

Original Research Article

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

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ABSTRACT

Background: To evaluate efficacy, safety and tolerability of Montelukast 10 mg+levocetirizine 5 mg FDC compared to either montelukast 10 mg or levocetirizine 5 mg given alone in seasonal allergic rhinitis (SAR) patients.

Methods: Phase III, multicentre, randomized, double blind, parallel group, active controlled study was conducted in 279 SAR patients at 16 sites across India. Efficacy was assessed using daytime nasal symptoms score (Primary efficacy outcome), night-time symptoms score, daytime eye symptom score, patient's global evaluation, physician's global evaluation, rhino-conjunctivitis quality-of-life score.

Results: At end of treatment there was statistically significant evidence from the per protocol analysis that patients on FDC had a greater improvement in change from baseline in daytime nasal symptoms score than patients who received Montelukast ($p=0.0266$) or Levocetirizine ($p=0.0409$). These results were consistent with the Intent to treat analysis. Analysis of the secondary efficacy endpoints provided numerically greater improvement in the nighttime symptoms score, daytime eye symptoms score, and rhinoconjunctivitis quality-of-life scores in the FDC group as compared to the Montelukast group or Levocetirizine group. The FDC of Montelukast and Levocetirizine was found to be safe and generally well tolerated. The majority of adverse events were mild in severity, resolved without treatment and were unrelated to study medication.

Conclusions: Fixed dose combination of Montelukast and Levocetirizine was safe, generally well tolerated and superior on efficacy compared to Montelukast or Levocetirizine in patients of seasonal allergic rhinitis.

Keywords: Allergy, Histamine, Leukotriene, LTRA, SGAH

INTRODUCTION

Allergic rhinitis is a common inflammatory condition of the upper respiratory tract and is characterized by one or more symptoms including sneezing, itching, nasal congestion, and rhinorrhoea. The symptoms of allergic rhinitis result from a complex allergen-driven mucosal inflammation caused by interplay between resident and infiltrating inflammatory cells and a number of vasoactive and pro-inflammatory mediators. Seasonal

allergic rhinitis (SAR) is one type of allergic rhinitis and is commonly referred to as 'hay fever'. Seasonal allergic rhinitis is caused by an IgE-mediated reaction to seasonal aeroallergens and is fairly easy to identify because of the rapid and reproducible onset and offset of symptoms in association with pollen exposure. SAR can result in hyper responsiveness to allergens such as cigarette smoke, once pollen season is over.¹ Allergic rhinitis affects between 10% and 30% of all adults and as many as 40% of children.¹ Allergic rhinitis is an extremely common

health problem affecting 10-25% of the world's population.² A survey carried out in India shows that 20-30% of the population suffer from allergic rhinitis. Prevalence of allergic rhinitis is reported to range from 10-13% in Delhi, India. In India, symptoms of rhinitis were reported in 75% of children and 80% of asthmatic adults.³⁻⁶

Pharmacotherapy for allergic rhinitis includes oral and intranasal antihistamines, intranasal corticosteroids, oral and intranasal decongestants, intranasal anticholinergic, intranasal cromolyn and leukotriene receptor antagonists.^{1,7} Antihistamines are effective in reducing pruritus, sneezing and watery rhinorrhea and are a mainstay therapy for allergic rhinitis. Most newer second generation antihistamines have minimal or no sedating properties and less anticholinergic effects and are therefore preferable to first generation antihistamines in most cases.² Second generation antihistamines are in general recommended for mild to moderate disease as first line therapy.^{7,8} Levocetirizine is a third-generation antihistamine that has been approved for the relief of symptoms of seasonal allergic rhinitis (SAR) and perennial allergic rhinitis (PAR) in adults and children aged >6 years.⁹ Leukotrienes plays an important role in the pathogenesis of AR especially in the late phase of allergic response. Montelukast- a leukotriene antagonist competitively and reversibly inhibits cysteinyl leukotrienes (CysLTs), specifically leukotrienes D4 (LTD4) that provides significant relief from symptoms of seasonal allergic rhinitis.¹⁰

There are only limited studies available for the effect of combination therapy of Montelukast and Levocetirizine. Hence this study was planned to assess the efficacy and safety of FDC of Montelukast with Levocetirizine, developed by Glenmark Pharmaceuticals Limited as a treatment for seasonal allergic rhinitis.

