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Intralesional versus Systemic Corticosteroid Therapy for Nasal Polyps in Chronic Rhinosinusitis: Clinical Outcomes Study

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العلاج بالكورتيكوستيرويد داخل الآفة (موضعي) مقابل العلاج الجهازي للزوائل الأنفية في التهاب الجيوب الأنفية المزمن: دراسة النتائج السريرية

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Abstract:
IPSI is defined as the local delivery of steroids directly into sinonasal polyposis in the management of diseases associated with CRSwNP. It should be noted that IPSI differs from systemic steroids treatment in terms of direct effect and lack of side effects due to administration of the drug. Here, we examine how IPSI and SC treatment differ in their effectiveness and efficacy when used in patients with CRSwNP. In total, 100 participants with a diagnosis of CRSwNP were enrolled in this prospective study and randomly assigned into two treatment groups. Healthy tackles to the polyps were added to IPSI every 2 weeks to 250 mcg/250 ml in sinus for 3 times in the first group and in the second group budesonide was injected directly into the polyps at 250 mcg/250 ml, once every 2 weeks for three times. The latter were given oral prednisolone at a rate of 1 mg/kg/day for three days, after which it was lowered to 5 mg/day for two weeks. Both the IPSI and SCs treatments had positive effects on the health status of the CRSwNP patients. Following SCs therapy, the nasal polyp volume decreased more (8.67 ± 2.6 vs. 10.15 ± 3.01, $p < 0.001$), the sense of smell improved (27.32 ± 10.68 vs. 23.32 ± 10.05, $p < 0.001$), and the SNOT-22 value decreased (36.32 ± 9.13 vs. 45.7 ± 12.66, $p < 0.001$).

Keywords: CRSwNP; Intrapolyp steroid injection; Intralesional budesonide; Systemic corticosteroids; SNOT-22; Serum cortisol; Quality of life; Lund-Mackay score.

الملخص
يُعرف الحقن الستيرويدي داخل الزوائل الأنفية (IPSI) بأنه الإعطاء الموضعي للستيرويدات مباشرة في الزوائل الأنفية الجيبية كجزء من إدارة الأمراض المرتبطة بالتهاب الجيوب الأنفية المزمن المصحوب بزوائل أنفية (CRSwNP). وتجدر الإشارة إلى أن الحقن الستيرويدي داخل الزوائل يختلف عن علاج الستيرويدات الجهازية من حيث التأثير المباشر وغياب الآثار الجانبية الناتجة عن طريقة إعطاء الدواء. هنا، قمنا بفحص كيفية اختلاف الحقن الستيرويدي داخل الزوائل والعلاج بالستيرويدات الجهازية (SC) من حيث الفعالية والكفاءة عند استخدامهما لدى مرضى التهاب الجيوب الأنفية المزمن المصحوب بزوائل

أنفية. في المجموع، تم إدراج 100 مشارك ممن تم تشخيص إصابتهم بـ CRSwNP في هذه الدراسة الاستباقية، وتم تعيينهم عشوائياً في مجموعتي علاج. تلقت المجموعة الأولى حقناً ستيرويدياً داخل الزوائل كل أسبوعين بجرعة 250 ميكروجرام/250 مل في الجيوب الأنفية لثلاث مرات، بينما في المجموعة الثانية، تم حقن بوديسونيد مباشرة في الزوائل بجرعة 250 ميكروجرام/250 مل، مرة كل أسبوعين لثلاث مرات. وقد أعطيت المجموعة الأخيرة بريدنيزولون عن طريق الفم بمعدل 1 مجم/كجم/يوم لمدة ثلاثة أيام، وبعد ذلك تم خفض الجرعة إلى 5 مجم/يوم لمدة أسبوعين. كان لكل من الحقن الستيرويدي داخل الزوائل والعلاج بالستيرويدات الجهازية آثار إيجابية على الحالة الصحية لمرضى CRSwNP. بعد العلاج بالستيرويدات الجهازية، انخفض حجم الزوائل الأنفية بشكل أكبر (8.67 ± 2.6 مقابل 10.15 ± 3.01، $p < 0.001$)، وتحسنت حاسة الشم (27.32 ± 10.68 مقابل 23.32 ± 10.05، $p < 0.001$)، وانخفضت قيمة اختبار SNOT-22 (36.32 ± 9.13 مقابل 45.7 ± 12.66، $p < 0.001$).

