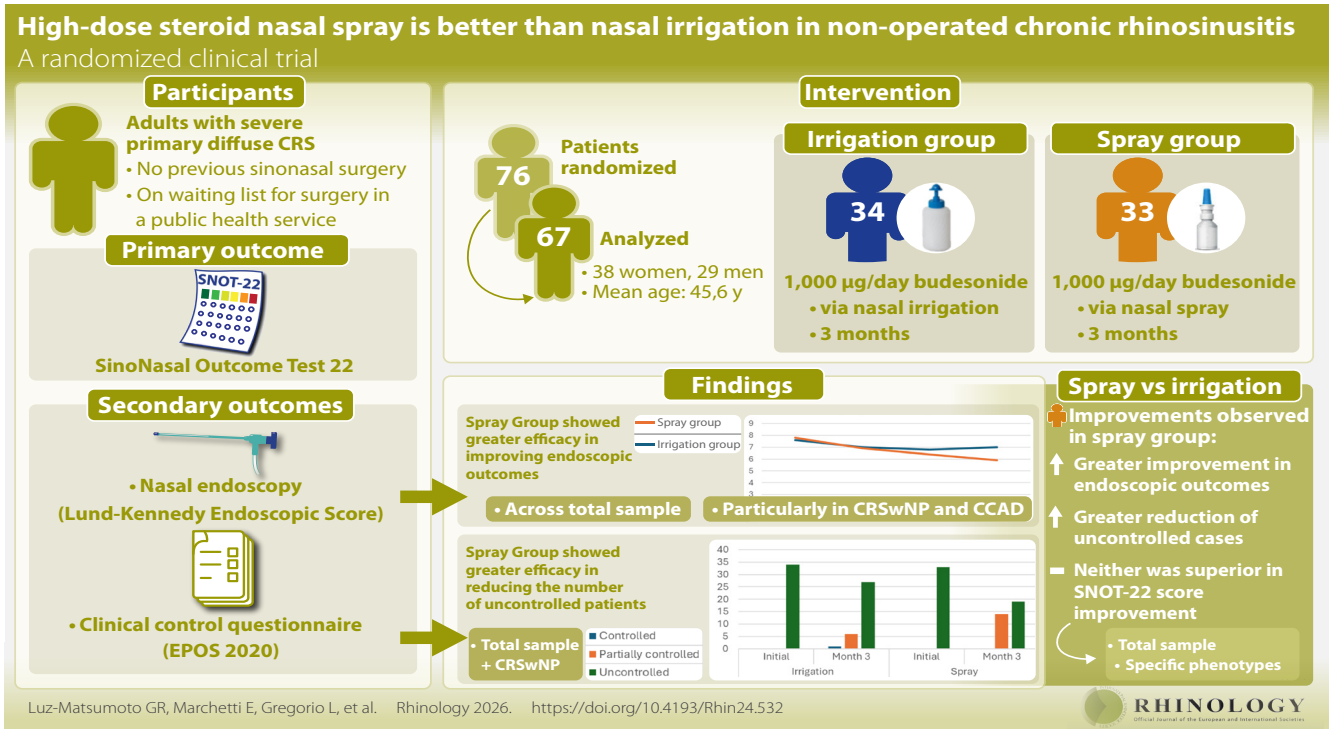
# High-dose steroid nasal spray is better than nasal irrigation in non-operated chronic rhinosinusitis: a randomized clinical trial

Gabriela Ricci Lima Luz-Matsumoto[1], Erika Cabernite Marchetti[1], Luciano Lobato Gregorio[1], Fabiano Mesquita Callegari[2], Eduardo Macoto Kosugi[1]

**Rhinology 64: 2,** 0 - 0, 2026
https://doi.org/10.4193/Rhin24.532




## Abstract

**Background**: To compare the efficacy of high-dose nasal steroid administered via high-volume irrigation versus spray delivery in patients with chronic rhinosinusitis (CRS) who have not undergone previous sinonasal surgery. **Methodology**: A double-blind randomized clinical trial was conducted. The study comprised two groups receiving 1,000 µg/day of nasal budesonide through two distinct methods over a 3-month period: irrigation and spray delivery. Patients with severe CRS who had never undergone surgery and were on the waiting list for surgery in a public health service were included. Primary outcomes included changes in quality-of-life scores and secondary outcomes included changes in clinical control questionnaire results and nasal endoscopy findings. Assessments were conducted on the total sample, CRS with nasal polyps (CRSwNP), CRS without nasal polyps (CRSsNP), and according to the newly defined phenotypes of diffuse primary CRS (central compartment atopic disease [CCAD], eosinophilic chronic rhinosinusitis [eCRS] and non-eosinophilic CRS [neCRS]). **Results**: Sixth-seven patients completed the study, with 34 in the Irrigation Group and 33 in the Spray Group. The Spray Group demonstrated superior efficacy in improving endoscopic outcomes across the total sample, particularly among CRSwNP and CCAD. No treatment demonstrated superiority in improving the SNOT-22 score. Furthermore, the Spray Group revealed greater efficacy in reducing the number of uncontrolled patients, as evaluated by the clinical control questionnaire, both in the total sample and CRSwNP. **Conclusions**: High-dose steroid nasal spray outperformed high-volume steroid nasal irrigation in improving nasal endoscopy outcomes across the total sample, especially in CRSwNP and CCAD.

**Key words**: steroids, nasal lavage, nasal sprays, preoperative period, sinusitis

## Introduction

The current approach to managing chronic rhinosinusitis (CRS) emphasizes disease control, primarily through nasal medications, a treatment that is low-cost and has proven safety for use. This strategy underscores systemic medications should not be routinely utilized owing to their potential adverse effects, particularly with oral steroids, and high costs associated with treatments such as immunobiologics. Additionally, endoscopic sinus surgery (ESS) plays a crucial role by enhancing the penetration of topical therapies to the inflamed mucosa of the paranasal sinuses [1-3].

High-volume steroid nasal irrigation is widely employed and has demonstrated superior efficacy compared to steroid nasal spray in post-operative [4]. Although the surgical status of the ostia influences solution penetration, certain medical and socioeconomic factors, such as public healthcare waiting lists, may delay ESS [5]. These patients require treatment, with nasal saline irrigation and steroid nasal spray being the most highly recommended treatment modalities for those who have not undergone surgery yet [1,2].

Nasal irrigation achieves superior sinus penetration than sprays in healthy, non-operated individuals [6,7], although less than in operated sinuses [8]. Consequently, in non-operated patients, steroid nasal irrigation is considered a viable treatment option for CRS, although nasal spray remains the first-line therapy [3]. Furthermore, corticosteroids for nasal irrigation are more expensive than corticosteroids in spray, making it important to understand the most cost-effective delivery methods for corticosteroids in non-operated patients. Thus, it is essential to compare delivery methods for high dose steroid in patients with CRS who have not undergone previous sinonasal surgery.

