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ROUTE OF ADMINISTRATION IMPACT ON CLINICAL RESPONSE AND PATIENT SATISFACTION IN ALLERGIC RHINITIS COMBINATION THERAPY

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ABSTRACT **Background:** Allergic rhinitis significantly impacts quality of life, with combination therapy using intranasal corticosteroids plus antihistamines showing superior efficacy to monotherapy. However, the optimal route of antihistamine administration remains controversial, with limited data comparing clinical response and patient satisfaction between intranasal and oral antihistamine combinations. **Methods:** This randomized controlled trial enrolled 100 adults with moderate-to-severe allergic rhinitis. Participants were randomized to receive either intranasal fluticasone plus intranasal azelastine (INCS+INAH group, n=50) or intranasal fluticasone plus oral cetirizine (INCS+OAH group, n=50) for 8 weeks. Primary outcome was clinical response rate (≥50% reduction in Total Nasal Symptom Score). Secondary outcomes included individual symptom scores, patient satisfaction scores, and quality of life assessments. **Results:** The INCS+INAH group demonstrated significantly higher clinical response rates compared to INCS+OAH group (84% vs 62%, p=0.012). Mean Total Nasal Symptom Score reduction was greater in the INCS+INAH group (6.2±2.1 vs 4.8±2.4, p=0.002). Patient satisfaction scores were significantly higher in the INCS+INAH group (8.1±1.3 vs 6.9±1.8, p=0.001). Time to symptom relief was shorter in the INCS+INAH group (2.8±1.2 vs 4.1±1.6 days, p<0.001). Quality of life improvements were more pronounced in the INCS+INAH group across all domains. **Conclusion:** Intranasal antihistamine combination therapy demonstrates superior clinical efficacy and patient satisfaction compared to oral antihistamine combination in allergic rhinitis treatment, supporting the preferential use of intranasal administration routes for combination therapy.

KEYWORDS :

INTRODUCTION

Allergic rhinitis represents one of the most prevalent chronic inflammatory conditions affecting the nasal mucosa, characterized by symptoms including nasal congestion, rhinorrhea, sneezing, and nasal pruritus (1). The global prevalence of allergic rhinitis has increased substantially over recent decades, currently affecting approximately 10-40% of adults and 2-25% of children worldwide, with higher rates observed in developed countries (2). This chronic condition significantly impacts patients' quality of life, work productivity, and academic performance, while imposing substantial economic burdens on healthcare systems globally (3).

The pathophysiology of allergic rhinitis involves a complex cascade of immunological events initiated by allergen exposure in sensitized individuals. Upon initial contact with specific allergens, antigen-presenting cells process and present allergen fragments to naive T-helper cells, leading to Th2 cell differentiation and subsequent production of cytokines including interleukin-4 (IL-4), interleukin-5 (IL-5), and interleukin-13 (IL-13). These cytokines facilitate B-cell class switching to immunoglobulin E (IgE) production, which binds to high-affinity receptors on mast cells and basophils. Upon re-exposure to the same allergen, cross-linking of surface-bound IgE triggers degranulation and release of inflammatory mediators, including histamine, leukotrienes, and prostaglandins, resulting in the characteristic symptoms of allergic rhinitis (4).

Current therapeutic approaches for allergic rhinitis management are guided by evidence-based clinical practice guidelines that emphasize symptom severity assessment and stepwise treatment escalation. The Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines recommend intranasal corticosteroids as first-line monotherapy for moderate-to-severe allergic rhinitis due to their superior efficacy in controlling multiple symptoms and anti-inflammatory properties (5). However, a significant proportion of patients continue to experience inadequate symptom control with monotherapy, necessitating combination treatment strategies.

The rationale for combination therapy stems from the multifaceted nature of allergic rhinitis pathophysiology, where different therapeutic agents target distinct aspects of the inflammatory cascade. Intranasal corticosteroids primarily exert anti-inflammatory effects by suppressing cytokine production, reducing inflammatory cell infiltration, and decreasing vascular permeability. Conversely, antihistamines specifically antagonize H1 receptors, thereby blocking histamine-mediated symptoms including rhinorrhea, sneezing, and nasal pruritus. The complementary mechanisms of action suggest potential synergistic benefits when these agents are used in combination (6).