الكلمات المفتاحية: التهاب الجيوب الأنفية المزمن المصحوب بزوائل أنفية (CRSwNP)؛ الحقن الستيرويدي داخل الزوائل؛ بوديسونيد داخل الآفة؛ الستيرويدات القشرية الجهازية؛ اختبار SNOT-22؛ كورتيزول المصل؛ جودة الحياة؛ مقياس لوند-ماكاي.

Introduction:

CRSwNP is a chronic inflammatory condition of the mucosa lining of the nasal cavity and the paranasal sinuses which consists of the growth of benign polypoid tissue along the inner lining of the nasal cavity [1]. It tends to weigh heavily on patients' quality of life, largely through symptoms such as nasal obstruction, reduced or absent sense of smell, facial pressure, and rhinorrhoea [2]. However, despite the many possible causes or etiological factors that have been suggested to be at the center of the disease, CRSwNP is still viewed as a complex disease that is still not fully understood [3]. The reason behind this is that there are several factors involved in its pathogenesis such as inflammation mediators, immunological disorders, tissue changes, biofilms, genetics, and environment [4-6].

The immunopathology of CRSwNP is dominated by type-2 inflammation, in which the cytokines IL-4, IL-5, and IL-13 are upregulated, eosinophils accumulate throughout the sinonasal mucosa, and local IgE production rises within the diseased tissue [4]. At the same time, the expression of tight junction proteins and the decrease in the number of ciliated cells of the nasal mucosa reduces the barrier function and facilitates the passage of inhaled allergens and microorganisms into the body, maintaining the inflammatory process [7]. Structural reorganization of the affected tissue, culminating in polyp outgrowth, is likewise a hallmark of the disease process. Despite research linking nasal polyps' development to epithelial to mesenchymal transition, the cause of polypogenesis is unknown [8]. The impacted area with nasal polyps formation includes edema, hyperplasia, fibroblast accumulation, and extra cellular matrix deposition [9].

The conventional methods of treatment entail the use of INCS, systemic corticosteroids (SCs), saline nasal irrigation, and surgical management [1,10]. The application of INCS directly is widely known to be one of the main approaches in the treatment of CRSwNP, which provides effective anti-inflammatory effects without causing any side effects related to the use of systemic SCs [11]. It has been proved that the INCS application can effectively manage the symptoms related to polypgenesis, nasal obstruction, and hyposmia [12]. Nevertheless, some reports indicated a number of limitations caused by the INCS application in patients with extensive polypgenesis or inflammatory reaction [13]. Another approach in the treatment of CRswNP is the administration of SCs, which is mainly used in patients having aggravation of disease and in those who recalcitrant to INCS therapies [14]. However, there are a few reports indicating that extended treatment with SCs may also have severe adverse effects, especially in individuals with comorbidities like diabetes mellitus, osteoporosis and adrenal insufficiency

[15]. This makes INCS/SC compromise to be a question yet to be answered in research and in practice.
A similar method, IPSI, has also been shown to be effective in treating sinonasal polyposis [17]. Similar results have been achieved for both symptom relief and decrease in polyp size for IPSI and SCs [17-20] and IPSI has been shown to achieve a higher concentration of steroid in the polyp tissue with minimal systemic exposure [17]. One previous study showed that IPSI was significantly associated with a decrease in Lund-Mackay score, polyp score, and symptom score [17–20]. The effectiveness of IPSI has been established in more situations than nasal sprays and irrigations, and IPSI lasts longer (at least three months) [18,20,21].However, limitations were mentioned when treating with IPSI in cases where polyps of significant size could not be completely resorbed by IPSI [18] and there are some minor side effects recorded such as nasal dryness and crusting [22]. The safety and effectiveness of IPSI compared with SCs have yet further to be established. The present study was undertaken with that gap in mind, setting out to directly compare IPSI and SCs in the treatment of CRSwNP.

Materials and methods:

A total of 100 patients diagnosed with CRSwNP were recruited from the Otorhinolaryngology (ENT) outpatient department at Al-Zahraa Teaching Hospital, located in Kut City, Iraq, over the period spanning December 2023 to January 2024. They were randomly assigned in equal numbers to the two treatment arms: Group 1 (n = 50) received IPSI therapy and Group 2 (n = 50) received SCs therapy. The Ethics Committee of College of Medicine, University of Wasit, Iraq, approved the ethical clearance. Consenting participants were recruited after the objective of this study was presented.Each patient was informed about the purpose of the study and gave written informed consent.
Patients with symptoms of CRSwNP lasting 12 weeks without evidence of remission were included. Patients who had unilateral nasal polyps, were pregnant or nursing, had a history of smoking, had asthma, had a history of aspirin-induced airway disease, had had sinus surgery in the past, or had systemic conditions (diabetes mellitus, osteoporosis, adrenal insufficiency, cardiovascular disease) were not included in the study. Patients who had recently received prior treatment with steroids in the past three months were also excluded from the study.
All enrolled patients had a thorough otorhinolaryngological examination based on CRSwNP, including assessment of the dimensions of the polyps, the olfactory function and the patients' quality-of-life scores. The levels of cortisol in their blood samples were also measured before commencing the treatment process. The data gathered from the above analyses acted as benchmarks for comparing data obtained after treatment.
The IPSI procedure, which was used among the group 1 subjects, was done as per the method described by Elzayat et al. (2023). Following placement of the patients in a semi-upright position, intralesional injection of budesonide was administered via a 28-gauge needle at a total dose of 250 µg/ml/sinus. Every sinus with polypoid development received an equal dosage. To eliminate operator variability, the procedure was performed by a single specialist throughout the study. Group 2 patients, by contrast, were started on oral prednisolone at 1 mg/kg/day for three days, followed by a taper of 5 mg/day over two weeks. All the patients were instructed not to use any other drug in addition to those used during this period. Follow-up was done after three months of the treatment initiation, after which the results were obtained by evaluating nasal polyp size, nasal congestion score, sense of smell test, cortisol levels, and quality of life. The size of the nasal polyps was measured after implementing the Lund-Mackay scoring system, applied to computed tomography (CT) images of the paranasal sinuses. This measurement included a score for the degree of opacity of each nasal sinus on a scale of 0 (totally free of any opacity), 1 (partially opaque), and 2 (totally opaque). There was another score assigned for obstruction in the osteomeatal complex, which could either be zero (no

obstruction) or two (blocked). Lund-Mackay scoring ranged between 0 and 24; the higher the score, the worse the condition of the patient.
Sniffin' Sticks test was used for evaluating olfactory function. Odour threshold, odour discrimination, and odour identification were the three components of the evaluation procedure. Patients were given some scented sticks were asked to identify the various fragrances, describe the aroma, and indicate how one scent differed from the others. The test's results are a number from one to forty-eight. The test was conducted on two occasions; before initiation of the treatment and after the completion of three months' period. This was done to assess any improvement in olfactory function following IPSI or SCs therapy.
The Sino-Nasal Outcome Test-22 (SNOT-22) was used to evaluate the impact on patients' quality of life. This validated instrument captures the impact of the condition on nasal, sleep, and emotional well-being, and was administered both at baseline and three months after the intervention. Patients were asked to respond to the 22 questions using a Likert scale (0 – no problem at all and 5 – severe problem). Higher scores indicate increased disease load.
Cortisol levels were also measured in serum prior to and following treatment in order to evaluate the influence of treatment on levels of steroids in the body systemically. All participants had blood drawn in the morning, and their serum cortisol level was determined in the hospital's laboratory unit using a chemiluminescence immunoassay. The comparison was done between intrapolyp steroid injection and systemic steroid treatment.
All data was analysed statistically using SPSS version 26 (IBM, USA). The continuous data e.g., age, BMI etc., which fall under the scale categories, were given as mean ± S.D. The differences among these variables across the groups were assessed with an independent sample t-test. Categorical variables such as sex were described by numbers and percentage (%). Differences among categorical variables across groups were assessed using the chi-square test. Between-group shifts in the principal endpoints — serum cortisol concentration, polyp size, smell perception, and quality-of-life scoring — were compared between the pre-treatment and post-treatment time points via repeated-measures ANOVA, with Bonferroni adjustment applied to control for multiple comparisons. A threshold of $p < 0.05$ was adopted to denote statistical significance. Linear regressions were used to determine the effect of the intervention plan on the outcome variables, where Beta is the effect of the intervention plan on the outcomes after three months of treatment.

