Original Article

Comparison Of Flunisolide Nasal Spray With Combined Oral Antihistamine And Antileukotriene Therapy In Allergic Rhinitis In Relation To Patients' Symptoms

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Abstract

Objective: To compare the efficacy of flunisolide nasal spray with combined oral antihistamine and leukotriene receptor inhibitor therapy in improving symptoms among patients with allergic rhinitis (AR).

Methods: This quasi-experimental comparative study was conducted in the Department of Otorhinolaryngology over nine months after ethical approval. A total of 100 adults (18–45 years) with AR were enrolled and divided into two groups (n = 50 each) using a non-probability consecutive sampling method. Group A received oral loratadine (10 mg) plus montelukast (10 mg), whereas Group B received flunisolide nasal spray (100 µg, two puffs per nostril twice daily). Total nasal symptom scores (TNSS) were recorded at baseline, 2 weeks, and 4 weeks after treatment. Data were analysed using SPSS version 23, and the Mann–Whitney U test was applied to compare treatment outcomes using TNSS between both groups, with $P \leq .05$ considered significant.

Results: A total of 100 patients (50 per group) were included in the study. Baseline TNSS was comparable between the groups ($P = .659$). No significant difference was observed at 1st follow-up ($P = .979$), while at 2nd follow-up, Group B showed a significantly lower TNSS ($P < .001$). After adjusting for age and baseline TNSS, the results at 2nd follow-up remained significant, favouring flunisolide therapy ($B = -0.719$, 95% CI: −1.181 to −0.257; $P = .003$) with a moderate effect size ($r=.35$).

Conclusion: Flunisolide nasal spray was more effective than combined oral antihistamine–leukotriene therapy and may be preferred as a first-line treatment for AR.

Keywords: Allergic rhinitis, Flunisolide, Intranasal corticosteroids, Loratadine, Montelukast, Nasal congestion, Rhinorrhea.

Introduction

Allergic rhinitis (AR) is clinically described as the presence of one or more of the following symptoms: nasal congestion, rhinorrhea, sneezing, and nasal itch, for more than 1 h per day for most of the days.[1] This may be perennial or seasonal.

Up to 400 million people are affected across the globe by AR worldwide, with varying prevalence across different regions. It is thought to arise as an immunoglobulin E-mediated type I hypersensitivity inflammatory response of the nasal mucosa against an allergen.[1]

Its pathophysiology involves early-phase mediator release, causing acute symptoms such as sneezing, rhinorrhea, and nasal congestion, followed by a late-phase inflammatory response that sustains mucosal oedema and prolonged nasal obstruction, providing the rationale for pharmacological intervention targeting histamine-mediated symptoms, as well as leukotriene-driven inflammation and chronic mucosal oedema.[4] The diagnosis is mostly made based on clinical symptomatology, supported by the presence of pale or bluish discoloration of the nasal mucosa. Laboratory investigations, which are quite challenging, are selected based on an individual's needs, including skin prick testing (SPT), radio-allergo-sorbent test (RAST)-IgE, nasal provocation tests, and others.[5]

Pharmacotherapy remains debatable, encompassing allergen avoidance, antihistamines (AH), leukotriene receptor antagonists (LTRA), short courses of systemic glucocorticoids, and intranasal glucocorticoids.[6]

AH therapy is prescribed in 75% of patients with AR as first-line therapy. AHs (H1 receptor blockers) control the early phase response by reducing vascular permeability, thus reducing the symptoms of sneezing, congestion, pruritus, and rhinorrhea.[8]

Leukotrienes (C4, D4, and E4) are inflammatory mediators from the 5-lipoxygenase pathway that participate in the pathogenesis of AR.4 Leukotriene receptor antagonists (LTRA), such as montelukast, block cysteinyl leukotriene receptor 1 on inflammatory and mucosal cells, leading to a reduction in inflammation, oedema, and mucus secretion in the upper and lower airways.[9]

The role of systemic steroids is limited because of their potential systemic side effects.[6] Currently, Intranasal Corticosteroid (INCS) preparations, such as Mometasone, Beclomethasone, and Fluticasone, are considered first-line monotherapy for controlling AR.[10] Flunisolide is a potent synthetic corticosteroid that efficiently binds to the nasal mucosa and suppresses inflammation in patients with AR by inhibiting the release of histamine, cytokines, prostaglandins, and leukotrienes and reducing the activity of immune cells, such as eosinophils and mast cells. As it is delivered directly to the nasal passages, it relieves sneezing, itching, rhinorrhea, and congestion more effectively than oral AH, while minimising systemic side effects.[12]

In Pakistan, rising urbanisation, environmental pollution, and increased exposure to multiple allergens have contributed to the growing burden of AR. Limited data are available directly comparing flunisolide nasal spray with combined oral AH and LTRA therapy in the Pakistani population. The rationale of this study was to address this gap by evaluating which therapy provides more effective and rapid symptom relief, thereby guiding evidence-based treatment strategies tailored to the local patient needs.

