039$) and 2 months (2.9% vs 4.3%, $\chi^2=1.430$, $p=0.042$).

**Table 1: Baseline Demographic and Clinical Characteristics**

| Characteristic | Group A (n=139) | Group B (n=138) | Statistic | p-value |
|---|---|---|---|---|
| **Age group (years)** | | | $\chi^2=2.033$ | 0.362 |
| 10–30 | 37 | 41 | | |
| 31–50 | 57 | 63 | | |
| 51–70 | 45 | 34 | | |
| **Sex** | | | $\chi^2=0.031$ | 0.860 |
| Female | 76 | 74 | | |
| Male | 63 | 64 | | |
| **Residence** | | | $\chi^2=1.313$ | 0.252 |
| Rural | 71 | 61 | | |
| Urban | 68 | 77 | | |
| **Socioeconomic status** | | | $\chi^2=1.752$ | 0.416 |
| Lower | 43 | 51 | | |

| | | | | |
|---|---|---|---|---|
| Middle | 52 | 42 | | |
| Upper | 44 | 45 | | |
| BMI (kg/m²), mean±SD | 25.65 ± 5.90 | 25.76 ± 5.64 | t=−0.163 | 0.870 |
| Duration of symptoms (months), mean±SD | 29.83 ± 16.23 | 27.95 ± 16.12 | t=0.970 | 0.333 |
| **Type of rhinitis** | | | $\chi^2$=0.811 | 0.368 |
| Perennial | 65 | 72 | | |
| Seasonal | 74 | 66 | | |
| **Known allergies** | | | $\chi^2$=1.940 | 0.585 |
| Dust | 43 | 36 | | |
| Food | 28 | 34 | | |
| Pollen | 33 | 28 | | |
| None | 35 | 40 | | |

**Table 2: Biomarker and Symptom/QoL Scores across Follow-up**

| Parameter | Time Point | Group A Mean±SD | Group B Mean±SD | t-value | p-value |
|---|---|---|---|---|---|
| **Serum IgE (IU/mL)** | Baseline | 120.67 ± 27.91 | 120.01 ± 27.42 | 0.199 | 0.843 |
| | 15 Days | 115.55 ± 27.84 | 114.70 ± 27.40 | 0.254 | 0.800 |
| | 1 Month | 106.05 ± 27.75 | 104.85 ± 27.42 | 0.361 | 0.718 |
| | 2 Months | 98.52 ± 27.65 | 97.23 ± 27.42 | 0.391 | 0.696 |
| | 3 Months | 90.99 ± 27.59 | 89.61 ± 27.46 | 0.419 | 0.750 |
| **AEC (cells/mm³)** | Baseline | 353.98 ± 83.07 | 346.41 ± 76.74 | 0.787 | 0.432 |
| | 15 Days | 303.76 ± 72.53 | 297.93 ± 66.07 | 0.698 | 0.486 |
| | 1 Month | 294.97 ± 82.59 | 286.45 ± 77.22 | 2.887 | **0.047** |
| | 2 Months | 240.51 ± 59.26 | 232.15 ± 54.02 | 1.226 | 0.221 |
| | 3 Months | 235.09 ± 83.05 | 226.95 ± 76.25 | 3.850 | **0.039** |
| **TNSS** | Baseline | 10.05 ± 1.43 | 9.02 ± 1.40 | −0.002 | 0.998 |
| | 15 Days | 8.47 ± 1.55 | 8.54 ± 1.49 | −0.375 | 0.708 |
| | 1 Month | 7.04 ± 1.48 | 7.01 ± 1.47 | 0.121 | 0.904 |
| | 2 Months | 5.56 ± 1.49 | 5.57 ± 1.49 | −0.063 | 0.950 |
| | 3 Months | 4.02 ± 1.58 | 4.07 ± 1.53 | −0.273 | 0.785 |
| **TOSS** | Baseline | 5.84 ± 1.39 | 5.80 ± 1.43 | 0.263 | 0.793 |
| | 15 Days | 4.39 ± 1.58 | 4.26 ± 1.44 | 2.703 | **0.048** |
| | 1 Month | 3.40 ± 1.76 | 3.30 ± 1.73 | 0.471 | 0.638 |
| | 2 Months | 2.90 ± 1.80 | 2.83 ± 1.72 | 0.346 | 0.729 |
| | 3 Months | 2.44 ± 1.83 | 2.38 ± 1.71 | 0.291 | 0.771 |
| **VAS** | Baseline | 4.11 ± 0.79 | 3.95 ± 0.81 | 4.641 | **0.042** |
| | 15 Days | 3.09 ± 0.82 | 2.97 ± 0.84 | 2.234 | 0.058 |
| | 1 Month | 2.09 ± 0.86 | 1.96 ± 0.97 | 1.174 | 0.241 |
| | 2 Months | 1.10 ± 0.93 | 1.03 ± 0.93 | 0.644 | 0.520 |
| | 3 Months | 0.42 ± 0.60 | 0.36 ± 0.58 | 5.879 | **0.038** |
| **RQLQ** | Baseline | 5.31 ± 0.98 | 5.46 ± 1.05 | −1.269 | 0.206 |
| | 15 Days | 4.49 ± 0.91 | 4.60 ± 1.02 | −0.965 | 0.336 |
| | 1 Month | 3.60 ± 0.91 | 3.78 ± 1.05 | −1.512 | 0.132 |
| | 2 Months | 2.71 ± 0.97 | 2.91 ± 1.01 | −2.797 | **0.042** |
| | 3 Months | 1.86 ± 1.00 | 2.07 ± 1.04 | −2.770 | **0.048** |

