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**Original Research Article**

# Expert perspectives on the prescription pattern of levocetirizine+montelukast and fexofenadine+montelukast for the management of allergic rhinitis in the Indian settings

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## ABSTRACT

**Background:** Studies have shown that oral antihistamines are considered as the gold-standard therapy for allergic rhinitis. However, there is dearth of studies among clinicians, so this study aimed to gather expert opinion on the prescribing pattern of levocetirizine+montelukast and fexofenadine+montelukast for managing AR in India.
**Methods:** This cross-sectional study, conducted through a multi-response questionnaire comprising 24 questions, gathered insights from experts across diverse Indian settings. It explored perspectives on clinical observations, experiences, demographic profiles, treatment characteristics in AR, and the utilization of fexofenadine+montelukast and levocetirizine+montelukast for AR management in clinical practice. The data were analyzed through descriptive analysis.
**Results:** Majority of clinicians (52%) preferred levocetirizine+montelukast for AR, with half of them recommending a 2-week course. Additionally, 38% of clinicians noted its effectiveness in addressing all AR symptoms. Most clinicians agreed that levocetirizine and montelukast combination therapy was effective in improving nighttime nasal symptoms (74%) and nasal congestion (69%). Furthermore, majority of clinicians acknowledged that the combination offers both immediate (74%) and long-term (56%) relief from AR symptoms. Approximately 58% of the healthcare providers reported overall improvement across categories with fexofenadine+montelukast, encompassing daytime nasal symptoms, nighttime nasal symptoms, and daytime eye symptoms.
**Conclusion:** Clinicians recommended the combination of levocetirizine+montelukast and fexofenadine+montelukast to manage AR. Levocetirizine+montelukast combination was preferred by clinicians for its efficacy in alleviating nighttime nasal symptoms and congestion. Fexofenadine+montelukast combination was also endorsed for overall improvement across various symptoms.

**Keywords:** Allergic rhinitis, Nasal symptoms, Fexofenadine, Levocetirizine, Montelukast

## INTRODUCTION

Allergic rhinitis (AR) is one of the most common chronic diseases worldwide, affecting patients of all ethnic groups and all ages, with approximately 400 million people affected globally. The prevalence of AR has increased over the years, alongside increased urbanization and environmental pollutants, which are thought to be some of the leading causes of the disease. AR is estimated to affect 10-30% of adults and 40% of children, and its prevalence is still on the rise globally, particularly in developing countries.[1] The results of the coexistence of allergic rhinitis and asthma (CARAS) survey highlight the high prevalence of concomitant AR in Indian patients with asthma.[2] Allergic rhinitis has economic, clinical, and social negative consequences. It can lead to workday loss

in adults and school day loss and learning disabilities in children. In a study conducted by Seedat et al, 39.4% of the students suffering from AR reported frequently feeling tired and 19.5% of the students with AR said they felt miserable because of their nasal symptoms. If AR is uncontrolled and untreated, it may lead to secondary diseases such as conjunctivitis, sinusitis, middle ear infections, jaw and teeth development disorders, and asthma or delay in the treatment of such existing diseases.[3-6]

Oral antihistamines are considered the gold-standard therapy for allergic rhinitis.[7] Leukotrienes are lipid mediators produced by inflammatory cells and play a role in the pathogenesis of allergic inflammation in the upper and lower airways.[8,9] Montelukast, a leukotriene antagonist, competitively and reversibly inhibits cysteinyl leukotrienes, specifically leukotrienes D4. By blocking the action of these leukotrienes, montelukast provides significant relief from symptoms of seasonal allergic rhinitis, including nasal congestion, sneezing, itching, and runny nose.[10]Fexofenadine hydrochloride is a potent, selective, nonsedating H1-receptor antagonist. It works by blocking histamine receptors, thereby preventing allergic responses. Fexofenadine has proven efficacy in clinical symptom relief and in improving quality of life in patients with allergic rhinitis and chronic idiopathic urticaria.[11] The current survey aims to gather expert opinion on the prescription pattern of levocetirizine+montelukast and fexofenadine+montelukast for the management of AR in Indian settings.