Results:

There were no meaningful differences between the arms of the study on initial demographic and body-composition parameters (age, BMI, and sex ratio) ($p > 0.05$; Table 1). Serum cortisol was collected at the beginning and end of treatment to reflect a surrogate for the amount of systemic glucocorticoid exposure associated with each treatment option. Mean concentration at entry was almost the same in both cohorts; 12.66 ± 1.45 µg/dL in IPSI and 12.13 ± 1.41 µg/dL in the SC. Inter-group differences were statistically significant after intervention ($p = 0.001$): the inter-group difference for cortisol in the IPSI arm was 13.22 ± 5.78 µg/dL, while it was 15.57 ± 5.35 µg/dL in the SC arm. This was confirmed by regression analysis, which identified systemic route of corticosteroid administration as a significant predictor of increased post-treatment cortisol (Table 2; $\beta = 0.21$, $p = 0.037$).
The Lund-Mackay endoscopic index was used to grade the severity of polyp disease. The scores for the two arms were almost the same at enrolment (16.88 ± 3.75 for IPSI and 16.64 ± 4.08 for SC), showing that the burden of disease was comparable at the start. After three months, however, the reduction observed in the SC arm substantially outpaced that of the IPSI arm (-10.15 ± 3.01 versus -8.67 ± 2.6; $p < 0.001$). This trend was reinforced by the regression analysis, in which a negative β value signalled that systemic steroid therapy delivered the greater drop in score.

Olfaction significantly increased in both treatment groups. The IPSI group's baseline mean score was 15.67 ± 5.79, whereas the SCs group's was 14.79 ± 5.28. At the 3-month follow-up, these had increased to 23.32 ± 10.05 in the first group and 27.32 ± 10.68 in the second group respectively, suggesting that olfaction was enhanced in the second group more effectively than in the first one ($p < 0.001$). Yet, the regression analysis did not reveal any significant difference between the two treatment groups ($p = 0.056$). Therefore, it may be assumed that both treatment methods were equally effective for patients.

Quality-of-life impairment at enrolment, captured by the SNOT-22 questionnaire, was substantial and broadly similar across the two cohorts, averaging 64.11 ± 32.21 in the IPSI arm and 69.27 ± 27.88 in the SC arm. Both groups had a significant decline after treatment in their scores, with IPSI and SCs group postoperative scores of 45.7 ± 12.66 ($p < 0.001$) and 36.32 ± 9.13 ($p < 0.001$), respectively, representing a better effect on patients treated with SCs. Regression analysis backed this up, with SCs linked to greater improvement than IPSI ($\beta = -0.39$, $p < 0.001$) (Table 2).

Table 1: Baseline and clinical features of patients with IPSI and SCs treatments.

Patients' characteristics		Treatment groups				P value
		Group 1 (IPSI)		Group 2 (SCs)		
		Mean ± S.D.	Count (%)	Mean ± S.D.	Count (%)	
Age (years)		39.3 ± 11.8		42.79 ± 11.9		0.144
BMI (kg/m²)		24.23 ± 2.97		25.09 ± 3.29		0.171
Sex	Male		35 (52.24%)		32 (47.76%)	0.532
	Female		15 (45.45%)		18 (54.55%)	
Serum cortisol level (µg/dL)	Before treatment	12.66 ± 1.45		12.13 ± 1.41		0.001*
	3 months post-treatment	13.22 ± 5.78		15.57 ± 5.35		
Nasal polyp size (Lund Mackay Scores)	Before treatment	16.88 ± 3.75		16.64 ± 4.08		<0.001*
	3 months post-treatment	10.15 ± 3.01		8.67 ± 2.6		
Olfactory function (Sniffin' Sticks test)	Before treatment	15.67 ± 5.79		14.79 ± 5.28		<0.001*
	3 months post-treatment	23.32 ± 10.05		27.32 ± 10.68		
Quality of life score (SNOT-22 questionnaire)	Before treatment	64.11 ± 32.21		69.27 ± 27.88		<0.001*
	3 months post-treatment	45.7 ± 12.66		36.32 ± 9.13		

*Significant difference.

Table 2. Linear regression analysis examining how corticosteroid treatment influenced serum cortisol concentrations, polyp dimensions, olfactory ability, and quality-of-life measures at the three-month review.

Outcome	Standardized Coefficients (Beta) †	St. E.	P- value	95% Cl for Beta	
				lower bound	upper bound
Level of serum cortisol	0.21	1.11	0.037*	0.14	4.56
Polyp burden (graded by Lund-Mackay scoring; lower values are more favourable)	-0.26	0.56	0.01*	-2.6	-0.36
Olfactory function (greater is better on the Sniffin' Sticks test)	0.19	2.07	0.056	-0.11	8.12
Quality of life score (lower is better) on the SNOT-22 questionnaire	-0.39	2.21	<0.001*	-13.76	-4.99

*Significant difference

Discussion:

The pathophysiology of CRSwNP involves type-2 inflammatory signalling, breakdown of the mucosal barrier, and neurogenic inflammation — all of which can contribute to loss of smell [23]. Other factors are eosinophilic infiltration, high cytokine levels, sinus oedema and hyperproduction of mucus [1]. The use of corticosteriods is thought to be the first line of treatment due to its anti-inflammatory and immune dysregulation properties associated with CRSwNP [10]. Corticosteroids have been administered in CRSwNP via several different routes, including topical nasal sprays, oral systemic medications, and injection directly into the polyp tissue (particularly in polyposis-predominant or recurrent CRSwNP) [17-20,24]. Every modality has its own risk/benefit ratio. In this context, the current study aimed to directly compare the therapeutic effectiveness of IPSI with the SCs in CRSwNP patients. The results of the current study showed that for CRSwNP patients, both IPSI and SC treatment programs facilitated improvements in nasal polyp size, in their ability to smell, and in their quality of life. That said, SCs produced consistently stronger results across each of these outcomes.

In addition, the use of oral steroids is common in the management of CRSwNP patients [25]. Research focused on the short time use of SCs rather than long time use, highlighting their major importance [26]. Some studies have found that the short-term use of SCs worked well for moderate and severe symptoms of CRSwNP and especially when there is an acute exacerbation prior to sinus surgery procedures [27,28]. Similarly, in individuals with nasal polyps, SC has been linked to a notable decrease in sinus fibrosis and tissue eosinophilia [29]. When compared to ESS patients, patients treated with SCs did demonstrate significant improvements over endoscopic sinus tests (including CT scores) and polyp exams (containing symptom ratings) in one clinical trial [30]. However, due to short-term benefits and adverse effects associated with prolonged use, other therapeutic approaches were recommended. Papadakis et al. (2021) noted that the integration of nasal spray and oral steroid could produce long-lasting benefits with no risk of adverse effects that could compromise patients' physical

well-being [32]. Extended use of systemic corticosteroids can lead to elevated systemic cortisol levels and potentially interfere with various metabolic, cardiovascular, and immunologic functions [33]. This is cause for serious worry when deciding on an approach for treating CRSwNP, particularly in those who have a tendency toward corticosteroid complications.

The advent of IPSI as a therapy regime has attracted considerable interest in recent years. It relies on delivering corticosteroid directly into the polyp tissue itself, with the goal of cutting down on swelling and shrinking polyp size [17-20]. Although its overall role in CRSwNP management is still being established, IPSI appears to match oral steroids in effectiveness while producing fewer side effects than SCs [20]. Additionally, IPSI treatment was found more effective and efficient than nasal spray and oral steroids regimes[34]. Kiris et al. study also showed that IPSI treatment for nasal polyps was equally effective with minimal side effects as compared to the short-term use of SCs, while maintaining cortisol levels[17]. Other authors have documented such findings, which go against the outcomes of the current study that demonstrated that SCs are superior to IPSI in reducing symptoms in patients with CRSwNP. Similarly, serum cortisol levels were found to be lower in our IPSI group compared with the SCs group as previously reported [18-20]. Taken together, these findings support IPSI as a reasonable alternative to SCs in patients at greater risk of side effects driven by raised cortisol levels. Besides, it may also be used on patients with nasal polyps that are resistant and recurring [35]. Nevertheless, a recent report showed that IPSI may cause nasal dryness and crusting, contrary to the current study.

The most recent data suggest that IPSI is most effective in combination with other measures in CRSwNP, such as saline nasal irrigation, intranasal corticosteroid sprays, specific allergen immunotherapy, and new biologic agents [36]. In addition to choosing the therapy, the reasons for the development of CRswNP should also be taken into account before starting a therapy, since allergic sensitization, structural abnormalities of the nose, genetic and environmental factors are all factors that can have a significant impact on the therapeutic results and make recovery more difficult [37]. But, IPSI has its challenges. It is a procedural technique and generally needs to be specifically trained and instrumented. Also, there are known risks associated with the injection of steroid into polyp tissue, including perforation of the nasal septum and adrenal axis suppression [18,22,38].

While SCs effectively manage clinical symptoms of CRSwNP, their well-defined safety and efficacy in routine clinical practice has not been fully established [14]. For instance, the response to corticosteroid treatment is different for different people. Some patients only get a short term benefit, which is followed by a recurrence of symptoms, and they are then usually advised to take more or use it for longer; others experience side effects that are so significant as to make the clinical benefit worthless [11]. Corticosteroids have an effect on the symptoms and signs of the condition, but do not treat the underlying causes (such as concurrent infection and allergic disease) [39]. If an assessment tool is not available to assess the outcomes, the patient may lose faith in any regimen currently available, and may not achieve long-lasting resolution but only symptom relief.

