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TARGETING TYPE 2 INFLAMMATION IN CHRONIC RHINOSINUSITIS WITH NASAL POLYPS: CURRENT EVIDENCE AND FUTURE PERSPECTIVES ON INTRANASAL CORTICOSTEROID THERAPY

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Abstract

Chronic Rhinosinusitis with nasal polyps (CRSwNP) is a chronic inflammatory disorder of the nasal and paranasal sinus mucosa characterized by persistent sinonasal inflammation, benign polyp formation, nasal obstruction, rhinorrhea, facial pressure, and olfactory dysfunction. Type 2 inflammation, mediated predominantly by eosinophils, immunoglobulin E (IgE), and cytokines such as interleukin (IL)-4, IL-5, and IL-13, plays a central role in disease pathogenesis. Intranasal corticosteroids (INCS) remain the cornerstone of pharmacological management because of their potent local anti-inflammatory effects, minimal systemic absorption, and favorable safety profile. This review comprehensively evaluates the current evidence regarding the mechanism of action, clinical efficacy, safety, postoperative benefits, and future therapeutic role of INCS in the management of CRSwNP. Available evidence consistently demonstrates that INCS effectively reduce nasal polyp size, suppress eosinophilic inflammation, improve nasal obstruction, rhinorrhea, postnasal drip, facial pressure, and olfactory dysfunction, and enhance patients' quality of life. Furthermore, long-term maintenance therapy following functional endoscopic sinus surgery (FESS) significantly reduces postoperative recurrence and decreases the need for systemic corticosteroids. Newer-generation corticosteroids, including fluticasone and mometasone, exhibit very low systemic bioavailability, making them suitable for prolonged use. Overall, intranasal corticosteroids remain the first-line medical therapy for CRSwNP owing to their proven efficacy, excellent safety profile, and ability to provide sustained disease control. Future treatment strategies may involve integrating INCS with biologic therapies to achieve personalized management in patients with severe or refractory disease.

Keywords:

Chronic rhinosinusitis, Intranasal corticosteroids, Eosinophilic inflammation, Nasal polyps, Functional endoscopic sinus surgery, Corticosteroids, Sinonasal inflammation.

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1. INTRODUCTION:

Chronic rhinosinusitis with nasal polyps (CRSwNP) is a chronic inflammatory disorder of the nasal cavity and paranasal sinuses characterized by benign edematous polyps, persistent nasal obstruction, rhinorrhea, facial pressure, postnasal drip, and impaired olfaction. The disease significantly affects patients' quality of life by impairing sleep, work productivity, and psychological well-being, while contributing substantially to healthcare burden.

The pathogenesis of CRSwNP is multifactorial and is predominantly driven by type 2 inflammation, characterized by eosinophilic infiltration, elevated immunoglobulin E (IgE), and increased production of cytokines such as interleukin (IL)-4, IL-5, and IL-13. These inflammatory mediators promote mucosal edema, tissue remodeling, and progressive nasal polyp formation.

Management aims to control inflammation, relieve symptoms, restore nasal function, and prevent disease recurrence. Current treatment options include saline irrigation, corticosteroids, biologic agents, and functional endoscopic sinus surgery (FESS). Among these, intranasal corticosteroids (INCS) remain the cornerstone of medical therapy because of their potent local anti-inflammatory effects, minimal systemic absorption, and favorable safety profile.

Extensive evidence from randomized controlled trials, systematic reviews, and international guidelines has demonstrated that INCS effectively reduce nasal polyp size, improve nasal airflow and olfactory function, enhance postoperative healing following FESS, and reduce recurrence. This review summarizes the current evidence on the mechanisms, clinical efficacy, postoperative benefits, and safety of intranasal corticosteroids, while highlighting future perspectives for optimizing long-term management of CRSwNP.

2. Mechanism of Action of Intranasal Corticosteroids

Intranasal corticosteroids (INCS) are synthetic glucocorticoids that provide potent local anti-inflammatory effects with minimal systemic absorption. Commonly used agents include fluticasone, mometasone, budesonide, beclomethasone, ciclesonide, and triamcinolone. After intranasal administration, they bind to intracellular glucocorticoid receptors and regulate gene transcription by inhibiting inflammatory transcription factors such as nuclear factor-kappa B (NF-κB) and activator protein-1 (AP-1). This suppresses the production of pro-inflammatory cytokines, including IL-4, IL-5, IL-13, TNF-α, and GM-CSF, thereby reducing eosinophilic inflammation, mucosal edema, and tissue remodeling.

