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Efficacy comparison of combined montelukast-antihistamine and montelukast monotherapy in allergic rhinitis: a meta-analysis of randomized controlled trials

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Key words

Montelukast; allergic rhinitis; antihistamine; drug combinations; meta-analysis.

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Impact statement

This meta-analysis provides evidence that symptom-specific efficacy of montelukast–antihistamine combinations may inform personalized pharmacologic strategies in allergic rhinitis management.

Summary

Background. *Combination therapy with montelukast and oral antihistamines is commonly used in allergic rhinitis (AR), but its comparative benefit over montelukast monotherapy remains unclear. This meta-analysis aimed to evaluate the efficacy of combination therapy compared to monotherapy, with a focus on symptom-specific outcomes.* ***Methods.*** *A comprehensive search of PubMed, SCOPUS, Embase, Web of Science, and Cochrane databases was conducted through April 2025. We systematically reviewed randomized controlled trials comparing montelukast combined with oral antihistamines to montelukast monotherapy in patients with AR. Outcomes included total symptom scores, Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) scores, and individual symptom domains. Pooled effects were analyzed using standardized mean differences (SMDs) with 95% confidence intervals (CIs).* ***Results.*** *Thirteen RCTs enrolling 2,950 patients were identified. Combination therapy significantly improved daytime symptoms (SMD = 0.25; 95%CI 0.15 to 0.35), with limited benefit for nighttime symptoms (SMD = 0.10; 95%CI -0.01 to 0.21) or RQLQ scores (SMD = 0.11; 95%CI -0.05 to 0.26). In subgroup analysis, all combinations with loratadine, desloratadine, or levocetirizine showed greater efficacy than monotherapy in improving daytime symptoms. However, only the levocetirizine-based combination demonstrated a significant benefit for nighttime symptoms. When analyzed by individual symptoms, the levocetirizine combination resulted in significantly better outcomes than monotherapy, improving sneezing, nasal itching, nasal obstruction, and rhinorrhea.* ***Conclusions.*** *Montelukast combined with antihistamines improves daytime and individual nasal symptoms more effectively than monotherapy. However, the effectiveness of each drug combination varied by symptom domain. These findings may assist clinicians in selecting appropriate combination regimens based on individual symptom patterns.* ***Study registration.*** *We registered study protocol on Open Science Framework (https://osf.io/4sedu/).*

Introduction

Allergic rhinitis (AR) is a common chronic inflammatory disorder of the upper respiratory tract, characterized by symptoms such as nasal congestion, rhinorrhea, sneezing, and nasal itching. It affects approximately 10-30% of the global population, with rising prevalence in both developed and developing countries (1). Beyond its physical symptoms, AR imposes a significant burden on patients' quality of life, including impaired sleep, decreased cognitive performance, and reduced work productivity (2). Despite the availability of various treatment options, many patients with AR remain poorly controlled due to suboptimal symptom relief and limited adherence, contributing to a substantial economic burden (3).

Current pharmacological options for AR include oral and intranasal antihistamines, intranasal corticosteroids, leukotriene receptor antagonists (LTRAs), and decongestants. Among these, second-generation oral antihistamines – such as loratadine, desloratadine, and levocetirizine –are commonly used as first-line therapy due to their rapid onset of action and minimal sedative effects. According to the ARIA (Allergic Rhinitis and its Impact on Asthma) guidelines, these agents are recommended as the initial treatment for mild intermittent AR, given their favorable safety profile and symptom-relieving efficacy (4). Montelukast, a LTRA, is often used as an alternative or adjunct, particularly in patients with poor response to antihistamines or comorbid asthma (5). The recent International Consensus Statement on Allergy and Rhinology supports that LTRAs are consistently more effective than placebo and may provide additional benefits for specific symptom domains such as nighttime control. They are not generally recommended as first-line therapy but may be considered in selected patients, particularly in combination strategies to enhance efficacy (6).

The rationale for combining montelukast with antihistamines is based on their complementary mechanisms. Antihistamines target histamine-mediated responses, while montelukast acts on leukotriene pathways, offering broader symptom control (7). This pathophysiological basis supports their potential synergistic effects, especially in patients with moderate-to-severe AR or those with partial response to monotherapy (8). In clinical practice, such combination therapy is frequently employed, although supporting evidence has been inconsistent. While several randomized controlled trials (RCTs) have evaluated the efficacy of combination therapy compared to monotherapy, the results remain inconsistent (9, 10). Importantly, limited number of meta-analyses have comprehensively addressed this specific comparison, leaving a gap in synthesized evidence that could inform guideline recommendations. The objective of this meta-analysis is to systematically evaluate the efficacy of combination therapy with montelukast and antihistamines compared to montelukast monotherapy in patients with AR. Primary outcomes include changes in total symptom scores and quality of life measures, while secondary analyses focus on individual symptom domains. This study also aims to identify whether certain antihistamine combinations provide greater benefit, thereby offering a clearer understanding of the clinical value of combination therapy and guiding optimal treatment strategies for AR.

