Medical therapies for adult chronic sinusitis: a systematic review

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ABSTRACT

Chronic sinusitis is an inflammatory disease of the paranasal sinuses that usually manifests as chronic sinonasal symptoms. Since the pathophysiology of chronic rhinosinusitis in children and adults varies significantly, as do the medical and surgical treatments, this review exclusively discusses adult chronic rhinosinusitis and explores the medical therapies used to treat chronic sinusitis in adult patients. A systematic review was performed involving studies of medical therapies used to treat chronic sinusitis in adult patients between 2016 and 2022. The PubMed and Google scholar databases were used to explore studies regarding our subject. The keywords included “Medical therapy, treatment, chronic, sinusitis, rhinosinusitis, and adult” and were used in various combinations. Original research reporting medical therapies used in treating chronic sinusitis in adult patients and full-text publications served as the inclusion criterion. Though 166 articles were obtained, only eight met the inclusion criteria. The studies included 2,884 participants; all the studies were clinical trials. The review found Dupilumab to be well-tolerated and provided rapid, significant, and clinically meaningful improvements for patients with chronic sinusitis and nasal polyposis (CRSwNP). In addition, it produced rapid and sustained improvement in the sense of smell, alleviating a cardinal symptom of severe CRSwNP. Furthermore, Dupilumab improved upper and lower airway outcome measures and health-related quality of life in patients with severe CRSwNP and comorbid asthma. Another therapy was Omalizumab, which produced positive outcomes on all endpoints in participants who switched from placebo to Omalizumab through week 52. In addition, endoscopic sinus surgery, combined with medical therapy, was found to be more efficacious than medical therapy alone in patients with CRSwNP.

Keywords: Medical therapy, treatment, chronic, sinusitis, rhinosinusitis.

Introduction

Chronic rhinosinusitis is a paranasal sinus inflammatory disorder that most frequently results in chronic sinonasal symptoms. The prevalence of chronic rhinosinusitis in the US ranges from 1% to 5%. It is an easily curable condition that causes direct and indirect medical costs in the United States to reach billions annually [1-2]. This review only addresses adult chronic rhinosinusitis since the pathophysiology of chronic rhinosinusitis in children differs from that in adults. The medicinal and surgical treatment varies significantly between children and adults [3]. The most severe effects of chronic rhinosinusitis are cerebral and orbital complications, but they are exceedingly rare and often only occur in people with concurrent acute sinusitis. Periorbital cellulitis, orbital cellulitis, and orbital abscess are all orbit problems. Meningitis, cavernous sinus thrombosis, and epidural abscess are intracranial problems [4]. Comorbid pulmonary disorders may become worse because of chronic rhinosinusitis. Cystic fibrosis patients nearly always develop chronic rhinosinusitis, and the paranasal sinuses of these patients might act as a reservoir for bacterial flora that seeds pulmonary illnesses [5]. Comorbid chronic rhinosinusitis is linked to worse asthma control, more trips to the emergency room for asthma-related issues, and systemic corticosteroid use in people with asthma [6]. The main effect of chronic rhinosinusitis is reduced quality of life (QOL) brought on by burdensome chronic sinonasal symptoms and acute exacerbations [7]. In individuals with chronic rhinosinusitis, treatment aims to control symptoms...
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and enhance or preserve the QOL. The goal of treatment is to improve mucociliary clearance, nasal drainage, and outflow, reduce local infection and inflammation, and facilitate topical medicament access. Medical medication is the first line of treatment, followed by endoscopic sinus surgery (ESS) if necessary [8]. Numerous studies have shown that patients with chronic rhinosinusitis benefit from at least daily saline irrigations, which lessen symptoms and enhance the QOL. Saline irrigation with low pressure and high volume (240 ml) is more effective at reducing sinonasal symptoms than nasal saline spray in 50% of patients [9]. Intranasal corticosteroid sprays have been shown in numerous randomized controlled trials (RCTs) to improve sinonasal symptoms and endoscopic findings in chronic rhinosinusitis [10]. No evidence was found to support the claims that one spray is superior to another or that using more of it will make it more effective [11]. When using intranasal corticosteroid sprays, the head should be bent forward to face the floor, and the spray should be applied laterally (away from the nasal septum). After spraying, the patient should not inhale too deeply [8]. The current systematic review aims to explore the medical therapies used to treat chronic sinusitis in adult patients.

