International Journal of Otorhinolaryngology and Head and Neck Surgery
Manjula S et al. Int J Otorhinolaryngol Head Neck Surg. 2024 Apr;10(2):192-196
http://www.ijorl.com
pISSN 2454-5929 | eISSN 2454-5937

DOI: https://dx.doi.org/10.18203/issn.2454-5929.ijohns20240697

Original Research Article

Expert opinion on the clinical use of a combination of antihistamines with leukotriene receptor antagonists in the management of allergic rhinitis in Indian settings

Manjula S.*, Krishna Kumar M.

Department of Medical Services, Micro Labs Limited, Bangalore, Karnataka, India

Received: 05 January 2024
Accepted: 01 March 2024

***Correspondence:**
Dr. Manjula S.,
E-mail: drmanjulas@gmail.com

ABSTRACT

Background: Various clinical studies have reported that the combination of montelukast and levocetirizine was effective in alleviating residual symptoms and the improvement of quality of life associated with allergic rhinitis. However, there was a dearth of data regarding the prescription practice among clinical practitioners. So, this study aims to gather clinicians' opinion regarding the use of antihistamines, with a special focus on the combined use of antihistamines with leukotriene receptor antagonists for the management of AR in Indian settings.
Methods: The multiple-response questionnaire-based survey involving 19 questions gathered information on current recommendations, clinical observations, clinical experience of specialists in AR management, and the use of montelukast with levocetirizine in routine settings.
Results: Out of 388 participants, approximately 84% of respondents preferred a combination of antihistamines and leukotriene receptor antagonists for managing AR. Additionally, 36% stated that 26 to 50% of patients presenting to routine practice may require montelukast and antihistamine combination as treatment. Around 61% endorsed the combination of antihistamines with leukotriene receptor antagonists as the preferred AR treatment strategy. In long-term AR management, 65% of clinicians rated montelukast with levocetirizine as excellent, and 78% of respondents reported montelukast confers additive benefits when combined with antihistamines.
Conclusions: The significant preference for the combined use of antihistamines and leukotriene receptor antagonists underscores their perceived efficacy in AR treatment. The combination of antihistamines with leukotriene receptor antagonists emerges as the favored strategy for managing AR.

Keywords: Allergic rhinitis, Montelukast, Antihistamines, Levocetirizine, Leukotriene receptor antagonists

INTRODUCTION

The burden of allergic rhinitis (AR), characterized by nasal congestion, clear rhinorrhea, sneezing, postnasal drip, and nasal pruritus, is substantial, both in terms of individual suffering and societal impact.[1] It significantly affects the quality of life of affected subjects and can lead to productivity loss in the workplace and increased healthcare utilization.[2] AR affects approximately 18 to 40% of adults globally and 20 to 30% of individuals in India. Symptoms of AR are frequently reported in 75% of children and 80% of asthmatic adults in the country.[3] Antihistamines have been recognized as the mainstay of treatment for managing AR, as they help in alleviating associated symptoms by blocking histamine receptors on nerve cells. However, as a standalone therapy, antihistamines may not comprehensively alleviate all AR symptoms. Therefore, they are often combined with

leukotriene receptor antagonists like montelukast, which inhibit leukotriene production, to achieve more comprehensive symptom management.[4]

Approximately 70% of individuals with asthma also experience AR, and 10% of AR are reported to have asthma. The use of a combination of antihistamine and montelukast provides a therapeutic approach for AR, aiming to alleviate ongoing inflammation and provide tangible benefits for patients.[5] Various studies have reported that the combination of montelukast and levocetirizine was effective, reliable and hold promise for the alleviation of residual symptoms and the improvement of quality of life associated with AR.[6] Furthermore, such combination of montelukast and levocetirizine resulted in greater efficacy compared to the monotherapy of either levocetirizine or montelukast in the treatment of chronic AR.[4,7] Understanding the prescription practice of antihistamines in Indian settings may help improve patient management and develop consensus to optimize the treatment for AR. The present survey-based study aims to gather clinicians' perspectives regarding the use of antihistamines, with a special focus on the combined use of antihistamines with leukotriene receptor antagonists for the management of AR in Indian settings.

METHODS

We carried out a cross sectional, multiple-response questionnaire-based survey among clinicians specialized in treating AR patients in the major Indian cities from June 2022 to December 2022.

Questionnaire

The questionnaire booklet titled ARIS (Allergic Rhinitis in Indian clinician's perspective Study) study was sent to the physicians who were interested to participate. The ARIS study questionnaire included 19 items about current recommendations, clinical observations, and clinical experience of specialists in the management of AR with the combination of antihistamines and montelukast. 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.