**Table 3: End-of-Study Symptom Reduction and Patient Satisfaction**

| Parameter | Group A (n=139) | Group B (n=138) | t-value | p-value |
|---|---|---|---|---|
| TNSS reduction | 6.04 ± 0.58 | 5.99 ± 0.59 | 0.715 | 0.475 |
| Overall satisfaction score | 7.86 ± 1.26 | 8.01 ± 1.16 | −1.037 | 0.300 |
| Nasal congestion score (0–3) | 1.60 ± 0.81 | 1.62 ± 0.79 | −0.273 | 0.785 |
| Rhinorrhea score (0–3) | 1.50 ± 0.87 | 1.71 ± 0.71 | −2.242 | **0.026** |
| Patient satisfaction (VAS) | 8.09 ± 1.45 | 7.97 ± 1.33 | 1.689 | **0.049** |

**Table 4: Safety and Tolerability Profile**

| Adverse Event | Time Point | Group A, n (%) | Group B, n (%) | Statistic | p-value |
|---|---|---|---|---|---|
| **Drowsiness** | Baseline | 5 (3.6) | 2 (1.4) | $\chi^2$=1.297 | 0.05 |
| | 15 Days | 14 (10.1) | 18 (13.0) | $\chi^2$=0.533 | 0.465 |
| | 1 Month | 9 (6.5) | 15 (10.9) | $\chi^2$=2.690 | 0.04 |
| | 2 Months | 8 (5.8) | 6 (4.3) | $\chi^2$=0.286 | 0.593 |
| | 3 Months | 4 (2.9) | 2 (1.4) | $\chi^2$=3.667 | 0.014 |
| **GI symptoms** | Baseline | 3 (2.2) | 4 (2.9) | $\chi^2$=0.199 | 0.793 |
| | 15 Days | 11 (7.9) | 9 (6.5) | $\chi^2$=0.200 | 0.654 |
| | 1 Month | 7 (5.0) | 9 (6.5) | $\chi^2$=1.810 | 0.039 |
| | 2 Months | 4 (2.9) | 6 (4.3) | $\chi^2$=1.430 | 0.042 |
| | 3 Months | 2 (1.4) | 3 (2.2) | $\chi^2$=0.142 | 0.754 |
| **Other adverse events** (any time) | Dizziness | 32 (23.0) | 36 (26.1) | $\chi^2$=3.526 | **0.047** |
| | Headache | 10 (7.2) | 10 (7.2) | | |
| | Nausea | 30 (21.6) | 36 (26.1) | | |
| | Rash | 38 (27.3) | 25 (18.1) | | |
| | None | 29 (20.9) | 31 (22.5) | | |
| **Residual symptoms** (overall) | Sneezing | 106 (76.3) | 116 (84.1) | $\chi^2$=4.647 | **0.04** |
| | Eye symptoms | 117 (84.2) | 105 (76.1) | $\chi^2$=3.845 | **0.032** |