Additionally, INCS stabilize mast cells, inhibit histamine and leukotriene release, reduce vascular permeability and mucus secretion, and improve mucociliary clearance. These effects result in reduced nasal polyp size, improved nasal airflow and olfactory function, relief of nasal obstruction and rhinorrhea, prevention of postoperative recurrence, and long-term control of sinonasal inflammation. Their extremely low systemic bioavailability, particularly with fluticasone and mometasone, minimizes systemic corticosteroid-related adverse effects, making them the preferred long-term therapy for CRSwNP.

2.1 Role of Intranasal Corticosteroids in Reducing Nasal Polyp Size and Disease Progression

Intranasal corticosteroids are the cornerstone of CRSwNP management because they suppress type 2 eosinophilic inflammation responsible for nasal polyp formation and progression. By reducing inflammatory cytokine production, vascular permeability, and eosinophilic infiltration, INCS decrease mucosal edema and promote gradual shrinkage of nasal polyps. Randomized controlled trials have consistently demonstrated significant reductions in endoscopic polyp scores and sustained clinical improvement with long-term therapy.

Newer-generation corticosteroids, including fluticasone, mometasone, and budesonide, provide effective disease control with minimal systemic absorption and excellent safety. Continuous maintenance therapy suppresses persistent inflammation, delays disease progression, reduces exacerbations and systemic corticosteroid use, and lowers the need for surgical intervention. Accordingly, EPOS 2020 recommends INCS as the first-line treatment for both newly diagnosed and postoperative patients with CRSwNP.

2.2 Postoperative Role of Intranasal Corticosteroids and Prevention of Recurrence

Functional endoscopic sinus surgery (FESS) is recommended for patients with persistent CRSwNP despite optimal medical therapy; however, surgery alone does not eliminate the underlying inflammation. Postoperative intranasal corticosteroids are therefore essential to suppress residual inflammation, promote mucosal healing, reduce postoperative edema, and restore mucociliary function. Clinical studies have shown that regular postoperative INCS improve nasal patency, reduce endoscopic polyp scores, lower recurrence rates, and decrease the need for revision surgery. Budesonide nasal irrigation may further enhance corticosteroid delivery to postoperative sinonasal cavities. Consequently, international guidelines, including EPOS 2020 and ICAR, recommend long-term postoperative INCS to maintain disease control and prevent recurrence.

2.3 Safety Profile of Intranasal Corticosteroids

Intranasal corticosteroids have an excellent safety profile owing to their potent local anti-inflammatory effects and minimal systemic absorption. Newer-generation agents such as fluticasone, mometasone, and ciclesonide have systemic bioavailability of less than 1%, greatly reducing the risk of hypothalamic–pituitary–adrenal axis suppression and other systemic adverse effects. Most adverse events are mild and localized, including nasal irritation, dryness, burning sensation, sore throat, and occasional epistaxis, while serious complications are rare with appropriate administration. Compared with older agents such as beclomethasone dipropionate, newer corticosteroids provide a superior balance of efficacy and safety, supporting their use as first-line therapy for long-term disease control and prevention of recurrence in patients with CRSwNP.

3. RESULTS:

The literature consistently demonstrates that intranasal corticosteroids (INCS) are the most effective first-line pharmacological therapy for patients with chronic rhinosinusitis with nasal polyps (CRSwNP). Evidence from randomized controlled trials, systematic reviews, meta-analyses, and international clinical guidelines indicates that INCS significantly reduce nasal polyp size, improve sinonasal symptoms, restore olfactory function, and enhance overall quality of life while maintaining an excellent safety profile.

3.1 Reduction in Nasal Polyp Size

Most randomized controlled trials reported significant reductions in endoscopic nasal polyp scores following regular administration of intranasal corticosteroids. Continuous suppression of eosinophilic inflammation resulted in decreased mucosal edema, reduced inflammatory cell infiltration, and gradual regression of polyp tissue. These improvements were consistently observed with commonly prescribed corticosteroids including fluticasone propionate, mometasone furoate, budesonide, fluticasone furoate, and ciclesonide. Long-term therapy maintained these benefits and delayed disease progression.