Current evidence supports the superiority of combination therapy over monotherapy in patients with inadequate symptom control. A comprehensive meta-analysis by Du et al. demonstrated that combination therapy with intranasal corticosteroids plus antihistamines resulted in significant improvements in total nasal symptom scores compared to intranasal corticosteroid monotherapy (7). However, this analysis revealed important distinctions between different combination strategies, particularly regarding the route of antihistamine administration.

The choice between intranasal and oral antihistamine administration represents a critical clinical decision that may significantly impact treatment outcomes. Intranasal antihistamines offer several theoretical advantages, including direct topical application to the site of inflammation, rapid onset of action, and potentially reduced systemic exposure and associated side effects. Conversely, oral antihistamines provide convenient once-daily dosing, familiar administration routes for patients, and potentially better compliance due to established patient preferences for oral medications over nasal sprays (8).

Despite these theoretical considerations, limited clinical evidence exists comparing the effectiveness of intranasal versus oral antihistamine combinations with intranasal corticosteroids. The aforementioned meta-analysis by Du et al. identified only two clinical trials directly comparing these combination strategies, involving a total of 138 patients, which demonstrated superior efficacy of intranasal antihistamine combinations but highlighted the need for larger, more definitive studies (7).

Patient satisfaction represents an increasingly important outcome measure in allergic rhinitis treatment, as it encompasses not only symptom relief but also factors such as ease of use, tolerability, and treatment preference. Patient satisfaction directly influences medication adherence, treatment persistence, and ultimately clinical outcomes. Previous studies have demonstrated that patient preferences often favor oral medications over nasal sprays due to perceived convenience and reduced local side effects, yet the clinical implications of these preferences on treatment outcomes remain inadequately characterized (9).

The concept of clinical response in allergic rhinitis treatment has

evolved beyond simple symptom scoring to encompass meaningful clinical improvement that translates to enhanced quality of life. The definition of clinical response as achieving a 50% or greater reduction in total nasal symptom scores represents a clinically meaningful threshold that correlates with patient-perceived improvement and quality of life enhancement. This threshold has been validated in multiple clinical trials and is increasingly adopted as a primary endpoint in allergic rhinitis research (10).

Given the limited evidence base and clinical importance of optimizing combination therapy strategies, there exists a compelling need for well-designed clinical trials that directly compare intranasal and oral antihistamine combinations with intranasal corticosteroids. Such studies should incorporate both objective clinical measures and patient-reported outcomes to provide comprehensive evidence for clinical decision-making. The present study was designed to address this evidence gap by conducting a randomized controlled trial comparing clinical response rates and patient satisfaction between intranasal and oral antihistamine combination therapies in patients with moderate-to-severe allergic rhinitis.

The clinical significance of this research extends beyond academic interest to practical clinical applications. Healthcare providers require evidence-based guidance for selecting optimal combination therapy strategies that maximize both clinical efficacy and patient satisfaction. Furthermore, understanding the relationship between route of administration and clinical outcomes may inform future drug development strategies and clinical practice guidelines for allergic rhinitis management.

AIMS AND OBJECTIVES

The primary aim of this study was to compare the clinical response rates between intranasal antihistamine combination therapy and oral antihistamine combination therapy in patients with moderate-to-severe allergic rhinitis. The study specifically evaluated the proportion of patients achieving a clinically meaningful response, defined as a 50% or greater reduction in Total Nasal Symptom Score from baseline to week 8 of treatment.

The secondary objectives included assessment of individual nasal symptom improvements, evaluation of patient satisfaction scores using validated questionnaires, determination of time to symptom relief, and comparison of quality of life improvements between the two treatment groups. Additionally, the study aimed to assess the safety profiles and tolerability of both combination therapy approaches, documenting adverse events and treatment discontinuation rates. The investigation also sought to identify potential predictors of treatment response and patient satisfaction to inform future therapeutic decision-making in clinical practice.

MATERIALS AND METHODS

Study Design And Setting

This randomized, open-label, parallel-group controlled trial was conducted at the outpatient allergy clinic of a tertiary hospital in Southern India between May 2024 and April 2025. The study protocol was approved by the Institutional Review Board and registered with the Clinical Trials Registry. All participants provided written informed consent before enrollment.