This study compared the efficacy of flunisolide nasal spray with combined oral antihistamine and leukotriene receptor inhibitor therapy in improving symptoms in patients with AR.

Materials And Methods

This comparative quasi-experimental study was conducted in the Department of Otorhinolaryngology at Pak Emirates Hospital, Rawalpindi, from 1st January to 30th September 2025 after obtaining approval from the Institutional Review Board (Reference # ERC/116/24).

The formula for two independent groups was applied, that is, $n = [2 \times (SD^2) \times (Z\alpha/2 + Z\beta)^2] / (\Delta^2)$. Based on a mean TNSS difference of 0.83,[12] an estimated standard deviation of 1.0, a significance level of 0.05, and 80% power, the minimum sample size was 23 patients per group. However, considering possible dropouts and to enhance statistical power, 50 patients per treatment group were enrolled.

The eligibility criteria included adult patients (18-45 years) clinically diagnosed with AR based on a history of recurrent sneezing, rhinorrhea, nasal congestion, and nasal pruritus, supported by clinical findings of pale or bluish discoloration of the nasal mucosa. Participants were enrolled irrespective of sex or ethnicity. As the study was conducted in Pakistan, the study population primarily reflected the local South Asian demographics.

The exclusion criteria were acute airway infections, chronic obstructive lung disease, cardiac disease, and immunocompromised status.

Participants fulfilling the eligibility criteria were consecutively enrolled using a non-probability sampling technique and allocated to study groups using a non-random allocation method, whereby patients with odd sequence numbers were assigned to Group A (combined oral therapy), and those with even sequence numbers were assigned to Group B (intranasal flunisolide therapy). Group A patients were prescribed a daily dose of loratadine (10 mg) and montelukast (10 mg). Group B patients were advised to use flunisolide (100 µg per puff formulation) intranasal preparation (two puffs in each nostril twice daily). Total nasal symptom scores (TNSS) were recorded at the time of 1st visit, on 1st follow-up (after 2 weeks), and 2nd follow-up (after 4 weeks), encompassing nasal congestion, rhinorrhea, sneezing, and nasal itch. TNSS scores were graded 0–3 each, with mild (1–4) meaning symptoms were noticeable but not disruptive, moderate (5–8) meaning symptoms were interfering with daily activities, and severe (9–12) meaning symptoms were disrupting normal activities. Outcome assessment was performed by an independent assessor blinded to the treatment allocation. SPSS version 23 was used for data recording and statistical analyses. The normality of continuous variables (age and TNSS at all visits) was assessed using the Shapiro–Wilk test. The data were non-normally distributed ($P < .05$); therefore, continuous variables were expressed as medians with interquartile ranges (IQR: Q1–Q3). Categorical and ordinal variables are presented as frequencies and percentages. For inferential analysis, the Mann–Whitney U test was used to compare the TNSS between the two independent groups at each time point. A P-value of $\leq .05$ was considered statistically significant.

Results

A total of 100 eligible participants were enrolled, all of whom completed the follow-up, with 50 patients allocated to each treatment group (n = 50 per group).
In Group A, there were 31 males (62%) and 19 females (38%) with a median age of 35.50 (30.0-40.0) years. The distribution of symptom severity according to the TNSS is shown in Table 1.

Table 1: Total nasal symptom scores (Frequency with Percentage) in Oral Therapy-Treated Group 'A' (N=50)

Severity of symptoms	Pretreatment				1st follow-up				2nd follow-up			
	Nasal obstruction	Rhinorrhea	Sneezing	Itch	Nasal obstruction	Rhinorrhea	Sneezing	Itch	Nasal obstruction	Rhinorrhea	Sneezing	Itch
None	0	0	0	0	0	14(28%)	0	32(64%)	13(26%)	29(58%)	35(70%)	46(92%)
Mild	11(22%)	6 (12%)	0	28(56%)	14 (28%)	31(62%)	50(100 %)	17 (34%)	30(60%)	21(42%)	15(30%)	4(8%)
Moderate	27(54%)	34(68%)	46 (92%)	21(42%)	31(62%)	5(10%)	0	1(2%)	6(12%)	0	0	0
Severe	12(24 %)	10(20%)	4(8%)	1(2%)	5(10%)	0	0		1(2%)	0	0	0

Group B consisted of 32 males (64%) and 18 females (36%) with a median age of 26.0 (21.75-32.25) years.
The TNSS scores are mentioned in Table 2.