Literature Search Strategy

This systematic review complies with the PRISMA checklist guidelines for systematic reviews and meta-analyses [12]. Google Scholar and PubMed were the two databases that were searched. The two databases were utilized to survey for studies on our main topic, “medical therapies used in the treatment of chronic sinusitis in adult patients.” The studies were published between 2016 and 2022. The searching process involved using different keywords, including “Medical therapy, treatment, chronic, sinusitis, rhinosinusitis, and adult.” In addition, the involved keywords were employed to collect all relevant articles. This initial exploration resulted in the revision of all titles.

Eligibility criteria

Only papers focusing on the medical therapies used in treating chronic sinusitis in adult patients were included after reviewing the titles of the retrieved articles. In contrast, articles on the medical therapies used to treat chronic sinusitis in adult patients before 2016 were excluded. The second phase involved selecting only original, English-language studies on the medical treatments used in treating chronic sinusitis in adult patients after evaluating the abstracts of the remaining articles. On the other hand, review articles, editor letters, and case reports were not included. The final stage included original English-language articles discussing the medical therapies used in treating chronic sinusitis in adult patients. These articles were further examined to exclude duplicates, non-full-text articles, and articles with unsatisfactory content, such as overlapped or incomplete data. Figure 1 displays a detailed explanation of the search approach.

Data reviewing and analysis

The full text and abstracts of the articles were evaluated to extract the relevant data and transfer it to a pre-made excel sheet. The chosen data were then amended in the excel sheet, and the data were combined to summarize the data to facilitate data analysis.

Results

Eight studies met the eligibility criteria for this systematic review [13-20] (Table 1). The included studies were either published in 2016 [14] or 2019 [17] or 2020 [18], 2021 [13,15], or 2022 [16,19,20]. All the studies were clinical trials. The included studies involved 2,884 participants; 1,966 adults with chronic sinusitis and 918 placebo controls. Three studies included patients on a background of mometasone furoate nasal spray [13,1,18,19], whereas five studies involved patients with chronic sinusitis and nasal polyposis (CRSwNP) [14,16,17,20]. In five studies [13-17], the patients received Dupilumab, while in two studies, patients were administered Omalizumab [18,19]. In only one study, patients were assigned to ESS plus medical therapy [20].

Three studies investigated the effect of Dupilumab on Intractable Chronic Rhinosinusitis with Nasal Polygyn, its impact on the sense of smell and outcome measures of the upper and lower airways, and health-related quality of life (HRQoL) [13-15]. In addition, two studies assessed the efficacy and safety of Dupilumab and the inhibition of interleukins 4 and 13 in patients with CRSwNP with previous treatment with systemic corticosteroids [16-17]. Another two studies evaluated the continued efficacy, safety, and durability of the response of Omalizumab in adults with CRSwNP [18,19]. Only one study compared the effectiveness of ESS in addition to medical therapy versus medical therapy in patients with CRSwNP [20]. The safety and efficacy of Dupilumab were demonstrated in five studies [13-17]. One study [13] showed that Dupilumab provided rapid, significant, and clinically meaningful improvements for patients with CRSwNP. In addition, it was well tolerated, and safety and efficacy were consistent with the study population. In another study [14], Dupilumab produced rapid and sustained improvement in the sense of smell, alleviating a cardinal symptom of severe CRSwNP. One more study [15] revealed that Dupilumab improved upper and lower airway outcome measures and HRQoL in patients with severe CRSwNP and comorbid asthma and was well tolerated. Finally, two studies [16,17] showed that patients with symptomatic CRS and nasal polyposis refractory compared to intranasal corticosteroids, adding subcutaneous Dupilumab to mometasone furoate nasal spray decreased endoscopic nasal polyp size, sinus opacification, and severity of symptoms in comparison to mometasone alone. Two studies reported the safety and
efficacy of Omalizumab in managing chronic sinusitis in adult patients [18,19]. In one study [18], positive outcomes on all endpoints were seen in participants who switched from placebo to Omalizumab through week 52, comparable to POLYP 1 and 2 at week 24. This study’s efficacy and safety profile supported continued omalizumab treatment for CRSwNP with insufficient response to nasal corticosteroids for up to 1 year. [19]. Compared to Dupilumab and Omalizumab, ESS plus medical therapy was more efficacious than medical therapy alone in patients with CRSwNP [20].