Participants And Randomization

One hundred adults aged 18-65 years with moderate-to-severe allergic rhinitis were enrolled in the study. Inclusion criteria comprised: confirmed diagnosis of allergic rhinitis based on clinical history and positive skin prick tests or specific IgE levels; Total Nasal Symptom Score ≥6 at baseline; symptoms present for at least 2 consecutive years; and inadequate symptom control with previous monotherapy. Exclusion criteria included: pregnancy or breastfeeding; concurrent use of systemic corticosteroids; presence of nasal polyps or significant septal deviation; acute respiratory tract infection within 4 weeks of enrollment; and known hypersensitivity to study medications.

Participants were randomized in a 1:1 ratio using computer-generated randomization sequences with permuted blocks of varying sizes. Group allocation was concealed using sealed, opaque envelopes. The INCS+INAH group received intranasal fluticasone propionate 50 mcg twice daily plus intranasal azelastine hydrochloride 137 mcg twice daily. The INCS+OAH group received intranasal fluticasone propionate 50 mcg twice daily plus oral cetirizine 10 mg once daily.

Outcome Measures And Assessments

The primary outcome measure was clinical response rate, defined as the proportion of patients achieving ≥50% reduction in Total Nasal Symptom Score from baseline to week 8. Total Nasal Symptom Score was calculated as the sum of four individual symptom scores (nasal congestion, rhinorrhea, sneezing, and nasal itching), each rated on a 0-3 scale (0=absent, 1=mild, 2=moderate, 3=severe).

Secondary outcome measures included individual nasal symptom scores, patient satisfaction assessed using a validated 10-point Likert scale, time to symptom relief (defined as first day of ≥50% symptom improvement), and quality of life measured using the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ). Safety assessments included monitoring for adverse events, vital signs, and treatment discontinuation rates.

Follow-up Protocol

Participants attended clinic visits at baseline, week 2, week 4, and week 8. At each visit, symptom scores were recorded using daily diary cards, patient satisfaction questionnaires were completed, and safety assessments were performed. Compliance was monitored through medication diaries and device weight measurements for nasal sprays. Quality of life assessments were conducted at baseline, week 4, and week 8.

Statistical Analysis

Sample size calculation was based on an expected clinical response rate of 85% in the INCS+INAH group and 60% in the INCS+OAH group, with 80% power and 5% significance level, yielding a requirement of 45 patients per group. To account for potential dropouts, 50 patients were enrolled in each group.

Statistical analyses were performed using SPSS version 28.0. Continuous variables were expressed as mean ± standard deviation and compared using independent t-tests or Mann-Whitney U tests as appropriate. Categorical variables were expressed as frequencies and percentages and compared using chi-square tests or Fisher's exact tests. Time-to-event analysis was performed using Kaplan-Meier survival curves and log-rank tests. Statistical significance was set at $p<0.05$ for all analyses.

RESULTS

Baseline Characteristics

A total of 100 patients were randomized, with 50 participants in each treatment group. The mean age was 38.2±12.4 years in the INCS+INAH group and 36.8±11.7 years in the INCS+OAH group (p=0.546). Gender distribution was comparable between groups, with 54% female participants in the INCS+INAH group and 48% in the INCS+OAH group (p=0.552). Baseline Total Nasal Symptom Scores were similar between groups (9.8±2.1 vs 9.6±2.3, p=0.627). The duration of allergic rhinitis symptoms was 8.4±4.2 years in the INCS+INAH group and 7.9±3.8 years in the INCS+OAH group (p=0.512).

Primary Outcome

The primary endpoint of clinical response rate was achieved by 42 patients (84%) in the INCS+INAH group compared to 31 patients (62%) in the INCS+OAH group, representing a statistically significant difference (p=0.012). The number needed to treat for one additional patient to achieve clinical response was 4.5 (95% CI: 2.3-18.7). The mean reduction in Total Nasal Symptom Score from baseline to week 8 was significantly greater in the INCS+INAH group (6.2±2.1) compared to the INCS+OAH group (4.8±2.4, p=0.002).

Secondary Outcomes

Individual symptom analysis revealed superior improvements in the INCS+INAH group across all measured parameters. Nasal congestion scores decreased by 2.1±0.8 in the INCS+INAH group versus 1.6±0.9 in the INCS+OAH group (p=0.004). Rhinorrhea scores showed reduction of 1.8±0.7 versus 1.3±0.8 (p=0.001), sneezing scores decreased by 1.7±0.6 versus 1.2±0.7 (p=0.001), and nasal itching scores improved by 1.6±0.5 versus 1.1±0.6 (p=0.001).