## METHODS

The study was carried out a cross sectional, multiple-response questionnaire-based survey among clinicians specialized in managing AR patients in the major Indian cities from June 2023 to December 2023. The study was conducted after receiving approval from Bangalore Ethics, an Independent Ethics Committee which is recognized by the Indian Regulatory Authority, Drug Controller General of India. An invitation was sent to leading clinicians in managing AR in the month of March 2023 for participation in this Indian survey.

The questionnaire booklet titled PEARL (Expert perspectives on Fexofenadine+Montelukast or Levocetirizine+Montelukast in allergic Rhinitis) study was sent to the physicians who were interested to participate and were included.

The PEARL study questionnaire comprised 24 questions addressing current feedback, clinical observations, and experiences regarding the use and prescription patterns of levocetirizine+montelukast and fexofenadine+montelukast in the management of AR. Clinicians were instructed to answer the questionnaire on their own, without contacting any of their colleagues. Prior to the study implementation, each doctor provided their written informed permission before the initiation of the study. Those who did not accepted the invite were excluded. Also, incomplete answer and those who did not provide consent were excluded.

### *Statistical analysis*

The data were analyzed using descriptive statistics. Categorical variables were presented as percentages to provide a clear insight into their distribution. The frequency of occurrence and the corresponding percentage were used to represent the distribution of each variable. To visualize the distribution of the categorical variables, graphs were created using Microsoft excel 2013 (version 16.0.13901.20400).

## RESULTS

The survey involved a total of 153 participants. Approximately 42% of the clinicians reported encountering over 20 cases of AR per week in their clinical practice. According to 24% and 20% of clinicians, respectively, AR was more prevalent within the age groups of under 10 years and 31-40 years. According to most clinicians (82%), both males and females are equally affected by AR. Majority (67%) of the clinicians noted compliance with medications for AR across all socioeconomic statuses: upper, middle, and lower.

According to 35% of the clinicians, the most common symptom observed in AR in their clinical practice is runny nose (35%). As per 63% of the clinicians, levocetirizine is the preferred antihistamine for the management of AR. Around 29% of the experts endorsed fexofenadine due to its combined advantages, including selectivity, long-lasting effects, effectiveness against AR symptoms, non-sedating nature, and better tolerability profile. The majority (94%) of the respondents preferred the combination of antihistamine and leukotriene receptor antagonists for managing AR. According to 57% of healthcare providers, a 10-tablet pack is the preferred package for antihistamine combinations.

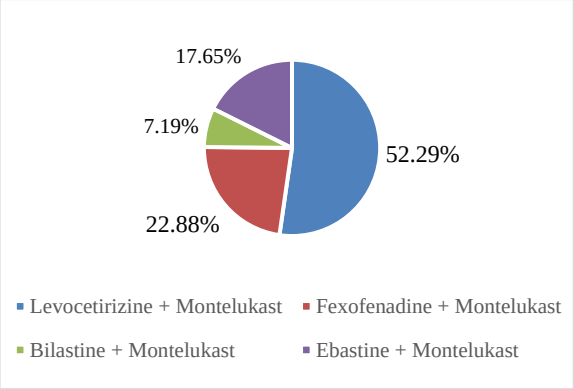


**Figure 1: Distribution of response to preference for antihistamine combinations for the management of AR.**

Over half of the clinicians (53%) indicated that 26-50% of patients require a combination of montelukast with an antihistamine. Majority of the clinicians (72%) preferred the combination of oral antihistamine with oral antileukotriene as the most common polytherapy for AR. Approximately 52% endorsed levocetirizine+montelukast as the preferred combination of antihistamines for managing AR (Figure 1). According to the majority of clinicians, the combination of levocetirizine+montelukast offers both immediate (74%) and long-term (56%) relief from symptoms associated with AR (Table 1).