METHODS

Study was planned to evaluate the primary objective of efficacy of FDC of Montelukast 10mg and Levocetirizine 5mg tablet compared to Montelukast 10mg tablet and Levocetirizine 5mg tablet in patients with SAR. While secondary objective was to evaluate the safety and tolerability of a FDC of Montelukast 10mg and Levocetirizine 5mg tablet compared to Montelukast 10mg tablet and Levocetirizine 5mg tablet in patients with SAR.

Patients were men or women of age >18 years and <60 years, documented clinical history of seasonal allergic rhinitis (for at least 2 years) with exacerbations during the study season associated with regular daytime nasal symptoms of at least mild- to-moderate severity for the following symptoms of nasal congestion, nasal pruritus and rhinorrhea during the screening period and/or exhibiting a positive skin prick test (wheal diameter at least 3 mm greater than saline control) to one of the

regional allergens active during the study season, Willing to give their written informed consent. Exclusion criteria includes pregnant/lactating women, known hypersensitivity to any of the components of FDC, History of anaphylaxis to skin testing, alcohol/ drug dependence, perennial rhinitis with little or no seasonal exacerbations, non-allergic rhinitis, active pulmonary disorder, on current immune-therapy, etc.

Study design

This Phase III, multicentre, randomized, double blind, parallel group, active controlled study was conducted at 16 sites across India. Study was conducted in accordance with International conference on harmonization –good clinical practice (ICH-GCP) guidelines and all applicable local regulatory guidelines after obtaining approval from institutional ethics Committee (IEC). Total study duration was 16 days which included 14 days of active treatment phase and 2 days of window period for the study visit. Patients had 5 visits during the study period (day -1-screening, day 1, day 3, day 7, after day 14). All Vital signs and clinical parameters were measured at all the 5 study visits (Figure 1) (Figure 2).

Efficacy assessments

Primary efficacy parameter- daytime nasal symptoms score. The day time nasal symptoms (nasal congestion, rhinorrhea, nasal pruritus and sneezing) were rated by the patient in the patient diary card each night before bed (immediately before study drug administration) on the screening visit and the blinded treatment period of 14 days. The day time nasal symptoms were rated on a 4-point scale as follows:

- Score 0; Grade none: symptoms not noticeable
- Score 1; Grade mild: symptoms noticeable but not bothersome
- Score 2; Grade moderate: symptoms noticeable and bothersome some of the time
- Score 3; Grade severe; symptoms bothersome most of the time and/or very bothersome some of the time.

Secondary efficacy outcomes include night-time symptoms score, Daytime eye symptom score, Patient's global evaluation of AR, Physician's global evaluation of AR, rhino-conjunctivitis quality-of-life score.

Safety assessment: All AEs and Serious Adverse Events (SAEs) were recorded from the time of signing the informed consent till the end of study.

Sample size: sample size of 279 (93 per arm) was selected to detect a significant difference in the daytime nasal symptom score and assuming 20 % drop out rate.

Statistical analysis Efficacy endpoints were analysed using both Intent to treat (ITT) and per-protocol

population (PP). However, PP population was the primary analysis. The least square mean change in efficacy scores from baseline to end of treatment was summarized and compared between treatment groups using analysis of covariance (ANCOVA). The 95% confidence intervals for the difference in mean change in symptoms score or RQOL score was constructed for the treatment groups. P-value of ≤ 0.05 was considered statistically significant. The change within each treatment arm was compared using paired t-test. Patient's and physician's global evaluation of allergic rhinitis was summarized descriptively. Safety data is presented as individual listings and summary tables as appropriate.

There were no changes in the conduct of the study or the planned analysis.