Materials and methods

Search strategy

A comprehensive literature search was conducted in PubMed, Embase, MEDLINE, Scopus, and the Cochrane Library through April 2025. The search strategy was developed in collaboration with an experienced medical librarian specialized in clinical research synthesis. Studies were eligible if they compared combination therapy with montelukast and oral antihistamines *versus* montelukast monotherapy in patients with AR, with outcomes assessing symptom scores or health-related quality of life. Two reviewers independently screened titles and abstracts, assessed full texts, and resolved discrepancies through consensus with a third reviewer. The study flow is shown in **figure 1**.

Data extraction and risk of bias assessment

Data extraction was performed using a standardized form, capturing study characteristics including patient demographics, treatment allocation, and outcome measures (11, 12). Extracted data included changes from baseline to post-treatment in individual nasal symptoms (sneezing, itching, nasal congestion, and rhinorrhea), eye symptoms, total daytime and nighttime symptom scores, and Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) scores. Outcomes were compared between combination therapy groups (montelukast plus loratadine, levocetirizine, or desloratadine) and monotherapy controls (montelukast alone) to assess the added benefit of combination treatment. Risk of bias for each included randomized controlled trial was evaluated using the Cochrane Risk of Bias 2.0 tool (13).

Statistical analysis

Statistical analyses were performed using R version 4.3.1 (R Foundation for Statistical Computing, Vienna, Austria). Outcomes were pooled using standardized mean differences (SMDs) to account for variations in measurement scales across studies. Heterogeneity was assessed using Cochran's Q and the I^2 statistic. Publication bias was evaluated through funnel plots and Egger's regression test. Subgroup analyses were conducted to investigate sources of heterogeneity and to examine potential effect modifiers.

Results

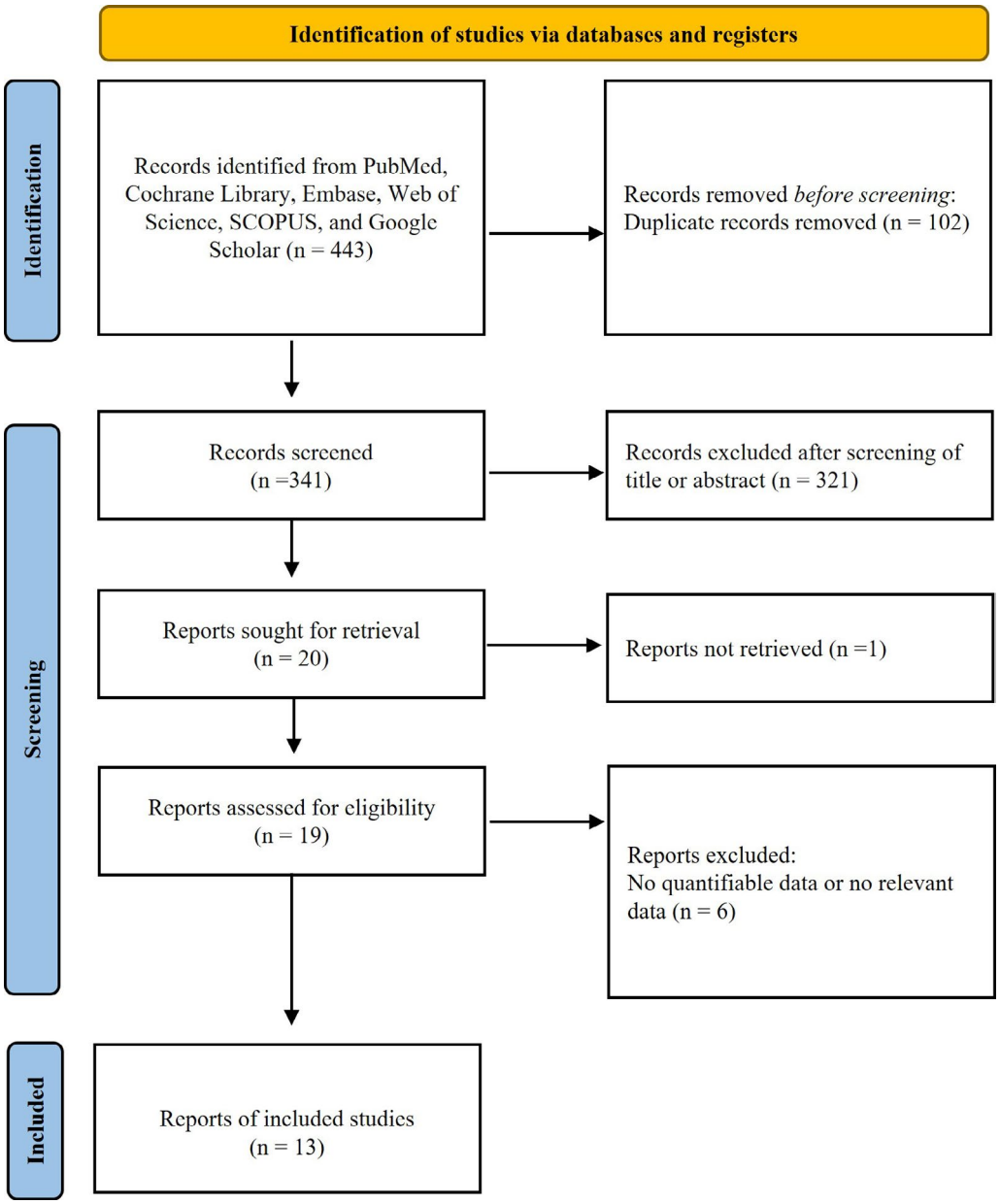
We ultimately analyzed 2,950 subjects evaluated in 13 studies (7, 10, 14-24). The studies are summarized in **table I** and the individual randomized controlled trial methodological quality are listed in **table I(Suppl)**.