**Discussion**

Chronic sinusitis is a clinical syndrome that includes a variety of conditions, all defined by inflammation of the sinonasal mucosa. The goal of treatment is to locate and control the various triggers that contribute to inflammatory pathophysiology [21]. The numerous disorders represented by CRSsNP and CRSwNP share some of the same symptoms. Nasal irrigation, topical and oral steroids, and management of CRSsNP and CRSwNP are essential. While topical antibiotics may cure resistant diseases, oral antibiotic usage is debatable. Recognizing and treating any confounding comorbidities and underlying systemic conditions is essential [22]. Therefore, the current systematic review aims to explore the different medical therapies used in managing chronic sinusitis in adult patients.

The safety and efficacy of Dupilumab were demonstrated in five studies Fujieda et al. [13], Mullol et al. [14], Laidlaw et al. [15], and Laidlaw et al. [15]. First, Fujieda et al. [13] showed that Dupilumab provided rapid, significant, and clinically meaningful improvements for patients with CRSwNP. In addition, it was well tolerated, and safety and efficacy were consistent with the study population. Second, Mullol et al. [14] found that Dupilumab produced
**Table 1. Selected studies.**

<table>
<thead>
<tr>
<th>Author and publication year</th>
<th>Study design</th>
<th>Population, sample size, and characterization</th>
<th>Main points</th>
<th>Results and main findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Fujieda et al. [13]</td>
<td>Clinical trial</td>
<td>• 45 Patients on a background of mometasone furoate nasal spray received Dupilumab 300 mg</td>
<td>• The effect of Dupilumab on intractable chronic rhinosinusitis with nasal polyps in Japan</td>
<td>Dupilumab provided rapid, significant, and clinically meaningful improvements for patients with CRSwNP in Japan. Dupilumab was well tolerated, and safety and efficacy were consistent with the overall study population.</td>
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<td>2. Mullol et al. [14]</td>
<td>RCTs</td>
<td>• 724 patients with severe CRSwNP. (286 placebo, 438 Dupilumab)</td>
<td>• To assess the impact of Dupilumab on the sense of smell in severe CRSwNP.</td>
<td>Dupilumab produced rapid and sustained improvement in the sense of smell, alleviating a cardinal symptom of severe CRSwNP.</td>
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<td>3. Laidlaw et al. [15]</td>
<td>Randomized, double-blind, placebo-controlled trials</td>
<td>• On a mometasone furoate nasal spray background, 724 patients were administered subcutaneous Dupilumab 300 mg (n = 438) or placebo (n = 286) every 2 weeks. Upper and lower airway outcome measure changes from baseline at week 24 are presented.</td>
<td>• The impact of Dupilumab against a placebo on upper and lower airway outcome indicators and HRQoL in the combined group of patients with CRSwNP.</td>
<td>In individuals with severe CRSwNP and concomitant asthma, Dupilumab improved upper and lower airway outcome measures, HRQoL, and was well tolerated.</td>
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<td>4. Bachert et al. [16]</td>
<td>A randomized, double-blind, placebo-controlled parallel-group study was conducted at 13 United States and European sites between August 2013 and 2014.</td>
<td>• With a 16-week follow-up, 60 adults with CRSwNP were unresponsive to intranasal corticosteroids.</td>
<td>• To examine if Dupilumab inhibits interleukins 4 and 13 in those with CRSwNP.</td>
<td>When combined with mometasone furoate nasal spray, subcutaneous Dupilumab reduced endoscopic nasal polyp load at 16 weeks in persons with symptomatic CRSwNP unresponsive to intranasal corticosteroids.</td>
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<td>5. Bachert et al. [17]</td>
<td>Two multicentre, randomized, double-blind, placebo-controlled, parallel-group phase 3 trials</td>
<td>• First trial: At least one study drug dose was administered to 143 CRSwNP patients in the Dupilumab group and 133 individuals in the placebo group. In the second study, 153 people received at least one Placebo dosage, 150 people received at least one dose of Dupilumab every two weeks, 145 people received at least one dose of Dupilumab every 2 weeks for the first 24 weeks, and then every week. 4 weeks after that. To evaluate the effectiveness and safety of Dupilumab in individuals with CRSwNP despite prior systemic steroid, surgical, or both treatments. Dupilumab decreased polypp size, sinus opacification, and severity of symptoms in adult patients with severe CRSwNP and was well tolerated. These outcomes demonstrate the advantages of including Dupilumab in the daily treatment regimen for individuals with severe CRSwNP who otherwise have few therapeutic options.</td>
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*Continued*
6. Gevaert et al. [18]  
**Clinical trial**  
- Patients in POLYP 1 (n = 148) and POLYP 2 (n = 127) demonstrated severe CRSwNP and significant QOL impairment, as shown by a mean NPS greater than 6 and SNOT-22 score of roughly 60.  
- Phase 3 trials assess omalizumab’s safety and effectiveness in CRSwNP (POLYP 1 and POLYP 2).  
In severe CRSwNP with poor response to intranasal corticosteroids, omalizumab dramatically improved endoscopic, clinical, and patient-reported outcomes and was well tolerated.

