

Topical Therapies for Refractory Chronic Rhinosinusitis



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KEYWORDS

- Topical therapy • Chronic rhinosinusitis • Anti-inflammatory • Antimicrobial
- Surfactant • Stents

KEY POINTS

- Chronic rhinosinusitis (CRS) is a common disease that has a substantive impact on quality of life. CRS treatments are aimed at reducing sinonasal inflammation, infection, and re-establishing mucociliary clearance.
- Sinus surgery is an effective adjunct for topical sinonasal drug delivery for patients with CRS.
- With a 5% to 10% failure rate from surgery, there is an additional subset of patients who are recalcitrant to conventional medical and surgical therapies, leading to alternative therapies centered on anti-infective and anti-inflammatory nasal irrigations.
- Topical therapies have become an integral component in the management plan for CRS.
- Although topical therapy is not a panacea, it can, because of its safety profile, be repeated and/or sustained over extended periods, thus avoiding the risks of prolonged oral corticosteroids, intravenous antibiotics, and/or repeat surgery.

OVERVIEW

Chronic rhinosinusitis (CRS) is a multifactorial disorder that is heterogeneous in presentation and clinical course. Treatment of CRS is based on several factors including the type of rhinosinusitis (acute, chronic, or fungal), presence of nasal polyposis, concurrent medical comorbidities, symptom severity, and response to previous medical treatments.¹ Medical treatment should be considered the cornerstone of disease treatment of CRS, with sinus surgery reserved for medical failures or patients' complications. However, with a 5% to 10% failure rate from surgery, there is an additional

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subset of patients who are refractory to conventional medical and surgical therapies.² The focus of this article is on therapies centered on topical delivery and application for refractory CRS.

CRS has been simplified to two subgroups: CRS with nasal polyps (NP) and CRS without NP.³ In the past, these two entities were considered to be a spectrum of one disease where CRS with NP was thought to be the end point of CRS. However, it has been shown that these two diseases have distinct differences and patients can respond differently to medical treatment.^{3,4} This article mentions specific recommendations based on the CRS subgroup when possible.

Generally, the treatment of CRS is intended to reduce symptoms, improve quality of life, and prevent disease progression or recurrence. More specifically, topical therapies are aimed at reducing mucosal inflammation, reducing pathogenic bacterial burden and improving mucociliary clearance and sinonasal function. Clinicians often try to minimize systemic medical therapies and favor the use of topical therapies to focus drug delivery locally. Major factors that impact topical therapy success include the patient's anatomy and the dynamics of the delivery device. Advantages of topical medical therapy include direct delivery onto diseased tissue, potential for delivering higher local drug concentrations, and minimizing systemic absorption. Disadvantages of topical medical therapy include challenges with application technique; local adverse effects, such as epistaxis or patient discomfort; and variable sinus penetration. Because of the accessible nature of the sinonasal cavity, it is amenable to topical medical therapy and this has become an integral strategy in the management of refractory CRS.

Effective drug delivery to the involved tissue is a challenge that all topical drug therapies must overcome during the management of CRS. Endoscopic sinus surgery (ESS) is an important component in the management of medically refractory CRS, clinically and economically.^{5,6} One major advantage of ESS is creating an open and accessible cavity. This has been demonstrated to optimize sinonasal penetration of topical medical therapy.⁷ Potential topical sinonasal therapy strategies include topical saline irrigations, topical corticosteroids, topical antibiotics, topical antifungals, topical stents, and topical alternative medications.

METHODS OF DELIVERY

The main factors associated with particle penetration include the size of the sinus ostia, the size of the particle, and the flow rate (liters per minute) of the aerosol. Particles greater than 10 μm in size typically do not make it past the nasal cavity, and particles less than 5 μm enter the lungs.⁸ Early studies estimated that the ideal particle size for maxillary sinus penetration is between 3 μm and 10 μm . Further studies concluded that smaller particle size, 45-degree insertion angle of the topical therapy, and higher flow rate (5 L/min compared with 1 L/min as demonstrated by Saijo and colleagues⁹) improved maxillary sinus penetration.⁸

Nasal sprays are a popular option for topical drug delivery because of their ease of use and diverse available formulations. Typical nasal sprays generate droplets of 50 μm to 100 μm in diameter and deliver 70 μL to 150 μL of drug per puff, at velocities of 7.5 L/min to 20 L/min.¹⁰ However, a large fraction of the spray is deposited in the anterior nasal cavity without any paranasal sinus penetration. Also, half of the spray is cleared within 15 minutes from the nasal cavity, with minimal activity occurring at 6 hours.¹⁰

Nebulizers deliver medications in mist form and are commonly used for treating disease of the lower airway. Multiple nebulizers exist for topical sinonasal topical delivery. Some studies on pulsating aerosol nebulizers demonstrated increased deposition in

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