Direct comparison of changes in total symptom scores and quality of life between combination therapy and montelukast monotherapy

Combination therapy demonstrated a statistically significant improvement in daytime nasal and eye symptoms compared to montelukast alone (SMD [95%CI] = 0.25 [0.15 to 0.35], I^2 = 51.2%) (**figure 2**). However, no significant differences were observed in nighttime symptoms (SMD [95%CI] = 0.10 [-0.01 to 0.21], I^2 = 0%) or RQLQ scores (SMD [95%CI] = 0.11 [-0.05 to 0.26], I^2 = 0%) (**table II**).

Subgroup analyses based on the type of antihistamine revealed that the combination of levocetirizine and montelukast consistently provided greater benefit in daytime symptoms (SMD [95%CI] = 0.42 [0.03 to 0.81], I^2 = 66.9%) and nighttime symptoms (SMD [95% CI] = 0.22 [0.05 to 0.39], I^2 = 0%) (**table II**). In contrast, loratadine in combination with montelukast showed a

Figure 1 *- Study selection diagram.*



more modest benefit in daytime symptoms (SMD [95%CI] = 0.18 [0.07 to 0.30], I^2 = 0%) with no significant effects on nighttime symptoms or quality of life. Desloratadine combined with montelukast showed a relatively large effect size for daytime symptoms (SMD [95%CI] = 0.83 [0.18 to 1.48]), although based on a single study. Subgroup analyses indicated that levocetirizine-montelukast combinations showed numerically greater benefit in both daytime and nighttime symptoms. However, these trends should be interpreted with caution, as formal tests for subgroup differences did not reach statistical significance (**table II**).

Direct comparison of changes in individual symptom scores between combination therapy and montelukast monotherapy

Combination therapy with montelukast and antihistamines was generally more effective than montelukast monotherapy in relieving most nasal symptoms, including sneezing, itching, obstruction, and rhinorrhea (**figure 3**). Considerable heterogeneity (I^2 > 50%) was observed in several outcomes. The analysis was based on pooled data without stratification by the type of antihistamine. Subgroup comparisons were performed to explore differences in treatment response across antihistamines (**table III**). For sneezing, combination therapy demonstrated a clear benefit over monotherapy (SMD = 0.54 [0.23 to 0.84], I^2 = 62.4%). The largest effect was observed in the desloratadine group (SMD = 0.72 [0.23 to 1.21], I^2 = 0%), followed by levocetirizine (SMD = 0.66 [0.14 to 1.18], I^2 = 66.2%). Loratadine-based therapy did not show a statistically significant improvement (SMD = 0.18 [-0.01 to 0.38]). In nasal itching, the overall effect of combination therapy was modest (SMD = 0.23 [0.09 to 0.37], I^2 = 0%). Desloratadine (SMD = 0.53 [0.05 to 1.01]) and levocetirizine (SMD = 0.32 [0.09 to 0.55]) both showed meaningful improvements, while loratadine did not result in a significant effect (SMD = 0.12 [-0.07 to 0.31]). Nasal obstruction improved significantly with combination therapy overall (SMD = 0.58 [0.21 to 0.95], I^2 = 79.2%). Deslorata-

Table I *- Summary of the studies included in our meta-analysis.*

Study	Year	Study Type	Total number	Age (yrs)	Country	Rhinitis Type	Treatment	Duration (wks)	Outcomes
Meltzer	2000	Multicenter RCT with 5 parallel treatment groups (placebo-controlled)	460	15-75	USA	SAR	Montelukast (10/20 mg), loratadine 10 mg, combination (montelukast + loratadine), or placebo	2	Daytime nasal symptoms, Daytime eye symptoms, Nighttime nasal symptoms
Nayak	2002	Multicenter double-blind RCT (placebo-controlled)	758	15-82	USA	SAR	Montelukast (10/20 mg), loratadine 10 mg, combination (montelukast + loratadine), or placebo	2	Daytime nasal symptoms, individual nasal symptoms, Daytime eye symptoms, Nighttime nasal symptoms, Rhinoconjunctivitis Quality-of-Life
Ciebiada	2006	Double-blind, placebo-controlled crossover RCT	40	18-65	Poland	PAR	Montelukast 10 mg, desloratadine 5 mg, combination, or placebo	6	Daytime nasal symptoms, individual nasal symptoms, Daytime eye symptoms
Ciebiada	2008	Double-blind, placebo-controlled crossover RCT	40	18-65	Poland	PAR	Montelukast 10 mg, desloratadine 5 mg, combination, or placebo	6	Nighttime nasal symptoms, Rhinoconjunctivitis Quality-of-Life
Lu (study 1)	2009	Phase 2 randomized parallel-group study	402	15-85	Belgium	SAR	Beclomethasone 200 µg, placebo, combination (montelukast 10 mg + loratadine 10 mg), montelukast 10 mg, or loratadine 10 mg	2	Daytime nasal symptoms