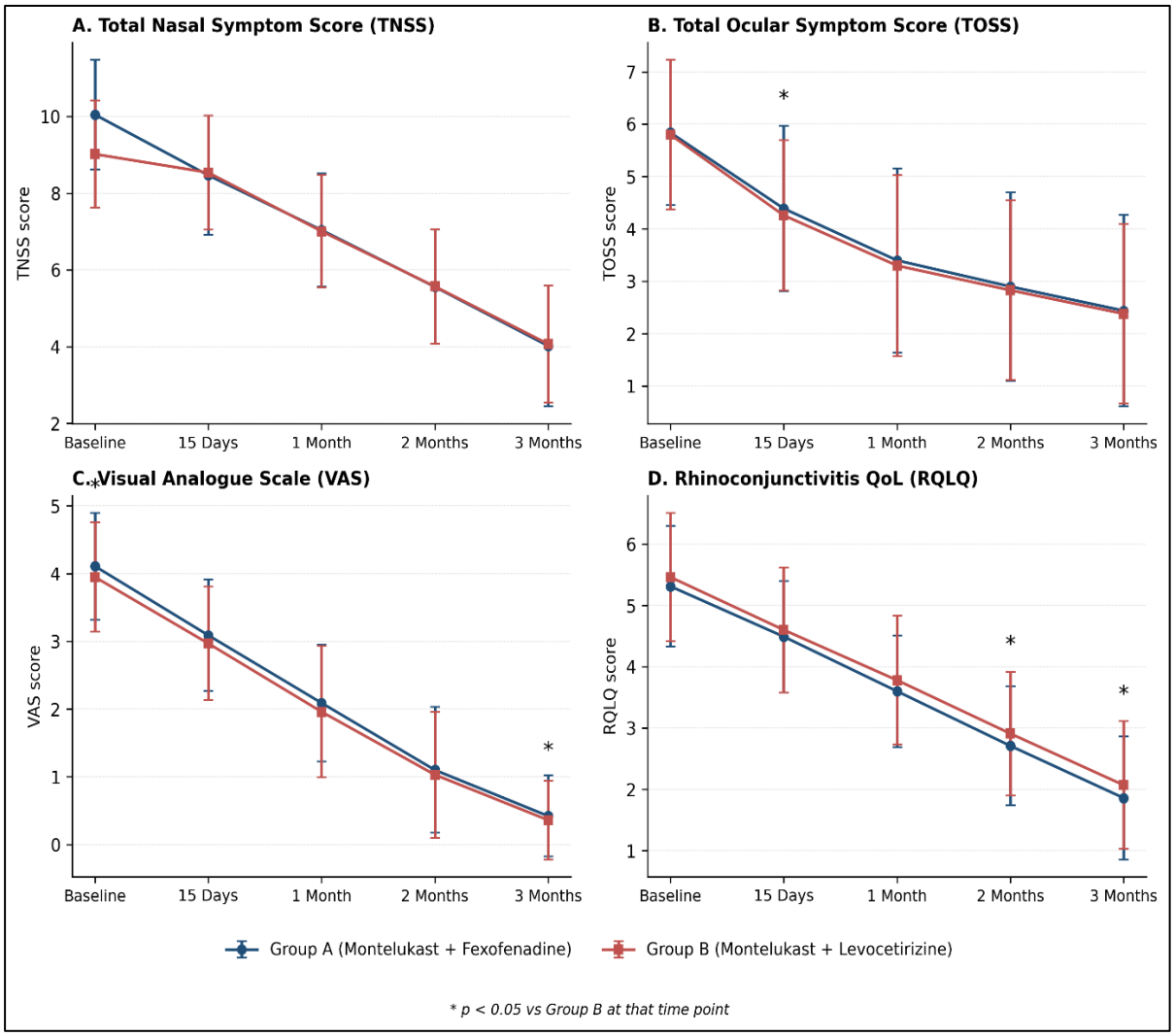


**Figure 1: Comparative Trends in Symptom Severity and Quality-of-Life Scores over the Follow-up Period**

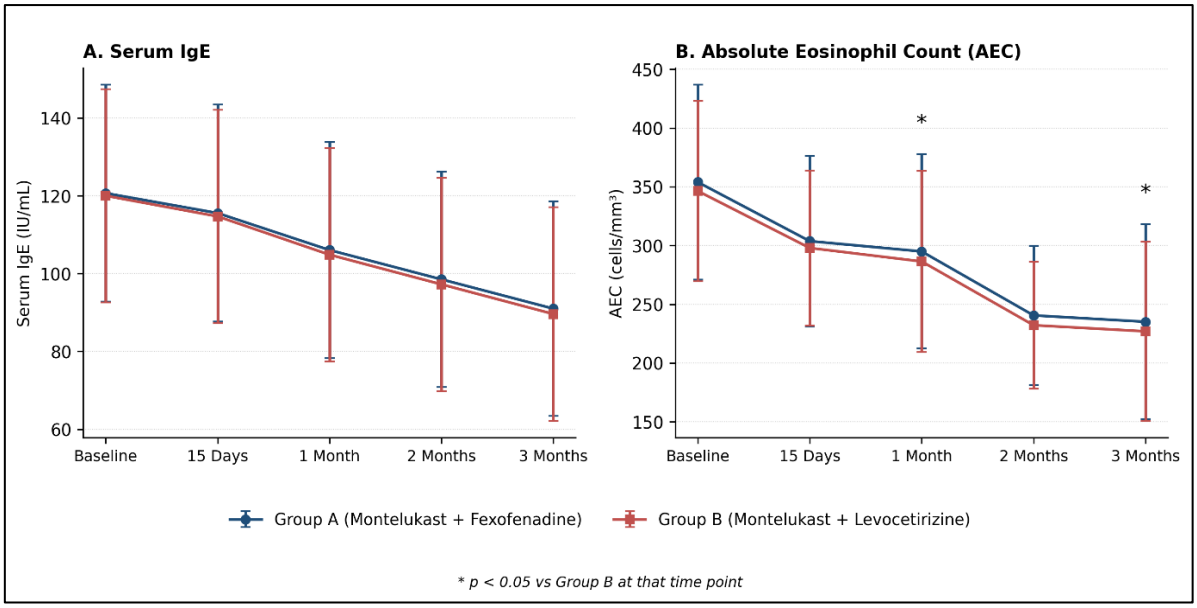


**Figure 2: Comparative Trends in Serum IgE and Absolute Eosinophil Count Over the Follow-up Period**

## Discussion

The present study demonstrated that both montelukast–fexofenadine and montelukast–levocetirizine combinations produced significant and progressive improvement in nasal symptoms, ocular symptoms, quality of life, and inflammatory biomarkers over the three-month follow-up. However, no significant difference was observed in the primary efficacy outcome (TNSS), suggesting that both regimens provide comparable overall clinical benefit in patients with allergic rhinitis. These findings support the current concept that simultaneous blockade of histamine- and leukotriene-mediated pathways offers greater symptom control than targeting either pathway alone, particularly in patients with persistent or moderate-to-severe disease [7,8].