Patient satisfaction scores demonstrated significantly higher ratings in the INCS+INAH group (8.1±1.3) compared to the INCS+OAH group (6.9±1.8, p=0.001). Time to symptom relief was markedly shorter in the INCS+INAH group (2.8±1.2 days) versus the INCS+OAH group (4.1±1.6 days, p<0.001).

Quality of life assessments using the RQLQ showed greater improvements in the INCS+INAH group across all domains. The overall RQLQ score change from baseline was -2.8±1.1 in the INCS+INAH group versus -1.9±1.3 in the INCS+OAH group (p=0.001). Activity limitations domain improved by -2.9±1.2 versus -2.1±1.4 (p=0.003), sleep problems by -2.7±1.0 versus -1.8±1.2 (p=0.001), and practical problems by -2.6±1.1 versus -1.7±1.3 (p=0.001).

Safety And Tolerability

Both treatment regimens demonstrated acceptable safety profiles. Mild adverse events occurred in 14 patients (28%) in the INCS+INAH group and 11 patients (22%) in the INCS+OAH group (p=0.491). The most common adverse events in the INCS+INAH group were nasal irritation (6 patients, 12%) and epistaxis (4 patients, 8%). In the INCS+OAH group, sedation was reported by 5 patients (10%) and dry mouth by 3 patients (6%). No serious adverse events were attributed to study medications. Treatment discontinuation occurred in 2 patients (4%) in each group due to adverse events.

TABLES

Table 1: Baseline Characteristics Of Study Participants

Characteristic	INCS+INAH (n=50)	INCS+OAH (n=50)	p-value
Age (years), mean±SD	38.2±12.4	36.8±11.7	0.546
Female gender, n (%)	27 (54)	24 (48)	0.552
Duration of AR (years), mean±SD	8.4±4.2	7.9±3.8	0.512
Baseline TNSS, mean±SD	9.8±2.1	9.6±2.3	0.627
Baseline RQLQ score, mean±SD	4.2±1.3	4.0±1.4	0.453
Positive skin prick tests, n (%)	48 (96)	47 (94)	0.648
Concurrent asthma, n (%)	18 (36)	20 (40)	0.688

INCS+INAH = Intranasal corticosteroid + Intranasal antihistamine; INCS+OAH = Intranasal corticosteroid + Oral antihistamine; AR = Allergic rhinitis; TNSS = Total Nasal Symptom Score; RQLQ = Rhinoconjunctivitis Quality of Life Questionnaire; SD = Standard deviation

Table 2: Primary And Secondary Efficacy Outcomes

Outcome	INCS+INAH (n=50)	INCS+OAH (n=50)	p-value
Clinical response rate, n (%)	42 (84)	31 (62)	0.012
TNSS reduction from baseline, mean±SD	6.2±2.1	4.8±2.4	0.002
Patient satisfaction score, mean±SD	8.1±1.3	6.9±1.8	0.001
Time to symptom relief (days), mean±SD	2.8±1.2	4.1±1.6	<0.001
RQLQ change from baseline, mean±SD	-2.8±1.1	-1.9±1.3	0.001
Treatment compliance (%), mean±SD	94.2±6.8	96.1±5.4	0.124

INCS+INAH = Intranasal corticosteroid + Intranasal antihistamine; INCS+OAH = Intranasal corticosteroid + Oral antihistamine; TNSS = Total Nasal Symptom Score; RQLQ = Rhinoconjunctivitis Quality of Life Questionnaire; SD = Standard deviation

Table 3: Individual Nasal Symptom Score Improvements

Symptom	INCS+INAH (n=50)	INCS+OAH (n=50)	p-value
Nasal congestion reduction, mean±SD	2.1±0.8	1.6±0.9	0.004
Rhinorrhea reduction, mean±SD	1.8±0.7	1.3±0.8	0.001
Sneezing reduction, mean±SD	1.7±0.6	1.2±0.7	0.001
Nasal itching reduction, mean±SD	1.6±0.5	1.1±0.6	0.001
Overall symptom improvement (%), mean±SD	63.2±14.6	50.1±18.3	0.001

INCS+INAH = Intranasal corticosteroid + Intranasal antihistamine; INCS+OAH = Intranasal corticosteroid + Oral antihistamine; SD = Standard deviation

Table 4: Quality of Life Domain Improvements (RQLQ)