Table 2: Total nasal symptom scores (Frequency with Percentage) in Flunisolide Spray-Treated Group 'B' (N=50)

Severity of symptoms	Pretreatment				1st follow-up				2nd follow-up			
	Nasal obstruction	Rhinorrhea	Sneezing	Itch	Nasal obstruction	Rhinorrhea	Sneezing	Itch	Nasal obstruction	Rhinorrhea	Sneezing	Itch
None	0	0	0	0	0	0	0	12(24%)	42 (84%)	35 (70%)	33(66%)	43(86%)
Mild	7(14%)	1(2%)	4(8%)	31(62%)	37(74%)	47(94%)	50(100%)	38(76%)	8(16%)	15(30%)	17(34%)	7(14%)
Moderate	29(58%)	35(70%)	43(86%)	19(38%)	13(26%)	3(6%)	0	0	0	0	0	0
Severe	14(28%)	14(28%)	3(6%)	0	0	0	0	0	0	0	0	0

The Mann-Whitney U test was used to compare the median TNSS before treatment and on subsequent follow-ups with ongoing treatment between the two groups (Table 3).

Table 3: Comparison of Total Nasal Symptom Scores (Median; IQR) Between Treatment Groups Over Time (N= 50 versus 50)

Assessment duration	Total nasal symptom scores Median (IQR: Q1-Q3)		Mann-Whitney U (2 -sided P value)	Effect Size (r)
	Group A	Group B		
Pre-treatment	8.0 (7.75-8.0)	8.0 (8.0-8.0)	1203.0 (.659)	.04
1st Follow-up	4.0(3.75-5.0)	4.0 (4.0-4.0)	1246.500(.979)	.00
2nd Follow-up	2.0 (1.0-2.0)	1.0 (0.0-2.0)	756.500(<.001)	.35

**Data are expressed as median (interquartile range) and compared using the Mann–Whitney U test.*

A significant age difference was observed between the two groups at baseline (Mann–Whitney U test); therefore, multiple linear regression analysis was performed to adjust for age, baseline TNSS (TNSS1), and treatment group. A moderate effect size (r=.35) was observed at the 2nd follow-up.
For TNSS at the 1st follow-up, the overall model was significant (F = 2.919, P = .038; R^2 = 0.084). Baseline TNSS was a significant predictor (B = 0.368, P = .006), whereas the treatment group (P = .683) and age (P = .316) were not significant, indicating no independent treatment effect at this stage.
For TNSS at the 2nd follow-up, the model was also significant (F = 4.802, P = .004; R^2 = 0.130). The treatment group was a significant independent predictor (B = −0.719, 95% CI: −1.181 to −0.257, P = .003), showing that flunisolide spray was associated with significantly lower TNSS compared with montelukast after adjustment. Age (B = 0.005,

95% CI: −0.025 to 0.035, P = .745) and baseline TNSS (B = −0.032, 95% CI: −0.362 to 0.298, P = .847) were not significant.

Clinically, this suggests that while early outcomes were influenced mainly by baseline severity, a clear treatment advantage of flunisolide therapy emerged at 4 weeks after adjustment for confounders.

Discussion

In the present study, baseline demographics were comparable between the two treatment groups, except for age. This baseline age difference was statistically adjusted for in the analysis to ensure that the observed differences in treatment outcomes were attributable to the therapeutic interventions rather than population variability.

In this study, the maximum improvement in the LTRA combined with the AH group was observed in nasal itch and sneezing, where symptom-free cases increased from 0% at baseline to 92% and 70%, respectively, by the 2nd follow-up. This determines the efficacy of H1 receptor blockers combined with leukotriene receptor inhibitors in improving histamine-mediated symptoms.

Rajput et al. recorded the individual benefits of montelukast therapy in controlling AR, reducing the mean TNSS from 8.25 to 2.43 after four weeks of therapy (P =.005).

Wang et al. reported that combined loratadine–montelukast therapy was significantly more effective than monotherapy with either loratadine (SMD = −1.00, P < 0.001) or montelukast alone (SMD = −0.46, P < 0.001), with superior improvement in nasal symptoms, as evidenced by lower TNSS and quality of life.[14]

Krishnamoorthy et al. demonstrated in their results that combined montelukast and oral antihistamine therapy significantly improved day (MD = −0.15, P = .010), night (MD = −0.16, P = .006), and overall symptom scores (MD = 0.10, P = .007) compared to either montelukast or antihistamine monotherapy, where montelukast alone (MD = −0.07, P = .04) and antihistamine alone (MD = −0.06, P = .05) showed modest improvements.[15]

Considering the results of this study for group B, mild improvement was observed after 2 weeks of therapy, but significant benefits (Table II) were observed after 4 weeks of therapy compared to group A.

