Annals of Otolaryngology Head and Neck Surgery
Case Report (ISSN 2835-7132)

Impact of Systemic Corticosteroid and Antibiotic Use on Tissue Eosinophilia in Nasal Polyps of Patients with Chronic Rhinosinusitis

Cárita Lopes Macêdo[1*], Jordanna Lousek[1], Rogério Pezato[2], Wilder Alves[1], Claudiney Candido Costa[1], Hugo Valter Lisboa Ramos[1], Leandro Castro Velasco[1]

[1]Centro Estadual de Reabilitação e Readaptação Dr. Henrique Santillo, CRER, Goiânia, Goiás, Brazil

[2]Universidade Federal de São Paulo – UNIFESP, São Paulo, São Paulo, Brazil

Citation: Cárita Lopes Macêdo, Jordanna Lousek, Rogério Pezato, Wilder Alves, Claudiney Candido Costa, Hugo Valter Lisboa Ramos, et al. Impact of Systemic Corticosteroid and Antibiotic Use on Tissue Eosinophilia in Nasal Polyps of Patients with Chronic Rhinosinusitis. Annal of Otol Head and Neck Surg. 2025;4(6):1-6.

Received Date: 09 December, 2025; **Accepted Date:** 12 December, 2025; **Published Date:** 14 December, 2025

***Corresponding author:** Cárita Lopes Macêdo, Centro Estadual de Reabilitação e Readaptação Dr. Henrique Santillo, CRER Goiânia, Goiás, Brazil

ABSTRACT

Aim: To assess the impact of systemic corticosteroid and antibiotic therapy on tissue eosinophilia in nasal polyps of patients with Chronic Rhinosinusitis with Nasal Polyps (CRSwNP)

Methods: This prospective cohort study included adult patients with CRSwNP undergoing endoscopic sinus surgery (ESS) between May 2023 and September 2024 at the Centro de Reabilitação e Readaptação Dr. Henrique Santillo (CRER), Goiânia, Brazil. A nasal polyp biopsy was performed seven days before surgery, after which patients were prescribed oral prednisone and amoxicillin–clavulanate. During ESS, additional polyp fragments were collected for histopathological evaluation. All analyses were performed by experienced pathologists blinded to the timing of sample collection, with eosinophilic inflammation defined as >10 eosinophils/HPF.

Results: The study included 22 patients. The number of tissue eosinophils was significantly lower in intraoperative samples following the use of corticosteroids and antibiotics.

Conclusion: Systemic corticosteroid and antibiotic therapy prior to surgery, while improving operative conditions, may confound the histopathological classification of CRSwNP, with implications for prognosis and the use of biologics targeting type 2 inflammation.

Keywords: Chronic Rhinosinusitis; Nasal Polyps; Corticosteroids; Antibiotics;

INTRODUCTION

Chronic rhinosinusitis (CRS) is a persistent inflammatory condition of the nasal and paranasal sinus mucosa, clinically classified into two main groups: CRS with nasal polyps (CRSwNP) and CRS without nasal polyps (CRSsNP). This distinction is essential due to the clinical presentation, inflammatory profile, prognosis and response to treatment between the two subgroups [1]. While CRSsNP is usually associated with predominantly neutrophilic inflammation

and a more favorable disease course, CRSwNP-especially in cases with eosinophilic polyps-is characterized by more severe inflammation on both endoscopic and radiologic findings, along with higher recurrence rates and treatment resistance [2,3].

In recent years, the classification of CRS has undergone significant updates, particularly with the publication of the EPOS 2020 consensus, which introduced a broader approach based on disease phenotypes and endotypes. Unlike previous classifications that prioritized anatomical and clinical features, EPOS 2020 emphasizes the role of eosinophils as central inflammatory markers in CRSwNP [1].

Although eosinophils play a role in tissue repair and immune defense, the tissue damage they cause is believed to be the central pathophysiological mechanism in CRS. Their degranulation leads to tissue edema, epithelial desquamation, and fibrosis, contributing to the persistence of a chronic inflammatory state. Thus, tissue eosinophilia is considered a biomarker of severe and recurrent disease [4,5]. The recruitment, activation, and survival of eosinophils are driven by epithelial cytokines-especially IL- 4, IL-5, and IL-13-as well as complement proteins and other factors. There is evidence that eosinophils have a prolonged lifespan in nasal tissue due to the presence of local cytokines like IL-5 and granulocyte-macrophage colony-stimulating factor (GM-CSF), which protect them from apoptosis.[4]

CRSwNP demonstrates marked geographic variability in its pathophysiology. In Western countries such as the United States and Europe, type 2 inflammation with significant tissue eosinophilia predominates. In contrast, in many Asian countries, CRSwNP is often associated with a predominantly neutrophilic infiltrate [1]. This heterogeneity underscores the importance of both local and global studies to better understand the factors influencing the inflammatory profile of the disease.

