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# COST-EFFECTIVENESS AND QUALITY-OF-LIFE OUTCOMES OF MONTELUKAST–LEVOCETIRIZINE VERSUS MONTELUKAST–BILASTINE IN ALLERGIC RHINITIS: A PROSPECTIVE OBSERVATIONAL STUDY

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## ABSTRACT

**Background:** Allergic rhinitis (AR) substantially impairs quality of life and imposes direct and indirect economic burdens, particularly in countries with high out-of-pocket health expenditure. Fixed-dose combinations of montelukast with second-generation antihistamines are widely prescribed, yet comparative data on cost-effectiveness and patient well-being in the Indian setting are limited.

**Methods:** Current prospective observational study was conducted in a tertiary care centre and included 60 patients with AR, with or without coexisting asthma. Group A(n=30) participants received montelukast 10 mg + levocetirizine 5 mg whereas Group B(n=30) participents recieved montelukast 10 mg + bilastine 20 mg once daily. Quality of life was assessed using the WHO-5 Well-Being Index at baseline and day 28. Direct drug costs were estimated from market prices of ten widely available brands per group. Cost-effectiveness ratio (CER) was calculated as cost per unit reduction in Total Nasal Symptom Score (TNSS).

**Results:** Findings revealed that baseline characteristics were comparable between groups. Both regimens significantly improved WHO-5 well-being scores (mean improvement: 9.43 ± 3.24 in Group A vs 9.24 ± 2.57 in Group B; and reduced TNSS (6.64 ± 1.60 vs 6.54 ± 1.38; p=0.81). The average 28-day cost was lower in Group A (₹403.84 ± 212.90) than Group B (₹457.99 ± 139.56). CER was numerically lower for montelukast–levocetirizine (₹60.82 ± 32.06) compared to montelukast–bilastine (₹70.03 ± 21.34), not statistically significant (p=0.511).

**Conclusions:** Both combinations effectively improved well-being and symptom control. Montelukast–levocetirizine offered a modest economic advantage, whereas montelukast–bilastine provided a non-sedating alternative. These findings support patient-centred, value-conscious prescribing decisions in AR management.

**Keywords:** Allergic rhinitis, montelukast, levocetirizine, bilastine, cost-effectiveness, quality of life.

## INTRODUCTION

Allergic rhinitis (AR) is among the most prevalent chronic inflammatory airway conditions and remains a major public-health challenge in India. Recent nationally representative data from the Global Asthma Network (Phase I, India) estimate AR prevalence at 7.7% in children (6–7 years), 23.5% in adolescents (13–14 years), and 9.8% in adults, underscoring a substantial symptomatic burden across the life course[1]. Evidence suggests the burden has risen over recent decades in Indian cohorts, particularly among older children, mirroring trends captured across ISAAC phases[2].

Beyond nasal and ocular symptoms, AR impairs health-related quality of life (HRQoL) and productivity. Systematic evidence indicates that work effectiveness is disproportionately affected (presenteeism), often exceeding absenteeism-related losses[3, 4]. Early health-economic analyses similarly highlighted that indirect costs tied to at-work performance—exacerbated by sedating antihistamines—can dominate overall economic impact[5].Contemporary real-world studies continue to link poor AR control with decreased productivity and higher indirect costs, especially in patients with concomitant asthma[6]. In the Indian setting—where out-of-pocket expenditure constitutes a large share of health spending—the value proposition of AR therapies must be weighed carefully against affordability[7].

Guideline-directed pharmacotherapy for AR is well defined. The ARIA 2016 update and subsequent iterations recommend second-generation H1-antihistamines and intranasal corticosteroids as core options, with leukotriene receptor antagonists (LTRAs) considered in selected patients—particularly when rhinitis coexists with asthma as part of a unified airway paradigm[8, 9, 10]. Montelukast, a cysteinyl-leukotriene receptor antagonist, has supportive evidence in AR and comorbid asthma, complementing antihistaminic control of the early allergic phase[11, 12].

Within the second-generation antihistamine class, levocetirizine has demonstrated efficacy and tolerability in randomized studies of seasonal and perennial AR, with improvements in symptom control and HRQoL versus placebo[13, 14]. Bilastine—a newer second-generation agent—exhibits a favourable CNS safety profile: it is a P-glycoprotein substrate with minimal blood-brain barrier penetration, shows practically no cerebral H1-receptor occupancy on PET at therapeutic doses, and does not impair driving performance in controlled studies[15, 16]. These pharmacodynamic distinctions are clinically relevant for patients who prioritize daytime alertness.