**Table 1: Distribution of response to drug combination that provides more immediate and long-term relief from AR symptoms.**

| Drug combination | Response rate (n=153) | |
|---|---|---|
| | Immediate relief (%) | Long-term relief (%) |
| **Levocetirizine+montelukast** | 114 (74.51) | 86 (56.21) |
| **Fexofenadine+montelukast** | 35 (22.88) | 63 (41.18) |
| **Bilastine+montelukast** | 3 (1.96) | 4 (2.61) |
| **Ebastine+montelukast** | 1 (0.65) | 0 (0) |

Majority of the clinicians (44%) advocated prescribing the combination of levocetirizine+montelukast for all allergic conditions, encompassing the nose, skin, lower respiratory tract, upper respiratory tract, and eyes. Majority of the clinicians (53%) recommended prescribing the combination of fexofenadine+montelukast for all allergic conditions, encompassing the nose, skin, lower respiratory tract, upper respiratory tract, and eyes (Table 2). Majority of the clinicians (48%) recommended a 2-week course of fexofenadine+montelukast combination for treating AR in adults (Figure 2). Half of the clinicians recommended a 2-week course of the levocetirizine+montelukast combination for treating AR in adults (Table 3).

**Table 2: Distribution of response to patient types for prescribing fexofenadine + montelukast combination (n=153).**

| Patient type | Response rate N (%) |
|---|---|
| **Adult working patients** | 34 (22.22) |
| **All patients Group** | 4 (2.61) |
| **All allergic conditions including nose, skin, lower respiratory tract, upper respiratory tract, eyes** | 82 (53.59) |
| **For long term and working-class people** | 6 (3.92) |
| **Geriatric patients** | 4 (2.61) |
| **Young age** | 5 (3.27) |
| **Others** | 18 (11.76) |

**Table 3: Distribution of response to duration of levocetirizine+montelukast combination therapy in adult patients (n=153).**

| Duration | Response rate N (%) |
|---|---|
| **1 week** | 27 (17.65) |
| **2 weeks** | 77 (50.33) |
| **6 weeks** | 37 (24.18) |
| **12 weeks** | 10 (6.54) |
| **3 weeks** | 1 (0.65) |
| **Depends upon allergy severity** | 1 (0.65) |

**Table 4: Distribution of responses to combination therapy, indicating superiority in improving nighttime nasal symptoms and nasal congestion (n=153).**

| Combination therapy | Response rate (n=153) | |
|---|---|---|
| | Night time nasal symptoms (%) | Nasal congestion (%) |
| **Levocetirizine+montelukast** | 113 (73.86) | 106 (69.28) |
| **Fexofenadine+montelukast** | 38 (24.84) | 42 (27.45) |
| **Bilastine+montelukast** | 2 (1.31) | 5 (3.27) |

Approximately 38% of the clinicians cited that the advantage of the levocetirizine+montelukast combination therapy is its effectiveness in addressing all symptoms of AR (Figure 3). Majority of clinicians indicated that the combination therapy of levocetirizine and montelukast yields superior improvement in nighttime nasal symptoms (74%) and nasal congestion (69%) (Table 4).