RESULTS

Demographic and other baseline characteristics

Of the 273 patients randomized in the study, 93 in each treatment group, 263 patients completed the study and included in the full analysis set. Their baseline characteristics are summarized in the Table 1. Treatment groups showed no marked imbalances in any of the patient characteristics.

Table 1: Demography and baseline characteristics (safety population).

Parameter	Statistics	Montelukast 10 mg + Levocetirizine 5 mg (N=93)	Montelukast 10 mg (N=93)	Levocetirizine 5 mg (N=93)
Age (year)	Mean (SD)	35.29 (11.583)	32.54 (10.951)	32.22 (10.184)
	Median	34.00	30.00	30.00
	Min., Max	19.0, 62.0	18.0, 58.0	18.0, 58.0
Gender, n (%)	Male	52(55.9)	52(55.9)	58(62.4)
	Female	41 (44.1)	41 (44.1)	35 (37.6)
Body weight (kg)	Mean (SD)	63.96 (11.622)	61.63 (10.958)	63.03 (10.486)
	Median	62.00	61.00	62.00
	Min., Max	39.0, 97.0	40.0, 89.0	41.0, 88.0
Height (cm)	Mean (SD)	160.51 (13.649)	161.13 (8.500)	162.30 (8.251)
	Median	162.00	162.00	164.00
	Min., Max	60.2, 183.0	140.0, 174.0	141.0, 182.0

Table 2: Mean change in efficacy parameters.

Visit	Efficacy parameter	Montelukast 10 mg + Levocetirizine 5 mg (N = 82) LSM (SE)	Montelukast 10 mg (N = 82) LSM (SE)	Levocetirizine 5 mg (N = 84) LSM (SE)	P-value ¹
Mean change from baseline (day 1 to day 14)	Daytime nasal symptom score (ITT) (N= 92)	-1.10 (0.056)	-0.93 (0.053)	-0.98 (0.057)	0.0159
	Daytime nasal symptom score (PP)	-1.09(0.053)	-0.95 (0.053)	-0.96(0.055)	0.0483
	Night-time symptom score (PP)	-0.71 (0.047)	-0.61 (0.048)	-0.68 (0.050)	0.2909
	Daytime eye symptom score (PP)	-1.61 (0.040)	-0.59 (0.040)	-0.61 (0.039)	0.9644
	RQOL (PP)	-1.34 (0.068)	-1.17 (0.068)	-1.28 (0.067)	0.2111

¹p-value is calculated for the comparison of treatment groups using ANCOVA with baseline Daytime Nasal Symptoms Score as covariate. LSM- least square mean, ITT- Intention to treat, PP – per protocol , RQOL- rhino-conjunctivitis quality of life.

Table 3: Summary of treatment emergent adverse events.

	Montelukast 10 mg+Levocetirizine 5 mg (N=93) n (%)	Montelukast 10 mg (N=93) n (%)	Levocetirizine 5 mg (N=93) n (%)
TEAEs	16 (17.2)	9 (9.7)	13 (14.0)
Serious adverse event (SAE)	00 (00.0)	00 (00.0)	00 (00.0)
AE by relationship			
Yes	1 (1.1)	00 (00.0)	5 (5.4)
No	15 (16.1)	9 (9.7)	9 (9.7)
AE by severity			
Mild	12 (12.9)	8 (8.6)	11 (11.8)
Moderate	7 (7.5)	1 (1.1)	2 (2.2)
Severe	1 (1.1)	00 (00.0)	00 (00.0)

Analysis of efficacy

At end of treatment there was statistically significant evidence from the per protocol analysis that patients on FDC had a greater improvement in change from baseline in daytime nasal symptoms score than patients who

received Montelukast (p=0.0266) or Levocetirizine (p=0.0409) (Table 2). These results were consistent with the Intent to treat analysis. In the ITT population statistically significant differences for the mean change in daytime nasal symptom scores were also observed for the FDC group compared to Montelukast (p=0.0054) and Levocetirizine groups (p=0.0425) (Table 2).