Thus, this study aims to compare the efficacy of high-dose nasal steroid administered via high-volume nasal irrigation versus nasal spray in managing CRS, measured by a quality-of-life questionnaire, a disease control questionnaire and nasal endoscopy, in patients with primary diffuse CRS without previous sinonasal surgery who are awaiting ESS.

## Materials and methods

### Study population

The sample included patients with primary diffuse CRS according to the European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS)2020 [2]. These patients had failed initial appropriate medical therapy, which included 400 µg/day of steroid nasal spray and nasal saline irrigation for 90 days, in addition to a 15-day oral steroid cycle (prednisone or prednisolone 1 mg/kg/day for 5 days, followed by tapering doses). They were candidates for surgical intervention, with SinoNasal Outcome Test 22 (SNOT-22) [9] questionnaire score ≥ 40 points and Lund–Kennedy endoscopic score (LKES) [10,11] indicating diseased mucosa (at least one of following: presence of polyps [except grade 3, due to inability to perform nasal irrigation], polypoid edema, and/or thick/mucopurulent secretions). These patients were on the waiting list for surgery and had no history of previous ESS.

Pregnant and breastfeeding women, secondary CRS, and prior diagnosis of sinonasal neoplasms were excluded. Patients with absolute contraindications for the use of steroids, those who had taken systemic steroids within 30 days prior to study enrollment, individuals who had received immunobiological (anti-IgE, anti-IL-5 or anti-IL-4/13) within 180 days before study inclusion, and those who used systemic steroids during the study period were also excluded.

### Study design

This study received approval by the local Research Ethics Committee under number 27729519.0.000.5505 and registered at ensaiosclinicos.gov.br under number RBR-7qt7vk. A double-blind, randomized clinical trial was conducted comparing two groups receiving 1,000 µg/day of budesonide administered via either nasal irrigation or nasal spray.

After considering the inclusion and exclusion criteria, patients were instructed to abstain from steroids, both nasal and systemic, for 1 month and to perform high-volume nasal irrigation with 250 mL/day of isotonic alkaline saline solution. This washout phase aimed to eliminate the effects of previously used topical medication and rule out improvement solely due to high-volume nasal irrigation. Eligible patients meeting all the inclusion criteria (which remained with SNOT-22 ≥ 40 and diseased mucosa after washout phase) were randomly assigned to treatment groups using block randomization with blocks of six patients following the washout phase.

Patients received a kit containing a 15-mL dropper bottle, four 25-mL spray applicator bottles, a nasal irrigation device consisting of a 125-mL squeeze bottle with Soniclear® nozzle and ninety sachets to produce isotonic alkaline solution containing 1.03 g of sodium chloride and 1.59 g of sodium bicarbonate.

For patients assigned to the "steroid irrigation + placebo spray" treatment (Irrigation Group), the dropper bottle contained 1% budesonide diluted in 5% glycerin solution, while the spray bottle contained 5% glycerin solution. In patients assigned to the "Placebo irrigation + steroid spray" (Spray Group), the dropper bottle contained 5% glycerin solution, while the spray bottle contained budesonide 100 µg/actuation. The kits were visually indistinguishable, and the medications were diluted in 5% glycerin, ensuring similarity in taste and smell.

To prepare an isotonic alkaline solution, patients were instructed to dissolve one sachet in 250 mL of filtered water. Thereafter, two drops from the dropper bottle were applied to the saline solution and 125 mL was instilled into each nostril once daily using the nasal irrigation device. Following nasal irrigation, patients were instructed to administer 5 sprays from the nasal spray bottle into each nostril. This treatment was administered once daily

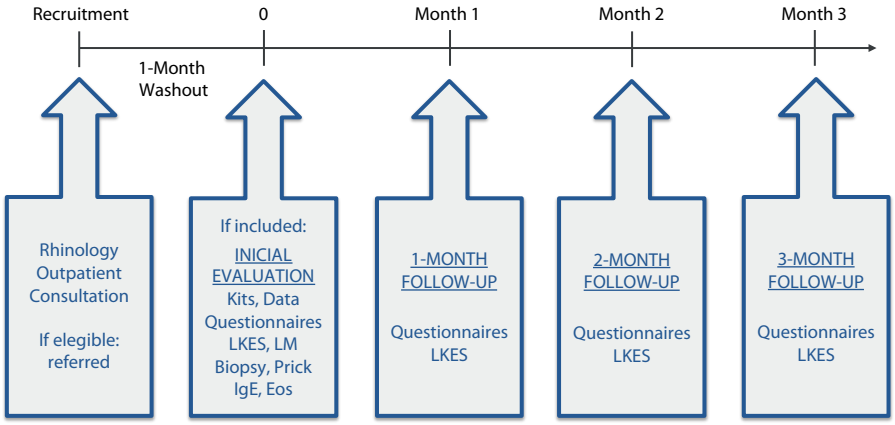



Figure 1. Timeline. LKES = Lund-Kennedy Endoscopic Score; LM = Lund-Mackay Computed Tomography Score; Prick = Skin prick test; IgE = Total immunoglobulin E; Eos = Serum eosinofilia.

for 3 months, with patients undergoing monthly reassessments. During the initial consultation, clinical and epidemiological characteristics were collected along with CT evaluation using the Lund–Mackay CT score [12]. Endophenotyping tests were conducted, including skin allergy testing, serum eosinophilia, total immunoglobulin E (IgE), and biopsy of polyp or middle turbinate mucosa for tissue eosinophil count (conducted after washout). The diagnostic criteria for distinguishing the newly defined phenotypes of diffuse primary CRS were: 1) central compartment atopic disease (CCAD): presence of tissue eosinophilia and characteristic CT findings with the halo sign (partial or total opacification of the ethmoid sinuses and obstruction of the ostiomeatal complex, with mild involvement of the maxillary sinuses and no involvement of the frontal and/or sphenoid sinuses); 2) eosinophilic chronic rhinosinusitis (eCRS): presence of tissue eosinophilia and CT with diffuse involvement (partial or total opacification of the maxillary, frontal, and/or sphenoid sinuses); 3) non-eosinophilic CRS (neCRS): absence of tissue eosinophilia [13]. Reference values for the biomarkers were: tissue eosinophilia ≥ 10 eosinophils per high-power field (eos/HPF), serum eosinophilia ≥ 250/µL and IgE ≥ 100 IU/mL [14]. SNOT-22(9) and the EPOS2020 Clinical Control Questionnaire [2] were administered at all consultations, in addition to the LKES [10,11]. A timeline figure is presented in Figure 1.