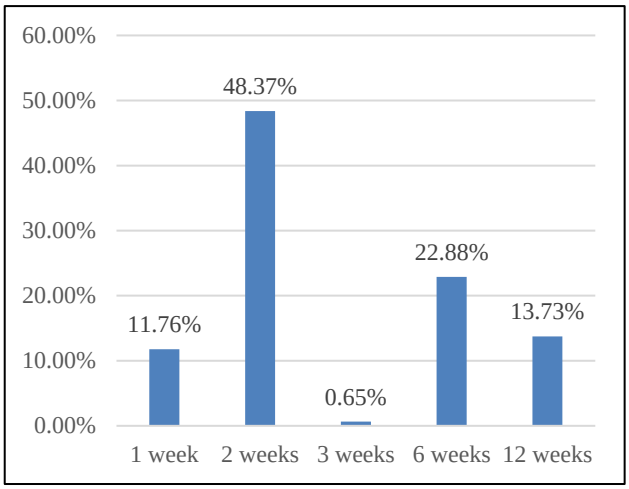


**Figure 2: Distribution of response to duration of fexofenadine+montelukast combination therapy in adult AR patients.**

Approximately 58% of the clinicians reported that the combination of montelukast+fexofenadine provides improvement in all evaluated categories, including

daytime nasal symptoms, nighttime nasal symptoms, and daytime eye symptoms (Figure 4). An equal number of healthcare providers (49.67%) indicated both "Yes" and "No" regarding whether demographic or geographic factors influence the choice between levocetirizine+montelukast or fexofenadine+montelukast.

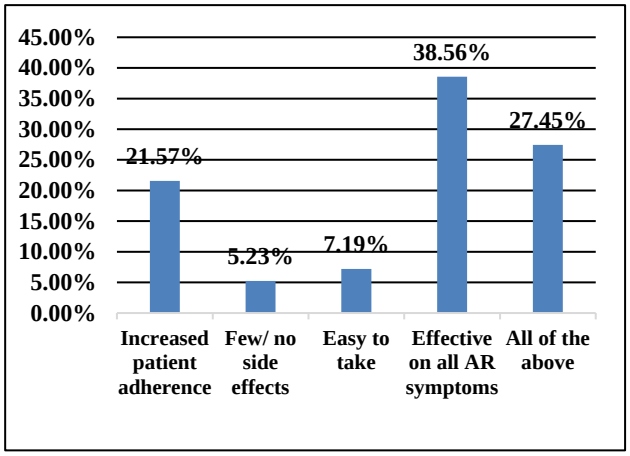


**Figure 3: Distribution of response to advantages of levocetirizine + montelukast combination therapy.**

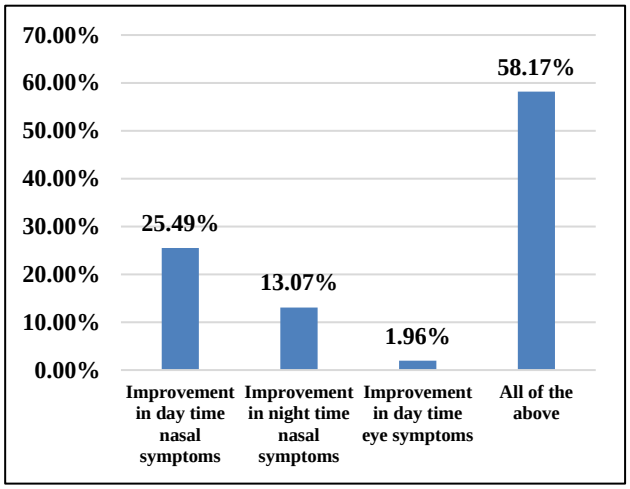


**Figure 4: Distribution of responses to perceived benefits of montelukast+fexofenadine combination therapy according to clinicians.**

## DISCUSSION

The current survey highlights the preference and effectiveness of combinations of levocetirizine+montelukast and fexofenadine+montelukast for managing AR in routine clinical practice. In the present study, majority of the clinicians largely favored the combination of levocetirizine and montelukast for AR management, with many advocating for a two-week treatment regimen. A notable consensus among clinicians highlights the efficacy of this combination in addressing the full spectrum of AR symptoms. A post-marketing surveillance study by Kiran et al revealed that the fixed-dose combination (FDC) of montelukast 10 mg and levocetirizine 5 mg per tablet demonstrated both efficacy and safety in the treatment of AR.[12] The FDC of montelukast 10 mg and levocetirizine 5 mg exhibited superiority over montelukast 10 mg monotherapy or levocetirizine 5 mg monotherapy in effectively treating patients with seasonal AR.[13] A review by Adsule et al. demonstrated the superior efficacy of the combination therapy of levocetirizine and montelukast in treating persistent AR compared to montelukast monotherapy alone.[14] Several clinical trials also reported the efficacy of levocetirizine+montelukast combination therapy in the management of AR.[12,15,16]

