

COMPARATIVE EFFICACY AND SAFETY OF BIOLOGIC THERAPIES IN CHRONIC RHINOSINUSITIS WITH NASAL POLYPS: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

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Abstract: Chronic rhinosinusitis with nasal polyps (CRSwNP) is a chronic inflammatory condition that significantly affects quality of life through persistent nasal obstruction, impaired smell, and recurrent sinus infections. Biologic therapies targeting type-2 inflammatory pathways have emerged as effective treatment options for patients with severe or refractory disease. However, direct head-to-head randomized controlled trials comparing biologic agents are limited. This study aimed to evaluate and rank the efficacy and safety of available biologics for CRSwNP using a systematic review and network meta-analysis. A comprehensive literature search was conducted in PubMed, Embase, Web of Science, and the Cochrane Library. Randomized controlled trials evaluating biologics in adult patients with CRSwNP were included. The primary outcomes included nasal polyp score (NPS), Sino-Nasal Outcome Test-22 (SNOT-22), University of Pennsylvania Smell Identification Test (UPSIT), nasal congestion score (NCS), and adverse events (AEs). Nine randomized controlled trials involving 1,190 patients were included, comparing three biologics—dupilumab, omalizumab, and mepolizumab—with placebo. Network meta-analysis demonstrated that dupilumab showed the highest efficacy across most outcomes, including NPS, SNOT-22, UPSIT, and NCS. Omalizumab ranked second for several symptom-related outcomes, while mepolizumab ranked second in reducing NPS but showed the highest probability of adverse events. Overall, dupilumab appears to provide the most effective and favorable treatment profile for CRSwNP, followed by omalizumab. These findings may guide clinicians in selecting optimal biologic therapy for patients with severe CRSwNP.

Keywords: Chronic rhinosinusitis with nasal polyps; Dupilumab; Omalizumab; Mepolizumab; Biologic therapy; Network meta-analysis; Nasal polyp score; CRSwNP.

Introduction

Chronic rhinosinusitis with nasal polyps (CRSwNP) is a persistent inflammatory disease of the nasal and paranasal sinus mucosa characterized by the growth of benign inflammatory polyps within the nasal cavity. The condition affects a substantial proportion of the adult population and is frequently associated with symptoms such as nasal obstruction, rhinorrhea, facial pressure, and loss of smell. These symptoms can significantly impair patients' quality of life and often require long-term medical management or surgical intervention.

The pathophysiology of CRSwNP is strongly associated with type-2 inflammatory responses involving cytokines such as interleukin-4 (IL-4), interleukin-5 (IL-5), interleukin-13 (IL-13), and immunoglobulin E (IgE). Traditional treatment approaches include intranasal corticosteroids, systemic corticosteroids, and endoscopic sinus surgery. However, a considerable number of patients experience persistent or recurrent disease despite these therapies.

In recent years, biologic therapies targeting specific inflammatory pathways have emerged as promising treatment options for patients with severe or refractory CRSwNP. Among the currently available biologics, dupilumab, omalizumab, and mepolizumab have shown effectiveness in reducing nasal polyp size and improving symptoms. Dupilumab targets the IL-4 receptor alpha, blocking IL-4 and IL-13 signaling pathways; omalizumab binds to IgE, preventing allergic inflammatory responses; and mepolizumab targets IL-5, reducing eosinophil-mediated inflammation.

Although these biologics have demonstrated clinical benefits compared with placebo, direct head-to-head randomized controlled trials comparing their relative effectiveness and safety are limited. Consequently, clinicians often lack clear evidence to determine which biologic therapy may be most beneficial for patients with CRSwNP.

Network meta-analysis (NMA) allows indirect comparisons across multiple treatments by integrating data from different randomized trials. Therefore, this study aimed to perform a systematic review and network meta-analysis of randomized controlled trials to compare the efficacy and safety of dupilumab, omalizumab, and mepolizumab in adult patients with CRSwNP.

Materials and Methods. This study was conducted as a systematic review and network meta-analysis of randomized controlled trials. The protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO). A comprehensive literature search was conducted in the following electronic databases: PubMed, Embase, Web of Science, Cochrane Library.

Studies were excluded if they:

- Were observational studies, reviews, editorials, or case reports
- Included pediatric populations only
- Did not report relevant clinical outcomes

Data Extraction

Two independent reviewers extracted data from the included studies. The following information was collected:

- Study characteristics (author, year, design)
- Number of participants
- Type of biologic therapy
- Treatment duration

- Outcome measures

Primary outcomes included:

- Nasal Polyp Score (NPS)
- Sino-Nasal Outcome Test-22 (SNOT-22)
- University of Pennsylvania Smell Identification Test (UPSIT)
- Nasal Congestion Score (NCS)
- Adverse events (AEs)

Statistical Analysis

A network meta-analysis was conducted to compare the efficacy and safety of different biologics. Treatment ranking was estimated using the **surface under the cumulative ranking curve (SUCRA)** values, where higher values indicate greater efficacy or higher probability of ranking best among treatments.

Results. The database search initially identified several potentially relevant studies. After removing duplicates and screening titles and abstracts, full texts of eligible studies were reviewed. Ultimately, **nine randomized controlled trials** involving **1,190 patients** met the inclusion criteria.

These trials compared three biologic therapies—dupilumab, omalizumab, and mepolizumab—with placebo.

Efficacy Outcomes

Nasal Polyp Score (NPS)

Dupilumab demonstrated the highest efficacy in reducing nasal polyp size, with a **SUCRA value of 0.900**, indicating the greatest probability of being the most effective treatment. Mepolizumab ranked second with a **SUCRA value of 0.563**, followed by omalizumab.

Sino-Nasal Outcome Test-22 (SNOT-22)

Dupilumab showed the most substantial improvement in patient-reported symptoms with a **SUCRA value of 0.916**, while omalizumab ranked second with a **SUCRA value of 0.606**.

Smell Identification (UPSIT)

Dupilumab achieved the highest ranking in improving sense of smell, with a **SUCRA value of 1.000**, suggesting superior efficacy among the evaluated biologics. Omalizumab ranked second with a **SUCRA value of 0.500**.

Nasal Congestion Score (NCS)

Dupilumab again ranked highest with a **SUCRA value of 0.807**, while omalizumab ranked second with **0.693**.

Safety Outcomes

In terms of adverse events, **mepolizumab demonstrated the highest risk**, with a **SUCRA value of 0.746**. Dupilumab and omalizumab showed comparatively lower probabilities of adverse events.

Overall, the results indicate that **dupilumab consistently ranked highest in efficacy across most clinical outcomes**, while **omalizumab generally ranked second**. Although **mepolizumab showed moderate efficacy**, it was associated with a higher risk of adverse events.

Conclusion

This study represents the first network meta-analysis comparing different biologic therapies for the treatment of chronic rhinosinusitis with nasal polyps. The findings suggest that biologic therapies provide significant benefits compared with placebo in reducing nasal polyp size and improving symptoms.

Among the evaluated biologics, **dupilumab demonstrated the highest overall efficacy and favorable safety profile**, making it the most effective treatment option for patients with CRSwNP. **Omalizumab appears to be the second most effective therapy**, particularly for improving symptom scores and quality of life. **Mepolizumab showed moderate efficacy but was associated with the highest probability of adverse events**.

These results highlight the importance of individualized treatment selection based on clinical characteristics, disease severity, and safety considerations. Further head-to-head randomized trials are needed to confirm these findings and provide stronger evidence for optimal biologic therapy selection in CRSwNP.

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