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Review

Review of evidence supporting the use of nasal corticosteroid irrigation for chronic rhinosinusitis

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Key Messages

- Corticosteroid irrigation (CSI) is commonly used for management of chronic rhinosinusitis; however, evidence supporting its safety and efficacy is weak, deriving primarily from small studies in postoperative patients. Corticosteroid irrigation is not approved by the US Food and Drug Administration, and no systematic surveillance of safety data exists.
- Variability in the prescribed regimen and the preparation by compounding pharmacies or patients may influence safety and effectiveness. Furthermore, recommended methods for CSI may result in poor patient adherence.
- No convincing evidence supports the use of CSI in patients who have not been operated on. Small studies in postoperative patients have shown improved outcomes with CSI compared with standard intranasal corticosteroid nasal sprays; however, little evidence supports benefits of CSI over saline irrigation.
- Adequately powered and well-controlled safety and efficacy studies of CSI should be conducted before recommending its routine use in patients with CRS.

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ABSTRACT

Objective: To analyze published reports on the efficacy and safety of CSI in CRS and evaluate the clinical implications of current gaps in evidence. Corticosteroid irrigation (CSI) is commonly used for management of chronic rhinosinusitis (CRS) with nasal polyps; however, such use is not approved by the US Food and Drug Administration (FDA).
Data Sources: Publications were obtained through PubMed searches through January 2022.
Study Selection: Searches were conducted using 2 terms: "chronic rhinosinusitis" or "nasal polyps" as the first term and "corticosteroid irrigation," "steroid nasal lavage," or "sinus rinse" as the second term. We reviewed relevant, peer-reviewed literature (19 original research [9 controlled, 10 uncontrolled trials], 7 reviews, and 1 meta-analysis) reporting safety and efficacy of CSI in patients with CRS.

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Results: Studies were difficult to compare because they used a variety of solution volumes (60 mL to 125 mL per nostril), corticosteroid agents (budesonide, betamethasone, mometasone, or fluticasone), corticosteroid doses, preparation protocols (by compounding pharmacy or by patient), and administration (frequency, time of day, body positioning). It is difficult to determine which parameters might substantially influence clinical effects because studies were generally small, showed marginal benefits, and rarely assessed safety. To date, no studies evaluating CSI have shown statistically significant differences in a type-I error–controlled primary end point over any comparator, possibly owing to small sample sizes.

Conclusion: Designing more robust clinical trials may help determine whether CSI is a valid treatment option. Until more evidence supporting CSI use exists, health care professionals should strongly consider choosing FDA–approved therapies for the treatment of CRS.

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Introduction

Chronic rhinosinusitis (CRS) with or without nasal polyps (CRSwNP, CRSsNP) is an inflammatory condition affecting up to 13.8% of individuals in the United States.[1,2] The symptoms of CRS, which include nasal congestion, obstruction or drainage, facial pain, sinus pressure and hyposmia, substantially impair patient quality of life (QoL).[3–5] Many patients with CRS report depression, fatigue, impaired workplace activity, and sleep disorders.[5,6]

Topical corticosteroid therapy is a mainstay of recommended treatment for CRS, preoperatively and postoperatively.[6] "Standard" intranasal corticosteroid sprays (INCS) are first-line treatments; however, many patients report inadequate symptom relief with INCS.[5] The narrow openings of sinonasal cavities prevent medication delivered by standard INCS from reaching target regions,[7–11] including the ostiomeatal complex and middle meatus, where sinuses drain and ventilate.[12]

The inaccessibility of key anatomic areas poses a major challenge to CRS management. Nasal irrigation using a large volume of saline solution may penetrate posterior regions of the nasal cavity. The International Consensus Statement on Allergy and Rhinology (ICAR) recommends saline irrigation as a first-line therapeutic option to improve CRS symptoms and patient QoL.[6] A short burst of systemic corticosteroids may be prescribed for symptom relief in CRSwNP; however, ICAR recommends that prescribers consider the risks associated with systemic corticosteroids, including adrenal suppression, sleep disturbances, and bone metabolism alterations.[6,13] Repeated courses of oral corticosteroids, even as infrequently as twice yearly, increase the risk of adverse events (AEs).[14–18] When symptoms persist despite appropriate use of systemic and topical corticosteroids and saline irrigation, sinus surgery may be warranted. Sinus surgery aims to decrease inflammation, increase ventilation, and enlarge drainage pathways to facilitate topical drug delivery.[6] Surgery is not curative, however, and patients require ongoing postoperative management of chronic inflammation with topical corticosteroids to mitigate symptom recurrence.[2]