Despite the wide real-world use of montelukast + antihistamine fixed-dose combinations (FDCs), comparative evidence that integrates cost-effectiveness with patient-reported well-being remains limited in the Indian context. Meanwhile, brief, responsive measures of well-being—such as the WHO-5 Well-Being Index—are validated across diverse conditions and settings and are suitable as outcome measures capturing meaningful change over short horizons[17, 18].

Accordingly, the present 28-day prospective observational study was designed to compare cost-effectiveness and quality-of-life outcomes between two commonly used FDCs—montelukast–levocetirizine and montelukast–bilastine—in Indian patients with allergic rhinitis. By aligning with ARIA-consistent pharmacotherapy and incorporating well-validated patient-centred endpoints alongside pragmatic cost assessments, this work aims to inform value-based treatment choices in routine care[8, 17].

## METHODS

### Study Design and Setting

This was a 28-day, prospective, observational study conducted in the Department of Pharmacology at a tertiary care teaching hospital in North India. The study was approved by the Institutional Ethics Committee prior to initiation, and all participants provided written informed consent before enrolment.

### Study Population

Patients diagnosed with allergic rhinitis (AR) on clinical grounds were included. Diagnosis was established based on characteristic nasal and ocular symptoms such as sneezing, rhinorrhoea, nasal obstruction, nasal itching, and conjunctival irritation, persisting for at least one year.

**Inclusion criteria:**
- Age ≥18 years.
- Both sexes.
- Patients with a confirmed diagnosis of allergic rhinitis with or without concomitant asthma.
- Willingness to provide informed consent and adhere to study procedures.

**Exclusion criteria:**
- Patients with chronic sinusitis, nasal polyps, or upper respiratory tract infection during the study period.
- History of hypersensitivity to study drugs.
- Pregnant or lactating women.
- Patients with significant hepatic, renal, or cardiovascular comorbidities.
- Patients on concomitant medications likely to interfere with study outcomes (e.g., systemic corticosteroids, immunotherapy).

**Study Groups and Treatment**

Eligible patients were assigned to one of the following groups based on physician prescription patterns:
- **Group A:** Montelukast 10 mg + Levocetirizine 5 mg fixed-dose combination, once daily.
- **Group B:** Montelukast 10 mg + Bilastine 20 mg fixed-dose combination, once daily.

Both groups received treatment for 28 consecutive days. Drug formulations included both branded and generic products available in the Indian market.

**Study Assessments**

1. *Quality of Life Assessment:* Quality of life was evaluated using the WHO-5 Well-Being Index at baseline and day 28. This self-reported tool consists of five positively phrased items scored on a 6-point Likert scale. Higher scores indicate better subjective well-being.
2. *Cost Analysis:* Direct medical cost was calculated based on the average retail price of ten widely available branded and generic fixed-dose combinations of each regimen. The 28-day treatment cost for each participant was derived and averaged for both groups.
3. *Cost-effectiveness ratio (CER):* defined as the cost per unit reduction in TNSS from baseline to day 28.

**Sample Size**

The study enrolled patients consecutively until 60 eligible participants completed follow-up, with 30 patients in each treatment group. Sample size was based on feasibility and the observational design, rather than a priori power calculation.

**Statistical Analysis**

Data were entered into Microsoft Excel and analyzed using SPSS software. Continuous variables were expressed as mean ± standard deviation. Intergroup comparisons were made using the unpaired Student's t-test for continuous variables and the chi-square test for categorical variables. A p value $<0.05$ was considered statistically significant.

