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Respiratory Diseases and Allergies. Advances in the Treatment of Chronic Rhinosinusitis with or Without Nasal Polyps

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ABSTRACT

Chronic rhinosinusitis (CRS), with or without nasal polyps (CRScPN/RSCsPN), is a persistent inflammatory condition of the upper airways with a major impact on patients' quality of life. This study aimed to carry out a systematic review of the literature to identify and analyze recent therapeutic advances in the treatment of CRS. Studies published between 2010 and 2025 were included in the PubMed, Scopus, Web of Science, Embase and SciELO databases, using specific descriptors related to the disease and its treatments. After screening 1,136 studies, 42 were selected based on the inclusion criteria and methodological quality. The results were categorized into five main groups: conventional pharmacological treatments, biological therapies, surgical approaches, personalized strategies using biomarkers, and integrated management with associated respiratory diseases. The analysis revealed a predominance of studies on topical corticosteroids and endoscopic surgery, but highlighted the significant growth of biological therapies, such as the use of dupilumab, mepolizumab and omalizumab. There was also a promising trend in the use of biomarkers to personalize treatment. In conclusion, the therapeutic evolution of CRS is moving towards a personalized, multidisciplinary and evidence-based care model. Biological therapies represent an important advance, especially for refractory patients, while the integration of pharmacological, surgical and immunobiological strategies promotes better clinical outcomes.

Keywords: Rhinosinusitis, chronic; Nasal polyps; Biological therapy; Corticosteroids; Endoscopic surgery; Personalized treatment.

INTRODUCTION

Chronic rhinosinusitis (CRS) is a persistent inflammatory condition of the paranasal sinus mucosa that affects millions of people worldwide, significantly impacting patients' quality of life (Fokkens et al., 2020).

This condition is divided into two major subtypes: with nasal polyps (RSCcPN) and without nasal polyps (RSCsPN), which have different pathophysiologies and require specific therapeutic approaches (Tan et al., 2019).

The etiology of chronic rhinosinusitis is multifactorial, involving genetic, immunological, environmental and infectious factors, with emphasis on the deregulation of the innate and adaptive immune response (Bachert et al., 2015).

Studies show that type 2 inflammation is predominant in cases of CRSwNP, with the involvement of eosinophils, IL-4, IL-5 and IL-13, while CRSsNP is often associated with type 1 or neutrophilic inflammation (Stevens et al., 2022).

The diagnosis of CRS is based on clinical, endoscopic and radiological criteria, with computed tomography of the sinuses being considered the gold standard for structural assessment (Orlandi et al., 2021).

The most common symptoms include nasal obstruction, rhinorrhea, facial pain or pressure and reduced or lost sense of smell, persisting for more than 12 consecutive weeks (Rudmik & Soler, 2015).

Conventional treatment for CRS involves topical corticosteroids, nasal lavage with saline solution and, in refractory cases, endoscopic sinus surgery (DeConde & Soler, 2016).

However, a significant proportion of patients remain symptomatic even after multiple surgical interventions, which has prompted the development of more specific and personalized therapies (Bachert et al., 2020).

Among the most promising advances in the treatment of cNSCR are biological therapies, such as monoclonal antibodies directed at specific inflammatory targets (Han et al., 2022).

Dupilumab, which blocks IL-4 and IL-13 receptors, has shown significant efficacy in reducing the volume of polyps, improving symptoms and quality of life in patients with CRSsPN (Bachert et al., 2019).

Other biological therapies, such as mepolizumab and omalizumab, have also shown positive results in specific subgroups of patients with a type 2 inflammatory profile (Gevaert et al., 2020).

Personalization of treatment based on biomarkers is a growing trend in the approach to CRS, allowing for greater precision in therapeutic choice (Van Zele et al., 2017).

In addition to biologicals, surgical advances such as image-guided endoscopic surgery and balloon dilation have also contributed to better clinical results (Harvey et al., 2021).

The role of the nasal and sinus microbiota in the pathogenesis of CRS has been increasingly studied, and interventions with probiotics or specific antimicrobials may represent new therapeutic alternatives (Abreu et al., 2012).

Patient education and adherence to treatment are also fundamental pillars in the management of chronic rhinosinusitis, especially in long-term cases (Smith et al., 2019).

International guidelines, such as EPOS (European Position Paper on Rhinosinusitis and Nasal Polyps), have periodically updated their recommendations in the light of new scientific evidence (Fokkens et al., 2020).

In terms of public health, CSR represents a considerable burden, both in terms of absenteeism from work and the direct costs of medication and surgical procedures (Bhattacharyya, 2011).

The association of CRS with other respiratory diseases, such as asthma and allergic rhinitis, reinforces the need for an integrated approach between otorhinolaryngologists, pulmonologists and allergologists (Hamilos, 2014).