Shahzad et al. also supported these findings; they recorded a significant reduction in the mean nasal score in the intranasal steroid spray therapy group (1.04 ± 0.33) compared to the cetirizine plus montelukast group (2.21 ± 0.38).[16]

The present study demonstrated that flunisolide spray produced a greater improvement in nasal obstruction (84% vs. 58%) and rhinorrhea (70% vs. 58%), indicating its late but sustained therapeutic efficacy.

Asghar et al. compared the efficacy of flunisolide nasal spray with that of beclomethasone dipropionate and found it to be superior in improving symptom scores after 14 days of treatment in patients with AR(85% vs. 79.6%, P = .035).[17]

Interestingly, Sitompul et al. in their randomised clinical trial (RCT) comparing INCs plus AH versus INCs plus LTRA found that the INCs-LTRA group showed greater improvement in nasal obstruction and rhinorrhea (P < 0.05), suggesting that adding montelukast may enhance the control of congestion-related symptoms compared to cetirizine.[18]

Another meta-analysis found the superior benefits of INCs in improving TNSS, that is, MD = –0.86 vs oral antihistamines, MD = –1.05 vs leukotriene antagonists.[12]

Junaid et al. in their RCT found a 94.5% response to INCs therapy compared to oral loratadine plus montelukast therapy (75.3%).[19]

Zhang et al. in their meta-analysis reported that overall, INCS resulted in a clinically and statistically meaningful improvement in TNSS (MD 0.90; P = .002) and PNIF (MD 13.31 L/min; P = .0007), while oral AH improved quality of life (RQLQ MD 0.36; P < .001) but had no significant effect on nasal airflow.[20]

In contrast to the above findings, a review study indicated that no significant difference occurred between INCS + LTRA and INCS monotherapy in composite nasal symptom score, total daytime and nighttime symptom scores, or disease-specific quality of life.[21]

Another study reported that combined oral AH and LTRA improved nasal symptoms in patients with perennial AR, whereas adding LTRA or AH to INCS offered no advantage over INCS alone.[22]

The present study provided local data on the efficacy of INCs (flunisolide spray) over combined oral therapy (AH plus LTRA). The limitations of this study include its single-centre design and short follow-up duration, which may not fully capture the long-term efficacy or seasonal variations in AR symptoms. Data should be gathered from different regions, incorporating a longitudinal study design with extended follow-up in the future to validate these findings and explore the long-term efficacy, effects of seasonal variation, and probable side effects of multiple treatment options in cases of AR

Conclusions

Intranasal corticosteroids may be considered an effective first-line monotherapy for patients with AR.