### Statistical analysis

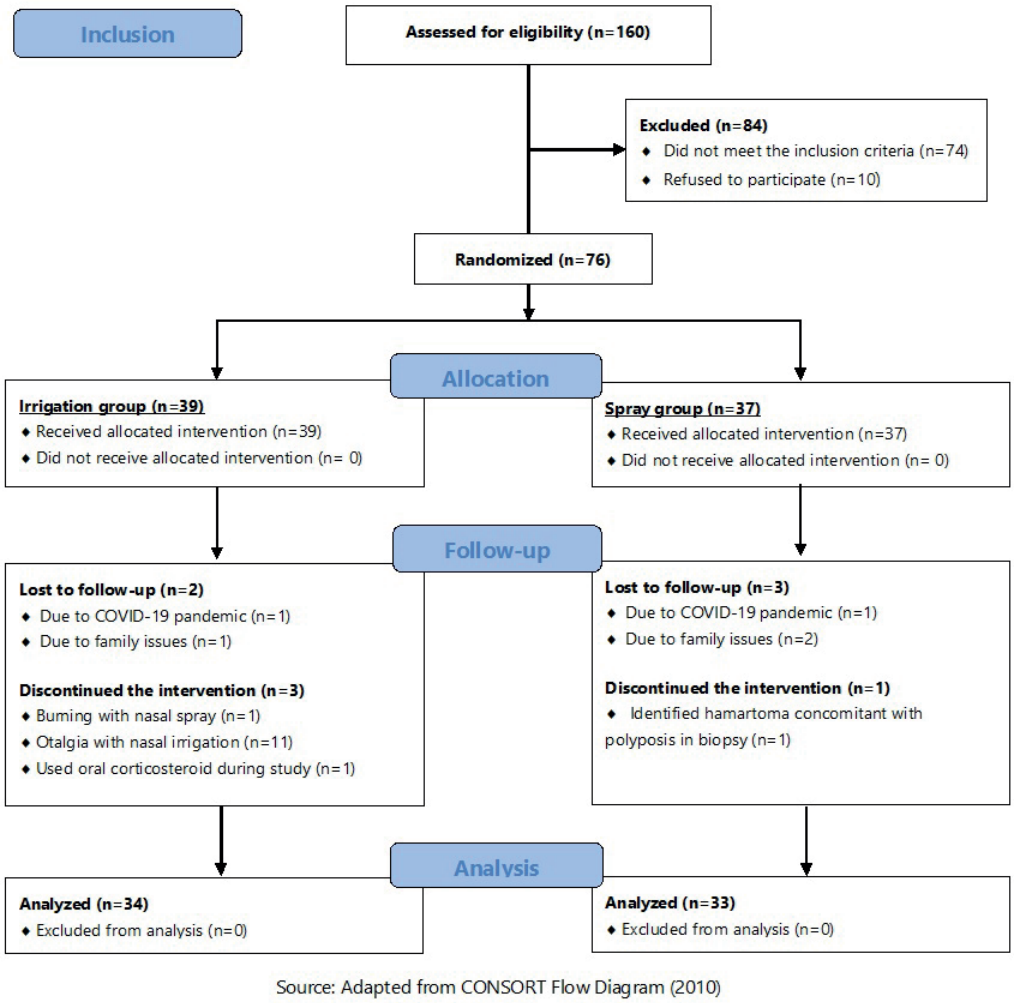
The sample size calculation was conducted to compare SNOT-22 scores' difference between groups. Based on the previously published studies and using a significance level of 5% (α = 0.05) and a statistical power of 80%, the required sample size for this study was calculated to be 60 patients to detect an minimal clinically important difference (MCID) of 14 points or greater in SNOT-22 from before to after treatment between the 2 treatment groups (considering the MCID found in the validation of the SNOT-22 questionnaire in our country) [9]. Assuming a 10% loss rate, 33 patients would need to be recruited in each group. Assessments were conducted between treatment groups for the total sample, CRS with nasal polyps (CRSwNP), CRS without nasal polyps (CRSsNP), and according to the newly defined phenotypes of diffuse primary CRS [13]. Quantitative parameters were expressed as mean ± standard deviation. Categorical variables were expressed as absolute frequencies (n) and percentages (%). Quantitative parameters were compared using Student's t-test or Mann–Whitney test, depending on data normality as measured by the Kolmogorov–Smirnov test. The association between the qualitative variables was evaluated using Pearson's chi square test or Fisher's exact test. Two tailed tests were conducted for all the analyses. The level of significance was set at $p \leq 0.05$. The software used was SPSS version 25.0.

## Results

A total of 76 patients were included and randomized, with 39 in the Irrigation Group and 37 in the Spray Group. Two patients in the Irrigation Group and three in the Spray Group lost follow-up, while three patients in the Irrigation Group and one in the Spray Group discontinued the intervention. Consequently, 67 patients completed the study, with 34 in the Irrigation Group and 33 in the Spray Group. The recruitment and randomization flowchart are presented in Figure 2.

The mean age of the total sample was 45.6 years (±13.4), with a predominance of women in the Irrigation Group (70.6% vs. 42.4%; p=0.02*). All investigated parameters related to comorbidities and CRS data were equally distributed between groups in the total sample. Majority of patients had polyps, accounting for 80.6% of cases. Regarding the new CRS phenotypes, 28.4% of the sample was classified as CCAD, 35.8% as eCRS, and 35.8% as neCRS. The clinical and epidemiological characteristics of the total sample are presented in Table 1.

Regarding tomographic, laboratory, histopathological, and allergy features in the total sample, the only parameter that de-




Source: Adapted from CONSORT Flow Diagram (2010)

Figure 2. Recruitment and randomization flowchart.

monstrated unequal distribution between groups was total IgE, with the Spray Group containing more patients with elevated total IgE (75% vs. 51.5%; p=0.05*). The tomographic, laboratory, histopathological, and allergy features of the total sample are presented in Table 2.

Regarding primary outcome in the total sample, there were no differences in the SNOT-22 between the groups at the end of the treatments (Irrigation: 69.1 to 51.6; Spray: 69.0 to 49.2; p=0.490). Regarding secondary outcomes in the total sample, in the LKES, only the Spray Group revealed significant improvement, demonstrating superiority compared to Irrigation (Irrigation: 7.6 to 7.0; Spray: 7.8 to 5.9, p=0.030*). The SNOT-22 and LKES comparisons are presented in Table 3.

The EPOS2020 Clinical Control Questionnaire was analysed according to the number of controlled, partially controlled, and uncontrolled individuals. The Spray Group showed superior disease control results at the end of the third month in the total sample, with a significant reduction in the number of uncontrolled cases (Irrigation: 34 to 27; Spray: 33 to 19; p=0.05*). The analysis of the EPOS2020 Clinical Control Questionnaire questionnaire can be seen in Table 4.