## RESULTS

**Participant baseline characteristics**

Sixty patients completed follow-up (n=30 per group). Baseline characteristics were comparable between groups. Mean baseline TNSS was 9.15 ± 1.17 in the montelukast–levocetirizine group (Group A) and 9.57 ± 1.27 in the montelukast–bilastine group (Group B). Baseline WHO-5 was 11.61

± 2.52 (Group A) and 10.70 ± 2.12 (Group B). Age and the distribution of AR alone vs AR + asthma were also balanced. (Table-1)

***Table 1: Baseline characteristics of study participants***

| ***Parameter*** | ***Group A (Montelukast + Levocetirizine, n=30)*** | ***Group B (Montelukast + Bilastine, n=30)*** | ***p value*** |
|---|---|---|---|
| *Age (years), mean ± SD* | 32.33 ± 11.88 | 31.50 ± 9.30 | NS |
| *AR alone (%)* | 17 (56.7%) | 21 (70%) | – |
| *AR with asthma (%)* | 13 (43.3%) | 9 (30%) | – |
| *Baseline TNSS, mean ± SD* | 9.15 ± 1.17 | 9.57 ± 1.27 | 0.31 |
| *Baseline WHO-5, mean ± SD* | 11.61 ± 2.52 | 10.70 ± 2.12 | 0.22 |

**Quality of life (WHO-5 wellbeing score) & Asthma subgroup ACQ-7 score**

Both regimens produced large and comparable gains in well-being over 28 days. Mean WHO-5 improvement was +9.43 ± 3.24 (Group A) versus +9.24 ± 2.57 (Group B), p = 0.80; median improvements were 9.25 and 9.65, respectively (ranges: 2.5–16.2 and 3.7–13.4).

In the subgroup of patients with asthma, the mean reduction in ACQ-7 scores from baseline to day 28 was 2.52 ± 0.91 in Group A and 2.88 ± 0.45 in Group B. Although numerically higher in Group B, this difference did not reach statistical significance (p = 0.28) (Table-2, Figure-1)

***Table 2: Change in TNSS, WHO-5 and* Asthma Subgroup ACQ-7 *scores from baseline to day 28***

| ***Outcome*** | ***Group A (n=30)*** | ***Group B (n=30)*** | ***p value*** |
|---|---|---|---|
| *TNSS reduction, mean ± SD* | 6.64 ± 1.60 | 6.54 ± 1.38 | 0.81 |
| *WHO-5 improvement, mean ± SD* | 9.43 ± 3.24 | 9.24 ± 2.57 | 0.80 |
| *WHO-5 improvement, median (range)* | 9.25 (2.5–16.2) | 9.65 (3.7–13.4) | – |
| *Mean ACQ-7 Reduction* | 2.52 ± 0.91 | 2.88 ± 0.45 | 0.28 |

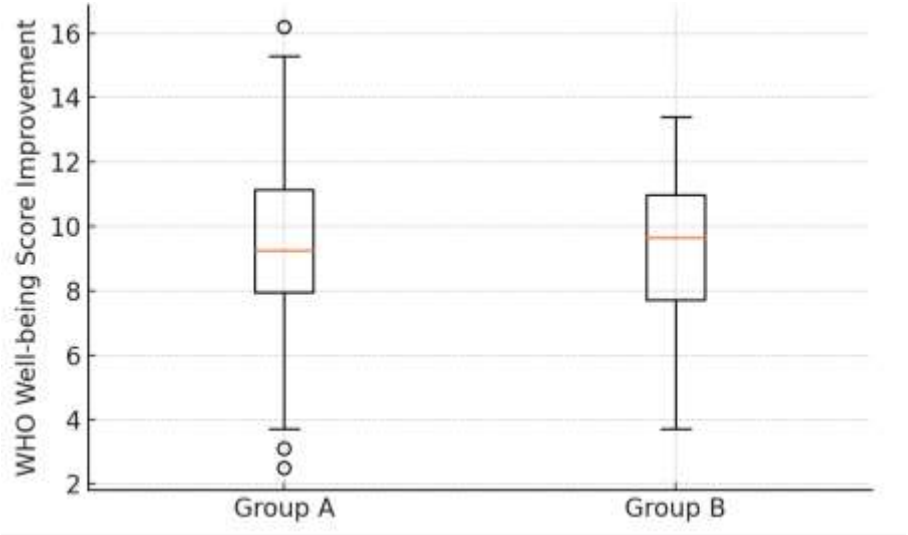


**Figure 1: Box plot showing the change in WHO-5 Well-Being Index scores from baseline to day 28 in both groups. Both combinations produced significant intra-group improvement with no statistically significant difference between groups (p = 0.80).**