7. Gevaert et al. [19]  
**Patients (n = 249) in duplicate phase 3, randomized, placebo-controlled trials**  
- Received background nasal mometasone therapy along with open-label omalizumab therapy for 28 weeks before being monitored for an additional 24 weeks after stopping the omalizumab.  
- Omalizumab’s ongoing effectiveness, safety, and longevity of response in adults with CRSwNP  
were assessed. Through 52 weeks, coprimary and secondary outcomes showed further benefits in patients who kept taking omalizumab. Through week 52, patients who moved from placebo to omalizumab showed positive results across endpoints comparable to POLYP 1 and POLYP 2 at week 24. This trial’s efficacy and safety profile justify prolonged omalizumab treatment for CRSwNP with insufficient response to nasal corticosteroids for up to 1 year.

8. To compare the effectiveness of ESS with medical therapy alone in patients with CRSwNP, Lourijsen et al. [20]  
**Conducted a multicenter, RCT, controlled trial**  
- 238 with CRSwNP patients randomly assigned to ESS plus medical therapy (n = 121) or medical therapy (n = 117).  
- In patients with CRSwNP  
ESS combined with medical therapy is more effective than medical therapy alone.
rapid and sustained improvement in the sense of smell, alleviating a cardinal symptom of severe CRSwNP. Third, Laidlaw et al. [15] revealed that Dupilumab improved upper and lower airway outcome measures and HRQoL in patients with severe CRSwNP and comorbid asthma and was well tolerated. Finally, Laidlaw et al. [15] showed that in symptomatic CRSwNP refractory compared to intranasal corticosteroids patients, adding subcutaneous Dupilumab to mometasone furoate nasal spray decreased endoscopic nasal polyp size, sinus opacification, and severity of symptoms in comparison to mometasone alone. One of the most uncomfortable and difficult symptoms of CRSwNP is a loss or reduction in scent. In accordance with earlier publications about the significant burden associated with loss of smell in CRSwNP, our results identified “Decreased sense of smell/taste” as the most significant HRQoL item [23,24]. The findings of this study provide credence to the idea that asthma in people with CRSwNP appears to represent a spectrum of the same underlying type 2 inflammation-mediated disease. A bidirectional interaction between structural (such as an inflammatory response in the sinonasal and pulmonary compartments) and functional (such as upper and lower airflow) events are brought about by thin bronchial crosstalk [25]. Maspero et al. [26] observed a similar pattern in the phase 3 QUEST study for Dupilumab effectiveness in patients with uncontrolled, moderate-to-severe asthma, where those with comorbid CRS improved more quickly than the non-CRS category in terms of asthma control. The higher efficacy shown with comorbid disease may be because of Dupilumab’s ability to simultaneously manage the type 2 inflammation that underlies CRSwNP and asthma, improving both upper and lower airway outcomes. Gevaert et al. [18] and Gevaert et al. [19] reported the safety and efficacy of Omalizumab in managing chronic sinusitis in adult patients. Gevaert et al. [18] showed that positive outcomes on all endpoints were seen in participants who switched from placebo to