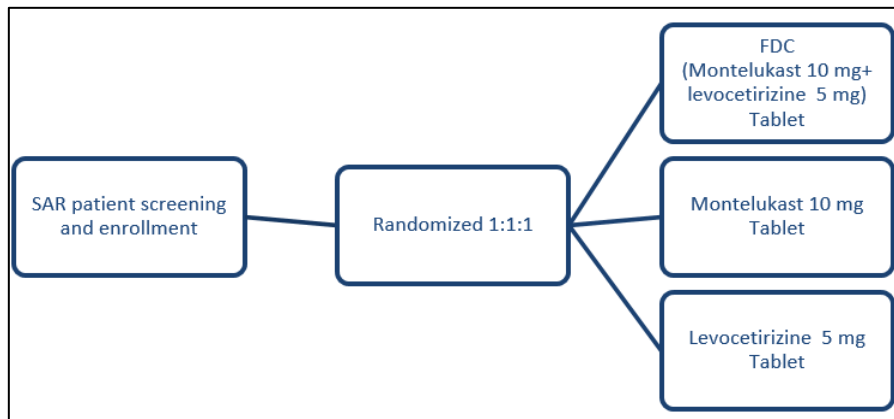


Figure 1: Study design.

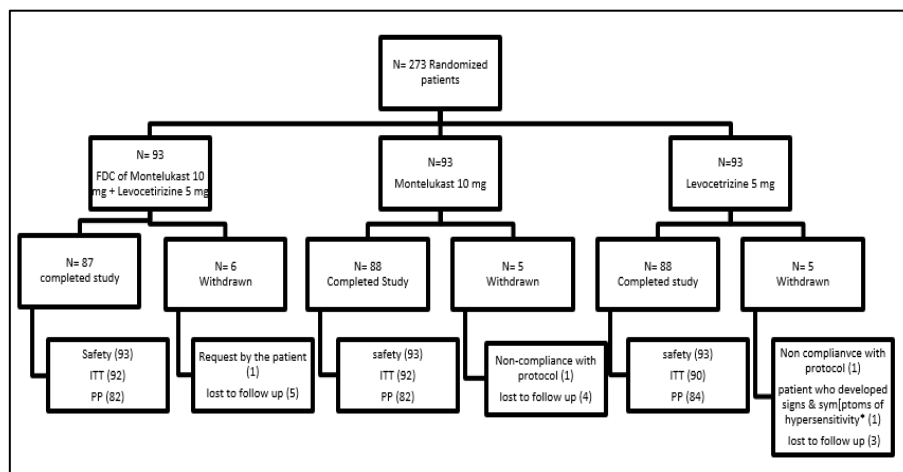


Figure 2: Clinical trial participant flowchart.

*Patient was withdrawn from the study due to signs and symptoms of hypersensitivity.

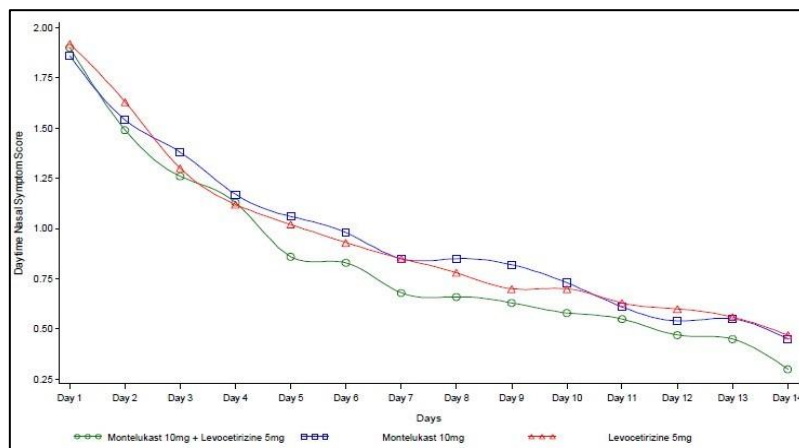


Figure 3: Daily mean daytime nasal symptoms score (PP).