Adverse events were reported in 8.9% of the total sample, with no significant difference observed between the Irrigation Group (14.7%) and Spray Group (3%) (p=0.21). Within the Irrigation Group, the documented adverse events included otalgia in one patient, which led to discontinuation, a burning sensation in the nasal cavity during spray application in three patients (with one discontinuing) and sneezing during spray application in one patient. In the Spray Group, only one patient reported experiencing aural fullness.

Considering CRSwNP and CRSsNP patients, neither treatment demonstrated superiority in improving SNOT-22 (CRSwNP = Irrigation: 69.8 to 54.1; Spray: 69.6 to 47.8; p=0.131 / CRSsNP = Irrigation: 67.0 to 44.6; Spray: 64.8 to 59.5; p=0.076). The LKES exhibited significant improvement only in the Spray Group for CRSwNP patients, with superior results compared to irrigation (Irrigation: 8.3 to 7.7; Spray: 8.1 to 6.0; p=0.037*). Neither treatment significantly improved the LKES in CRSsNP sample (Irrigation: 5.8 to 5.1; Spray: 5.8 to 5.3; p=0798).

For the EPOS2020 Clinical Control Questionnaire in CRSwNP,

Table 1. Clinical and epidemiological characteristics of the total sample.

| Characteristics | | Irrigation n=34 | | Spray n=33 | | Total n=67 | | Test | p-value |
|---|---|---|---|---|---|---|---|---|---|
| Age (years) | M/SD | 47,6 | [12,3] | 43,1 | [14,3] | 45,6 | [13,4] | T | 0,18 |
| Female | n/% | 24 | [70,6] | 14 | [42,4] | 38 | [56,7] | Chi | 0,02* |
| Comorbidities | | | | | | | | | |
| Asthma | | | | | | | | | |
| Childhood | n/% | 3 | [8,8] | 2 | [6,1] | 5 | [7,5] | Fisher | 0,80 |
| Adult-onset | n/% | 10 | [29,4] | 12 | [36,4] | 22 | [32,8] | | |
| Allergic rhinitis | | | | | | | | | |
| Limited to childhood | n/% | 1 | [2,9] | 1 | [3,0] | 2 | [3,0] | Fisher | 0,10 |
| Since childhood | n/% | 14 | [41,2] | 16 | [48,5] | 30 | [44,8] | | |
| Adult-onset | n/% | 0 | [0] | 4 | [12,1] | 4 | [6,0] | | |
| Dermatitis/Conjunctivitis | n/% | 4 | [11,8] | 1 | [3,0] | 5 | [7,5] | Fisher | 0,36 |
| N-ERD | n/% | 3 | [8,8] | 5 | [15,2] | 8 | [11,9] | Fisher | 0,48 |
| CRS data | | | | | | | | | |
| Phenotypes | | | | | | | | | |
| CRSwNP | n/% | 25 | [73,5] | 29 | [87,9] | 54 | [80,6] | Fisher | 0,21 |
| CRSsNP | n/% | 9 | [26,5] | 4 | [12,1] | 13 | [19,4] | | |
| CCAD | n/% | 10 | [29,4] | 9 | [27,3] | 19 | [28,4] | Fisher | 0,50 |
| eCRS | n/% | 10 | [29,4] | 14 | [42,4] | 24 | [35,8] | | |
| neCRS | n/% | 14 | [41,2] | 10 | [30,3] | 24 | [35,8] | | |
| Onset age (years) | | | | | | | | | |
| <20 | n/% | 4 | [11,8] | 8 | [24,2] | 12 | [17,9] | Fisher | 0,32 |
| 20-30 | n/% | 1 | [2,9] | 3 | [9,1] | 4 | [6,0] | | |
| 31-50 | n/% | 24 | [70,6] | 20 | [60,6] | 44 | [65,7] | | |
| >50 | n/% | 5 | [14,7] | 2 | [6,1] | 7 | [10,4] | | |
| Obesity | | | | | | | | | |
| Overweight | n/% | 15 | [44,1] | 9 | [27,3] | 24 | [35,8] | Fisher | 0,15 |
| Obesity (I-III) | n/% | 9 | [26,5] | 9 | [27,3] | 18 | [26,9] | | |
| Smoking | | | | | | | | | |
| Active smoking | n/% | 2 | [5,9] | 0 | [0] | 2 | [3,0] | Fisher | 0,60 |
| Former smoker | n/% | 6 | [17,6] | 7 | [21,2] | 13 | [19,4] | | |
| Baseline | | | | | | | | | |
| SNOT-22 | M/SD | 69,1 | [17,8] | 69,0 | [18,4] | 69,1 | [17,9] | Mann | 0,980 |
| LKES | M/SD | 7,6 | [1,7] | 7,8 | [1,7] | 7,7 | [1,7] | Mann | 0,582 |
| Uncontrolled EPOS 2020 | n/% | 34 | [100] | 33 | [100] | 67 | [100] | Fisher | N/A |

M=mean; SD=standard deviation; n=number; %=percentage; T=Student's t-test; Chi=Pearson's chi-square test; Fisher=Fisher's exact test; Mann=Mann-Whitney U test; N-ERD=NSAID exacerbated respiratory disease; CRS=chronic rhinosinusitis; CRSwNP=chronic rhinosinusitis with nasal polyps; CRSsNP=chronic rhinosinusitis without nasal polyps; CCAD=central compartment atopic disease; eCRS=eosinophilic chronic rhinosinusitis; neCRS=non-eosinophilic chronic rhinosinusitis; SNOT-22=SinoNasal Outcome Test-22 (Brazilian Portuguese); LKES=Lund-Kennedy Endoscopic Score; EPOS 2020=EPOS 2020 Clinical Control Questionnaire; N/A=not applicable.

there was a statistically significant reduction in the number of uncontrolled patients in the Spray Group (Irrigation: 25 to 21; Spray: 20 to 15; p=0.02*). In the CRSsNP sample, no significant improvement was noted among uncontrolled patients (EPOS2020), with scores decreasing from 9 to 6 in the Irrigation Group and remaining unchanged at 4 in the Spray Group (p = 0.66).