Current findings, in addition, point out another balance that needs to be achieved during the therapeutic process, namely, the compromise between effectiveness and systematic impact. While SCs produce more favorable results concerning the shrinkage of polyps, the improvement in olfactory function, and quality of life, these procedures have a higher possibility of producing a significant systemic effect and even lead to adrenal suppression. IPSI, meanwhile, ensures that the effect remains localized with minimal absorption in the system, which makes this procedure preferable to patients vulnerable to systemic side-effects of steroids.

This study has certain limitations as well. To begin with, the follow-up period of only three months did not allow for evaluating the sustainability of the results as well as the probability

of adverse side effects developing over time. In addition, cortisol was used to reflect systemic steroid absorption, although other endocrine parameters should have been evaluated as well. Finally, although certain validated measures were used, such as Lund-Mackay score, Sniffin' Sticks, and SNOT-22 scale, other objective biological markers, such as cytokines and histopathological examination of nasal mucosa, were not taken into account. Such data could have helped improve the assessment of the therapeutic effect of the procedure.

Conclusion:

The findings clearly show that although IPSI and SCs were equally efficient in terms of shrinking polyps, restoring olfaction and improving QoL, SCs treatment produced significantly better results across all parameters. Nonetheless, the improved performance was achieved at the expense of increased systemic steroid uptake, indicated by the increased concentrations of cortisol in the blood plasma following the intervention among the SCs patients. Additional studies are needed for a thorough analysis of its long-term effectiveness and safety.

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References

[1] Marglani O, Al Abri R, Al Ahmad M, Alsaleh S, Abuzakouk M, Kamel R. Management of Chronic Rhinosinusitis with Nasal Polyps (CRSwNP) in the Pan-Arab Region: Consensus Recommendations from a Multidisciplinary Expert Working Group. J Asthma Allergy. 2023;16:1055-1063. doi:10.2147/jaa.S413610

[2] Maspero J, Philpott C, Hellings P, et al. Health-Related Quality of Life Impairment Among Patients With Severe Chronic Rhinosinusitis With Nasal Polyps in the SINUS-24 Trial. Journal of Allergy and Clinical Immunology. 2021;147(2):AB133. doi:10.1016/j.jaci.2020.12.485

[3] Kato A, Schleimer RP, Bleier BS. Mechanisms and pathogenesis of chronic rhinosinusitis. J Allergy Clin Immunol. May 2022;149(5):1491-1503. doi:10.1016/j.jaci.2022.02.016

[4] AlBloushi S, Al-Ahmad M. Exploring the immunopathology of type 2 inflammatory airway diseases. Front Immunol. 2024;15:1285598. doi:10.3389/fimmu.2024.1285598

[5] Amirapu S, Biswas K, Radcliff FJ, Wagner Mackenzie B, Ball S, Douglas RG. Sinonasal Tissue Remodelling during Chronic Rhinosinusitis. Int J Otolaryngol. 2021;2021:7428955. doi:10.1155/2021/7428955

[6] Zhou Q, Ma J, Biswal S, et al. Air pollution, genetic factors, and chronic rhinosinusitis: A prospective study in the UK Biobank. Science of The Total Environment. 2024/08/25/ 2024;940:173526. doi:https://doi.org/10.1016/j.scitotenv.2024.173526

[7] Huang Z-Q, Liu J, Sun L-Y, et al. Updated epithelial barrier dysfunction in chronic rhinosinusitis: Targeting pathophysiology and treatment response of tight junctions. Allergy. 2024;79(5):1146-1165. doi:https://doi.org/10.1111/all.16064

[8] Qureshi HA, G. Franks Z, Gurung A, Ramanathan M. Scientific Advancements That Empower Us to Understand CRS Pathophysiology. American Journal of Rhinology & Allergy. 2023;37(2):221-226. doi:10.1177/19458924221148026

[9] Lee K, Tai J, Lee SH, Kim TH. Advances in the Knowledge of the Underlying Airway Remodeling Mechanisms in Chronic Rhinosinusitis Based on the Endotypes: A Review. International Journal of Molecular Sciences. 2021;22(2):910.

[10] Norelli F, Schiappoli M, Senna G, et al. Adherence to Intranasal Steroids in Chronic Rhinosinusitis with Nasal Polyposis Prior to and during Biologic Therapy: A Neglected Matter. Journal of Clinical Medicine. 2024;13(4):1066.