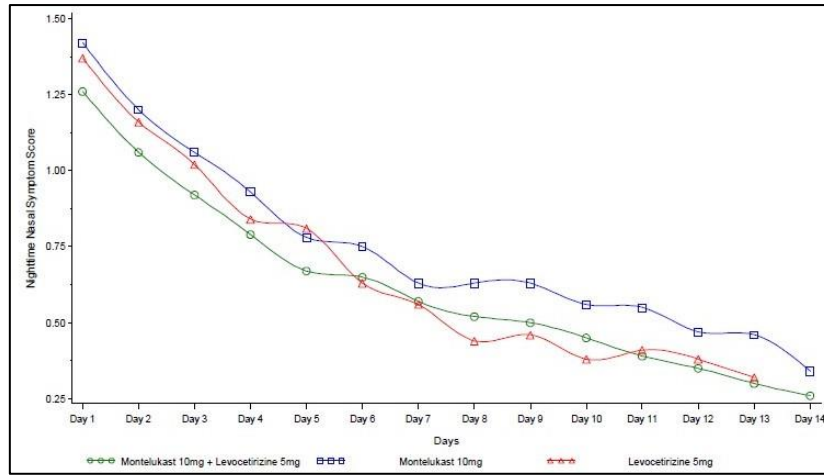


Figure 4: Daily mean night time symptoms score (PP).

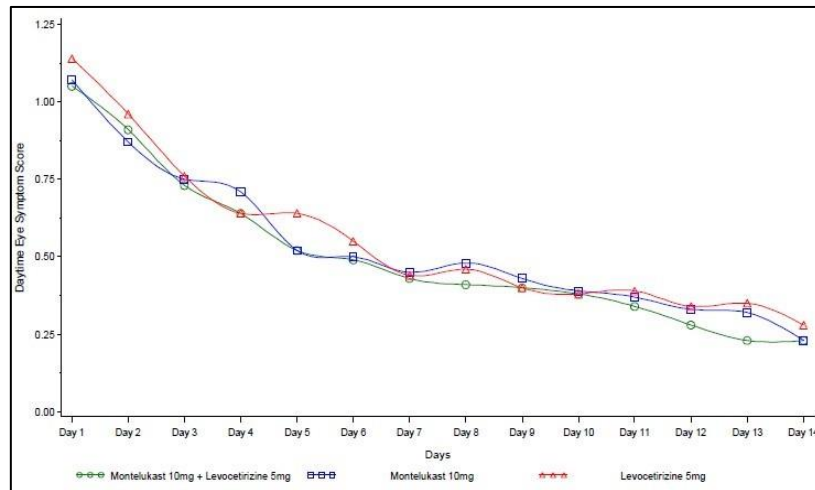


Figure 5: Daily mean daytime eye symptoms score (PP).

Analysis of the secondary efficacy endpoints (nighttime symptoms score, daytime eye symptoms score, and rhinoconjunctivitis quality-of-life score) provided numerically greater improvement in the nighttime symptoms score, daytime eye symptoms score, and rhinoconjunctivitis quality-of-life scores in the FDC group as compared to the Montelukast group or Levocetirizine group. It was also noted that a greater number of patients in the FDC group demonstrated improvement in symptoms of allergic rhinitis as compared to patients in the Montelukast group and Levocetirizine group for the Physician's and Patient's global evaluation of allergic rhinitis at end of study (Figure 4-6).

Safety evaluation

A total of 38 out of 279 patients (13.6%) experienced at least one adverse event during the study; after randomization (treatment emergent adverse events). Adverse events were reported for 17.2% (16/93) patients in the FDC of Montelukast 10mg and Levocetirizine 5mg

group, 9.7% (9/93) patients in the Montelukast 10mg group, and 14% (13/93) patients in the Levocetirizine 5mg group. A total of 69 AEs were reported during the study. The majority of adverse events were mild in severity and resolved without treatment. Most of the AEs reported in this study were assessed by the investigator as not related to study drug.