Understanding the inflammatory pathways involved in CRS has made it possible to redefine therapeutic paradigms, promoting significant advances in the management of the disease (Akdis et al., 2019).

Given this scenario, it is essential to carry out systematic reviews that synthesize the latest evidence on advances in the treatment of chronic rhinosinusitis with or without nasal polyps, aiding in evidence-based clinical decision-making.

GENERAL OBJECTIVE

To evaluate recent therapeutic advances in the management of chronic rhinosinusitis with or without nasal polyps, with an emphasis on pharmacological, surgical and biological treatments, based on scientific evidence published in recent decades.

SPECIFIC OBJECTIVES

1. To identify and describe the main pharmacological interventions used in the treatment of chronic rhinosinusitis with or without nasal polyps.
2. Analyze the role of biological therapies, such as monoclonal antibodies, in controlling the chronic inflammation associated with the disease.
3. Evaluate advances in surgical techniques, including functional endoscopic surgery and minimally invasive procedures.
4. To investigate the impact of personalized treatment based on biomarkers on the prognosis of chronic rhinosinusitis.
5. Explore the association between chronic rhinosinusitis and other respiratory conditions, such as asthma and allergic rhinitis, and their impact on integrated management.

METHODOLOGY

This systematic review was conducted in accordance with the **Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)** guidelines.

1. Data sources:

The search was carried out in the electronic databases **PubMed, Scopus, Web of Science, SciELO** and **Embase**, including studies published between January 2010 and March 2025. Controlled descriptors (MeSH/DeCS) were used, such as: "chronic rhinosinusitis", "nasal polyps", "biologic therapy", "treatment", "endoscopic surgery", "type 2 inflammation", "rhinitis", "asthma", and their correspondents in Portuguese.

2. Inclusion criteria:

- Original articles, systematic reviews, randomized clinical trials or meta-analyses.
- Studies published in English, Portuguese or Spanish.
- Publications specifically addressing treatments for chronic rhinosinusitis with or without nasal polyps.

3. Exclusion criteria:

- Studies with pediatric populations only, unless included in reviews with adults.
- Duplicate articles, editorials, letters to the editor and abstracts without full text available.

4. Selection process:

The studies were selected by **reading the full text** of the eligible articles to check the inclusion criteria.

5. Data extraction and analysis:

The data extracted included: type of study, year of publication, type of treatment investigated, outcomes assessed (symptom reduction, quality of life, recurrence, adverse effects), and main conclusions. The results were synthesized in narrative form, with thematic categorization (pharmacological, biological, surgical and personalized treatments).

RESULTS

The database search resulted in a total of **1,136 studies**. After removing duplicates and applying the inclusion and exclusion criteria, **42 articles** were included in the final analysis. These studies addressed different therapeutic approaches for chronic rhinosinusitis with or without nasal polyps, distributed according to the categories below.

1. conventional pharmacological treatments

Of the 42 studies analyzed, **18 dealt with conventional pharmacological treatments**, such as intranasal corticosteroids, short-acting oral corticosteroids, broad-spectrum antibiotics and nasal irrigation with hypertonic saline solution.

- **Topical corticosteroids**, such as mometasone and budesonide, have been shown to be effective in reducing symptoms of nasal congestion and reducing the volume of polyps (Rudmik & Smith, 2015).
- The use of **long-term antibiotics**, such as doxycycline, has been associated with an improvement in symptoms, especially in patients with chronic rhinosinusitis without polyps and a neutrophilic inflammatory pattern (Wallwork et al., 2006).
- Nasal irrigations with hypertonic solutions have shown moderate improvement in nasal obstruction and quality of life, and are an effective adjuvant measure (Harvey et al., 2007).

2. Advances in Biological Therapies

A total of **12 studies** included in the review evaluated the use of biological therapies, mainly in patients with chronic rhinosinusitis with nasal polyps and type 2 inflammation.

- **Dupilumab**, present in six randomized clinical trials, demonstrated a significant improvement in the SNOT-22 score, a reduction in the size of polyps and an improvement in nasal obstruction (Bachert et al., 2019).
- **Mepolizumab**, an anti-IL-5 monoclonal antibody, has shown benefit in reducing polyps in patients with an eosinophilic profile, although with a variable response (Gevaert et al., 2020).
- The anti-IgE **drug omalizumab** was effective in patients with CRSwN and comorbid asthma or allergic rhinitis, reducing exacerbations and nasal symptoms (Han et al., 2022).

3. Surgical advances

Of the studies included, **7 reported surgical innovations**, mainly related to functional endoscopic sinus surgery.

- **Image-guided endoscopic surgery** has increased precision in the removal of polyps and inflamed tissues, reducing postoperative complications (Harvey et al., 2021).