**Direct drug costs (28-day horizon)**

Using a market-basket of ten brands per combination, the average 28-day cost was ₹403.84 ± ₹212.90 for montelukast–levocetirizine and ₹457.99 ± ₹139.56 for montelukast–bilastine. Example price dispersion illustrates wide brand-level variation (e.g., levocetirizine FDCs ranged from ₹1.80 to ₹23.04 per tablet; bilastine FDCs from ₹5.00 to ₹23.00 per tablet). (Table-3)

***Table 3: Average 28-day cost of therapy***

| *Combination* | *Mean ± SD cost (₹)* | *Cost per tablet range (₹)* |
|---|---|---|
| *Montelukast + Levocetirizine* | 403.84 ± 212.90 | 1.80 – 23.04 |
| *Montelukast + Bilastine* | 457.99 ± 139.56 | 5.00 – 23.00 |

**Cost-effectiveness**

From baseline to Day 28, mean TNSS reduction was 6.64 ± 1.60 in Group A and 6.54 ± 1.38 in Group B; the inter-group difference was not significant (p = 0.81). The mean cost-effectiveness ratio (CER)—defined as cost per unit TNSS reduction—was ₹60.82 ± ₹32.06 for montelukast–levocetirizine and ₹70.03 ± ₹21.34 for montelukast–bilastine; the inter-group difference was not statistically significant (p = 0.511). (Figure-2)

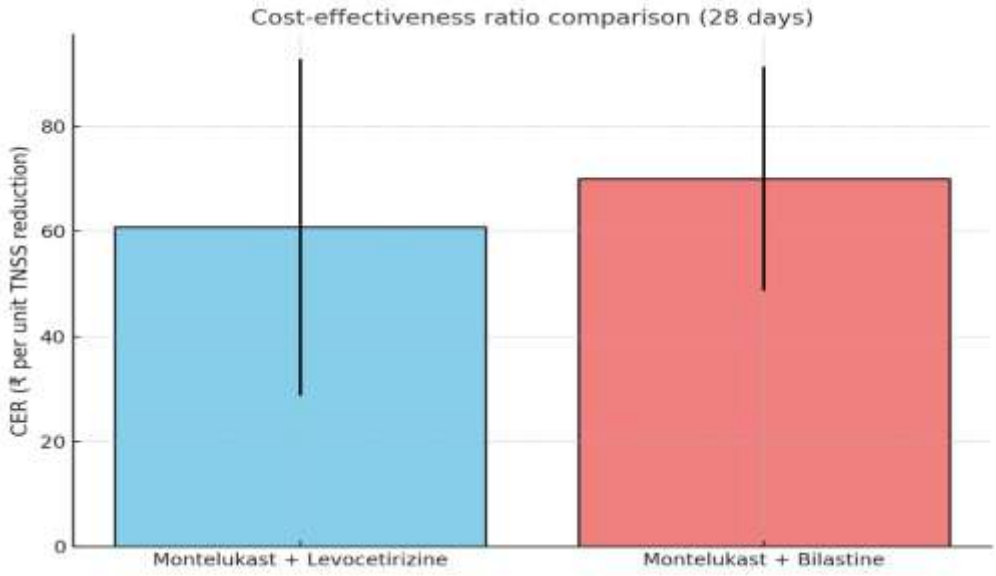


**Figure 2: Mean cost-effectiveness ratios.**Bar chart shows mean CER (cost per unit TNSS reduction) between montelukast–levocetirizine and montelukast–bilastine groups).

**DISCUSSION**

The present 28-day observational study found that both fixed-dose combinations—montelukast–levocetirizine and montelukast–bilastine—produced large, comparable gains in patient well-being (WHO-5) and similar reductions in symptom burden (TNSS). Although acquisition costs were modestly lower for the levocetirizine combination, between-group differences in the cost-effectiveness ratio (cost per unit TNSS reduction) did not reach statistical significance, indicating broadly equivalent short-term value in routine care.

Our pharmacoeconomic signal favouring levocetirizine is consistent with randomized evidence showing that a montelukast–levocetirizine regimen can deliver favourable cost-effectiveness relative to alternative second-generation antihistamine combinations, despite small differences in symptom scores[21]. Longer-horizon studies in persistent AR likewise report that levocetirizine improves quality of life while reducing overall disease costs, reinforcing the plausibility of the present short-term findings[23].

