

# Sinus surgery and delivery method influence the effectiveness of topical corticosteroids for chronic rhinosinusitis: Systematic review and meta-analysis

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## ABSTRACT

**Background:** Published randomized controlled trials (RCTs) on the efficacy of intranasal corticosteroid (INCS) in chronic rhinosinusitis (CRS) use either nasal delivery (nasal drop or nasal spray) or sinus delivery (sinus catheter or sinus irrigation) in patients with or without sinus surgery. This influences topical drug delivery and distribution. The effect of these factors on the published results of RCTs is assessed. This systematic review explores the strength of evidence supporting the influence of sinus surgery and delivery methods on the effectiveness of topical steroids in studies for CRS with meta-analyses.

**Methods:** A systematic review was conducted of RCTs comparing INCS with either placebo or no intervention for treating CRS. Data were extracted for meta-analysis and subgroup analyses by sinus surgery status and topical delivery methods.

**Results:** Forty-eight studies (3961 patients) met the inclusion criteria. INCS improved overall symptoms (standardized mean difference [SMD],  $-0.49$ ;  $p < 0.00001$ ) and the proportion of responders (risk ratio [RR],  $0.59$ ;  $p < 0.00001$ ) compared with placebo. It decreased nasal polyp size with a greater proportion of responders (RR,  $0.48$ ;  $p < 0.00001$ ) and prevented polyp recurrence (RR,  $0.59$ ;  $p = 0.0004$ ) compared with placebo. Reduction of polyp size was greater in patients with sinus surgery (RR,  $0.31$ ; 95% confidence interval [CI],  $0.20, 0.48$ ) than those without (RR,  $0.61$ ; 95% CI,  $0.46, 0.81$ ;  $p = 0.009$ ). Greater symptom improvement occurred when sinus delivery methods (SMD,  $-1.32$ ; 95% CI,  $-2.26, -0.38$ ) were compared with nasal delivery methods (SMD,  $-0.38$ ; 95% CI,  $-0.55, -0.22$ ;  $p < 0.00001$ ).

**Conclusion:** INCS is effective for CRS. Prior sinus surgery and direct sinus delivery enhance the effectiveness of INCS in CRS.

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Inflammatory dysfunction is considered an important part of chronic rhinosinusitis (CRS). Anti-inflammatory therapy, including corticosteroid,<sup>1</sup> doxycycline,<sup>2</sup> and low-dose macrolides,<sup>3</sup> plays a significant role in the treatment of CRS. Compared with oral corticosteroid administration, topical corticosteroids are more widely used as a treatment because they can be given for longer periods without the associated systemic side effects and potentially achieve better drug concentration in the sinus mucosa.

However, simply applying topical steroid through the nostrils does not imply delivery of the drug into the sinus. To deliver topical medicine into the sinuses, an appropriate access and delivery is required. Sinus surgery greatly affects the amount of corticosteroid, which comes into contact with paranasal sinus mucosa.<sup>4–6</sup> The edematous inflammatory mucosa and ostiomeatal occlusion often seen in CRS allows <1% of solution volume to enter the sinus cavities before surgery.<sup>7</sup> The extent of sinus surgery varies across institutions. This difference brings about variable access and sinus penetration. An

adequate ostial dimension has been shown to be necessary for appropriate topical drug distribution.<sup>4,8–10</sup> Additionally, an appropriate device and delivery technique is required for adequate administration.<sup>1,8</sup> Simple nasal delivery methods such as drops, sprays, aerosols, nebulizers, and atomizers provide good nasal cavity contact but poor sinus delivery. Nasal irrigation, with squeeze bottles and NETI pots, along with direct sinus cannulation, are likely to provide better delivery to the sinuses, especially in the post-sinus surgery setting.<sup>4,5</sup>

Studies investigating topical steroid for CRS have a high level of heterogeneity, and systematic reviews<sup>11–13</sup> rarely discuss or explore this heterogeneity of patient groups and outcomes. Trials studying the effectiveness of topical corticosteroid used various topical delivery methods and patients with both nonsurgical and post-endoscopic sinus surgery (ESS) cavities. This systematic review aims to assess the strength of evidence supporting the influence of sinus surgery and delivery methods on the benefit of topical steroids in CRS.

## MATERIALS AND METHODS

### Search Methods for Identification of Studies

Electronic systematic searches for randomized controlled trials (RCTs) were conducted with no language, publication year, or publication status restrictions. A search strategy was used with a combination of MESH terms and key words in collaboration with the Cochrane Ear, Nose, and Throat disorders group. The Cochrane Ear, Nose, and Throat Disorders group Trials Register; the Cochrane Central Register of Controlled Trials (CENTRAL); PubMed; EMBASE; CINAHL; Web of Science; BIOSIS Previews; Cambridge Scientific Abstracts; mRCT; and additional sources were searched for published and unpublished trials. The date of the last search was April 10, 2012.

### Criteria for Included Studies

**Types of Studies.** RCTs, which fulfilled the criteria described previously, were included.

**Types of Participants.** Both adults and children with CRS as defined by either European Position Paper on Rhinosinusitis and Nasal Pol-

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