Off-label use of corticosteroid products in nasal irrigation solutions has been recommended in postoperative patients.[2,6] Although corticosteroid irrigation (CSI) is used in clinical practice, no US Food and Drug Administration (FDA)–approved CSI product exists, and no standardized dosing and administration regimen is supported by evidence-based guidelines. In addition, there are many examples of approved drugs for which serious AEs were unknown until the medications were used in larger populations and AEs were discovered through rigorous postmarketing surveillance.[19] It is therefore quite concerning that no ongoing systematic safety monitoring exists for CSI—as is required for all approved pharmaceuticals—particularly because the safety of these compounded preparations has not been adequately established. Here, we review published studies on the efficacy and safety of CSI in CRS and evaluate the clinical implications of current gaps in evidence.

Corticosteroid Irrigation: An Unregulated Treatment Option

Irrigation is achieved through various methods: sinus rinse bottles are typically used to deliver high-volume saline or CSI; however, neti pots are also used. Experts propose that irrigation is a mechanical intervention that cleans the nasal mucosa; therefore, the effect may be the same regardless of solution composition.[20] Because both saline irrigation and CSI have been used in practice, it is important to determine whether efficacy or safety differ between these treatments.

One study[21] showed that solutions delivered by nasal irrigation devices minimally penetrate sinuses in patients who have not been operated on. Postoperatively, high volumes of solution have appeared to penetrate both the maxillary and frontal sinuses, with good coverage starting at approximately 100 mL.[22] Although CSI can reach the maxillary and frontal sinuses in patients after surgery, studies have shown that, for patients with CRS with mucosal edema (without nasal polyps or before sinus surgery), distribution may be < 2% of total CSI volume.[23,24] A nasal cast study by Harvey et al.[25] estimated that 1.4% of the suspension remained in the nose and sinus cavities of patients who have not undergone surgery, compared with 3.1% in those who have, suggesting that surgically opening sinuses facilitates drug delivery to an extent. Because distribution of topical solution to the sinus cavity is negligible in the patient before surgery, CSI generally is considered only after surgery.[2,6] Nasal saline irrigation (without corticosteroids) of postsurgical sinus cavities results in improved CRS outcomes compared with use of saline nasal sprays; therefore, high-volume saline irrigation has its own therapeutic benefit that may contribute substantially to benefits reported for CSI.[26–28]

Although it is well accepted that head position during irrigation affects the distribution of solution within sinonasal cavities, no standard position has been established. Common head positions used in corticosteroid administration are shown in Figure 1. For low-volume devices, for example, nasal drops, Mygind's position[29] is preferred.[30] The Mygind and Mecca positions were shown to be superior to the "head-back" position,[31] and the Mygind and Ragan positions were superior to Mecca and "head-back" positions in delivering drops to the middle meatus.[32] One study evaluated several positions with neti pot use,[33] but high-volume CSI has typically been administered in the head-forward 90° position.[30] For corticosteroid delivery to the sinuses through irrigation, a systematic review found the head-down-and-forward position to be more effective than the head-upright or head-back positions.[34] Computational fluid dynamic modeling showed that the nose-to-ceiling head position was superior to the nose-to-ground position in delivering a 120-mL irrigation to the sphenoid sinuses, whereas other sinuses were similarly penetrated in both head positions.[34] No standard protocol specifies which head position is optimal for low- or high-volume irrigation, and among the 9 controlled studies of CSI reviewed in Table 1,[24,36–43] only 1 indicated whether a standardized head position was used to ensure consistent delivery of high-volume CSI.[43]