In the present survey, clinicians widely agreed that combining levocetirizine and montelukast results in notable improvements in nighttime nasal symptoms and congestion. Additionally, they emphasized its effectiveness for both immediate and long-term relief from AR symptoms. In a multicenter, phase III trial conducted by Panchal et al, it was noted that at the end of treatment, the FDC of levocetirizine+montelukast group showed significantly greater improvement in nighttime symptoms score, daytime eye symptoms score, and rhino conjunctivitis quality-of-life scores compared to both the montelukast group and the levocetirizine group.[15] In a randomized controlled trial conducted by Ciebiada et al, the greatest improvement in nasal symptoms was observed with the combination treatment of levocetirizine and montelukast.[16] In a study conducted by Kiran et al, the combination of montelukast and levocetirizine resulted in nearly all trial subjects experiencing a reduction of more than 50% in their total symptom score at all visits, with the majority achieving complete relief from their symptoms.[12]

Majority of the current survey respondents advocated the use of fexofenadine+montelukast combination across various allergic conditions, including adult AR, with a preference for a 2-week treatment regimen. Clinicians observed overall improvement across various symptoms, endorsing montelukast+fexofenadine for its efficacy in addressing daytime and nighttime nasal symptoms, along with daytime eye symptoms. A post-marketing study found that the FDC of fexofenadine plus montelukast was effective and well-tolerated in Indian adult patients with AR. It significantly reduced the total symptom score, total nasal symptom score, and total ocular symptom score.[17] In a randomized, double-blind clinical trial conducted by Mahatme et al in patients with AR, the mean change in total nasal symptom score was significantly greater in the montelukast-fexofenadine combination group compared to the montelukast-levocetirizine combination group.[18] In a randomized controlled trial conducted by Cingi et al, the group receiving both fexofenadine and montelukast demonstrated significantly improved control of nasal congestion. This was evident subjectively through patient diaries and visual analog scale evaluations, as well as objectively through rhinomanometry and physical

examination, compared to groups receiving antihistamine alone or with a placebo.[19]

The survey contributes to enhancing the understanding of optimal treatment approaches for AR and supports evidence-based decision-making in clinical practice. It serves as a valuable resource for clinicians seeking to optimize patient outcomes and improve the management of AR. The survey findings support the clinical use of levocetirizine+montelukast and montelukast+fexofenadine combinations as effective treatments for AR among Indian patients. The survey highlights the clinical utility of these combinations in alleviating AR symptoms and improving the overall quality of life. Major strength of the survey is the use of a meticulously designed and validated questionnaire for collecting expert data. However, it is necessary to acknowledge that personal viewpoints and preferences may have influenced the survey findings, which introduces the possibility of bias. Therefore, interpreting the results while considering these limitations is crucial. Further research is required to confirm and expand upon the findings presented in this study.

## CONCLUSION

Experts recommended the combinations of levocetirizine+montelukast and fexofenadine+montelukast to manage AR patients. Clinicians' preference for the levocetirizine and montelukast combination in managing allergic rhinitis, citing its efficacy across the spectrum of AR symptoms. Clinicians concur on the combination's efficacy in alleviating nighttime nasal symptoms and congestion, emphasizing its dual benefits for immediate and long-term relief from allergic rhinitis symptoms. Clinicians also endorsed the combination of fexofenadine+montelukast for overall improvement across various symptoms, and its efficacy in addressing daytime and nighttime nasal symptoms, along with daytime eye symptoms.

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