Participants

An invitation was sent to leading clinicians in managing AR in the month of March 2022 for participation in this Indian survey. 388 doctors from major cities of all Indian states representing the geographical distribution shared their willingness to participate and provide necessary data. Physicians were asked to complete the questionnaire without discussing with peers. A written informed consent was obtained from each physicians prior initiation of the study.

Statistical analysis

The data were analyzed using descriptive statistics. Categorical variables were presented as percentages to depict 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, pie, and bar charts were created using Microsoft Excel 2013 (version 16.0.13901.20400).

RESULTS

According to 47% of the respondents, the monthly average number of AR cases encountered in clinical practice was about 21-30. Majority of the clinicians reported that about 57% experience morning AR symptoms. Around 32% of the clinicians noted that subjects between the age group of 5 to 10 years were commonly diagnosed with AR. Approximately 84% of the clinicians stated that AR was prevalent in both genders. About 43% of respondents reported rhinorrhea as the most common symptom, while 33% noted constant sneezing, rhinorrhea, and an itchy nose as the predominant symptoms.

Table 1: Distribution of response to the preferred drug class for managing AR (n=388).

Drugs indicated for AR	Response rate, N (%)
Only antihistamines	29 (7.47)
Only leukotriene receptor antagonists	30 (7.73)
Combination of antihistamine and leukotriene receptor antagonists	325 (83.76)
All the above	2 (0.52)

Table 2: Distribution of response to preferred duration of treatment with montelukast and levocetirizine for AR with asthma (n=388).

Preferred duration of treatment with montelukast and levocetirizine for AR with asthma	Response rate, N (%)
1 week	16 (4.12)
2 weeks	95 (24.48)
6 weeks	167 (43.04)
12 weeks	107 (27.58)
Any other	1 (0.26)

Nearly 83% of the participants stated that they prefer dual therapy over monotherapy as an oral treatment for AR. Around 56% of the clinicians reported morning symptoms as the primary complaint reported by patients with AR, while 38% reported it as general sleep problems. Around 50%, 29%, and 13% of the clinicians reported sinusitis, asthma, and allergic conjunctivitis as the common concomitant disease noted with AR in clinical practice, respectively. Majority of the

respondents (94%) preferred levocetirizine for managing AR. About 84% of the respondents stated they prefer a combination of antihistamines and leukotriene receptor antagonists for managing AR (Table 1).

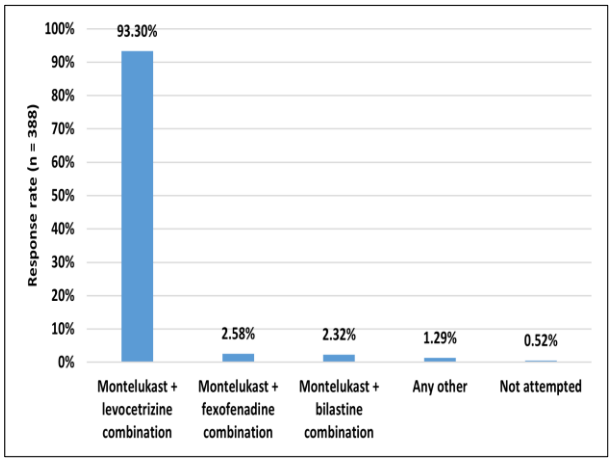

Figure 1: Distribution of response to a requirement of a combination of montelukast with antihistamines.

The proportion of patients requiring the combination of montelukast with antihistamines was 26 to 50% as per 36% of the respondents and 11 to 25% as per 35% of the respondents. Approximately less than 50% of respondents stated that about 26% of patients require a combination of montelukast with antihistamines (Figure 1). Around 54% of the clinicians stated that the combination of montelukast with levocetirizine leads to improvement in both nasal symptoms during the day and night time and eye symptoms during the daytime.

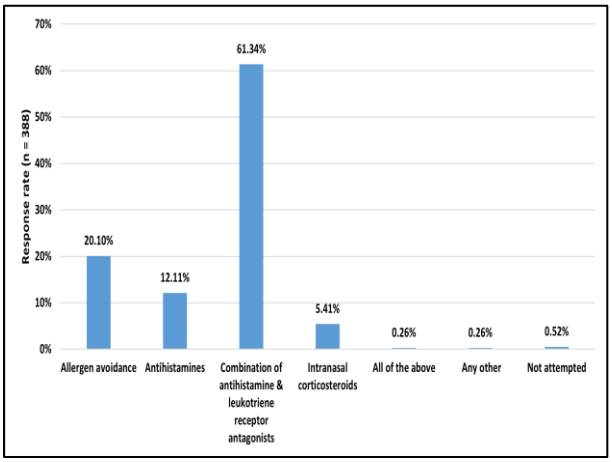

Figure 2: Distribution of response on preferred drug combination for managing morning symptoms of AR.