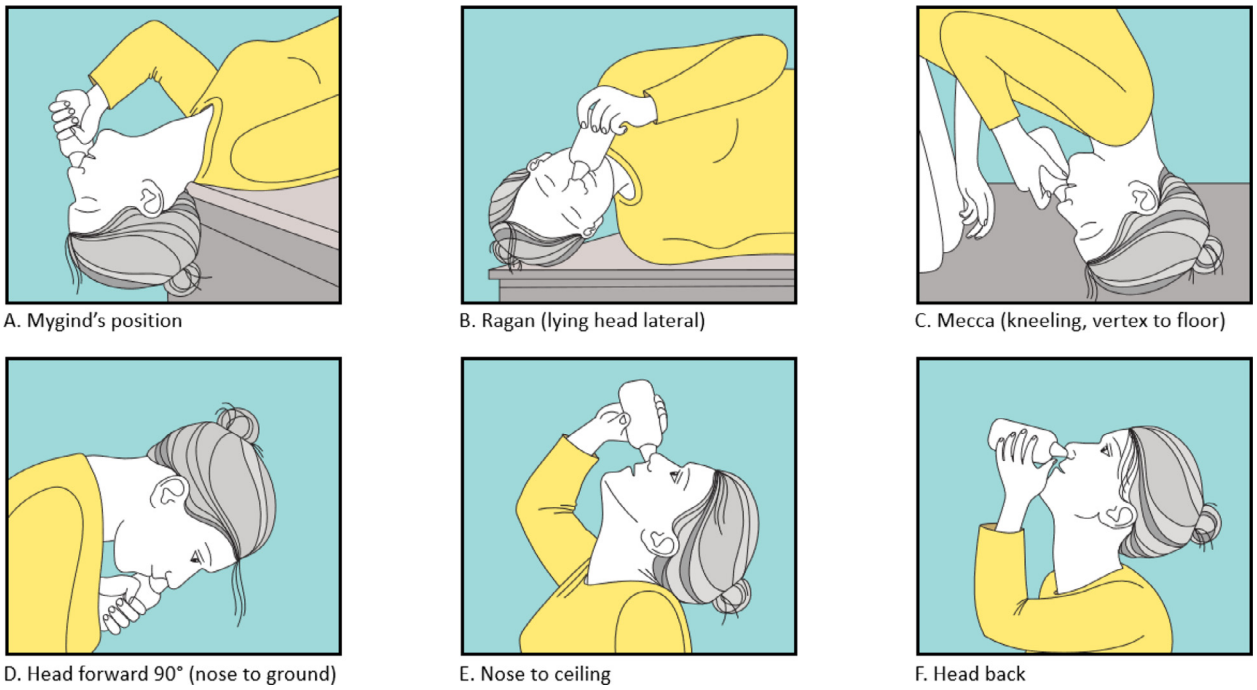

Figure 1. Head positions used for nasal irrigation. A, Mygind's position: lying recumbent, head hanging over the edge of a surface, nostrils facing upward. B, Ragan position: lying, with head lateral. C, Mecca position: kneeling, vertex to floor. D, Head forward 90°. E, Nose-to-ceiling position. F, Head-back position.

Role of Corticosteroid Irrigation in Chronic Rhinosinusitis Treatment Algorithms

International Consensus Statement on Allergy and Rhinology: Rhinosinusitis 2021

ICAR-RS-2021 details recommendations for "appropriate medical therapy prior to surgery," which include INCS and saline irrigation for both CRSwNP and CRSsNP. Short courses of oral corticosteroids and antibiotics (3 to 4 weeks) are recommended for CRSwNP but not for CRSsNP. When these treatments are insufficient, ICAR-RS-2021 recommends surgery followed by postoperative medical management. For both forms of CRS, ICAR-RS-2021 recommends topical corticosteroid sprays (Grade A) and saline irrigation (Grade B) as postoperative treatment options.[6]

For CRSwNP, ICAR-RS-2021 describes evidence supporting use of "nonstandard" delivery of corticosteroids, for example, through CSI, an exhalation delivery system with fluticasone (EDS-FLU), and atomizers. ICAR-RS-2021 recommends CSI (Grade A) on the basis of 5 randomized, controlled studies (4 studies also involving patients with CRSsNP),[24,37,40,42] and a meta-analysis.[44] For CRSsNP, ICAR-RS-2021 designates CSI as a treatment option (Grade A) on the basis of 3 prospective cohort studies[45–47] and 2 randomized clinical trials.[37,40]

European Position Paper on Rhinosinusitis and Nasal Polyps 2020

The European Position Paper on Rhinosinusitis and Nasal Polyps 2020 recommends 6 to 12 weeks of nasal corticosteroids (Level 1a) and saline irrigation (Level 1a) for patients with CRS but does not distinguish between CRSsNP and CRSwNP. Antibiotics and systemic corticosteroids may be used for patients with persistent disease (Level 1a).[48]

Corticosteroid steroid irrigation is classified as an alternative delivery method, without a specific level of recommendation. The European Position Paper on Rhinosinusitis and Nasal Polyps 2020 describes CSI studies and notes that it cannot advise on this delivery method because of the low quality of available evidence, particularly the lack of direct comparisons.[48]

Chronic Rhinosinusitis With Nasal Polyps

For patients with nasal polyps, Hopkins et al.[49] recommend that healthcare professionals prescribe corticosteroid drops (not FDA −approved) and saline irrigation for 4 weeks. If symptoms are not resolved, sinus surgery should be considered. After sinus surgery, they recommend use of standard INCS and saline irrigation. If polyps recur, corticosteroids may be considered, using different delivery methods (eg, delivery devices, irrigation, and stents).[49]