[11] Davis GE, Zeiger RS, Emmanuel B, et al. Systemic Corticosteroid-related Adverse Outcomes and Health Care Resource Utilization and Costs Among Patients with Chronic Rhinosinusitis with Nasal Polyposis. Clin Ther. Sep 2022;44(9):1187-1202. doi:10.1016/j.clinthera.2022.08.004
[12] Bognanni A, Chu DK, Rank MA, et al. Topical Corticosteroids for Chronic Rhinosinusitis with Nasal Polyposis: GRADE Systematic Review and Network Meta-Analysis. The Journal of allergy and clinical immunology. 2022;
[13] Ranford D, Hopkins C. Safety review of current systemic treatments for severe chronic rhinosinusitis with nasal polyps and future directions. Expert Opinion on Drug Safety. 2021;20:1177 - 1189.
[14] Tamene S, Dalhoff K, Schwarz P, Backer V, Aanaes K. Systemic corticosteroids in treatment of chronic rhinosinusitis-A systematic review. Eur Clin Respir J. 2023;10(1):2240511. doi:10.1080/20018525.2023.2240511
[15] Tavares LCP, Caetano LVN, Ianhez M. Side effects of chronic systemic glucocorticoid therapy: what dermatologists should know. An Bras Dermatol. Mar-Apr 2024;99(2):259-268. doi:10.1016/j.abd.2023.05.005
[16] De Corso E, Pipolo C, Cantone E, et al. Survey on Use of Local and Systemic Corticosteroids in the Management of Chronic Rhinosinusitis with Nasal Polyps: Identification of Unmet Clinical Needs. J Pers Med. May 29 2022;12(6)doi:10.3390/jpm12060897
[17] Kiris M, Muderris T, Yalciner G, Bercin S, Sevil E, Gul F. Intrapolyp steroid injection for nasal polyposis: Randomized trial of safety and efficacy. Laryngoscope. Aug 2016;126(8):1730-5. doi:10.1002/lary.25945
[18] Zamzam SM, Elshazly M, Salah M, Enayat A. Comparative study between intrapolyp steroid injection and oral steroid for treatment of sinonasal polyposis in Egyptian patients. The Egyptian Journal of Otolaryngology. 2020/12/14 2020;36(1):59. doi:10.1186/s43163-020-00062-w
[19] Elzayat S, Elgendy A, Lasheen H, El-Deeb ME, Aouf MM, Gehad I. The role of budesonide intrapolyp injection in the management of type 2 chronic rhinosinusitis with nasal polyps: a randomised clinical trial. J Laryngol Otol. Apr 2024;138(4):416-424. doi:10.1017/S0022215123001688
[20] Albazee E, Abu-Zaid A, Althaidy M, Alqunaee M. Intrapolyp Steroid Injection for Nasal Polyposis: A Systematic Review and Network Meta-Analysis. The Laryngoscope. 2024;
[21] Moss WJ. Can we please reconsider intranasal injections in refractory sinonasal inflammatory disease? International Forum of Allergy & Rhinology. 2021;11:1033 - 1034.
[22] Rollema C, van Roon EN, Ekhart C, van Hunsel F, de Vries TW. Adverse Drug Reactions of Intranasal Corticosteroids in the Netherlands: An Analysis from the Netherlands Pharmacovigilance Center. Drugs Real World Outcomes. Sep 2022;9(3):321-331. doi:10.1007/s40801-022-00301-x
[23] Backaert W, Steelant B, Hellings PW, Talavera K, Van Gerven L. A TRiP Through the Roles of Transient Receptor Potential Cation Channels in Type 2 Upper Airway Inflammation. Curr Allergy Asthma Rep. Mar 18 2021;21(3):20. doi:10.1007/s11882-020-00981-x
[24] Müskens WD, Dees MK, Stikkelbroeck MML, van Herwaarden N, Kramers C. [Systemic side effects of locally administered corticosteroids]. Nederlands tijdschrift voor geneeskunde. 2024;168
[25] Han J, Laidlaw T, Peters A, et al. Baseline Use of Oral Corticosteroids Among Patients With Chronic Rhinosinusitis With Nasal Polyps Enrolled In The Global AROMA Registry. Journal of Allergy and Clinical Immunology. 2024;153(2):AB251. doi:10.1016/j.jaci.2023.11.805
[26] Poetker DM, Jakubowski LA, Lal D, Hwang PH, Wright ED, Smith TL. Oral corticosteroids in the management of adult chronic rhinosinusitis with and without nasal polyps: an evidence-based review with recommendations. Int Forum Allergy Rhinol. Feb 2013;3(2):104-20. doi:10.1002/alr.21072
[27] Shao S, Wang Y, Zhang N, et al. A prospective single-arm study on the efficacy and safety of short-course oral corticosteroids followed by topical corticosteroids in patients with severe chronic rhinosinusitis with nasal polyps. Expert Review of Clinical Immunology. 2023;19:1029 - 1039.