When patients were analysed according to the new CRS phe-

Table 2. Tomographic, laboratory, histopathological and allergy characteristics of the total sample.

| Characteristics | | Irrigation n=34 | | Spray n=33 | | Total n=67 | | Test | p-value |
|---|---|---|---|---|---|---|---|---|---|
| Lund-Mackay score | M/SD | 17,8 | [3,6] | 18,6 | [4,1] | 18,2 | [3,8] | Mann | 0,26 |
| CT pattern | | | | | | | | | |
| Central | n/% | 13 | [38,2] | 13 | [39,4] | 26 | [38,8] | Chi | 1,0 |
| Diffuse | n/% | 21 | [61,8] | 20 | [60,6] | 41 | [61,2] | | |
| Immunoglobulin E (n=65) | | | | | | | | | |
| <100 | n/% | 16 | [48,5] | 8 | [25,0] | 24 | [36,9] | Chi | 0,05* |
| ≥100 | n/% | 17 | [51,5] | 24 | [75,0] | 41 | [63,1] | | |
| Serum eosinophils (n=66) | | | | | | | | | |
| <250 | n/% | 7 | [21,2] | 6 | [18,2] | 13 | [19,7] | Chi | 0,76 |
| ≥250 | n/% | 26 | [78,8] | 27 | [81,8] | 53 | [80,3] | | |
| Tissue eosinophils | | | | | | | | | |
| <10 | n/% | 13 | [38,2] | 11 | [33,3] | 24 | [35,8] | Chi | 0,06 |
| 10-100 | n/% | 16 | [47,1] | 9 | [27,3] | 25 | [37,3] | | |
| ≥100 | n/% | 5 | [14,7] | 13 | [39,4] | 18 | [26,9] | | |
| Prick-test | | | | | | | | | |
| Negative | n/% | 17 | [50,0] | 12 | [36,4] | 29 | [43,3] | Chi | 0,39 |
| Positive (1-2) | n/% | 11 | [32,4] | 16 | [48,5] | 27 | [40,3] | | |
| Multi-sensitive (>2) | n/% | 6 | [17,6] | 5 | [15,2] | 11 | [16,4] | | |

M=mean; SD=standard deviation; n=number; %=percentage; Chi=Pearson's chi-square test; Mann=Mann-Whitney U test.

notypes, SNOT-22 scores did not show statistically significant differences between interventions in any of the three new CRS phenotypes. The LKES, in turn, revealed a significant improvement in the Spray Group for CCAD, outperforming Irrigation (Irrigation: 6.9 to 7.3; Spray: 7.8 to 5.9, p=0.04*), but no significant difference was found between the groups in LKES for eCRS and neCRS.

Regarding the EPOS2020 Clinical Control Questionnaire, no statistically significant changes in the clinical control status were observed at the end of the third month for any of the interventions across the three new CRS phenotypes.

## Discussion

This study is the first to elucidate the clinical response to high-dose nasal steroid (1,000 µg/day of budesonide via irrigation or nasal spray) in patients with CRS who have never undergone surgery. Only one randomized clinical trial has compared steroid nasal irrigation to steroid nasal spray in non-operated patients without polyps; however, equivalent doses of nasal steroid were not utilized [15]. Furthermore, this study is the first to compare the clinical response to nasal steroid treatments across the newly identified phenotypes of diffuse primary CRS.

In this study, which included non-operated patients with significant inflammation in both paranasal sinuses and nasal cavities, steroid nasal spray outperformed steroid nasal irrigation in improving nasal endoscopy scores. This was noted in the total sample, in the nasal polyps' sample, and in the CCAD's sample (subpopulations with more pronounced inflammation in the central nasal cavity region). These outcomes confirm the efficacy of sprays as a nasal treatment, rather than sinus treatment, due to its known low penetration into the paranasal sinuses [8,16,17] but proper reach to middle turbinates and middle meatus [18].

Another three factors must be considered: 1) drug delivered by spray remains longer on the nasal mucosa than by irrigation; 2) the present study utilized higher doses of steroid nasal spray than the regular spray treatment, possibly allowing the persistence of a higher local concentration of the drug and leading to better results for Spray Group; and 3) high-volume nasal irrigation was used before the spray in both groups, which may have allowed for better contact of the corticosteroid spray with the nasal mucosa after the mucus was mechanically removed. The benefits of saline irrigation go beyond the mechanical action of mucus cleansing, also contributing to the improvement of mucociliary function, the reduction of mucosal edema and the elimination of inflammatory mediators [19].

Although endoscopic scores were usually weakly related to patients' symptoms and quality of life measures, we consider that endoscopic assessment could play an important role in CRS

Table 3. Comparison of SNOT-22 and Lund–Kennedy endoscopic scores between pre-treatment evaluation and after 1, 2 and 3 months of treatment in the total sample and chronic rhinosinusitis phenotypes.

| | | Pre | | | | 1 month | | | | 2 months | | | | 3 months | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Irrigation | | Spray | | Irrigation | | Spray | | Irrigation | | Spray | | Irrigation | | Spray | |
| **Total sample** | | | | | | | | | | | | | | | | | |
| SNOT-22 | M/SD | 69,1 | [17,8] | 69,0 | [18,4] | 57,0 | [23,3] | 54,3 | [24,1] | 54,8 | [26,0] | 50,8 | [21,2] | 51,6 | [24,6] | 49,2 | [24,1] |
| | p-value1 | | | | | | | | 0,7782 | | | | 0,3603 | | | | 0,4904 |
| LKES | M/SD | 7,6 | [1,7] | 7,8 | [1,7] | 7,0 | [2,0] | 6,9 | [2,6] | 6,8 | [2,3] | 6,4 | [2,5] | 7,0 | [2,7] | 5,9 | [2,5] |
| | p-value1 | | | | | | | | 0,2212 | | | | 0,1833 | | | | 0,0304* |
| **CRSwNP** | | | | | | | | | | | | | | | | | |
| SNOT-22 | M/SD | 69,8 | [18,8] | 69,6 | [18,9] | 56,1 | [24,3] | 53,1 | [23,5] | 58,5 | [26,4] | 49,7 | [21,0] | 54,1 | [25,9] | 47,8 | [24,4] |
| | p-value1 | | | | | | | | 0,6832 | | | | 0,0603 | | | | 0,1314 |
| LKES | M/SD | 8,3 | [1,4] | 8,1 | [1,7] | 7,6 | [1,9] | 7,0 | [2,8] | 7,6 | [2,1] | 6,5 | [2,7] | 7,7 | [2,9] | 6,0 | [2,6] |
| | p-value1 | | | | | | | | 0,1892 | | | | 0,0763 | | | | 0,0374* |
| **CRSsNP** | | | | | | | | | | | | | | | | | |
| SNOT-22 | M/SD | 67,0 | [15,3] | 64,8 | [16,0] | 59,4 | [21,7] | 62,8 | [30,6] | 44,4 | [23,2] | 58,3 | [24,3] | 44,6 | [20,4] | 59,5 | [21,0] |
| | p-value1 | | | | | | | | 0,3512 | | | | 0,1413 | | | | 0,0764 |
| LKES | M/SD | 5,8 | [0,4] | 5,8 | [0,5] | 5,4 | [1,3] | 5,8 | [0,5] | 4,6 | [0,7] | 5,3 | [1,0] | 5,1 | [1,1] | 5,3 | [1,1] |
| | p-value1 | | | | | | | | 0,4502 | | | | 0,1883 | | | | 0,7984 |
| **CCAD** | | | | | | | | | | | | | | | | | |
| SNOT-22 | M/SD | 68,1 | [14,2] | 71,1 | [19,2] | 48,1 | [15,2] | 54,1 | [30,2] | 52,1 | [17,5] | 57,3 | [24,1] | 50,1 | [13,8] | 55,4 | [24,3] |
| | p-value1 | | | | | | | | 0,7432 | | | | 0,7443 | | | | 0,8704 |
| LKES | M/SD | 6,9 | 1,2 | 7,8 | 1,4 | 6,6 | 1,6 | 6,0 | 2,3 | 6,7 | 1,7 | 5,1 | 1,6 | 7,3 | 2,6 | 5,9 | 2,5 |
| | p-value1 | | | | | | | | 0,0732 | | | | 0,0043* | | | | 0,0374* |
| **eCRS** | | | | | | | | | | | | | | | | | |
| SNOT-22 | M/SD | 81,6 | [16,2] | 75,4 | [17,1] | 64,5 | [22,1] | 64,7 | [16,1] | 68,0 | [25,8] | 55,9 | [16,9] | 65,9 | [25,2] | 55,0 | [23,5] |
| | p-value1 | | | | | | | | 0,5002 | | | | 0,1773 | | | | 0,2914 |
| LKES | M/SD | 9,2 | [1,2] | 8,5 | [1,7] | 7,9 | [2,3] | 8,3 | [2,9] | 8,5 | [2,3] | 7,7 | [2,6] | 8,8 | [3,2] | 7,2 | [2,2] |
| | p-value1 | | | | | | | | 0,5842 | | | | 0,6953 | | | | 0,2744 |
| **neCRS** | | | | | | | | | | | | | | | | | |
| SNOT-22 | M/SD | 60,9 | [17,0] | 58,3 | [16,1] | 57,9 | [27,9] | 39,8 | [21,9] | 47,2 | [29,1] | 37,7 | [19,7] | 42,4 | [26,7] | 35,5 | [20,8] |
| | p-value1 | | | | | | | | 0,1202 | | | | 0,4123 | | | | 0,7474 |
| LKES | M/SD | 7 | [1,5] | 6,9 | [1,9] | 6,6 | [1,8] | 5,7 | [1,4] | 5,6 | [1,9] | 5,6 | [2,4] | 5,5 | [1,5] | 4,2 | [1,9 |
| | p-value1 | | | | | | | | 0,1802 | | | | 0,9763 | | | | 0,1804 |