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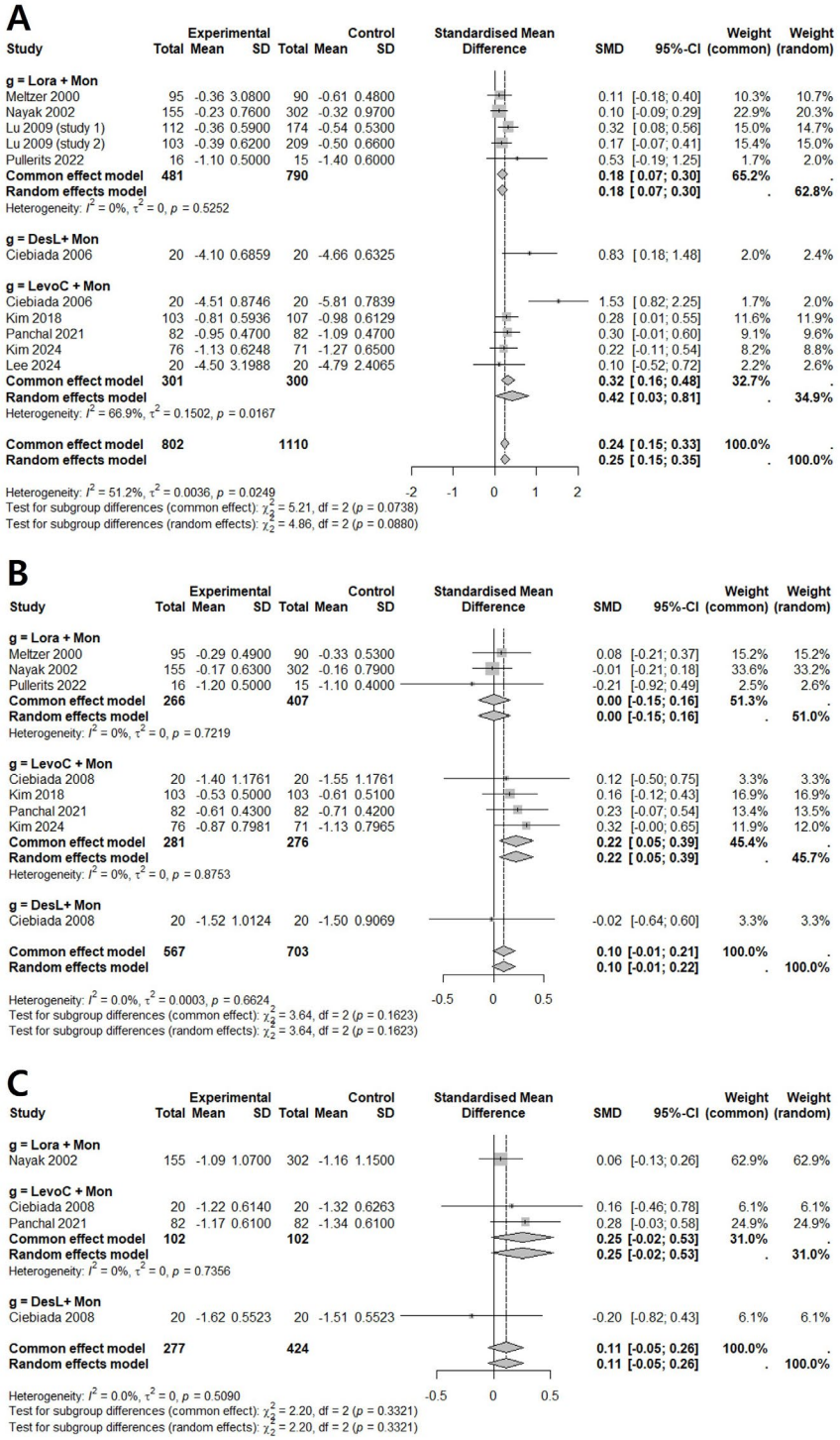
Study	Year	Study Type	Total number	Age (yrs)	Country	Rhinitis Type	Treatment	Duration (wks)	Outcomes
Lu (study 2)	2009	Phase 2 randomized parallel-group study	476	15-85	Belgium	SAR	Beclomethasone 200 µg (study 1 only), placebo, combination (montelukast + loratadine), montelukast, or loratadine	2	Daytime nasal symptoms
Ciebiada	2011	Double-blind, placebo-controlled, 2-arm crossover RCT	40	18-65	Poland	PAR	Montelukast 10 mg, desloratadine 5 mg, combination (montelukast 10 mg + desloratadine 5 mg), or placebo	6	individual nasal symptom
Andhale	2016	Prospective RCT	75	15-75	India	PAR	Montelukast 10 mg or combination (montelukast 10 mg + levocetirizine 5 mg), or levocetirizine 5mg alone	2	individual nasal symptoms, Daytime eye symptoms
Kim	2018	Phase 3 multicenter double-blind RCT	210	>15	Korea	Asthma and AR	Montelukast 10 mg or combination (montelukast 10 mg + levocetirizine 5 mg)	4	Daytime nasal symptoms, individual nasal symptoms, Nighttime nasal symptoms
Panchal	2021	Phase 3 multicenter double-blind RCT	186	18-60	India	SAR	Montelukast 10 mg or combination (montelukast 10 mg + levocetirizine 5 mg), or levocetirizine 5mg alone	2	Daytime nasal symptoms, Nighttime nasal symptoms, Rhinoconjunctivitis Quality-of-Life
Pullerits	2022	Double-blind, double-dummy, placebo-controlled parallel-group RCT	31	15-50	Estonia	SAR	Fluticasone 200 µg, montelukast 10 mg, combination (montelukast 10 mg + loratadine 10 mg), or placebo	6	Daytime nasal symptoms, Nighttime nasal symptoms,
Ghanbari	2024	Open-label RCT	45	6-14	Iran	Moderate to severe AR	Desloratadine syrup (2.5–5 mg/day), montelukast 5 mg, combination (desloratadine + montelukast)	8	Daytime nasal symptoms, individual nasal symptoms
Kim	2024	Open-label multicenter RCT	147	6-14	Korea	AR	Montelukast 5 mg or fixed-dose combination (montelukast 5 mg + levocetirizine 5 mg)	4	Daytime nasal symptoms, individual nasal symptoms, nighttime nasal symptom score
Lee	2024	Open-label randomized case-controlled study	40	6-14	Korea	PAR	Montelukast 5 mg or combination (montelukast 5 mg + levocetirizine 5 mg) for 4 weeks	4	Daytime nasal symptoms