Although overall efficacy was similar between the treatment groups, the montelukast–fexofenadine combination produced significantly greater improvement in RQLQ scores during the later follow-up period, whereas the montelukast–levocetirizine combination showed marginally better control of rhinorrhea at study completion. These differences may reflect the distinct pharmacodynamic characteristics of the two second-generation antihistamines. Fexofenadine exhibits minimal penetration across the blood-brain barrier, thereby maintaining excellent efficacy with negligible central nervous system effects, while levocetirizine possesses high H1-receptor affinity that may contribute to superior control of selected nasal symptoms in some patients. Recent evidence comparing oral H1-antihistamines has similarly reported that differences among agents are generally modest and that treatment selection should be individualized according to symptom profile and patient preference rather than efficacy alone [9,10].

Both treatment groups exhibited a steady decline in serum IgE concentration and absolute eosinophil count, indicating attenuation of allergic inflammation following therapy. Although statistically significant differences in AEC were observed at isolated follow-up visits, the magnitude of these differences was small and unlikely to be clinically meaningful, particularly in view of the similar improvement in symptom scores. Leukotriene receptor antagonists reduce eosinophilic inflammation, whereas antihistamines suppress histamine-mediated responses; therefore, the observed reduction in laboratory biomarkers is biologically consistent with the complementary mechanisms of these agents. Recent systematic reviews have also demonstrated that montelukast-based combination therapy improves both clinical symptoms and inflammatory indices in allergic airway disease [7].

Improvement in quality of life represents one of the principal therapeutic goals in allergic rhinitis because persistent nasal symptoms frequently impair sleep, daily activities, emotional well-being, and work productivity. In the present study, RQLQ scores improved substantially in both treatment arms, with slightly greater improvement observed in the montelukast–fexofenadine group during the final months of follow-up. This finding agrees with recent evidence indicating that effective control of both nasal and ocular symptoms translates into meaningful improvement in health-related quality of life and overall patient satisfaction [8,11].

Both regimens were well tolerated, with only mild adverse events reported throughout the study and no serious drug-related complications. Drowsiness

and gastrointestinal symptoms occurred infrequently and were comparable between groups despite isolated statistically significant differences at individual follow-up visits. The favorable safety profile observed in our study is consistent with recent evidence showing that second-generation antihistamines, particularly fexofenadine, possess excellent tolerability with minimal sedative effects, while combination therapy with montelukast generally does not substantially increase treatment-related adverse events when appropriately prescribed [7,10].

Our findings also have practical implications for routine clinical practice. Since both regimens achieved comparable improvement in the primary efficacy endpoint, clinicians may individualize treatment according to the predominant symptom pattern, previous treatment response, patient tolerance, availability, and economic considerations. Recent expert opinion from India similarly emphasizes that both levocetirizine–montelukast and fexofenadine–montelukast combinations remain valuable therapeutic options in routine management of allergic rhinitis, with prescribing decisions guided by patient-specific characteristics rather than a universal preference for either regimen [12].

The strengths of the present study include its prospective randomized design, relatively large sample size, serial assessment of validated symptom scores together with objective inflammatory biomarkers, and comprehensive evaluation of safety over three months. Nevertheless, certain limitations should be acknowledged. The study was conducted at a single tertiary care centre with an open-label design, which may limit external validity and introduce observer bias. In addition, longer follow-up would be necessary to evaluate sustained symptom control, seasonal variation, recurrence after treatment discontinuation, and long-term safety. Future multicentric, double-blind randomized controlled trials incorporating pharmacoeconomic analyses and patient-reported outcome measures would further clarify the optimal role of these combination therapies in personalized management of allergic rhinitis.

## Conclusion

The findings of this study indicate that both antihistamine–leukotriene receptor antagonist combinations are safe and effective options for managing allergic rhinitis, and the choice between them may be individualized based on patient symptom profile, sensitivity to sedation, and physician judgment, with further multicentric trials of longer duration warranted to confirm long-term efficacy, safety, and cost-effectiveness.

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