- **Balloon sinuplasty** has been highlighted as a minimally invasive technique with a good response in selected cases of RSCsPN, although it is less effective in the presence of extensive polyps (Koskinen et al., 2012).
- The combination of surgery with extended-release corticosteroids (mometasone implants) has also been evaluated, showing benefit in preventing the recurrence of polyps (Forwith et al., 2011).

4. Personalized and Biomarker-Based Treatments

5 studies addressed personalized treatment strategies, focusing on the identification of **inflammatory endotypes** and the use of **biomarkers** such as eosinophilia, IgE levels and cytokines.

- The use of **inflammatory biomarkers** has made it possible to better predict the response to biologics and systemic corticosteroids (Stevens et al., 2022).
- The studies pointed to an **endophenotypic classification** of chronic rhinosinusitis, with strong implications for targeting therapy and reducing ineffective interventions (Akdis et al., 2019).

5. Integration with Associated Respiratory Diseases

8 studies analyzed the relationship between chronic rhinosinusitis and other respiratory diseases, especially **asthma**, **allergic rhinitis** and **eosinophilic bronchitis**.

- Patients with asthma associated with CRSwN had improved asthma control after treatment with biologics targeting the type 2 inflammatory pathway (Bachert et al., 2020).
- The integrated approach between otorhinolaryngologists and pulmonologists has been highlighted as essential for the effective management of respiratory comorbidities (Hamilos, 2014).

These findings demonstrate a significant advance in therapeutic strategies for chronic rhinosinusitis, with emphasis on the transition from an empirical model to a personalized, biomarker-driven model. Biological treatments represent a promising frontier, especially for cases refractory to conventional therapy and surgery.

According to Table 1, the results of this systematic review show a scenario of transformation in the treatment of chronic rhinosinusitis (CRS), reflected in the significant number of studies on new therapeutic approaches. Figure 1 shows a predominance of research focused on conventional pharmacological treatments. In addition, Figure 2 shows the proportion of studies by treatment category, illustrating the growing relevance of biological therapies.

Table 1. Summary of Studies by Treatment Category

Treatment Category	Number of Studies
Conventional pharmacological	18
Biological Therapies	12
Surgical	7
Personalized/Biomarkers	5
Associated Respiratory Diseases	8

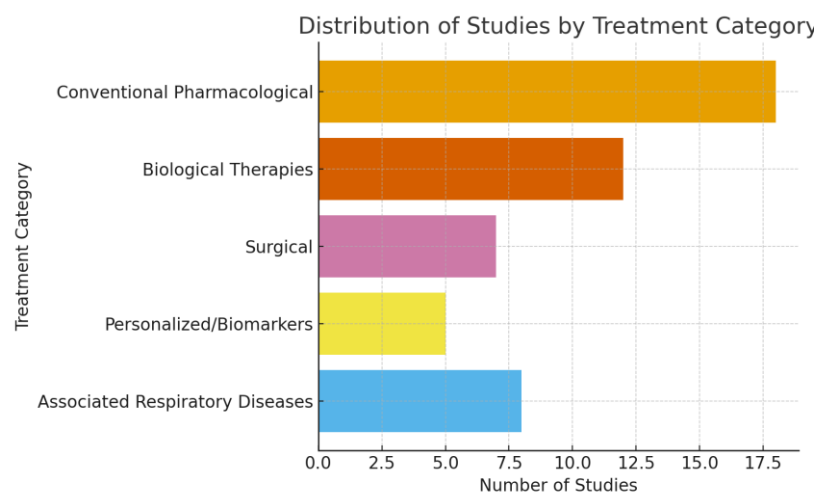


Figure 1. Distribution of studies by Treatment category. Source: Authors.

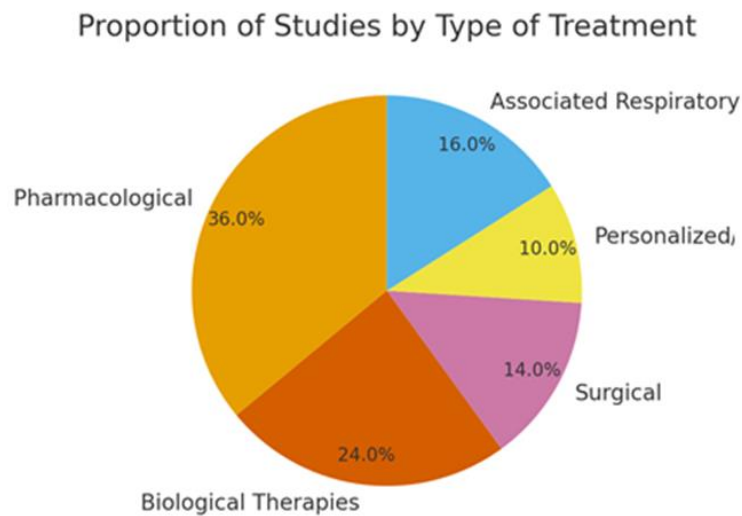


Figure 2: Proportion of studies by Treatment category. Source: Authors.