RCT: randomized controlled trial; SAR: seasonal allergic rhinitis; PAR: perennial allergic rhinitis; AR: allergic rhinitis.

***Figure 2** - Direct comparison of changes in total symptom scores and Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) scores between combination therapy and montelukast monotherapy.*



***(A)** Daytime total symptom score, **(B)** nighttime total symptom score, and **(C)** RQLQ score. Lora: loratadine; DesL: desloratadine; Levoc: levocetirizine; Mon: montelukast; SMD: standardized mean difference; CI: confidence interval.*

dine (SMD = 0.71 [0.25 to 1.16], I^2 = 28.0%) and levocetirizine (SMD = 0.68 [0.09 to 1.27], I^2 = 82.8%) showed substantial benefit. In contrast, loratadine showed no significant improvement (SMD = 0.02 [-0.17 to 0.21]).

For rhinorrhea, a moderate pooled effect was observed (SMD = 0.42 [0.09 to 0.83], I^2 = 85.5%), with only the levocetirizine subgroup demonstrating a significant improvement (SMD = 0.70 [0.12 to 1.29], I^2 = 87.9%). Desloratadine (SMD = 0.00 [-0.47 to 0.48]) and loratadine (SMD = 0.06 [-0.14 to 0.25]) showed no meaningful effect. Leave-one-out sensitivity analyses indicated that heterogeneity was largely driven by a few trials with large effect sizes, particularly Kim *et al*. (2024) (22) and Ciebiada *et al*. (2006) (7). Excluding Kim (2024) reduced heterogeneity to 60.3% (SMD = 0.23 [-0.02 to 0.47]) (22), and excluding Ciebiada (2006) yielded SMD = 0.31 [-0.04 to 0.65] with I^2 = 84.8% (7). When both studies were removed, the pooled effect remained modest but consistent (SMD = 0.21 [0.05 to 0.37]) with I^2 = 0%, suggesting that the overall direction of effect is robust while the magnitude is influenced by small but influential studies.

Eye symptoms had the largest pooled effect size (SMD = 1.04 [-0.18 to 2.26], I^2 = 97.7%), though the wide confidence interval and high heterogeneity limit the interpretability of this result. The strongest apparent benefit was observed in the levocetirizine group (SMD = 1.84 [-0.11 to 3.79], I^2 = 96.0%), while desloratadine (SMD = 0.42 [–0.21 to 1.05]) and loratadine (SMD = 0.08 [-0.11 to 0.28]) were not associated with significant improvement.

Discussion

In this meta-analysis, combination therapy with montelukast and antihistamines demonstrated superior efficacy compared to montelukast monotherapy in relieving several symptom domains associated with AR. The combination approach was particularly effective in improving daytime symptoms, with a statistically significant pooled effect size. However, it showed limited benefits for nighttime symptoms and health-related quality of life, as measured by the RQLQ. Among the antihistamines analyzed, levocetirizine-based combination therapy consistently provided the most favorable outcomes for both daytime and nighttime symptom scores. Desloratadine also showed a relatively large effect on daytime symptoms, although this finding was derived from a single study. In contrast, loratadine-based combinations did not produce statistically meaningful improvements in any symptom domain.

Cysteinyl leukotrienes (CysLTs) play a key role in the pathophysiology of AR by promoting vascular permeability, mucus secretion, and eosinophilic infiltration in the nasal mucosa (25). Montelukast, a selective CysLT1 receptor antagonist, has demonstrated efficacy in nasal obstruction by reducing mucosal edema, suppress sneezing and itching through inhibition of sensory nerve stimulation, and improve mucociliary clearance by decreasing mucus viscosity (5, 26). Chervinsky *et al*. demonstrated that montelukast monotherapy significantly improved daytime nasal symptoms in patients with seasonal AR, particularly during periods of high pollen exposure (27). Their multi-seasonal analysis supported the responsiveness of montelukast to allergen load, reinforcing its efficacy as a monotherapy.