Omalizumab through week 52, which were comparable to POLYP 1 and 2 at week 24. Gevaert et al. [19] claimed that this study’s efficacy and safety profile supported continued omalizumab treatment for CRSwNP with insufficient response to nasal corticosteroids for up to 1 year. The omalizumab-induced improvements reported here were comparable to the functional endoscopic sinus surgery-related improvements reported in a previous systematic review and meta-analysis by Le et al. [27] that included 3,048 patients. Our results thus corroborate those of Bidder et al. [28], who showed comparable gains in SNOT-22 score in individuals with CRSwNP who underwent surgery and omalizumab treatment. Lourijsen et al. [20] showed that when compared to Dupilumab and Omalizumab, ESS plus medical therapy was found to be more efficacious than medical therapy alone in patients with CRSwNP. ESS is possible when CRS is resistant to conventional treatment. In a multi-institutional prospective trial, Schlosser et al. [29] showed that ESS results in a better asthma-specific QOL and asthma control in patients with pre-existing asthma and CRS. Fewer patients in the ESS + medical therapy group suffered acute exacerbation of chronic rhinosinusitis in a recent RCT comparing ESS and medical therapy for CRS versus medical treatment alone. Additionally, the cumulative mean dose of systemic corticosteroids utilized by the ESS plus medical therapy group was less than half that of the medical therapy group [30]. A systematic review by Rimmer et al. [31] found no difference between the groups (ESS with topical steroids versus antibiotics plus high-dose topical steroids).

**Conclusion**

In this review, Dupilumab was well-tolerated and provided rapid, significant, and clinically meaningful improvements for patients with CRSwNP. In addition, it produced rapid and sustained improvement in the sense of smell, alleviating a cardinal symptom of severe CRSwNP. Patients with severe CRSwNP, and concomitant asthma responded better to Dupilumab regarding upper and lower airway outcome measures and HRQoL. When combined with mometasone furoate nasal spray, subcutaneous Dupilumab reduced endoscopic nasal polyp size, sinus opacification, and severity of symptoms in patients with symptomatic CRSwNP refractory in com intranasal corticosteroids. Regarding the safety and efficacy of Omalizumab in managing chronic sinusitis in adult patients, it was found that positive outcomes on all endpoints were seen in participants who switched from placebo to Omalizumab through week 52, which were comparable to POLYP 1 and 2 at week 24. This supported the continued omalizumab treatment for CRSwNP with insufficient response to nasal corticosteroids for up to 1 year. Furthermore, ESS plus medical therapy was found to be more efficacious than medical therapy alone in patients with CRSwNP.

**List of Abbreviations**

- **CRSwNP**: Chronic sinusitis and nasal polyposis
- **ESS**: Endoscopic sinus surgery
- **HRQoL**: Health-related quality of life

**Conflict of interest**

Not applicable.

**Funding**

None.

**Consent to participate**

Not applicable.

**Ethical approval**

Not applicable.

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**References**

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