A Multidisciplinary Consensus on a Stepwise Treatment Algorithm for Management of Chronic Rhinosinusitis With Nasal Polyps

Han et al.[2] recommend initial management of CRSwNP using standard INCS and a short burst of oral corticosteroids. In addition, EDS-FLU or short bursts of oral corticosteroids are recommended as a second step before surgery or biologics. Corticosteroid irrigation is not recommended for initial management but is listed as an option for postoperative management, along with saline irrigation, standard INCS, EDS-FLU, and sinus implants.[2]

Yardstick for the Medical Management of Chronic Rhinosinusitis

This expert consensus recommends intranasal corticosteroids as first-line therapy for patients presenting with symptoms of CRS. It recommends changing delivery mode if initial treatment yields inadequate response but does not recommend any specific agent or delivery method over another. Standard INCS, dry powder, drops, and nebulized particles are discussed within a single category of "Sprays and Drops," whereas large-volume irrigation and the exhalation delivery system are each discussed as distinct modes of intranasal corticosteroid delivery. The authors concluded that although high-volume nasal irrigations seem safe and effective for postoperative management, more research in larger study populations is needed. The authors noted that it is reasonable to consider EDS-FLU as an alternative for patients who do not respond to standard INCS. Second-line therapies for patients with CRSwNP include endoscopic

Table 1
Corticosteroid irrigation Literature Review Results: Controlled Trials, by Study Population Size[23,35–42]

Study	Cited in guidelines and key reviews	Patient population	Study treatment	Administration protocol	Treatment duration	Safety results	Efficacy results
Luz-Matsumoto et al,[36] 2021	Not cited	N = 257 Adults ≥ 18 y of age, diagnosed with CRSwNP and CRSsNP	Retrospective observational study • Group A: CSI (1% compounded budesonide drops [each drop presented 500 μg of budesonide] or betamethasone cream [0.5 mg/g betamethasone] diluted in 250 mL of alkaline homemade saline solution) • Group B: standard INCS (budesonide or betamethasone)	Not specified	Evaluation of electronic medical records from 2013-2019; use of drug was defined by cycles of use (3-6 mo)	Adverse events of ear fullness (n = 2), epistaxis (n = 2), nasal irritation (n = 1), epigastric pain (n = 1) and nausea (n = 1) occurred with CSI use, whereas standard INCS use caused only epistaxis in 1 patient.	For patients who were ESS naive, those who used CSI showed significant improvement on the SNOT-22 (mean [SD], 44.5 [21.9] to 39.7 [22.3]; $P = .04$). Patients who were ESS naive and used standard INCS showed significant improvement in LKS (mean [SD], 5.4 [3.0] to 4.7 [3.1]; $P < .001$). Patients using CSI had greater improvement in SNOT-22 score than did patients using INCS ($P = .008$). Patients who previously had ESS experienced more subjective symptom improvements and fewer exacerbations with CSI than did those using standard INCS ($P = .04$ and $P = .02$, respectively).
Tait et al,[37] 2018	Bernstein et al. *AAAAI*. 2019; Orlandi et al. *ICAR*. 2021; Fokkens et al. *EPOS*. 2020; Grayson et al. *IFAR*. 2019; Lee et al. *Immunol Allergy Clin North Am*. 2020; Marcias-Valle et al. *Ear Nose Throat J*. 2020; Tan et al. *Curr Opin Otolaryngol Head Neck Surg*. 2019	N = 61 Adults, mean age of 51 y, with a diagnosis of CRSwNP or CRSsNP, inflammation of the sinuses for ≥ 12 wk and ≥ 2 symptoms consistent with CRS	Patients were randomized to receive either 0.5 mg budesonide capsules or lactose capsules (placebo) into an 8-oz saline solution.	Patients dissolved 2 budesonide capsules into saline solution and irrigated both nostrils with half the bottle once daily for 30 days.	30 d	No related adverse events in either intervention group.	The average change in SNOT-22 score for patients who received BNI was numerically larger than in the saline irrigation placebo arm (mean [SD], 20.7 [17.9] vs 13.6 [18.8] points) (95% CI, −2 to 16). Twenty-three participants (79%) who received BNI experienced a clinically meaningful (not statistically significant) reduction in SNOT-22 score vs 19 (59%) in the placebo arm, for a difference of 20% (95% CI, −2.5% to 42.5%). Mean change in LKS was 3.4 points (SD, 2.3) in those treated with BNI and 2.7 points (1.9) in the placebo arm, for an average difference of 0.7 points (95% CI, −0.6 to 2).
Huang et al,[24] 2019	Orlandi et al. *ICAR*. 2021; Lee et al. *Immunol Allergy Clin North Am*. 2020; Marcias-Valle et al. *Ear Nose Throat J*. 2020; Tan et al. *Curr Opin Otolaryngol Head Neck Surg*. 2019	N = 60 Adults, median age 37.6 y, diagnosed with CRSwNP or CRSsNP, 3 mo after ESS	Patients with CRS after ESS • Group A: CSI (budesonide dissolved in saline [dosage not described]) • Group B: saline irrigation	Patients performed postoperative nasal irrigation once daily for 6 d after the first cleaning of the nasal cavity and sinus. Patients who continued to use budesonide or saline irrigation for 3 mo were included in this analysis.	3 mo	Adverse events were reported in both CSI and saline irrigation groups. The most common were nasal itching (7 vs 5), nasal pain (10 vs 6), and epistaxis (8 vs 5).	SNOT-22 scores, visual analog scale scores, and LKS improved; however, no statistical differences between the 2 groups were observed for SNOT-22 or visual analog scale. The CSI group had a significantly higher mean (±SD) LKS than the saline irrigation group (2.83 ± 1.782 vs 1.96 ± 2.822; $P = .009$). No significant differences between groups were observed in 36-Item Short Form Survey score, Self-Rating Anxiety Scale score, and Self-Rating Depression Scale.