3.2 Improvement in Sinonasal Symptoms

Treatment with intranasal corticosteroids was associated with substantial improvement in major clinical symptoms of CRSwNP, including nasal obstruction, rhinorrhea, postnasal drip, facial pressure, and sneezing. Reduction in mucosal inflammation and restoration of nasal airflow contributed to better symptom control and improved patient comfort. Numerous studies also demonstrated clinically meaningful improvement in olfactory function, which is often one of the most debilitating manifestations of the disease.

3.3 Quality of Life

Several clinical studies using validated assessment tools such as the Sinonasal Outcome Test (SNOT-22), visual analogue scales (VAS), and disease-specific quality-of-life questionnaires demonstrated significant improvement following treatment with intranasal corticosteroids. Improved sleep quality, enhanced work productivity, reduced psychological distress, and better overall health status were consistently reported among patients receiving long-term therapy.

3.4 Postoperative Outcomes

Evidence strongly supports the routine use of intranasal corticosteroids following functional endoscopic sinus surgery (FESS). Postoperative maintenance therapy significantly reduced mucosal inflammation, promoted epithelial healing, decreased postoperative edema, and lowered recurrence rates of nasal polyps. Budesonide nasal irrigation demonstrated additional benefits in selected postoperative patients by improving corticosteroid delivery to surgically opened sinonasal cavities.

3.5 Safety Outcomes

Across clinical trials, intranasal corticosteroids demonstrated excellent tolerability. The majority of adverse events were mild and localized, including nasal irritation, dryness, and occasional epistaxis. Serious systemic adverse effects were rarely observed because newer-generation corticosteroids exhibit extremely low systemic bioavailability. Long-term studies found no clinically significant hypothalamic-pituitary-adrenal axis suppression or other corticosteroid-related systemic complications when recommended therapeutic doses were used.

3.6 Guideline Recommendations

Major international clinical guidelines, including the European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS 2020) and the International Consensus Statement on Allergy and Rhinology (ICAR), consistently recommend intranasal corticosteroids as the cornerstone of both primary and maintenance therapy for CRSwNP. These recommendations are supported by high-quality evidence demonstrating sustained symptom control, reduced postoperative recurrence, and decreased reliance on systemic corticosteroids.

S. No.	Original Title	Journal	Methodology	Key Results	Short Conclusion
1	**European Position Paper on Rhinosinusitis and Nasal Polyps 2020 (EPOS 2020)**	*Rhinology*	International evidence-based clinical practice guideline developed by multidisciplinar y experts through systematic literature review and consensus recommendatio ns.	Updated definitions, diagnosis, classification and management of CRS/CRSwNP. Strong evidence supports intranasal corticosteroids (INCS) as first-line therapy, with surgery and biologics reserved for selected patients.	EPOS 2020 establishes INCS as the cornerstone of medical management and recommends individualized treatment based on disease severity and response.
2	**International Consensus**	*International Forum of*	Comprehensive international	Reaffirmed the effectiveness of	ICAR-RS 2021 supports
	Statement on Allergy and Rhinology: Rhinosinusitis 2021 (ICAR-RS 2021)	*Allergy & Rhinology*	consensus statement based on systematic review and evidence grading of available literature.	intranasal corticosteroids, saline irrigation and endoscopic sinus surgery. Provided evidence-based recommendati ons for diagnosis, medical treatment and postoperative care.	evidence-based multidisciplinary management, emphasizing topical corticosteroids as standard therapy for CRSwNP.
3	**Efficacy and Safety of Dupilumab in Patients with Severe Chronic Rhinosinusitis with Nasal Polyps (SINUS-24 and SINUS-52)**	*The Lancet*	Two multicenter, randomized, double-blind, placebo-controlled Phase III clinical trials evaluating dupilumab plus standard intranasal corticosteroids.	Dupilumab significantly reduced nasal polyp score, improved nasal congestion, restored smell, enhanced quality of life and reduced the need for systemic corticosteroids and surgery compared with placebo.	Dupilumab is an effective biologic therapy for severe CRSwNP inadequately controlled with conventional treatment, producing significant clinical improvement.