[1] Mann-Whitney U test; [2] Comparison before and after 1 month; [3] Comparison before and after 2 months; [4] Comparison before and after 3 months; M=mean; SD=standard deviation; SNOT-22=SinoNasal Outcome Test-22 (Brazilian Portuguese); LKES=Lund-Kennedy Endoscopic Score. CRSwNP=chronic rhinosinusitis with nasal polyps; CRSsNP=chronic rhinosinusitis without nasal polyps; CCAD=central compartment atopic disease; eCRS=eosinophilic chronic rhinosinusitis; neCRS=non-eosinophilic chronic rhinosinusitis.

disease control, as previously stated in EPOS2012 and EPOS2020 Clinical Control of Disease Assessment and NOSE modified staging system [2, 20]. Moreover, endoscopic findings could even bring early detections of inflammatory changes prior to symptoms, becoming a warning sign for possible loss of disease control [21].

Herein, in SNOT-22 scores, neither treatment demonstrated superiority over the other. Jiramongkolchai et al. (2020) [15] found similar results in the SNOT-22 evaluation of patients with CRS without polyps who had never undergone surgery, with no superiority between the treatments (mometasone nasal irrigation and nasal spray). SNOT-22 is an essential tool for clinical assessment and measuring the quality of life in patients with CRS, often exhibiting changes following nasal endoscopy [22]. Due to the brief follow-up period, our findings were likely more pronounced in demonstrating superiority among interventions

Table 4. Evaluation of clinical control using the EPOS 2020 questionnaire.

| Characteristics | Pre | 1 month | 2 months | 3 months | Pre | 1 month | 2 months | 3 months |
|---|---|---|---|---|---|---|---|---|
| Total sample | | | | | | | | |
| Controlled | 0 | 0 | 1 (2.9) | 1 (2.9) | 0 | 0 | 0 | 0 |
| Partially controlled | 0 | 4 (11.8) | 9 (26.5) | 6 (17.6) | 0 | 6 (18.2) | 5 (15.2) | 14 (42.4) |
| Uncontrolled | 34 (100) | 30 (88.2) | 24 (70.6) | 27 (79.4) | 33 (100) | 27 (81.8) | 28 (84.8) | 19 (57.6) |
| | | | | | | | p¶ = | 0.05* |
| CCAD | | | | | | | | |
| Controlled | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Partially controlled | 0 | 2 (20.0) | 4 (40.0) | 1 (10.0) | 0 | 2 (22.2) | 2 (22.2) | 3 (33.3) |
| Uncontrolled | 10 (100) | 8 (80.0) | 6 (60.0) | 9 (90.0) | 9 (100) | 7 (77.8) | 7 (77.8) | 6 (66.7) |
| | | | | | | | p¶ = | 0.30 |
| eCRS | | | | | | | | |
| Controlled | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Partially controlled | 0 | 1 (10.0) | 1 (10.0) | 1 (10.0) | 0 | 0 | 1 (7.1) | 5 (35.7) |
| Uncontrolled | 10 (100) | 9 (90.0) | 9 (90.0) | 9 (90.0) | 14 (100) | 14 (100) | 13 (92.9) | 9 (64.3) |
| | | | | | | | p¶ = | 0.34 |
| neCRS | | | | | | | | |
| Controlled | 0 | 0 | 1 (7.1) | 1 (7.1) | 0 | 0 | 0 | 0 |
| Partially controlled | 0 | 1 (7.1) | 4 (28.6) | 4 (28.6) | 0 | 4 (40.0) | 2 (20.0) | 6 (60.0) |
| Uncontrolled | 14 (100) | 13 (92.9) | 9 (64.3) | 9 (64.3) | 10 (100) | 6 (60.0) | 8 (80.0) | 4 (40.0) |
| | | | | | | | p¶ = | 0.21 |
| CRSwNP | | | | | | | | |
| Controlled | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Partially controlled | 0 | 3 (12.0) | 6 (24.0) | 4 (16.0) | 0 | 5 (17.2) | 5 (17.2) | 14 (48.3) |
| Uncontrolled | 25 (100) | 22 (88.0) | 19 (76.0) | 21 (84.0) | 29 (100) | 24 (82.8) | 24 (82.8) | 15 (51.7) |
| | | | | | | | p¶ = | 0.02* |
| CRSsNP | | | | | | | | |
| Controlled | 0 | 0 | 1 (11.1) | 1 (11.1) | 0 | 0 | 0 | 0 |
| Partially controlled | 0 | 1 (11.1) | 3 (33.3) | 2 (22.2) | 0 | 1 (25.0) | 0 | 0 |
| Uncontrolled | 9 (100) | 8 (88.9) | 5 (55.6) | 6 (66.7) | 4 (100) | 3 (75.0) | 4 (100) | 4 (100) |
| | | | | | | | p¶ = | 0.66 |

¶ Association between disease control and groups at 3 months. CRSwNP=chronic rhinosinusitis with nasal polyps; CRSsNP=chronic rhinosinusitis without nasal polyps; CCAD=central compartment atopic disease; eCRS=eosinophilic chronic rhinosinusitis; neCRS=non-eosinophilic chronic rhinosinusitis.

in endoscopy rather than in SNOT-22 scores.