The cutoff value for defining eosinophilic CRS based on tissue eosinophilia varies across the literature. Many studies, as well as EPOS 2020, adopt the threshold proposed by a 2010 study-≥10 eosinophils per high-power field (HPF) [1,6].

Corticosteroids remain the mainstay of CRSwNP management, both topical and systemic, reducing systemic eosinophil counts and inflammatory mediators such as IL-5 and eosinophil cationic protein (ECP) [2]. Endoscopic sinus surgery complements medical therapy by removing inflammatory burden, improving sinus ventilation, and enhancing topical drug delivery. Preoperative corticosteroids and antibiotics are frequently prescribed to reduce mucosal inflammation, improve surgical field visualization, and shorten operative time [7,8].

However, the influence of corticosteroids on eosinophil levels may interfere with the evaluation of these inflammatory markers. Quantifying eosinophils in nasal polyps without prior corticosteroid exposure may provide more accurate data on the pathophysiology of CRSwNP and its relationship with disease severity.

MATERIALS AND METHODS

The objective of the study was to assess the impact of systemic corticosteroid and antibiotic therapy on tissue eosinophilia in nasal polyps of patients with CRSwNP.

This prospective cohort study included adult patients (≥18 years) with a confirmed diagnosis of CRSwNP who underwent endoscopic sinus surgery (ESS) between May 2023 and September 2024 at the Centro de Reabilitação e Readaptação Dr. Henrique Santillo (CRER), Goiânia, Brazil. All participants provided written informed consent.

Inclusion criteria comprised:

- Clinical and endoscopic diagnosis of CRSwNP according to EPOS 2020 criteria [1].
  CRSwNP diagnostic criteria: Presence of two or more symptoms, one of which must be nasal obstruction/congestion or nasal discharge (anterior/posterior), possibly accompanied by facial pain/pressure and/or reduction or loss of smell, lasting for ≥12 weeks, with objective evidence of nasal polyps on nasal endoscopy and/or sinonasal inflammation on CT.
- Surgical indication for ESS.

Exclusion criteria were:

- Use of systemic corticosteroids within 30 days prior to the study protocol.
- Inability or refusal to undergo preoperative tissue collection.

Study protocol

At the preoperative consultation (seven days before ESS), a nasal polyp fragment was collected under local anesthesia and sent for histopathological evaluation. Following this, patients received a preoperative regimen of oral prednisone (40 mg/day for 5 days) and amoxicillin–clavulanate (875/125 mg twice daily for 7 days).

During ESS, additional nasal polyp fragments were obtained and submitted to the same pathology laboratory for eosinophil quantification. All analyses were performed by experienced pathologists blinded to the timing of sample collection. Eosinophil counts were expressed as the number of cells per high-power field (HPF, ×400). The inflammatory profile was categorized as eosinophilic when counts exceeded 10 eosinophils/HPF [1,6].

Variables were expressed as mean and standard deviation. A paired Student's t-test was used to compare the mean eosinophil counts between pre- and intraoperative samples. A p-value < 0.05 was considered statistically significant. Statistical analysis was performed using SAS 9.4 software.

RESULTS

The initial cohort of the study comprised 37 patients diagnosed with CRSwNP. Of these, 22 attended the preoperative consultation for the collection of the nasal polyp tissue fragment. The main reasons for non-participation preoperative stage were: the inability to present at the hospital facility at least seven days prior to the scheduled surgical procedure and the patients' refusal to undergo tissue fragment collection.

The final sample consisted of 22 patients with CRSwNP, of whom 50% were male and 50% were female. The mean age was 44 years (SD ± 13.17). Asthma was present in 54% of cases, 77% had no known drug allergies, and 86% had no history of previous sinonasal surgery.

Table 1 shows the mean eosinophil count in the nasal polyp in the preoperative and intraoperative periods. The mean eosinophil count in the intraoperative period was significantly lower than in the preoperative period (p = 0.0409).