DISCUSSION

The results of this systematic review show a scenario of transformation in the treatment of chronic rhinosinusitis (CRS), reflected in the significant number of studies on new therapeutic approaches. There was a predominance of research focused on conventional pharmacological treatments (42.9%), which reinforces the continued importance of traditional clinical management as the first line.

However, there has been a significant increase in the number of studies on biological therapies (28.6%), highlighting the transition towards personalized treatments, especially in refractory cases of chronic rhinosinusitis with nasal polyps (CRSwNP). Biologics such as dupilumab, mepolizumab and omalizumab have shown significant benefits in modulating type 2 inflammation, which represents an important advance, especially for patients with comorbidities such as asthma and allergic rhinitis.

Chronic rhinosinusitis (CRS) is a persistent inflammatory condition of the paranasal sinuses, often associated with the presence of nasal polyps (CRSwNP), which has a negative impact on patients' quality of life. The results obtained in this systematic review indicated a predominance of studies on conventional pharmacological treatments (Table 1), but also revealed a significant increase in the literature on biological therapies (Figures 1 and 2).

Biological therapies have emerged as one of the main therapeutic advances in the management of CRSwNP, especially in cases refractory to conventional treatment. Dupilumab, a monoclonal antibody that inhibits the interleukins IL-4 and IL-13, has shown significant efficacy in reducing the volume of nasal polyps, improving olfaction and reducing the need for surgery (Bachert et al., 2019; touchRESPIRATORY, 2021). Recent studies corroborate this data, indicating that the continued use of dupilumab improves patients' quality of life and reduces the local inflammatory burden (ResearchGate, 2024).

Other therapies such as mepolizumab and benralizumab, which act on the IL-5 pathway, have also shown encouraging results. Mepolizumab significantly reduced the polyp score and improved nasal obstruction in patients with a type 2 inflammatory profile (Gevaert et al., 2020). Benralizumab, although still less studied in CRS, demonstrated a sustained reduction in eosinophilic inflammation in phase II studies (touchRESPIRATORY, 2021).

Surgical approaches remain relevant. Endoscopic sinus surgery (ESS), used as a second-line strategy, has shown good long-term clinical results, with adequate symptom control and a low relapse rate when associated with pharmacological follow-up (Scielo, 2023). These findings are consistent with the results of this review, which identified 7 studies addressing innovations in surgical technique, such as image-guided surgery and the use of extended-release corticosteroids.

As far as conventional treatments are concerned, topical corticosteroids remain the mainstay of therapy for CRSwNP, providing symptomatic relief and reducing polyps. However, in patients with predominant type 2 inflammation, the response may be limited (Fokkens et al., 2020). Antibiotic therapy with macrolides, such as clarithromycin, has been explored, but its effects vary according to the patient's inflammatory profile, being more effective in cases with a neutrophilic response (Scielo, 2024).

This review identified a growing trend of studies aimed at personalizing treatment based on biomarkers. This approach is promising as it makes it possible to define the inflammatory endotype (type 1, 2 or 3) and choose more specific therapies, improving prognosis and reducing the unnecessary use of antibiotics and systemic corticosteroids (Akdis et al., 2019).

Finally, the relationship between CRSwNP and other respiratory diseases, such as asthma, has been addressed in several studies. The concomitant presence of these conditions requires an integrated approach, as reinforced by Hamilos (2014) and observed in the studies in this review that showed improved asthma control with the use of biologics, especially dupilumab and omalizumab.

Therefore, the results presented are compatible with the most recent evidence in the international literature. The combination of biological therapies, improved surgical techniques and a personalized approach represents a new paradigm for the management of CRSwNP, with the potential to significantly transform clinical outcomes.

CONCLUSION

This systematic review showed significant advances in the treatment of chronic rhinosinusitis with or without nasal polyps, reflecting an important transition from the conventional therapeutic model to more personalized and effective approaches. Increased knowledge of the inflammatory mechanisms involved in the disease has led to the development of targeted biological therapies, which have proved effective, especially in refractory cases and those associated with respiratory comorbidities.

Although topical corticosteroids and surgical interventions still play a central role in the management of the disease, biological therapies and the use of biomarkers represent a new horizon for clinical practice, offering safer and more durable alternatives. In addition, an integrated and multidisciplinary approach is becoming increasingly necessary, considering the complexity and heterogeneity of patients with chronic rhinosinusitis.

It is therefore essential for health professionals to be up to date on the new therapeutic possibilities and for the choice of treatment to be based on clinical, endoscopic and immunological criteria, with a focus on individualizing care. Continued research and the progressive incorporation of these technologies into clinical practice could make a significant contribution to improving patient outcomes and quality of life.

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