The presence or absence of nasal polyps was initially used to phenotype CRS, while endotyping aimed to better understand the underlying pathophysiological mechanisms. In Western populations, a predominance of type 2 response in patients with polyps (characterized by elevated eosinophils levels) and non-type 2 response in patients without polyps (characterized by increased neutrophil levels) have been documented [23]. In this sample, CRSwNP presented improvement in nasal endoscopy in the Spray Group. In patients with CRSsNP (19.4% of our patients), neither treatment modality yielded significant improvements in nasal endoscopy scores. These outcomes align with a previous Brazilian study, which presented that both steroid nasal irrigation and nasal spray failed to enhance endoscopy scores or SNOT-22 scores in patients without polyps [24].

Recent publications have focused on characterizing clinical criteria and biomarkers to differentiate the profiles of the new phenotypes of diffuse primary CRS [13]. All three phenotypes did

not demonstrate superiority in the improvement of SNOT-22 at the end of the treatments. The Spray Group demonstrated superiority in improving LKES in CCAD. DelGaudio et al. (2017) [25] described CCAD when examining atopic patients using nasal endoscopy, revealing polypoid degeneration of the middle turbinate or polyps affecting the middle turbinate, superior turbinate, and postero-superior nasal septum. We attribute the superiority of high-dose steroid nasal spray in improving endoscopic outcomes to its efficient targeting of the central area, which exhibits greater inflammation in these patients. eCRS, in turn, is widely known as a challenging disease to treat, often characterized by treatment failure and polyp recurrence following ESS [26]. The current sample with eCRS exhibited no significant improvement in LKES with any of the treatments, underscoring the challenge in managing the eosinophilic variant and the importance of ESS in these patients. Moreover, a Brazilian multicenter study demonstrated that the inflammatory profile of CRS in this population is mixed. Thus, the classification into eosinophilic and non-eosinophilic patterns may be of less importance in this situation [27].

The use of high-dose intranasal steroid is considered an off-label treatment for CRS due to concerns regarding systemic absorption and side effects. However, multiple studies analysing the effect of steroid nasal irrigation on the hypothalamic-pituitary axis have found no evidence of adrenal dysfunction with short-term or long-term use (ranging from 4 weeks to 12 months) [15,28-30]. Similarly, no studies to date have exhibited a significant increase in intraocular pressure or cataract formation in patients using steroid nasal irrigation [31-33].

Randomized controlled trials are widely regarded as the gold standard study design. However, they also face challenges, including participant dropout and loss to follow up. In this study, compliance was monitored biweekly through messaging, offering guidance and adjustments on the correct use of devices when needed. The primary limitation of the study was the short treatment period. In addition to this, other limitations of the study were: the inclusion of patients with more severe disease who had already failed appropriate medical therapy; the use of high-volume saline irrigation in both study arms, which by itself may have led to symptom improvement; and the underpowering of the results from the subgroup analyses, due to the low number of patients in phenotypes subgroups.

## Conclusion

A high-dose steroid nasal spray demonstrated greater efficacy than a high-volume steroid nasal irrigation in improving nasal endoscopy outcomes, both across the entire sample and specifically in CRSwNP and CCAD. Additionally, it reduced the number of uncontrolled cases in the overall sample and among CRSwNP patients. Neither intervention was superior in improving SNOT-22 scores across the entire sample or within specific phenotypes.

## Author contributions

GRLLM, ECM and LLG concepted the study and collected the data. FMC collected the data and analysed the biopsies. GRLLM analysed and interpreted the data and wrote the paper. EMK concepted the study, interpreted the data and critically revised this paper.

## Acknowledgments

We gratefully acknowledge the São Paulo State Research Foundation (FAPESP) for funding this study and to the Coordination for the Improvement of Higher Education Personnel (CAPES) for providing the doctoral scholarship.

## Conflict of interest

The authors declare no conflict of interest.

## Funding

This study was supported by São Paulo State Research Foundation (FAPESP).

## References

1. Rosenfeld RM, Piccirillo JF, Chandrasekhar SS, et al. Clinical practice guideline (update): adult sinusitis. Otolaryngol Head Neck Surg 2015; 152(2 Suppl): S1–39.
2. Fokkens WJ, Lund VJ, Hopkins C, et al. European position paper on rhinosinusitis and nasal polyps 2020. Rhinology 2020; 58(Suppl S29): 1–464.
3. Orlandi RR, Kingdom TT, Smith TL, et al. International consensus statement on allergy and rhinology: rhinosinusitis 2021. Int Forum Allergy Rhinol 2021; 11(3): 213-739.
4. Harvey RJ, Snidvongs K, Kalish LH, Oakley GM, Sacks R. Steroid nasal irrigations are more effective than simple sprays in a randomized double-blinded placebo-controlled trial for chronic rhinosinusitis after sinus surgery. Int Forum Allergy Rhinol 2018; 8(4): 461-470.
5. Sarmento Junior KM, Tomita S, Kos A. The problem of waiting lines for otorhinolaryngology surgeries in public services. Braz J Otorhinolaryngol 2005; 71(3): 256–62.
6. Wormald PJ, Cain T, Oates L, Hawke L, Wong I. A comparative study of three methods of nasal irrigation. Laryngoscope 2004; 114(12): 2224–2227.
7. Doellman M, Chen PG, McMains KC, Sarber KM, Weitzel EK. Sinus penetration of saline solution irrigation and atomizer in a cadaveric polyp and allergic fungal sinusitis model. Allergy Rhinol (Providence) 2015; 6(1): 8-11.
8. Harvey RJ, Debnath N, Srubiski A, Bleier B, Schlosser RJ. Fluid residuals and drug exposure in nasal irrigation. Otolaryngol Head Neck Surg 2009; 141(6): 757-761.
9. Kosugi EM, Chen VG, da Fonseca VMG, Cursino MMP, Neto JAM, Gregório LC. Translation, cross-cultural adaptation and validation of SinoNasal Outcome Test (SNOT): 22 to Brazilian Portuguese. Braz J Otorhinolaryngol 2011; 77(5): 663-669.
10. Lund VJ, Kennedy DW. Staging for rhinosinusitis. Otolaryngol Head Neck Surg 1997; 117(3 Pt 2): S35–40.
11. Lund VJ, Flood J, Sykes AP, Richards DH. Effect of fluticasone in severe polyposis. Arch Otolaryngol Head Neck Surg 1998; 124(5): 513-518.