Table 1: Comparison of mean eosinophil values in the preoperative and intraoperative periods

	Situation			
	Preoperative	**Intraoperative**	**Difference (Intra/Pre)**	**p-valor[2]**
Eosinophil count[1]	44,14 ± 35,08	29,23 ± 22,57	-14,91 ± 32,10	0,0409

1 Values expressed as mean ± standard deviation; ² Student's t-test

Overall, 77% of the patients exhibited an eosinophilic pattern (Figure 1), and 31% presented with more than 55 eosinophils per high-power field.

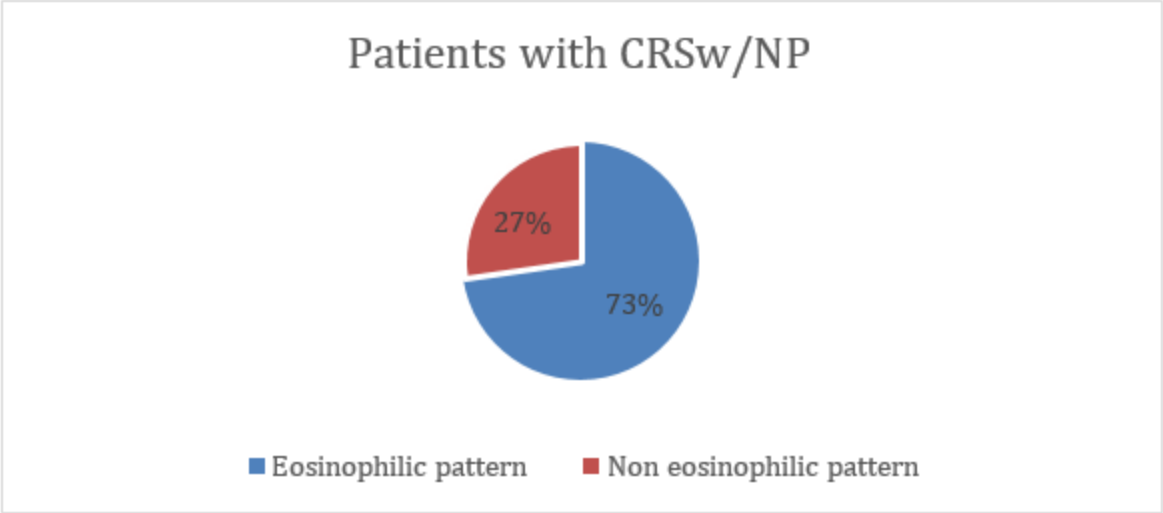

Figure 1: Distribution of eosinophilic vs. non-eosinophilic patterns in CRSwNP patients.

DISCUSSION AND CONCLUSION

This study demonstrated a significant reduction in tissue eosinophilia in nasal polyps following short-course systemic corticosteroid therapy and antibiotics, confirming previous evidence of corticosteroid effects on eosinophil-mediated inflammation. While several studies have reported reductions in inflammatory mediators and eosinophil counts with topical corticosteroid therapy [9-14], few have assessed pre- and post-treatment tissue eosinophilia after systemic corticosteroid administration. Our findings align with the limited available data showing that systemic corticosteroids reduce eosinophil infiltration [15,16].

The decrease in eosinophilia may occur through various mechanisms, including inhibition of eosinophil recruitment, suppression of their activation, and the promotion of cellular apoptosis. Corticosteroids directly induce eosinophil apoptosis and inhibit cytokine signaling pathways such as IL_3, IL_5, and granulocyte-macrophage colony- stimulating factor (GM-CSF), which are essential for eosinophil survival and recruitment [17].

Tissue eosinophilia can serve as a predictor of an increased likelihood of polyp recurrence after surgery. A meta-analysis suggested that >55 eosinophils/HPF is a predictor of nasal polyp recurrence [18]. In the present study, nearly one-third of patients met this threshold, underscoring the importance of pre-treatment histopathological evaluation.

All patients also received a short course of amoxicillin–clavulanate as part of the standard preoperative regimen. Although β-lactam antibiotics are not known to directly modulate eosinophilic inflammation, they may reduce bacterial load and local pro- inflammatory stimuli. Given the short duration and the mechanism of action of this drug class, its influence on tissue eosinophil counts is likely negligible compared to the potent anti-inflammatory effects of systemic corticosteroids.

Systemic corticosteroid and antibiotic therapy significantly reduced tissue eosinophil counts in nasal polyps of patients with CRSwNP.

Notably, systemic corticosteroid therapy before surgery—although beneficial in improving operative conditions-can confound the histopathological classification of CRSwNP. This may have implications for clinical decision-making, particularly when considering long-term prognosis and the potential use of biologic agents targeting type 2 inflammation.

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