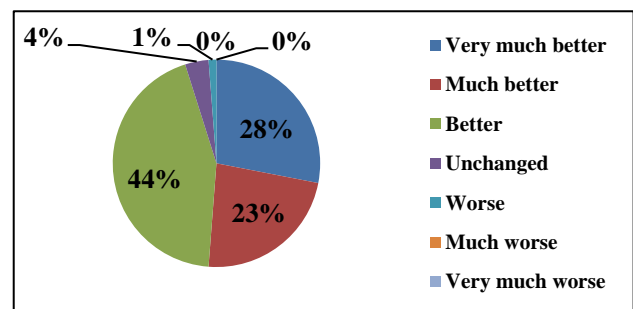


Figure 6: Summary of patient's global evaluation of allergic rhinitis (PP) with montelukast 10 mg +levocetirizine 5 mg.

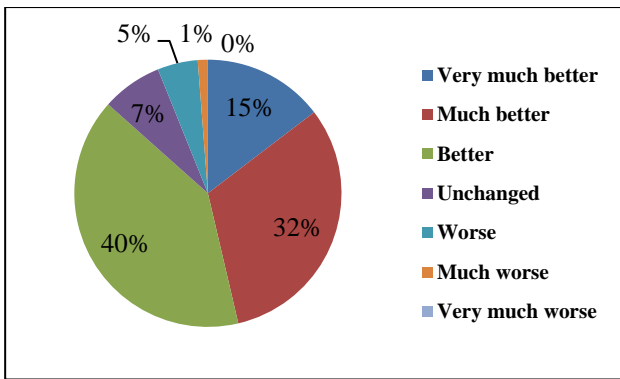


Figure 7: Summary of patient's global evaluation of allergic rhinitis (PP) with montelukast 10 mg

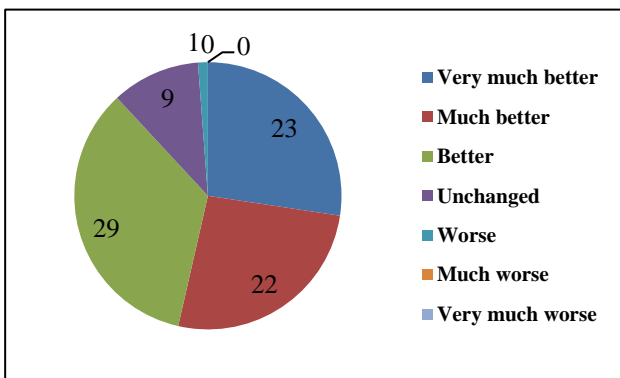


Figure 8: Summary of patient's global evaluation of allergic rhinitis (PP) with levocetirizine 5 mg.

Adverse events considered to be related to study medication were reported for 1.1% (1/93) (hypersomnia) and 5.4% (5/93) (sedation, somnolence, tremor and diarrhea) of patients in the FDC group and Levocetirizine 5mg group respectively. No adverse event was reported as related to study drug in the Montelukast 10 mg group. The most frequent AEs were nervous system disorders (11 patients across all groups), gastrointestinal disorders (9 patients across all groups) and respiratory disorders (7 patients across all groups). The most common single adverse event reported was headache and was reported in 5 patients across all treatment groups. Adverse events of pyrexia, urinary tract infection and cough were also common and each of these AEs were reported in 4 patients across all treatment groups. No serious adverse events or discontinuations due to adverse events were reported, and no deaths occurred during the study.

DISCUSSION

A total of 279 patients participated in the study with 93 patients in each treatment group. 263 patients completed the study. Clinical studies done in the past shows that Montelukast as monotherapy has been effective in improving daytime and night-time symptoms in patients with allergic rhinitis.^{11,12} Levocetirizine has been associated with significant improvements in symptom

scores for sneezing, rhinorrhea, and ocular/nasal pruritus. In a review of clinical trials, Levocetirizine was effective in relieving the nasal congestion associated with allergic rhinitis (AR) compared with placebo and was an appropriate option for the treatment of nasal congestion in patients with AR.^{9,13} Hence combining Montelukast with Levocetirizine does appear to have additional benefits in comparison to each agent alone and could be considered for the treatment of patients with allergic rhinitis.^{11,14}

In the present study significant improvement as compared to baseline occurred for all the efficacy measures in the three treatment groups. Analysis of the primary efficacy endpoint the daytime nasal symptoms score provided evidence that FDC of Montelukast 10mg and Levocetirizine 5 mg was superior to Montelukast 10mg monotherapy or Levocetirizine 5 mg monotherapy in the treatment of patients with seasonal allergic rhinitis.