[28] Chrysouli K, Kyrodimos E, Papanikolaou V. The Effect of the Premedication with Systemic Corticosteroids and Antibiotics on Inflammation and Intraoperative Bleeding During Sinonasal Endoscopic Surgery for Chronic Rhinosinusitis with Nasal Polyps (CRSwNP). Journal of Craniofacial Surgery. 2022;33:e405 - e408.
[29] Radajewski K, Kalińczak-Górna P, Zdrenka M, et al. Short Term Pre-Operative Oral Corticosteroids-Tissue Remodeling in Chronic Rhinosinusitis with Nasal Polyps. J Clin Med. Jul 29 2021;10(15)doi:10.3390/jcm10153346
[30] Kim J, Kim DH, Hwang SH. Effectiveness of Dupilumab Treatment to Treat Chronic Rhinosinusitis With Nasal Polyposis: A Systematic Review and Meta-Analysis. J Rhinol. 7 2023;30(2):62-68. doi:10.18787/jr.2023.00029
[31] Hopkins C. Surgery and uncontrolled chronic rhinosinusitis. The Lancet Respiratory Medicine. 2022;10(4):315-317. doi:10.1016/S2213-2600(21)00490-2
[32] Papadakis CE, Chimona TS, Chaidas K, Ladias A, Zisoglou M, Proimos EK. Effect of oral steroids on olfactory function in chronic rhinosinusitis with nasal polyps. European Annals of Otorhinolaryngology, Head and Neck Diseases. 2021/10/01/ 2021;138(5):343-348. doi:https://doi.org/10.1016/j.anorl.2020.06.028
[33] Chang MT, Hwang PH. Challenging our assumptions: oral corticosteroids and chronic rhinosinusitis without nasal polyposis. International Forum of Allergy & Rhinology. 2021;11
[34] Ali HK, Kadah SMS, Rashid RAA, EL-Din DAE-HS. Intrapolyp Corticosteroid Injection versus Oral Corticosteroid versus Topical Nasal Corticosteroid Spray in Treatment of Allergic Nasal Polyposis: Comparative Study. The Egyptian Journal of Hospital Medicine. 2020;
[35] Lee T-H, Nam J-G, Lee CK. Effects of intrapolyp steroid injection on intraocular pressure and recurrent polyp treatment. Eye. 2022/10/01 2022;36(10):1900-1904. doi:10.1038/s41433-021-01719-3
[36] Scadding GK, Scadding GW. Biologics for chronic rhinosinusitis with nasal polyps (CRSwNP). Journal of Allergy and Clinical Immunology. 2022;149(3):895-897. doi:10.1016/j.jaci.2021.10.029
[37] Petalas K, Goudakos J, Konstantinou GN. Targeting Epithelium Dysfunction and Impaired Nasal Biofilms to Treat Immunological, Functional, and Structural Abnormalities of Chronic Rhinosinusitis. Int J Mol Sci. Aug 3 2023;24(15)doi:10.3390/ijms241512379
[38] Bernstein JA, White AA, Han JK, Lang DM, Elkayam D, Baroody FM. Review of evidence supporting the use of nasal corticosteroid irrigation for chronic rhinosinusitis. Annals of Allergy, Asthma & Immunology. 2023;130(1):46-57. doi:10.1016/j.anai.2022.09.008
[39] Mansi A, Bui R, Chaaban MR. Oral Corticosteroid Regimens in the Management of Chronic Rhinosinusitis. Ear Nose Throat J. Feb 2022;101(2):123-130. doi:10.1177/0145561319876906
[40] Naclerio R, Baroody F, Bachert C, et al. Clinical Research Needs for the Management of Chronic Rhinosinusitis with Nasal Polyps in the New Era of Biologics: A National Institute of Allergy and Infectious Diseases Workshop. J Allergy Clin Immunol Pract. May 2020;8(5):1532-1549.e1. doi:10.1016/j.jaip.2020.02.023