Bilastine's clinical appeal resides in its non-sedating profile and preserved psychomotor performance—features that matter to patients who prioritize daytime alertness. Controlled driving studies show no meaningful impairment at therapeutic doses, and neuroimaging work demonstrates negligible central H1-receptor engagement compared with sedating comparators, aligning with real-world impressions of low CNS burden[15, 25]. These characteristics can justify selection of the bilastine combination for individuals whose occupations or daily activities are sensitive to even mild sedation.

Therapeutically, the combinations assessed here are congruent with guideline-consistent pharmacotherapy. ARIA's 2016 revision supports the use of second-generation H1-antihistamines and recognizes leukotriene receptor antagonists as an option in selected patients—particularly when rhinitis coexists with asthma as part of a unified airway concept—providing a mechanistic rationale for montelukast–antihistamine pairings in practice[8].

This study has limitations. Its 28-day horizon and observational design limit causal inference and preclude assessment of seasonal variability, adherence durability, or health-care utilization. Only direct drug costs were analysed; indirect costs (e.g., productivity losses) often dominate the economic burden of AR and should be incorporated in future evaluations. Larger, randomized, multicentre studies that include cost-utility endpoints and longer follow-up would strengthen the evidence base and allow subgroup analyses (e.g., comorbid asthma).

Overall, both combinations improved patient-reported well-being and symptoms over 28 days with broadly comparable short-term value. Montelukast–levocetirizine offers a small economic edge driven by lower acquisition cost, whereas montelukast–bilastine provides a non-sedating alternative that may be preferable for patients who prioritize cognitive performance. These findings support a tailored, value-conscious approach to AR management consistent with contemporary guidance[8].

## CONCLUSION

This prospective observational study demonstrated that both montelukast–levocetirizine and montelukast–bilastine fixed-dose combinations provide significant and comparable improvements in quality of life and symptom relief in patients with allergic rhinitis. While montelukast–levocetirizine showed a modest pharmacoeconomic advantage due to lower acquisition cost, the difference in overall cost-effectiveness was not statistically significant. Montelukast–bilastine, by contrast, offers the advantage of a non-sedating profile, which may be particularly valuable for patients whose occupational or academic performance requires sustained alertness.

## DECLARATIONS

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**Conflict of interest:** No conflict of interest

## REFERENCES

1. Barne M, Singh S, Mangal DK, Singh M, Awasthi S, Mahesh PA, et al. Global Asthma Network Phase I, India: Results for allergic rhinitis and eczema in 127,309 children and adults. J Allergy Clin Immunol Glob. 2022;1(2):51-60. doi- 10.1016/j.jacig.2022.01.004 PMID- 37780584
2. Krishna MT, Mahesh PA, Vedanthan P, Moitra S, Mehta V, Christopher DJ. An appraisal of allergic disorders in India and an urgent call for action. World Allergy Organ J. 2020;13(7):100446. doi- 10.1016/j.waojou.2020.100446 PMID- 32774662
3. Vandenplas O, Vinnikov D, Blanc PD, Agache I, Bachert C, Bewick M, et al. Impact of Rhinitis on Work Productivity: A Systematic Review. J Allergy Clin Immunol Pract. 2018;6(4):1274-86.e9. doi- 10.1016/j.jaip.2017.09.002 PMID- 29017832
4. Vandenplas O, D'Alpaos V, Van Brussel P. Rhinitis and its impact on work. Curr Opin Allergy Clin Immunol. 2008;8(2):145-9. doi- 10.1097/ACI.0b013e3282f63d92 PMID- 18317023
5. Crystal-Peters J, Crown WH, Goetzel RZ, Schutt DC. The cost of productivity losses associated with allergic rhinitis. Am J Manag Care. 2000;6(3):373-8. doi- PMID- 10977437
6. Vieira RJ, Azevedo LF, Pereira AM, Nogueira-Leite D, Rocha Gonçalves FN, Larenas-Linnemann DE, et al. Impact of Allergic Rhinitis Control on Work Productivity and Costs: A Real-World Data MASK-air Study. J Allergy Clin Immunol Pract. 2024;12(11):3107-15.e13. doi- 10.1016/j.jaip.2024.07.026 PMID- 39111363
7. Nanda M, Sharma R. A comprehensive examination of the economic impact of out-of-pocket health expenditures in India. Health Policy Plan. 2023;38(8):926-38. doi- 10.1093/heapol/czad050 PMID- 37409740