4	**Mepolizumab for Chronic Rhinosinusitis with Nasal Polyps (SYNAPSE Study)**	*The Lancet Respiratory Medicine*	Multicenter, randomized, double-blind, placebo-controlled Phase III trial evaluating mepolizumab as add-on therapy in patients with severe recurrent CRSwNP.	Mepolizumab significantly reduced nasal polyp size, improved nasal obstruction and symptom scores, and decreased the need for repeat sinus surgery compared with placebo.	Mepolizumab is an effective add-on biologic for severe CRSwNP, particularly in patients with recurrent disease despite standard therapy.
5	**Efficacy and Safety of Omalizumab in Chronic Rhinosinusitis with Nasal Polyps (POLYP 1 and POLYP 2)**	*Journal of Allergy and Clinical Immunology*	Two multicenter, randomized, double-blind, placebo-controlled Phase III clinical trials assessing omalizumab in adults with severe CRSwNP receiving intranasal corticosteroids.	Omalizumab significantly improved nasal polyp score, nasal congestion, smell function and overall quality of life while demonstrating a favorable safety profile.	Omalizumab is an effective biologic option for patients with severe CRSwNP inadequately controlled by conventional therapy.
6	**Endotypes of Chronic Rhinosinusitis with Nasal Polyps**	*Journal of Allergy and Clinical Immunology*	Comprehensive review of immunological and molecular mechanisms underlying CRSwNP, focusing on inflammatory endotypes.	Identified type-2 inflammation as the predominant endotype, involving IL-4, IL-5, IL-13 and eosinophilic inflammation, explaining disease heterogeneity and treatment response.	Understanding inflammatory endotypes enables personalized treatment and supports targeted biologic therapies in CRSwNP.
7	**Chronic Rhinosinusitis with Nasal Polyps**	*Journal of Allergy and Clinical Immunology: In Practice*	Narrative review discussing the epidemiology, pathophysiolog y, diagnosis, and management of CRSwNP.	Described the role of eosinophilic inflammation, epithelial barrier dysfunction, and type-2 immune response. Reviewed medical therapy, surgery, and emerging biologics.	CRSwNP is a chronic inflammatory disease requiring long-term medical management, with surgery and biologics reserved for refractory cases.
8	**Immunopathogen esis of Chronic Rhinosinusitis and Nasal Polyposis**	*Annual Review of Pathology: Mechanisms of Disease*	Comprehensive review of the molecular and cellular mechanisms involved in CRS and nasal polyposis.	Identified epithelial dysfunction, eosinophilic inflammation, cytokines (IL-4, IL-5, IL-13), and IgE-mediated responses as key drivers of disease.	Understanding disease immunopathogen esis provides the foundation for targeted therapies and personalized treatment approaches.

9	**Medical Therapies for Adult Chronic Sinusitis: A Systematic Review**	*JAMA*	Systematic review evaluating evidence on medical therapies for adult chronic rhinosinusitis from published clinical studies.	Intranasal corticosteroids demonstrated consistent symptom improvement. Saline irrigation showed additional benefit. Evidence for antibiotics and systemic steroids was limited for long-term management.	Intranasal corticosteroids and saline irrigation remain the primary evidence-based medical treatments for chronic rhinosinusitis.
10	**Intranasal Steroids versus Placebo for Chronic Rhinosinusitis**	*Cochrane Database of Systematic Reviews*	Systematic review and meta-analysis of randomized controlled trials comparing intranasal corticosteroids with placebo.	Intranasal corticosteroids significantly improved nasal obstruction, polyp size, symptom scores, and quality of life with minimal adverse effects.	High-quality evidence supports intranasal corticosteroids as first-line therapy for chronic rhinosinusitis with nasal polyps.
11	**Different Types of**	*Cochrane*	Systematic	No single	Selection of
	Intranasal Steroids for Chronic Rhinosinusitis	*Database of Systematic Reviews*	review comparing different formulations and types of intranasal corticosteroids used in CRS.	intranasal corticosteroid demonstrated clear superiority over others. Most agents showed comparable efficacy and safety when used appropriately.	intranasal corticosteroids should be based on patient preference, availability, cost, and tolerability rather than efficacy differences.
12	**Saline Irrigation and Topical Therapies for Chronic Rhino sinusitis**	*Cochrane Database of Systematic Reviews*	Systematic review of randomized controlled trials evaluating saline irrigation and other topical therapies for chronic rhinosinusitis.	Saline irrigation significantly improved symptom control, mucociliary clearance, and quality of life. Combined use with intranasal corticosteroids produced better outcomes than either therapy alone.	Saline irrigation is a safe and effective adjunctive treatment that enhances the benefits of intranasal corticosteroid therapy in CRS.
13	**International Consensus Recommendation s on the Management of Chronic Rhinosinusitis**	*International Forum of Allergy & Rhinology*	International expert consensus developed using systematic literature review and evidence grading.	Recommended intranasal corticosteroids and saline irrigation as first-line therapy, with endoscopic sinus surgery for refractory disease and biologics for selected patients with severe CRSwNP.	Evidence-based management combining medical and surgical approaches provides optimal long-term disease control.
14	**Mechanisms of Type 2**	*Journal of Allergy and*	Comprehensive review of	Demonstrated that IL-4, IL-5,	Targeting type-2 inflammatory