(*continued*)

Table 1 (*Continued*)

Study	Cited in guidelines and key reviews	Patient population	Study treatment	Administration protocol	Treatment duration	Safety results	Efficacy results
Rotenberg et al,[38] 2011	Bernstein et al. *AAAAI*. 2019; Fokkens et al. *EPOS*. 2020; Yoon et al,[44] 2018; Lee et al. *Immunol Allergy Clin North Am*. 2020; Marcias-Valle et al. *Ear Nose Throat J*. 2020	N = 60 Adults, mean age of 47.5 y, with a diagnosis of CRSwNP, a Samter's triad phenotype, failure of ≥ 6 mo of standard medical management before they underwent initial ESS, and documented severe disease	Patients with post-ESS were randomized into 3 groups: • Group A: saline irrigation alone (60 mL per nostril). • Group B: saline irrigation alone (60 mL per nostril) + separate budesonide nasal spray (64 μg metered dosage per nostril). • Group C: saline irrigation mixed with 2 mL of 0.5 mg/mL budesonide to irrigate each nostril.	Patients were instructed as to correct irrigation technique before hospital discharge, and were reminded of the technique at each postoperative visit. Irrigation was performed twice daily.	12 mo	No clinically significant changes in IOP; adrenocorticotropic hormone levels were within normal limits; no hypothalamic–pituitary–adrenal suppression detected.	No statistically or clinically significant differences were observed between groups at any time point ($P > .05$).
Jang et al,[39] 2013	Bernstein et al. *AAAAI*. 2019; Grayson et al. *IFAR*. 2019; Yoon et al,[44] 2018	N = 60 Adults, mean age of 45 y, who were post-FESS and had a lapse in BNI ≥ 1 month, while complying with nasal corticosteroid sprays and oral leukotriene antagonists. Patients were diagnosed with eosinophilic CRSwNP, eosinophilic CRSsNP, allergic fungal sinusitis, or Samter's triad.	0.5 mg ampules of budesonide in 3 oz of saline solution to irrigate each nostril with 1.5 oz Patients used BNI post-FESS and had a lapse in treatment when they were not using BNI. All patients served as their own controls.	Patients were instructed to irrigate each nostril twice daily.	Mean duration: 13.4 mo	None measured	SNOT-20 scores (mean ± SD) with BNI were significantly lower ($P < .05$) (12.5 ± 10.4 with BNI vs 15.1 ± 12.0 without BNI). The difference in LKS (mean ± SD) did not reach statistical significance (4.7 ± 3.5 with BNI vs 5.7 ± 3.6 without BNI) ($P = .08$). In the eosinophilic CRS subgroup, SNOT-20 scores and LKS significantly improved more with BNI than with no use of BNI ($P = .04$, $P = .02$).
Harvey et al,[40] 2018	Bernstein et al. *AAAAI*. 2019; Orlandi et al. *ICAR*. 2021; Fokkens et al. *EPOS* 2020; Grayson et al. *IFAR*. 2019; Hopkins,[49] 2019; Han et al,[2]. 2021; Marcias-Valle et al. *Ear Nose Throat J*. 2020; Tan et al. *Curr Opin Otolaryngol Head Neck Surg*. 2019	N = 44 Adults diagnosed with CRSwNP or CRSsNP who underwent endoscopic sinus surgery	After endoscopic sinus surgery, patients were randomized into either of 2 groups: • Group A: CSI with 240 mL saline solution mixed with 2 mg mometasone + placebo nasal spray • Group B: irrigated with placebo saline irrigation + standard INCS (0.1 mL mometasone nasal spray [2 mg])	Patients performed nasal irrigation followed by a nasal spray, once daily. The nasal irrigation was prepared with 2 pumps of the mometasone or placebo via a metered pump and mixed with the saline solution prepared per commercial guidelines.	12 mo	No medication reactions were observed in either group.	Mometasone CSI group had greater improvements (mean ± SD) in nasal blockage (−69.91 ± 29.37 vs −36.12 ± 42.94; $P = .03$), Lund-Mackay score (−12.07 ± 4.43 vs −7.39 ± 6.94; $P = .03$) and less inflammation on modified LKS (7.33 ± 11.55 vs 21.78 ± 23.37; $P = .02$) than did the group with standard mometasone INCS. 1 year after treatment, blockage, drainage, fever, and total visual analog scale scores in patient-reported outcomes were all statistically lower in the mometasone CSI group ($P = .06$, $P < .01$, $P = .03$, $P = .05$, respectively).