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References

1. Nur Husna SM, Tan HT, Md Shukri N, Mohd Ashari NS, Wong KK. Allergic rhinitis: a clinical and pathophysiological overview. Front Med (Lausanne). 2022;9:874114. https://doi.org/10.3389/fmed.2022.874114
2. Alnahas S, Abouammoh N, Althagafi W, Abd-Ellatif EE. Prevalence, severity, and risk factors of allergic rhinitis among schoolchildren in Saudi Arabia: a national cross-sectional study, 2019. World Allergy Organ J. 2023;16(10):100824. https://doi.org/10.1016/j.waojou.2023.100824
3. Zoabi Y, Levi-Schaffer F, Eliashar R. Allergic rhinitis: pathophysiology and treatment focusing on mast cells. Biomedicines. 2022;10(10):2486. https://doi.org/10.3390/biomedicines10102486
4. Charles N, Blank U. IgE-mediated activation of mast cells and basophils in health and disease. Immunol Rev. 2025;331(1):e70024. https://doi.org/10.1111/imr.70024
5. Bousquet J, Anto JM, Bachert C, Baiardini I, Bosnic-Anticevich S, Canonica GW, et al. Allergic rhinitis. Nat Rev Dis Primers. 2020;6(1):95. https://doi.org/10.1038/s41572-020-00227-0
6. Bernstein JA, Bernstein JS, Makol R, Ward S. Allergic rhinitis: a review. JAMA. 2024;331(10):866-77. https://doi.org/10.1001/jama.2024.0530
7. Sánchez G, Castro C. Prescription profile and clinical outcomes in patients with allergic rhinitis treated with oral antihistamines or nasal corticosteroids. Int Arch Otorhinolaryngol. 2019;23(3):e325-30. https://doi.org/10.1055/s-0039-1688968
8. Linton S, Hossenbaccus L, Ellis AK. Evidence-based use of antihistamines for treatment of allergic conditions. Ann Allergy Asthma Immunol. 2023;131(4):412-20. https://doi.org/10.1016/j.anai.2023.07.019
9. Meshram D, Bhardwaj K, Rathod C, Mahady GB, Soni KK. The role of leukotriene inhibitors in the management of chronic inflammatory diseases. Recent Pat Inflamm Allergy Drug Discov. 2020;14(1):15-31. https://doi.org/10.2174/1872213X14666200130095040
10. Levy DA, Bakare AB, Gurevich RE, McCoul ED. Aqueous versus aerosol intranasal corticosteroid spray for allergic rhinitis: systematic review and meta-analysis. Am J Rhinol Allergy. 2025 Nov;39(6):444-52. https://doi.org/10.1177/19458924251360917
11. McDonnell J, Weller K, Pien LC. Safety of intranasal steroids: an updated perspective. Curr Allergy Asthma Rep. 2020 Nov;20(11):69. https://doi.org/10.1007/s11882-020-00960-2
12. Torres MI, Gil-Mata S, Bognanni A, Ferreira-da-Silva R, Yepes-Nuñez JJ, Lourenço-Silva N, et al. Intranasal versus oral treatments for allergic rhinitis: a systematic review with meta-analysis. J Allergy Clin Immunol Pract. 2024;12(9):2400-11.e10. https://doi.org/10.1016/j.jaip.2024.09.001
13. Rajput MSA, Arain AA, Rajput AA, Adeel M, Ghaffar S, Suhail A. Effect of montelukast on the symptom severity score of allergic rhinitis. Cureus. 2020;12(3):e7403. https://doi.org/10.7759/cureus.7403
14. Wang H, Ji Q, Liao C, Tian L. A systematic review and meta-analysis of loratadine combined with montelukast for the treatment of allergic rhinitis. Front Pharmacol. 2023;14:1287320. https://doi.org/10.3389/fphar.2023.1287320
15. Krishnamoorthy M, Mohd Noor N, Mat Lazim N, Abdullah B. Efficacy of montelukast in allergic rhinitis treatment: a systematic review and meta-analysis. Drugs. 2020;80(17):1831-51. https://doi.org/10.1007/s40265-020-01406-9
16. Shahzad J, Ali SM, Khan MA, Hussain SS, Ibrahim M, Mustafa SH. Comparison of fluticasone furoate nasal spray versus combined oral anti-histamine and anti-leukotriene therapy in allergic rhinitis. Pak J Med Health Sci. 2019;13(4):1311-3. https://pjmhsonline.com/2019/oct_dec/
17. Asghar M, Rasheed MT, Akbar A, Malik FJ, Rai D, Ali L. Comparison of effects beclomethasone dipropionate with flunisolide in patients with allergic rhinitis. Life and Science. 2023;4(3):225-9. https://doi.org/10.37185/LnS.1.1.358

18. Sitompul BP, Suheryanto R, Surjotomo H. Comparison of fluticasone furoate and cetirizine versus fluticasone furoate and montelukast in allergic rhinitis. Oto Rhino Laryngol Indones. 2021;51(1):12-9. https://doi.org/10.32637/orli.v51i1.409
19. Junaid M, Muhammad N, Umair M, Arif AU, Din I. The effectiveness of topical intranasal steroids verses systemic anti-allergic drugs in allergic rhinitis: a randomized controlled trial. J Med Sci. 2020;28(1):50-4. https://jmedsci.com/index.php/Jmedsci/article/view/877
20. Zhang K, Li AR, Miglani A, Nguyen SA, Schlosser RJ. Effect of medical therapy in allergic rhinitis: a systematic review and meta-analysis. Am J Rhinol Allergy. 2022;36(2):269-80. https://doi.org/10.1177/19458924211041438
21. Seresirikachorn K, Mullol J, Limitlaohaphan K, Asvapoositkul V, Snidvongs K. Leukotriene receptor antagonist addition to intranasal steroid: systematic review and meta-analysis. Rhinology. 2021;59(1):2-9. https://doi.org/10.4193/Rhin20.126
22. Chitsuthipakorn W, Hoang MP, Kanjanawasee D, Seresirikachorn K, Snidvongs K. Combined medical therapy in the treatment of allergic rhinitis: systematic review and meta-analyses. Int Forum Allergy Rhinol. 2022;12(12):1480-1502. https://doi.org/10.1002/alr.23015