	Inflammation in Chronic Rhinosinusitis with Nasal Polyps	*Clinical Immunology*	molecular and immunological mechanisms underlying type-2 inflammation in CRSwNP.	IL-13, eosinophils, mast cells, and IgE are central mediators responsible for chronic inflammation and polyp formation.	pathways forms the scientific basis for newer biologic therapies in CRSwNP.
15	**Long-term Management of Chronic Rhinosinusitis with Nasal Polyps**	*Current Opinion in Otolaryngology & Head and Neck Surgery*	Narrative review summarizing long-term follow-up studies and current strategies for preventing recurrence of CRSwNP.	Emphasized long-term intranasal corticosteroid therapy, saline irrigation, postoperative follow-up, and appropriate use of biologics to reduce recurrence and improve quality of life.	Long-term maintenance therapy and regular follow-up are essential to minimize recurrence and achieve sustained symptom control in CRSwNP.

4. DISCUSSION:

Chronic rhinosinusitis with nasal polyps (CRSwNP) is a chronic inflammatory disease of the nasal and paranasal sinus mucosa, with type 2 inflammation playing a major role in many patients. It is characterized by eosinophilic infiltration and increased production of cytokines such as interleukin (IL)-4, IL-5, and IL-13, along with elevated immunoglobulin E (IgE). These inflammatory mediators contribute to mucosal edema, tissue remodeling, and nasal polyp formation, highlighting the need for sustained anti-inflammatory treatment.

Intranasal corticosteroids (INCS) remain the cornerstone of medical management for CRSwNP because of their potent local anti-inflammatory effects and favourable safety profile. They suppress pro-inflammatory cytokine production, reduce eosinophilic infiltration and mucosal edema, and thereby decrease nasal polyp size and improve nasal airflow.

Clinical evidence demonstrates that regular use of INCS improves major symptoms of CRSwNP, including nasal obstruction, rhinorrhea, postnasal drip, facial pressure, and olfactory dysfunction. These improvements contribute to better quality of life and overall disease control.

INCS are also particularly important following functional endoscopic sinus surgery (FESS). Since surgery does not eliminate the underlying inflammatory process, long-term postoperative INCS therapy helps

control inflammation, promote mucosal healing, reduce polyp recurrence, and maintain disease control. Budesonide nasal irrigation may further improve corticosteroid delivery to the postoperative sinonasal cavities.

Modern INCS formulations, including fluticasone and mometasone, have very low systemic bioavailability and an excellent safety profile. Most adverse effects are mild and localized, such as nasal dryness, irritation, and epistaxis, supporting their use as long-term maintenance therapy.

Although biologic therapies provide additional options for patients with severe or refractory CRSwNP, INCS remain the foundation of routine medical management. Overall, current evidence supports a long-term, multimodal approach combining INCS with surgery, saline irrigation, and biologics when indicated. Future research should focus on personalized treatment strategies, predictive biomarkers, and improved drug-delivery systems to optimize long-term disease control and reduce recurrence.

5. CONCLUSION:

Chronic rhinosinusitis with nasal polyps requires long-term control of sinonasal inflammation. Intranasal corticosteroids remain the first-line treatment because they effectively reduce inflammation, decrease nasal polyp size, improve symptoms and olfactory function, enhance quality of life, and reduce postoperative recurrence. Their excellent safety profile and low systemic bioavailability make them suitable for prolonged use.

Although biologic therapies have expanded treatment options for severe or refractory disease, current evidence and international guidelines continue to recommend intranasal corticosteroids as the foundation of long-term CRSwNP management. Future research should focus on

personalized therapy, improved drug-delivery systems, and integration of corticosteroids with biologic agents to optimize patient outcomes.

This version is approximately 40–45% shorter, making it more suitable for a review article while preserving the essential scientific content.

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