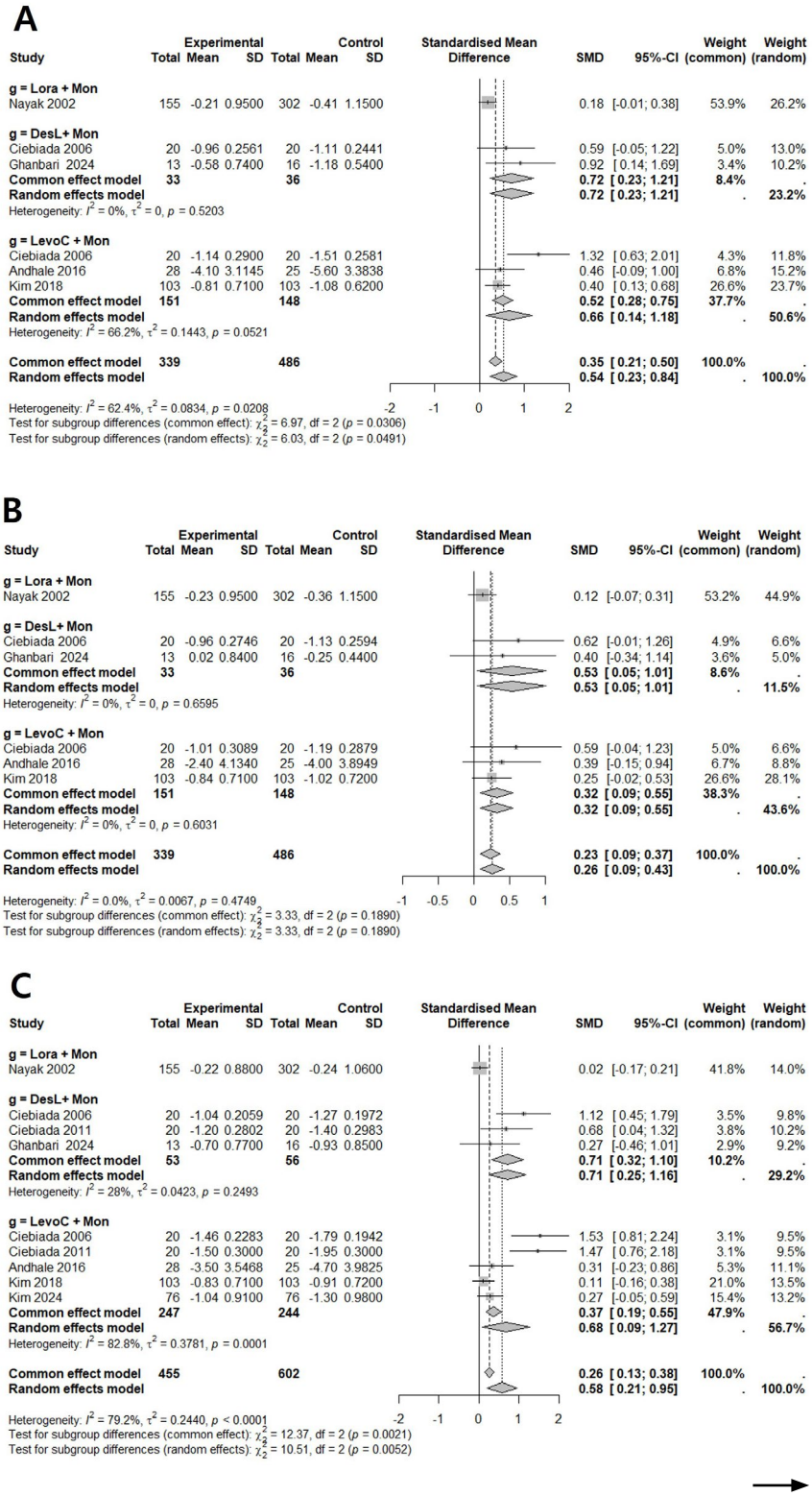
Histamine also plays a key role in the early-phase response of AR (28). Upon allergen exposure, activated mast cells rapidly release histamine, which binds to H_1 receptors in the nasal mucosa (29). These effects occur within minutes, inducing sneezing, itching, and rhinorrhea, and are central to the immediate hypersensitiv-