(*continued*)

Table 1 (*Continued*)

Study	Cited in guidelines and key reviews	Patient population	Study treatment	Administration protocol	Treatment duration	Safety results	Efficacy results
Jiramongkolchai et al,[41] 2020	Not cited	N = 43 Adults ≥ 18 y of age, with CRSsNP and no history of sinus surgery	Double-blind randomized clinical trial: • Group A: standard mometasone INCS (0.2 mg) and nasal saline irrigation • Group B: mometasone CSI (2.4 mg in 236 mL) and saline nasal spray	All participants were provided with an 8-oz sinus rinse bottle and supply of USP grade sodium chloride and sodium bicarbonate mixture in commercially prepared packets. Participants were instructed to perform nasal irrigation, followed by administration of nasal spray.	2 mo	No indication of hypothalamic–pituitary–adrenal axis suppression was detected after 8 weeks of intervention.	64% of patients (14/22) in the standard mometasone INCS group and 81% of patients (17/21) in the mometasone CSI group had clinically meaningful improvement in SNOT-22 score. The CSI group had incrementally more SNOT-22 score improvement than did the standard mometasone INCS group, a proportion difference of 17% (95% CI, −9% to 44%). The least squares mean difference between the 2 groups for SNOT-22 was −8.6 (95% CI, −17.7 to 0.58; $P = .07$) in favor of the mometasone CSI group. The least squares mean difference between LKS were similar (0.16 [95% CI, −0.84 to 1.15; $P = .75$]).
Rawal et al,[42] 2015	Bernstein et al. *AAAAI*. 2019; Orlandi, et al. *ICAR*. 2021; Fokkens,et al. *EPOS*. 2020; Grayson et al. *IFAR*. 2019; Yoon et al,[44] 2018; Marcias-Valle et al. *Ear Nose Throat J*. 2020	N = 42 Adults, median age 46.5 y, diagnosed with CRSwNP, who underwent functional endoscopic sinus surgery after failing medical management	After functional endoscopic sinus surgery, patients were randomly assigned to either saline irrigation alone or BNI (saline solution mixed with 2 mL of 0.5 mg/2 mL budesonide ampules). Patients irrigated each nostril with 60 mL.	Patients were given instructions on postoperative care. Patients created the saline solution reserve by mixing 1.5 tsp canning/pickling salt, 1.5 tsp baking soda, and 1 quart of distilled water. Patients in the BNI arm mixed BNI into their saline solution reserves. Patients were instructed to irrigate twice daily for a total of 240 mL using a high-volume, low-pressure irrigating device.	6 mo	None measured	Although both saline irrigation and BNI improved quality of life for postfunctional endoscopic sinus surgery patients, as measured by SNOT-22, Rhinosinusitis Outcomes Measurement Test-31, and Rhinosinusitis Disability Index. Neither intervention significantly increased quality of life compared with the other. Neither group of patients experienced significant olfactory improvement, as measured by Phenyl Ethyl Alcohol threshold test and the University of Pennsylvania Smell Identification Test, up through postoperative visit 3 (3-6 mo postoperatively).
Thamboo et al,[43] 2014	Bernstein et al. *AAAAI*. 2019; Orlandi et al. *ICAR*. 2021; Fokkens et al. *EPOS*. 2020; Marcias-Valle et al. *Ear Nose Throat J*. 2020	N = 20 Adults, ≥ 19 y of age, diagnosed with CRSsNP and who had received bilateral functional endoscopic sinus surgery in the past	Patients were randomized to either CSI with 1 mg BNI dissolved in 120 mL saline solution twice a daily (60 mL in each nostril) or 1 mg BNI via mucosal atomization device syringe twice daily.	Patients in the nasal saline irrigation arm were instructed to administer BNI twice daily using a NeilMed squeeze bottle. Patients in the mucosal atomization device arm were instructed to administer BNI twice daily via mucosal atomization device syringe. Patients assumed the lying, head-back position (Mygind's position).	2 mo	No indication of hypothalamic–pituitary–adrenal suppression in either group based on adrenocorticotropic hormone stimulation test results.	SNOT−22 scores did not differ between groups at 60 days ($P = .40$; 95% CI, −37.2 to 15.9).