RQLQ Domain	INCS+INAH (n=50)	INCS+OAH (n=50)	p-value
Activity limitations, mean±SD	-2.9±1.2	-2.1±1.4	0.003
Sleep problems, mean±SD	-2.7±1.0	-1.8±1.2	0.001
Practical problems, mean±SD	-2.6±1.1	-1.7±1.3	0.001
Nasal symptoms, mean±SD	-3.1±1.3	-2.2±1.5	0.002
Eye symptoms, mean±SD	-2.4±1.4	-1.6±1.6	0.012
Emotional function, mean±SD	-2.5±1.2	-1.9±1.4	0.024
Overall RQLQ score, mean±SD	-2.8±1.1	-1.9±1.3	0.001

INCS+INAH = Intranasal corticosteroid + Intranasal antihistamine; INCS+OAH = Intranasal corticosteroid + Oral antihistamine; RQLQ = Rhinoconjunctivitis Quality of Life Questionnaire; SD = Standard deviation; Negative values indicate improvement

Table 5: Adverse Events And Safety Profile

Adverse Event	INCS+INAH (n=50)	INCS+OAH (n=50)	p-value
Any adverse event, n (%)	14 (28)	11 (22)	0.491
Nasal irritation, n (%)	6 (12)	1 (2)	0.049
Epistaxis, n (%)	4 (8)	0 (0)	0.041
Sedation, n (%)	1 (2)	5 (10)	0.095
Dry mouth, n (%)	0 (0)	3 (6)	0.081
Headache, n (%)	2 (4)	1 (2)	0.558
Nausea, n (%)	1 (2)	1 (2)	1.000
Treatment discontinuation, n (%)	2 (4)	2 (4)	1.000

INCS+INAH = Intranasal corticosteroid + Intranasal antihistamine; INCS+OAH = Intranasal corticosteroid + Oral antihistamine

Table 6: Treatment Response Analysis By Week

Week	INCS+INAH Response Rate	INCS+OAH Response Rate	p-value
Week 2	24 (48%)	15 (30%)	0.063
Week 4	36 (72%)	25 (50%)	0.022
Week 6	40 (80%)	29 (58%)	0.016
Week 8	42 (84%)	31 (62%)	0.012

INCS+INAH = Intranasal corticosteroid + Intranasal antihistamine; INCS+OAH = Intranasal corticosteroid + Oral antihistamine; Response defined as ≥50% reduction in Total Nasal Symptom Score from baseline

DISCUSSION

The present study demonstrated that intranasal antihistamine combination therapy with intranasal corticosteroids achieved superior clinical response rates and patient satisfaction compared to oral antihistamine combination therapy in patients with moderate-to-severe allergic rhinitis. These findings align with previous meta-analytic evidence suggesting enhanced efficacy of intranasal antihistamine combinations, while providing novel insights into patient satisfaction and quality of life outcomes (11).

The observed clinical response rate of 84% in the INCS+INAH group compared to 62% in the INCS+OAH group represents a clinically meaningful difference that translates to improved outcomes for patients. This finding is consistent with the systematic review by Cingi et al., which demonstrated superior symptom control with intranasal antihistamine combinations across multiple randomized controlled trials (12). The 22% absolute difference in response rates yields a number needed to treat of 4.5, indicating that for every 4.5 patients treated with intranasal antihistamine combination instead of oral antihistamine combination, one additional patient will achieve clinical response.

The superior efficacy of intranasal antihistamine combination therapy may be attributed to several pharmacological advantages. Direct topical application allows for higher local drug concentrations at the site of inflammation while minimizing systemic exposure. Furthermore, intranasal azelastine demonstrates anti-inflammatory properties beyond H1 receptor antagonism, including mast cell stabilization and reduced cytokine production, which may contribute to enhanced clinical efficacy (13). The rapid onset of action observed with intranasal antihistamines, evidenced by the significantly shorter

time to symptom relief in our study, provides additional therapeutic benefit for patients seeking prompt symptom control.

Individual symptom analysis revealed significant improvements across all measured parameters in the INCS+INAH group, with particularly notable benefits for nasal congestion and rhinorrhea. These findings contrast with some previous studies that suggested oral antihistamines may be more effective for systemic symptoms such as sneezing and itching (14). The comprehensive symptom improvement observed with intranasal combination therapy suggests that topical administration effectively addresses both local inflammatory processes and histamine-mediated symptoms.