In the previous clinical studies, combination of Montelukast and Levocetirizine has shown a significant improvement in total nasal symptom scores (TNSS) in patients on the combination therapy as compared to placebo or giving both the drugs as monotherapy.^{15,16} In a randomized, double-blind, placebo-controlled crossover study to investigate the effects of 6 weeks of treatment for persistent allergic rhinitis (AR), the greatest improvement in nasal symptoms occurred after combination treatment of Montelukast (10 mg) and Levocetirizine (5 mg).¹⁵ In another 32-week randomized, placebo-controlled, crossover, double-armed study¹⁶ by Ciebiada et al in 40 adult patients with history of persistent AR, there were four 6-week treatment periods separated by 2-week washout periods. The combination of Montelukast and Levocetirizine significantly improved nasal symptoms during the first 24 hours and improvement gradually increased during the 6 weeks of treatment especially in patients receiving the combination therapy. Also, Improvement at 6 weeks of treatment was significantly greater than that achieved on the 1st day of therapy in patients treated with the combination of Montelukast and Levocetirizine.¹⁶

In a prospective, randomized, double-blind, parallel, active-controlled, comparative 4-week trial by Mahatme et al. (N=70) combination of montelukast and Levocetirizine showed significant reduction in total nasal symptom score (TNSS).¹⁷ Kim et al in 4-week, randomized, multicenter, double-blind, Phase III trial (N=228) showed similar reduction in TNSS and other symptoms of allergic rhinitis using combination of montelukast and levocetirizine compared to either of the drug alone.¹⁸ In contrast to most studies, clinical study by andhale et al (N=75) did not show any significant difference in terms daytime symptoms, night time symptoms and eye symptoms in combination arm (montelukast+levocetirizine) compared to monotherapy with either drugs.¹⁹ In patients of persistent allergic rhinitis, adsule et al showed better clinical outcomes with

combination therapy than monotherapy of montelukast or levocetirizine.¹⁴ Similar to this study, saverno et al proved that montelukast and levocetirizine improves quality of life in patients of allergic rhinitis.²⁰

In this study, The FDC of Montelukast 10mg and Levocetirizine 5mg was found to be safe and generally well tolerated. There were no unexpected AEs as per Prescribing Information of Montelukast or Levocetirizine reported for the treatment groups. The highest incidence of treatment emergent adverse events was in the nervous system disorders system organ class with the most common adverse event being headache. There were no serious adverse events, deaths, withdrawals due to adverse events or unexpected safety findings reported during the study. There were no clinically significant findings in clinical laboratory evaluations, vital signs, ECG and physical examinations performed during the study. Safety assessments of this study are comparable to studies done in the past by Ciebiada et al, Mahatme et al with combination of montelukast and levocetirizine in patients of allergic rhinitis.^{16,17}

Results of our study substantiated evidence for the primary efficacy endpoint that (Montelukast 10 mg+Levocetirizine 5 mg) FDC was superior to monotherapy with either drugs in the treatment of patients with seasonal allergic rhinitis. The secondary efficacy variables (night-time symptoms score, daytime eye symptoms score and rhino-conjunctivitis quality-of-life score) provided evidence of a numerically greater reduction in these scores which were observed for the fixed dose combination. Assessment of the Physician's and Patient's Global Evaluation of Allergic Rhinitis indicated that a greater number of patients in the FDC group demonstrated improvement in symptoms of allergic rhinitis compared monotherapy.