Abbreviations: BNI, budesonide nasal irrigation; CI, confidence interval; CRSsNP, chronic rhinosinusitis without nasal polyps; CRSwNP, chronic rhinosinusitis with nasal polyps; CSI, corticosteroid irrigation; ESS, endoscopic sinus surgery; FESS, functional endoscopic sinus surgery; INCS, intranasal corticosteroid spray; LKS, Lund-Kennedy score; SNOT, Sino-Nasal Outcome Test; USP, United States Pharmacopeia.

sinus surgery, biologics, and oral corticosteroids, and for patients with CRSsNP include surgical intervention, macrolide antibiotics, and intranasal decongestants. Saline irrigation is recommended as adjunctive therapy for CRSwNP or CRSsNP.[50]

Clinical Evidence Supporting the Use of Corticosteroid Irrigation

We identified 9 controlled trials including CSI as a treatment intervention (Table 1).[24,36–43]

Controlled Trials of Corticosteroid Irrigation vs Standard Intranasal Corticosteroid Spray

Harvey et al.[40] conducted a randomized, controlled trial over 12 months in which approximately 950 patients were screened for eligibility, of whom 44 patients with CRSwNP or CRSsNP agreed to participate, underwent surgery using a standardized surgical technique, and postoperatively received 2 mg daily of mometasone (delivered by mometasone spray [INCS group, n = 23] or by irrigation [CSI group, n = 21]). It is noteworthy that 2 mg daily of mometasone is 5 times the approved dosage for use in patients with CRSwNP (400 μg/d).[51] Patients prepared the CSI on each day of administration and instilled 240 mL of CSI or saline with a NeilMed bottle once daily, followed by a nasal spray; 1 device contained corticosteroid and the other saline. After 1 year, patients in the CSI group had greater improvement in nasal blockage, Lund-Mackay scores (LMS), and modified Lund-Kennedy scores (LKS) than did the standard INCS group, whereas there was no difference between treatment groups for visual analog score (VAS), Sino-Nasal Outcome Test 22 (SNOT-22), and global rating of sinonasal function (Table 1). No AEs were reported in either treatment group.[40]

Jiramongkolchai et al.[41] conducted a double-blind, randomized, controlled trial in patients with CRSsNP with no previous sinus surgery who received either mometasone CSI (2.4 mg diluted in 240 mL of saline) with a saline nasal spray, or a mometasone furoate spray (0.2 mg) with 240 mL of saline irrigation. Both groups experienced similar results with a minimally clinically improved difference in SNOT-22 scores between baseline and week 8 (Table 1). At week 8, the least squares mean difference between the 2 groups for SNOT-22 favored the mometasone CSI group. Change in LKS from baseline to week 8 was similarly improved for both groups (Table 1).[41] The authors tested for adrenal insufficiency by performing a cosyntropin stimulation test, the reference standard.[52] Postcosyntropin stimulation cortisol levels did not change significantly from baseline after 8 weeks of treatment for both treatment groups.[41]

Luz-Matsumoto et al.[36] conducted a retrospective observational study comparing patients with CRS (with or without polyps and surgery) who used corticosteroids (budesonide drops or betamethasone cream) through CSI or INCS. Both methods improved LKS among patients with CRSwNP; however, patients with CRSsNP showed no improvement in LKS using either method. Among patients with no previous sinus surgery, CSI was associated with greater SNOT-22 score improvements than was standard INCS. Patients who previously had sinus surgery experienced greater subjective improvement and fewer exacerbations with CSI than with INCS. Both treatment groups reported epistaxis; patients using CSI also reported ear fullness, nasal irritation, epigastric pain, and nausea (Table 1).[36]