12. Lund VJ, Mackay IS. Staging in rhinosinusitis. Rhinology 1993; 31(4): 183.814.
13. Grayson JW, Cavada M, Harvey RJ. Clinically relevant phenotypes in chronic rhinosinusitis. J Otolaryngol Head Neck Surg 2019; 48(1): 23.
14. Anselmo-Lima WT, Tamashiro E, Romano FR, et al. Guideline for the use of immunobiologicals in chronic rhinosinusitis with nasal polyps (CRSwNP) in Brazil. Braz J Otorhinolaryngol. 2022; 88(3): 471-480.
15. Jiramongkolchai P, Peterson A, Kallogjeri D, et al. Randomized clinical trial to evaluate mometasone lavage vs spray for patients with chronic rhinosinusitis without nasal polyps who have not undergone sinus surgery. Int Forum Allergy Rhinol 2020; 10(8): 936-943.
16. Snidvongs K, Chaowanapanja P, Aeumjaturapat S, Chusakul S, Praweswararat P. Does nasal irrigation enter paranasal sinuses in chronic rhinosinusitis? Am J Rhinol 2008; 22(5): 483-486.
17. Grobler A, Weitzel EK, Buele A, et al. Pre- and postoperative sinus penetration of nasal irrigation. Laryngoscope 2008; 118(11): 2078-2081.
18. Lam K, Tan BK, Lavin JM, Meen E, Conley DB. Comparison of nasal sprays and irrigations in the delivery of topical agents to the olfactory mucosa. Laryngoscope 2013; 123(12): 2950-2957.
19. Bastier PL, Lechot A, Bordenave L, et al. Nasal irrigation: From empiricism to evidence-based medicine. A review. Eur Ann Otorhinolaryngol Head Neck Dis. 2015; 132(5): 281-285.
20. Snidvongs K, Heller GZ, Sacks R, Harvey RJ. Validity of European position paper on rhinosinusitis disease control assessment and modifications in chronic rhinosinusitis. Otolaryngol Head Neck Surg. 2014; 150(3):479–86.
21. McCoul ED, Ganeshan V, Nguyen T. Nasal endoscopy: What have we been missing? Int Forum Allergy Rhinol. 2024; 14: 1277-81).
22. Kosugi EM, Moussalem GF, Simões JC, et al. Topical therapy with high-volume budesonide nasal irrigations in difficult-to-treat chronic rhinosinusitis. Braz J Otorhinolaryngol. 2016; 82(2): 191-197.
23. Fujieda S, Imoto Y, Kato Y, et al. Eosinophilic chronic rhinosinusitis. Allergol Int. 2019; 68(4): 403–412.
24. Luz-Matsumoto GR, Cabernite-Marchetti E, Sasaki LSK, et al. Nasal irrigation with steroids in Brazil: the clinical response of 1% compounded budesonide drops and betamethasone cream. Braz J Otorhinolaryngol 2022; 88 (Suppl 5): S32-S41.
25. DelGaudio JM, Loftus PA, Hamizan AW, Harvey RJ, Wise SK. Central compartment atopic disease. Am J Rhinol Allergy 2017; 31(4): 228-234.
26. Ho J, Hamizan AW, Alvarado R, Rimmer J, Sewell WA, Harvey RJ. Systemic predictors of eosinophilic chronic rhinosinusitis. Am J Rhinol Allergy 2018; 32(4): 252-257.
27. Romano FR, Valera FCP, Fornazieri MA, et al. Inflammatory profile of chronic rhinosinusitis with nasal polyp patients in Brazil: Multicenter study. Otolaryngol Head Neck Surg 2024; 171(5): 1552-1561.
28. Sachanandani NS, Piccirillo JF, Kramper MA, Thawley SE, Vlahiotis A. The effect of nasally administered budesonide respules on adrenal cortex function in patients with chronic rhinosinusitis. Arch Otolaryngol Head Neck 2009; 135(3): 303-307.
29. Welch KC, Thaler ER, Doghramji LL, Palmer JN, Chiu AG. The effects of serum and urinary cortisol levels of topical intranasal irrigations with budesonide added to saline in patients with recurrent polyposis after endoscopic sinus surgery. Am J Rhinol Allergy 2010; 24(1): 26-28.
30. Smith KA, French G, Mechor B, Rudmik L. Safety of long-term high-volume sinonasal budesonide irrigations for chronic rhinosinusitis. Int Forum Allergy Rhinol 2016; 6(3): 228-232.
31. Rotenberg BW, Zhang I, Arra I, Payton KB. Postoperative care for Samter's triad patients undergoing endoscopic sinus surgery: a double-blinded, randomized controlled trial. Laryngoscope 2011; 121(12): 2702-2705.
32. Soudry E, Wang J, Vaezeafshar R, Katznelson L, Hwang PH. Safety analysis of long-term budesonide nasal irrigations in patients with chronic rhinosinusitis post endoscopic sinus surgery. Int Forum Allergy Rhinol 2016; 6(6): 568-572.
33. Seiberling KA, Chang DF, Nyirady J, Park F, Church CA. Effect of intranasal budesonide irrigations on intraocular pressure. Int Forum Allergy Rhinol 2013; 3(9): 704-707.



Gabriela Ricci Lima Luz-Matsumoto
Department of Otorhinolaryngology and
Head and Neck Surgery
Federal University of São Paulo
Paulista School of Medicine
Rua Dr. Alceu de Campos Rodrigues
46 – Conjunto 161
Vila Nova Conceição
São Paulo 04544-000.
State of São Paulo
Brazil

Tel: +55 11 981831276
E-mail: gabirll@yahoo.com.br



Gabriela Ricci Lima Luz-Matsumoto[1], Erika Cabernite Marchetti[1], Luciano Lobato Gregorio[1], Fabiano Mesquita Callegari[2], Eduardo Macoto Kosugi[1]

[1] Rhinology Sector, Department of Otorhinolaryngology and Head and Neck Surgery, Federal University of São Paulo - Paulista School of Medicine, São Paulo, state of São Paulo, Brazil

[2] Department of Pathology, Federal University of São Paulo - Paulista School of Medicine, São Paulo, state of São Paulo, Brazil



**Rhinology 64: 2,** 0 - 0, 2026
https://doi.org/10.4193/Rhin24.532

**Received for publication:**
December 10, 2024
**Accepted:** November 13, 2025

**Associate Editor:**
Ahmad Sedaghat