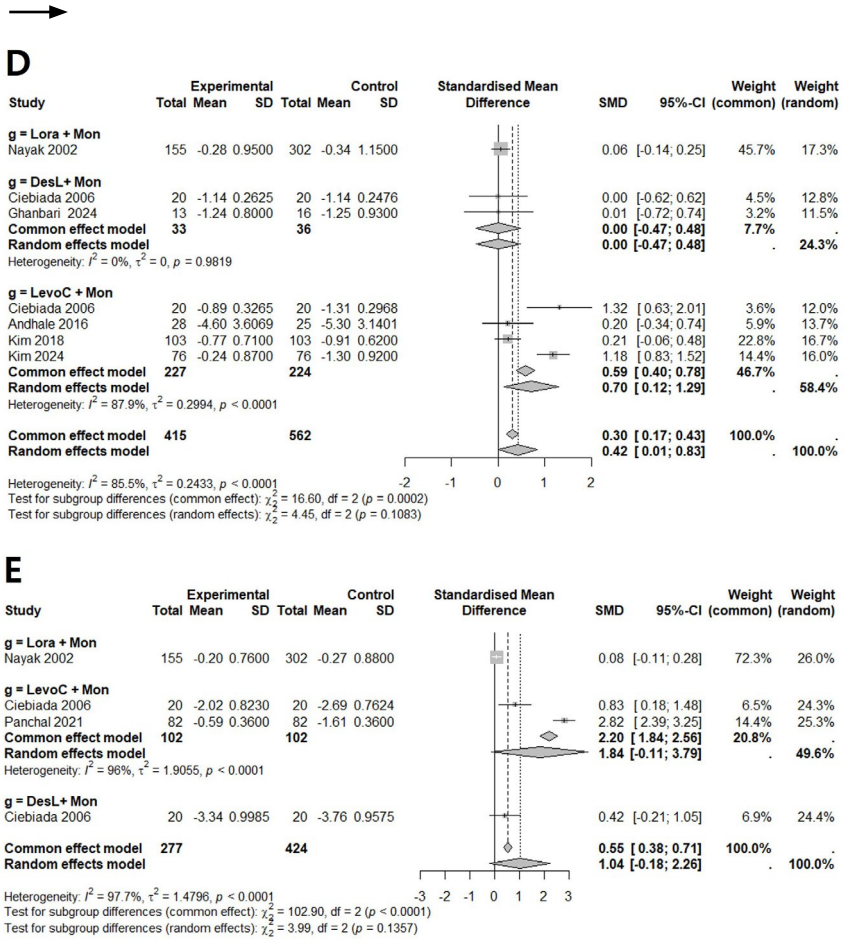
Table II *- Subgroup analysis of changes in total symptom scores and Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) scores between combination therapy (montelukast with antihistamines) and montelukast monotherapy.*

	Daytime	**Nighttime**	**RQLQ**
SMD	0.2498 [0.1478; 0.3518] I^2 = 51.2%	0.1018 [-0.0105; 0.2141] I^2 = 0%	0.1060 [-0.0476; 0.2595] I^2 = 0%
Lora + Mon	n = 5 0.1806 [0.0659; 0.2953] I^2 = 0%	n = 3 0.0037 [-0.1531; 0.1605] I^2 = 0%	n = 1 0.0622 [-0.1315; 0.2559] N/A
DesL+ Mon	n = 1 0.8319 [0.1832; 1.4806] N/A	n = 1 -0.0204 [-0.6402; 0.5994] N/A	n = 1 -0.1952 [-0.8166; 0.4262] N/A
LevoC + Mon	n = 5 0.4201 [0.0264; 0.8138] I^2 = 66.9%	n = 4 0.2216 [0.0549; 0.3883] I^2 = 0%	n = 2 0.2539 [-0.0218; 0.5295] I^2 = 0%
P-value	0.0880	0.1623	0.3321

Lora: loratadine; DesL: desloratadine; Levoc: levocetirizine; Mon: montelukast; SMD: standardized mean difference; CI: confidence interval; RQLQ: Rhinoconjunctivitis Quality of Life Questionnaire; N/A: not applicable.

Figure 3 *- Direct comparison of changes in individual nasal symptom scores and eye symptom scores between combination therapy and montelukast monotherapy.*





***(A)** Sneezing, **(B)** nasal itching, **(C)** nasal congestion, **(D)** rhinorrhea, and **(E)** eye symptoms. Lora: loratadine; DesL: desloratadine; Levoc: levocetirizine; Mon: montelukast; SMD: standardized mean difference; CI: confidence interval.*

***Table III** - Subgroup analysis of changes in individual nasal and eye symptom scores between combination therapy (montelukast with antihistamines) and montelukast monotherapy.*

	Sneezing	Itching	Obstruction	Rhinorrhea	Eye symptoms
SMD	0.5381 [0.2317; 0.8445] I² = 62.4%	0.2313 [0.0900; 0.3727] I² = 0%	0.5773 [0.2076; 0.9470] I² = 79.2%	0.4199 [0.0092; 0.8306] I² = 85.5%	1.0388 [-0.1797; 2.2574] I² = 97.7%
Lora + Mon	n = 1 0.1838 [-0.0102; 0.3778] N/A	n = 1 0.1195 [-0.0744; 0.3133] N/A	n = 1 0.0199 [-0.1737; 0.2136] N/A	n = 1 0.0551 [-0.1386; 0.2488] N/A	n = 1 0.0831 [-0.1107; 0.2768] N/A
DesL+ Mon	n = 2 0.7195 [0.2288; 1.2102] I² = 0%	n = 2 0.5306 [0.0481; 1.0131] I² = 0%	n = 3 0.7078 [0.2515; 1.1640] I² = 28.0%	n = 2 0.0046 [-0.4683; 0.4776] I² = 0%	n = 1 0.4208 [-0.2065; 1.0481] N/A
LevoC + Mon	n = 3 0.6587 [0.1407; 1.1766] I² = 66.2%	n = 3 0.3197 [0.0912; 0.5482] I² = 0%	n = 5 0.6779 [0.0900; 1.2658] I² = 82.8%	n = 4 0.7043 [0.1183; 1.2902] I² = 87.9%	n = 2 1.8391 [-0.1132; 3.7914] I² = 96.0%
P-value	0.0491	0.1890	0.0052	0.1083	0.1357