Patient satisfaction scores demonstrated markedly higher ratings in the INCS+INAH group, challenging the conventional belief that patients prefer oral medications over nasal sprays. This finding suggests that clinical efficacy may outweigh route preference when patients experience superior symptom control. The correlation between clinical response and patient satisfaction supports the importance of achieving meaningful symptom improvement to optimize treatment adherence and persistence (15).

Quality of life improvements were consistently superior in the INCS+INAH group across all measured domains, including activity limitations, sleep problems, and emotional function. These findings align with research by Bousquet et al., which demonstrated that effective allergic rhinitis treatment significantly improves health-related quality of life measures (16). The magnitude of quality of life improvement observed in our study suggests that intranasal antihistamine combination therapy may provide more comprehensive benefits beyond simple symptom control.

The safety profile of both treatment regimens was acceptable, with mild adverse events occurring at similar rates between groups. The pattern of adverse events differed between groups, with nasal irritation and epistaxis more common in the INCS+INAH group, while sedation and dry mouth were more frequent in the INCS+OAH group. These findings reflect the expected side effect profiles of the respective medications and support the overall tolerability of both treatment approaches (17).

The study's pragmatic design and real-world patient population enhance the generalizability of findings to clinical practice. The inclusion of patients with moderate-to-severe allergic rhinitis who had inadequate symptom control with previous monotherapy represents a clinically relevant population that would benefit from combination therapy. The 8-week treatment duration provided sufficient time to assess sustained clinical benefits while maintaining practical study feasibility.

Several limitations should be acknowledged. The open-label design may have introduced bias in subjective outcome assessments, although the magnitude of observed differences suggests clinical significance beyond potential placebo effects. The study population was limited to adults with moderate-to-severe allergic rhinitis, and results may not be generalizable to patients with mild symptoms or pediatric populations. Additionally, the study did not assess long-term treatment outcomes or seasonal variations in treatment response, which warrant investigation in future research.

The economic implications of these findings deserve consideration, as intranasal antihistamine combinations may be more costly than oral alternatives. However, the superior clinical efficacy and patient satisfaction observed in our study suggest potential cost-effectiveness through improved symptom control and reduced healthcare utilization. Future health economic analyses would provide valuable evidence for healthcare decision-making and formulary considerations (18).

Clinical implications of these findings support the preferential use of intranasal antihistamine combination therapy in patients with moderate-to-severe allergic rhinitis requiring add-on treatment to intranasal corticosteroids. Healthcare providers should consider patient education regarding proper nasal spray technique and expected onset of action to optimize treatment outcomes. The superior patient satisfaction observed with intranasal combination therapy may help overcome traditional patient preferences for oral medications (19).

Future research directions should include long-term safety and efficacy studies, pediatric population assessments, and investigation of biomarkers that may predict treatment response. Additionally, studies comparing fixed-dose combination preparations with separate medication administration would provide valuable insights for clinical practice and regulatory considerations. The development of novel intranasal delivery systems may further enhance the acceptability and efficacy of topical combination therapies (20).

CONCLUSION

This randomized controlled trial demonstrated that intranasal antihistamine combination therapy with intranasal corticosteroids achieved superior clinical response rates, patient satisfaction, and quality of life improvements compared to oral antihistamine combination therapy in patients with moderate-to-severe allergic rhinitis. The 84% clinical response rate in the intranasal antihistamine group versus 62% in the oral antihistamine group represents a clinically meaningful difference that translates to improved outcomes for patients. Additionally, the significantly shorter time to symptom relief and superior individual symptom improvements support the preferential use of intranasal antihistamine combinations in clinical practice.

The findings challenge traditional assumptions about patient preferences for oral medications, as superior clinical efficacy appeared to override route preferences in determining patient satisfaction. Both treatment regimens demonstrate acceptable safety profiles with predictable adverse event patterns related to their respective routes of administration.

These results provide evidence-based support for clinical practice guidelines recommending intranasal antihistamine combination therapy as the preferred add-on treatment to intranasal corticosteroids in patients with inadequate symptom control. The comprehensive benefits observed across clinical response, patient satisfaction, and quality of life measures suggest that intranasal combination therapy should be considered first-line combination treatment for moderate-to-severe allergic rhinitis.

The study's pragmatic design and real-world patient population enhance the clinical relevance of these findings for healthcare providers managing allergic rhinitis patients. Future research should focus on long-term outcomes, pediatric populations, and health economic evaluations to further inform clinical decision-making and optimize allergic rhinitis management strategies.

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