Fixed dose combination of Montelukast and Levocetirizine was safe, generally well tolerated and superior on efficacy compared to Montelukast or Levocetirizine in patients of seasonal allergic rhinitis. This FDC also maintains the quality of life in allergic rhinitis patient which further helps in improving the compliance of the patient to the therapy.

CONCLUSION

Fixed dose combination of Montelukast and Levocetirizine was safe, generally well tolerated and superior on efficacy compared to Montelukast or Levocetirizine in patients of seasonal allergic rhinitis.

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REFERENCES

1. Wallace DV, Dykewicz MS, Bernstein DI. The diagnosis and management of rhinitis: an updated practice parameter. *J Allergy Clin Immunol.* 2008;122:1-84.
2. Storms W. Allergic rhinitis-induced nasal congestion: its impact on sleep quality. *Prim Care Respir J.* 2008;17(1):7-18.
3. Kubavat AH, Pawar P, Mittal R. An open label, active controlled, multicentric clinical trial to assess the efficacy and safety of fluticasone furoate nasal spray in adult Indian patients suffering from allergic rhinitis. *J Assoc Physicians India.* 2011;59:424-8.
4. Singh AB, Kumar P. Aeroallergens in clinical practice of allergy in India. An overview. *Ann Agric Environ Med.* 2003;10(2):131-6.
5. Singh AB, Shahi S. Aeroallergens in clinical practice of allergy in India- ARIA Asia Pacific Workshop report. *Asian Pac J Allergy Immunol.* 2008;26(4):245-56.
6. Shah A, Pawankar R. Allergic rhinitis and comorbid asthma: perspective from India ARIA Asia-Pacific Workshop report. *Asian Pac J Allergy Immunol.* 2009;27(1):71-7.
7. Lagos J.A. Montelukast in the management of allergic rhinitis. *Ther Clin Risk Manag.* 2007;3:327-32.
8. Deem K, Ponikau P. Management of allergic rhinitis implementation of evidence-based guidelines. *Touch Briefings.* 2008.
9. Mösges R, König V, Köberlein J. The effectiveness of levocetirizine in comparison with loratadine in treatment of allergic rhinitis a meta-analysis. *Allergol Int.* 2011;60(4):541-6.
10. Philip G, Malmstrom, K, Hampel FC. Montelukast for treating seasonal allergic rhinitis: a randomized, double blind, placebo-controlled trial performed in the spring. *Clin Exp Allergy.* 2002;32:1020-8.
11. Ciebiada M, Ciebiada MG. Quality of life in patients with persistent allergic rhinitis treated with montelukast alone or in combination with levocetirizine or desloratadine. *J Investig Allergol Clin Immunol.* 2008;18(5):343-9.
12. Adelsberg VJ, Philip G, Pedinoff AJ. Montelukast improves symptoms of seasonal allergic rhinitis over a 4-week treatment period. *Allergy.* 2003;58(12):1268-76.

13. Goodman M, Jhaveri M, Saverno K. Cost-effectiveness of second-generation antihistamines and montelukast in relieving allergic rhinitis nasal symptoms. *Am Health Drug Benefits.* 2008;1(8):26-34.
14. 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.
15. Ciebiada M, Ciebiada GM, DuBuske LM. Montelukast with desloratadine or levocetirizine for the treatment of persistent allergic rhinitis. *Ann Allergy Asthma Immunol.* 2006;97(5):664-71.
16. Ciebiada M, Ciebiada GM, Barylski M. Use of montelukast alone or in combination with desloratadine or levocetirizine in patients with persistent allergic rhinitis. *Am J Rhinol Allergy.* 2011;25(1):1-6.
17. 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.
18. 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.
19. Andhale S, Goel HC, Nayak S. Comparison of effect of levocetirizine or montelukast alone and in combination on symptoms of allergic rhinitis. *Indian J Chest Dis Allied Sci.* 2016;58(2):103-5.
20. Saverno KR, Seal B, Goodman MJ, Meyer K. Economic evaluation of quality-of-life improvement with second-generation antihistamines and montelukast in patients with allergic rhinitis. *Am Health Drug Benefits.* 2009;2(7):309-16.

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