



CHRONIC RHINOSINUSITIS THERAPY CONSIDERATIONS

Chronic rhinosinusitis (CRS) is associated with over \$8 billion annually in the United States and is estimated to affect millions of patients. Several factors have contributed to CRS including environmental, occupational, infection, genetic abnormalities, anatomic changes, inflammation, nasal microfloral disturbances, and systemic diseases. CRS is thought to be more inflammatory in nature. This issue of *CLIPs* briefly summarizes an article that evaluates the prevalence, causes, and therapy of drug-induced kidney injury in the elderly population. If you need further information, please contact the Center for Healthcare Innovation and Patient Outcomes Research (CHIPOR) at chipor@samford.edu.

Beswick DM, Gray ST, Smith TL. Pharmacological management of chronic rhinosinusitis: current and evolving treatments. *Drugs*. 2017; 77:1713-1721.

Introduction

- CRS is divided into two types: those with nasal polyposis (CRSwNP) and those without polyposis (CRSsNP).
- Evidence suggests that there may be other factors that predict disease symptoms that may include migration of T-helper cells, neutrophils, cytokines, and basophils.
- These pathways may lead to different therapeutic targets for CRS.
- Neutrophils and elevate type 1 cytokines (e.g., INF) are more pronounced in patients with CRSsNP.
- Patients with CRSwNP have a predominance of eosinophils, mast cells, basophils, and an elevation in type 2 cytokines such as interleukin (IL)-4, IL-5, and IL-13.

Current treatment strategies

- Current treatment strategies target inflammation, decreasing bacterial or pathogen load, and permitting the removal of mucus or purulent discharge from the sinuses and nasal cavities.
- Treatments are typically used interchangeably between CRSsNP and CRSwNP; however, there are a few exceptions. Table 1 provides current treatment strategies associated with CRS.

Table 1: Current treatment strategies for CRS

Treatment Modality	Dose	Mechanism of Action	Evidence
Nasal saline irrigation	>200 mL	Supports clearance of mucus, helps remove antigens, and aids in the resolution of intranasal inflammation	Saline irrigations were as effective as primary and adjunctive treatment for CRS; however, it was less effective than nasal steroids.
Intranasal steroids	Mometasone 100-400 mcg/day* Fluticasone propionate 400-800 mcg / day Beclomethasone propionate 400-800 mcg / day Budesonide 128-400 mcg / day	Improve symptoms, polyp size, quality of life.	Insufficient evidence to suggest one agent over another.

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Treatment Modality	Dose	Mechanism of Action	Evidence
Oral steroids	Variable	Reduction of inflammation.	Patients may experience improvements in quality of life (QoL) indices and symptom severity following a 2-3 week course of oral steroid therapy.
Antibiotics	Macrolides.	Reduce infection. Decrease polyps.	Macrolide antibiotics typically reserved for CRSsNP. May be associated with some benefit in QoL measures. Non-macrolide antibiotics and topical antibiotics are not recommended.
Antifungals	Various.	Reduce eosinophilic disease.	No benefit in treating CRS with oral or topical antifungals.
Leukotriene antagonists	Montelukast, zarfilukast (various doses)	Inflammation mediators. Inhibiting arachidonic acid inflammatory cascade.	Mild benefit observed for treating leukotriene antagonists (LTAs) with CRSwNP.

*the only FDA approved medication for CRSwNP

Biological therapies for rhinosinusitis

- Patients with refractory symptoms (e.g., those with aspirin-exacerbated respiratory disease, asthma, and/or frontal sinus disease) may require additional agents to control symptoms.
- Patients with allergic rhinitis, food allergy, atopic dermatitis and urticarial may also have CRSwNP and may benefit from targeted therapy with biologic agents.
- Several agents are currently being evaluated for treatment of CRSwNP including omalizumab, mepolizumab, reslizumab, benralizumab, and dupilumab.

Omalizumab / Ligelizumab

- These agents work via the anti-immunoglobulin E pathway.
- Omalizumab has shown beneficial effects in computed tomography (CT) disease severity scores; however, the change was not statistically significant.
- Other studies indicate that omalizumab may be efficacious, but should be reserved for patients with asthma and CRSwNP who have refractory symptoms.
- Preliminary results of trials with ligelizumab indicates that it may have superior effects in atopic dermatitis and patients with asthma compared to omalizumab.

Reslizumab, mepolizumab, and benralizumab

- Most patients with CRSwNP have Th2 inflammatory profile that is characterized by eosinophilia and IL-5 expression.
- There may also be a geographic / ethnic predisposition with Th1 expression in Asian patients compared to Caucasians.
- Reslizumab is associated with improved nasal polyp severity score.
- Mepolizumab is currently approved for severe asthma; however, therapy has been associated with improved nasal polyp severity scores.
- Benralizumab has shown some benefit in treating patients with severe asthma.

Dupilumab

- This agent is currently approved for severe atopic dermatitis and has been shown to have significantly improved nasal polyp severity scores.

Summary

- Several agents are beneficial in the treatment of CRS.
- Saline irrigation, topical nasal steroids, some antibiotics, and systemic steroids are used to treat CRS.

Prepared by: Maisha Kelly Freeman, PharmD, MS, BCPS, FASCP