About 26% of the respondents stated that the drug combination improves only the night time nasal symptoms. Nearly 43% of the respondents preferred a six-week treatment with a combination of montelukast and levocetirizine for managing AR with asthma (Table 2). As per 93% of the respondents, the combination of montelukast and levocetirizine was preferred for a significant reduction of morning symptoms of AR compared to other combinations (Figure 2). As reported by around 61% of the clinicians, the combination of antihistamines with leukotriene receptor antagonists is the preferred treatment strategy for managing AR, while 20% reported that allergen avoidance helps in the management (Figure 3).

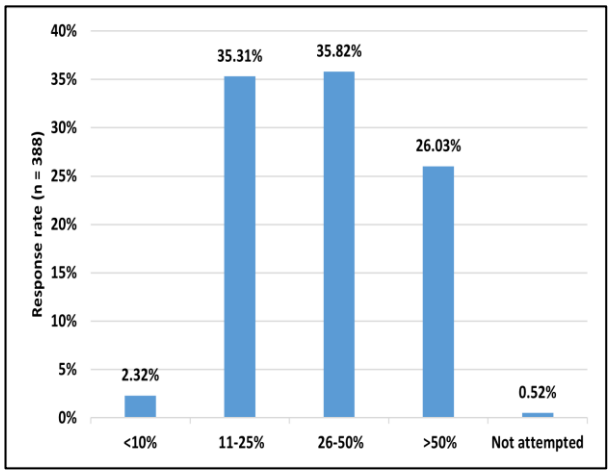

Figure 3: Distribution of response on the preferred strategy for managing AR.

In the long-term management of AR, approximately 65% of clinicians reported that the combination of montelukast with levocetirizine was excellent. Around 63% stated that AR was triggered by allergic reactions, while 27% reported it as being triggered by bacterial or viral infections. It has been stated that around 54% of individuals in urban areas with education tend to adhere well to their medication. Approximately 78% of the respondents reported the montelukast confers an additive effect when combined with antihistamines.

DISCUSSION

The study underscores the significant preference for combination therapies, particularly montelukast with levocetirizine, for managing AR. The findings also highlighted the additive effect of montelukast when combined with antihistamines, further emphasizing the potential synergy between these two medications for enhancing the treatment of AR. Most of the current respondents preferred a combination of antihistamines and leukotriene receptor antagonists for managing AR. This combination therapy, particularly montelukast with antihistamines, offers enhancing and complementary effects, effectively reducing symptoms.[8] In a comparative study conducted by Ciebiada et al on the treatment of AR with montelukast alone or in combination with an antihistamine, it was reported that the combination significantly improved nasal symptoms within the first 24 hours, and this improvement continued to steadily increase over six weeks.[9] A meta-analysis by Liu et al reported that the combination of antihistamines and

leukotriene receptor antagonists increases the therapeutic efficiency against daytime and composite nasal symptoms, such as rhinorrhea, sneezing, and itching. The combination therapy was more effective for those with persistent AR.[10]

More than half of the study participants reported that combining montelukast with levocetirizine improves both daytime and nighttime nasal symptoms, as well as daytime eye symptoms. In addition, 43% of respondents expressed a preference for a six-week treatment regimen with this combination for individuals with AR and asthma. In line with these findings a prospective, randomized, open, parallel by Gupta et al reported that the montelukast and levocetirizine combination group exhibited a significantly greater reduction ($p<0.05$) in total daytime nasal symptom scores, composite symptom scores, and night time nasal symptom scores compared to the levocetirizine alone group following a 6-week treatment course. Overall, the combination of montelukast with levocetirizine has been proven to be effective in reducing daytime, nighttime, composite, and daytime eye symptom scores when compared to levocetirizine alone.[6] Similarly, a randomized study conducted by Kim et al explored the effectiveness and safety of a fixed-dose combination of montelukast and levocetirizine in patients with perennial AR and mild to moderate asthma. The combination therapy was found to be more effective and safer than montelukast alone.[11]