8. Brożek JL, Bousquet J, Agache I, Agarwal A, Bachert C, Bosnic-Anticevich S, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines-2016 revision. J Allergy Clin Immunol. 2017;140(4):950-8. doi- 10.1016/j.jaci.2017.03.050 PMID- 28602936
9. Bousquet J, Hellings PW, Agache I, Bedbrook A, Bachert C, Bergmann KC, et al. ARIA 2016: Care pathways implementing emerging technologies for predictive medicine in rhinitis and asthma across the life cycle. Clin Transl Allergy. 2016;6:47. doi- 10.1186/s13601-016-0137-4 PMID- 28050247
10. Bousquet J, Schünemann HJ, Togias A, Bachert C, Erhola M, Hellings PW, et al. Next-generation Allergic Rhinitis and Its Impact on Asthma (ARIA) guidelines for allergic rhinitis based on Grading of Recommendations Assessment, Development and Evaluation (GRADE) and real-world evidence. Journal of Allergy and Clinical Immunology. 2020;145(1):70-80.e3. doi- 10.1016/j.jaci.2019.06.049 PMID-
11. Valovirta E. Managing co-morbid asthma with allergic rhinitis: targeting the one-airway with leukotriene receptor antagonists. World Allergy Organ J. 2012;5(Suppl 3):S210-1. doi- 10.1097/WOX.0b013e3181f4ea72 PMID- 23268480
12. Lagos JA, Marshall GD. Montelukast in the management of allergic rhinitis. Ther Clin Risk Manag. 2007;3(2):327-32. doi- 10.2147/tcrm.2007.3.2.327 PMID- 18360641
13. Potter PC. Efficacy and safety of levocetirizine on symptoms and health-related quality of life of children with perennial allergic rhinitis: a double-blind, placebo-controlled randomized clinical trial. Ann Allergy Asthma Immunol. 2005;95(2):175-80. doi- 10.1016/s1081-1206(10)61208-2 PMID- 16136768
14. Segall N, Gawchik S, Georges G, Haeusler JM. Efficacy and safety of levocetirizine in improving symptoms and health-related quality of life in US adults with seasonal allergic rhinitis: a randomized, placebo-controlled study. Ann Allergy Asthma Immunol. 2010;104(3):259-67. doi- 10.1016/j.anai.2009.12.003 PMID- 20377116
15. Farré M, Pérez-Mañá C, Papaseit E, Menoyo E, Pérez M, Martin S, et al. Bilastine vs. hydroxyzine: occupation of brain histamine H1 -receptors evaluated by positron emission tomography in healthy volunteers. Br J Clin Pharmacol. 2014;78(5):970-80. doi- 10.1111/bcp.12421 PMID- 24833043
16. Church MK, Labeaga L. Bilastine: a new H(1) -antihistamine with an optimal profile for updosing in urticaria. J Eur Acad Dermatol Venereol. 2017;31(9):1447-52. doi- 10.1111/jdv.14305 PMID- 28467671
17. Topp CW, Østergaard SD, Søndergaard S, Bech P. The WHO-5 Well-Being Index: a systematic review of the literature. Psychother Psychosom. 2015;84(3):167-76. doi- 10.1159/000376585 PMID- 25831962
18. Omani-Samani R, Maroufizadeh S, Almasi-Hashiani A, Sepidarkish M, Amini P. The WHO-5 Well-Being Index: A Validation Study in People with Infertility. Iran J Public Health. 2019;48(11):2058-64. doi- PMID- 31970105
19. 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. doi- 10.4103/0253-7613.194854 PMID- 28066101
20. Bachert C, Bousquet J, Canonica GW, Durham SR, Klimek L, Mullol J, et al. Levocetirizine improves quality of life and reduces costs in long-term management of persistent allergic rhinitis. J Allergy Clin Immunol. 2004;114(4):838-44. doi- 10.1016/j.jaci.2004.05.070 PMID- 15480324
21. Conen S, Theunissen EL, Van Oers AC, Valiente R, Ramaekers JG. Acute and subchronic effects of bilastine (20 and 40 mg) and hydroxyzine (50 mg) on actual driving performance in healthy volunteers. J Psychopharmacol. 2011;25(11):1517-23. doi- 10.1177/0269881110382467 PMID- 20855350