Lora: loratadine; DesL: desloratadine; Levoc: levocetirizine; Mon: montelukast; SMD: standardized mean difference; CI: confidence interval; N/A: not applicable.

ity reaction observed in AR (28). Second-generation oral antihistamines selectively block peripheral H_1 receptors and are widely recommended as first-line agents for patients with mild to moderate AR (4). Their rapid onset and low sedative potential make them appropriate for daily use. However, their therapeutic benefit is largely limited to histamine-mediated symptoms, with minimal efficacy against nasal obstruction and other manifestations driven by leukotrienes, cytokines, and other inflammatory mediators (30). Moreover, antihistamines exert little effect on the late-phase inflammatory response, which contributes to persistent symptoms and reduced treatment responsiveness in some patients (31). In this context, combination therapy with leukotriene receptor antagonists has been proposed to enhance therapeutic efficacy by targeting multiple inflammatory pathways (22, 24, 32).

Although the overall difference between montelukast-antihistamine combination therapy and montelukast monotherapy was small and RQLQ improvement was not significant, our analysis identified modest improvements in individual symptoms such as sneezing and nasal obstruction. These results are consistent with the modest role of montelukast and with recent evidence showing that intranasal treatments, particularly corticosteroids, are superior to oral therapies (33). However, intranasal corticosteroids are not feasible for all patients because of contraindications, side effects, or poor adherence. In such cases, oral therapy remains a relevant alternative. Our findings therefore suggest that adding an antihistamine to montelukast may provide incremental, symptom-specific benefits, particularly for patients whose predominant complaints are not adequately controlled with monotherapy. RQLQ showed limited responsiveness in our results, which may be because the questionnaire covers broader domains such as emotional well-being and daily functioning. These aspects may require longer treatment durations or stronger anti-inflammatory effects to show measurable improvement. Among the evaluated antihistamines, levocetirizine in combination with montelukast consistently showed statistically significant benefits across multiple studies, suggesting that this regimen may offer more reliable symptom control during both daytime and nighttime. Although desloratadine demonstrated the largest effect size for daytime symptoms, this finding was derived from a single study and should therefore be interpreted with caution until replicated in further trials.

In our analysis, desloratadine-based combinations showed the greatest improvements in sneezing, itching, and nasal obstruction, while levocetirizine-based combinations demonstrated more consistent and statistically robust effects, particularly for rhinorrhea. However, interpretation of the rhinorrhea outcome requires caution because of substantial heterogeneity. A small-scale study by Ciebiada *et al*. (2006) (7), which reported an unusually large effect and had concerns regarding risk of bias, disproportionately increased variability. In addition, the pediatric population in Kim (2024) (22) may have contributed to differences compared with adult studies. These findings suggest that although the overall direction of effect is consistent, the magnitude should be interpreted cautiously. Taken together, these results suggest that the choice of antihistamine in combination therapy may influence both the extent and profile of symptom relief. Analyzing outcomes by individual symptoms provides insights that composite scores may overlook. Since patients often present with distinct symptom patterns, identifying the most appropriate regimen for each profile may support more personalized treatment strategies.

This study has several limitations. Individual patient-level variables, particularly baseline symptom severity, were not consistently reported across studies. Because treatment response in AR varies with initial severity, the absence of severity-based stratification limits the interpretability of pooled effect sizes and may have led to over or underestimation in subgroups. In addition, most included studies had relatively short treatment durations, generally between two and four weeks, which may not be sufficient to capture meaningful changes in quality of life. Some subgroup findings, such as the large effect size observed with desloratadine, were derived from a single trial and should be interpreted with caution until replicated. In addition, most RQoL data were derived from SAR studies, with very limited evidence available for PAR, so the potential impact of rhinitis subtype on quality-of-life outcomes could not be assessed. This distinction may be clinically relevant, since patients with PAR often experience more persistent symptoms than those with SAR. Collectively, these limitations highlight the need for larger and stratified populations, longer follow-up, and standardized reporting of baseline severity. In particular, stratification by predominant symptom profiles will be essential to clarify whether certain AR phenotypes derive greater benefit from montelukast-antihistamine combination therapy.

Conclusions

This meta-analysis indicates that combining montelukast with oral antihistamines improves daytime and individual nasal symptoms more effectively than montelukast alone. Levocetirizine-based combinations showed the most consistent benefits, including nighttime symptom relief. However, treatment effects varied by symptom and antihistamine type. These findings support a personalized, symptom-targeted approach to treatment selection. Future studies should stratify patients by predominant symptoms or AR phenotypes to optimize combination strategies and better assess long-term impacts on quality of life.

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Contributions

JSK, GS, SHH: conceptualization, supervision. JSK, SHH: methodology, formal analysis, investigation data curation, writing - original draft, writing - review & editing, visualization. SHH: software, validation.

Conflict of interests

The authors declare that they have no conflict of interests.

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