Previous literature findings have corroborated that the addition of an antihistamine to montelukast confers added benefit.[8] Majority of the current respondents preferred the combination for significantly reducing morning AR symptoms and rated long-term treatment using montelukast with levocetirizine as excellent for AR management. The current survey has also validated the additive effect of montelukast in enhancing the management of AR when combined with antihistamines. A four-week prospective, randomized, double-blind, parallel, active-controlled trial conducted by Mahatme et al also noted that the combination of montelukast with levocetirizine contributed to significant reduction in AR symptoms and concluded it as cost-effective treatment option.[8] A phase 3 clinical trial study conducted by Burkate et al concluded on the safety, tolerability and effectiveness of the fixed drug combination of montelukast and levocetirizine when compared to montelukast or levocetirizine alone for patients with seasonal AR. The combination treatment contributed to a significant reduction in nighttime symptoms, daytime eye symptoms, and rhinoconjunctivitis and improved quality-of-life scores compared to the other groups.[12] The survey findings offer valuable insights to optimize patient care for AR. The use of a carefully designed and validated questionnaire for gathering expert data was the major strength of the study. Since personal perspectives and preferences might have influenced the conclusion, the dependence on expert judgments establishes the possibility of bias. Observing the results while keeping these limitations in mind was essential, and further research should be undertaken to confirm and broaden the scope of the current survey findings.

CONCLUSION

The clinician's preference for the combined use of antihistamines and leukotriene receptor antagonists highlighted their perceived effectiveness in treating AR. This combination stands out as the preferred strategy for managing AR. Montelukast provides an additive benefit when combined with antihistamines for the management of AR.

ACKNOWLEDGEMENTS

Authors would like to thank all the clinicians who were participated in this study.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Akhouri S, House SA. Allergic Rhinitis. In: Stat Pearls. Treasure Island (FL): Stat Pearls Publishing; 2023.
2. Adsule SM, Misra D. Long-term treatment with montelukast and levocetirizine combination in persistent allergic rhinitis: review of recent evidence. J Indian Med Assoc. 2010;108(6):381-2.
3. Kumar RS, Jain MK, Kushwaha JS, Patil S, Patil V, Ghatak S, et al. Efficacy and Safety of Fluticasone Furoate and Oxymetazoline Nasal Spray: A Novel First Fixed Dose Combination for the Management of Allergic Rhinitis with Nasal Congestion. JAA. 2022;15:783-92.
4. Kiran M, Pawaskar L, Sheikh S, Waghambare P. Efficacy and Safety for the combination of Montelukast and Levocetirizine in patients of allergic rhinitis: Post Marketing Surveillance study. Ann Int Med Dent Res. 2021;7(5):61-70.
5. Baççıoğlu A. Role of leukotriene antagonists and antihistamines in treatment of allergic rhinitis and asthma comorbidity. J Med Updates. 2013;3(1):34-9.
6. Gupta V, Matreja PS. Efficacy of montelukast and levocetirizine as treatment for allergic rhinitis. J Aller Ther. 2010;1:103.
7. Ciebiada M, Górska-Ciebiada M, DuBuske LM, Górski P. Montelukast with desloratadine or levocetirizine for the treatment of persistent allergic rhinitis. Ann Allergy Asthma Immunol. 2006;97(5):664-71.
8. Mahatme MS, Dakhale GN, Tadke K, Hiware SK, Dudhgaonkar SD, Wankhede S. Comparison of efficacy, safety, and cost-effectiveness of montelukast-levocetirizine and montelukast-fexofenadine in patients of allergic rhinitis: A

randomized, double-blind clinical trial. Indian J Pharmacol. 2016;48(6):649-53.
9. Ciebiada M, Gorska-Ciebiada M, Barylski M, Kmiecik T, Gorski P. Use of montelukast alone or in combination with desloratadine or levocetirizine in patients with persistent allergic rhinitis. Am J Rhinol Allergy. 2011;25:e1-6.
10. Liu G, Zhou X, Chen J, Liu F. Oral Antihistamines Alone vs in Combination with Leukotriene Receptor Antagonists for Allergic Rhinitis: A Meta-analysis. Otolaryngol Head Neck Surg. 2018;158(3):450-8.
11. Kim MK, Lee SY, Park HS, Yoon HJ, Kim SH, Cho YJ, et al. A randomized, multicenter, double-blind, phase iii study to evaluate the efficacy on allergic rhinitis and safety of a combination therapy of montelukast and levocetirizine in patients with asthma and allergic rhinitis. Clin Ther. 2018;40(7):1096-107.
12. Panchal S, Patil S, Barkate H. Evaluation of efficacy and safety of montelukast and levocetirizine FDC tablet compared to montelukast and levocetirizine tablet in patients with seasonal allergic rhinitis: a randomized, double blind, multicentre, phase III trial. Int J Otorhinolaryngol Head Neck Surg. 2020;7(1):83-90.

Cite this article as: Manjula S, Kumar KM. Expert opinion on the clinical use of a combination of antihistamines with leukotriene receptor antagonists in the management of allergic rhinitis in Indian settings. Int J Otorhinolaryngol Head Neck Surg 2024;10:192-6.