In a double-blind, randomized, controlled trial conducted by Rotenberg et al.,[38] no statistically or clinically significant differences were observed in patients with CRSwNP after sinus surgery receiving saline irrigation alone, saline irrigation and standard budesonide nasal spray, or budesonide irrigation alone, for 12 months. No clinically significant changes in intraocular pressure (IOP) were observed. Intraocular pressure was reported as mean (SD) values[38]; however, the authors did not report whether any patients experienced a clinically meaningful increase in IOP (ie, > 6 mm Hg).[38,53,54] Adrenocorticotropic hormone (ACTH) levels were within normal limits, and no hypothalamic–pituitary–adrenal (HPA) axis suppression was detected. Adrenal function was assessed through random ACTH evaluations rather than with the more rigorous cosyntropin stimulation test.[38]

Controlled Trials of Corticosteroid Irrigation vs Saline Irrigation

Three randomized clinical trials compared CSI with nonmedicated saline irrigations.[24,37,42] Huang et al.[24] conducted a randomized, controlled trial involving patients with CRS (with or without polyps) after sinus surgery. Patients received either CSI (budesonide) or saline irrigation. Improvements in LKS, VAS, and SNOT-22 score were observed; however, results showed no significant differences between the 2 groups for VAS or SNOT-22 scores. The CSI group had a significantly higher LKS than did the saline irrigation group. Both groups reported nasal itching, nasal pain, and epistaxis (Table 1).[24] Tait et al.[37] examined patients with CRS (with or without polyps) without sinus surgery within 6 weeks before enrollment. Corticosteroid irrigation resulted in numerically larger changes in LKS and SNOT-22 scores than did saline irrigation; however, these changes were not statistically significant. Safety was not assessed in this study (Table 1).[37] Rawal et al.[42] reported on patients with CRSwNP evaluated by QoL (SNOT-22, Rhinosinusitis Outcomes Measurement Test, Rhinosinusitis Disability Index) and olfaction measures before and after sinus surgery. There were no statistically significant differences between the normal saline arm vs saline plus budesonide at any postoperative visit. Safety was not assessed in this study.[42]

Uncontrolled Trials of Corticosteroid Irrigation

Most uncontrolled trials had small study populations (between N = 8 and N = 48) (Table 2).[45–47,55–61] The largest study evaluated change in symptom score (a Likert scale from 0 to 5 recorded nasal obstruction, postnasal discharge, thick nasal discharge, loss of smell and taste, and facial pain and pressure), SNOT-22, and LKS in 111 patients with CRS (with or without polyps) who underwent sinus surgery.[44] After surgery and CSI (budesonide or betamethasone), significant improvement from baseline measurements (before surgery) were observed (Table 2); the mean (SD) follow-up was 55.5 ± 33.9 weeks. Safety was not assessed in this study. Other studies also reported efficacy results in SNOT-20, SNOT-22, and/or LMS, showing improvement from baseline measurements in similar patient populations (Table 2).[46,47,56,60]

In studies assessing CSI safety (Table 2), Soudry et al.[55] evaluated the effect of long-term budesonide CSI on HPA axis function and in IOP in postoperative patients with CRS (N = 48). Eleven patients had abnormally low stimulated cortisol levels (< 18 μg/dL), as measured by cosyntropin stimulation test; mean duration of CSI was 22 months. Concomitant use of standard INCS and inhaled corticosteroid (for asthma), in addition to budesonide rinse, was associated with HPA axis suppression. Intraocular pressure, measured in 46 of 48 patients, did not increase (range, 13-18 mm Hg; mean, 16 mm Hg).[55] Smith et al.[56] evaluated HPA axis and adrenal suppression in 35 patients with CRSwNP or CRSsNP using twice-daily budesonide CSI (daily dosage of 2 mg) over a mean of 38.2 months. Adrenal function was initially assessed by mean ACTH levels, and a cosyntropin stimulation test was obtained only in patients with cortisol levels < 500 nmol/L. No patients showed signs of HPA axis suppression.[56] Sachanandani et al.[46] investigated daily use, over 30 days, of budesonide respules (0.25 mg, 1 respule per nostril) dissolved in 5 mL saline. No HPA axis suppression was detected, and no patients showed poststimulation cortisol below critical levels.[46] In a study by Welch et al.,[61] 10 patients with CRSwNP who previously underwent sinus surgery received CSI twice daily with 0.5 mg budesonide dissolved in 240 mL saline, for 6 weeks. The average serum cortisol and 24-hour urinary cortisol levels were all within normal limits, and no HPA

Table 2
CSI Literature Review Results: Uncontrolled Trials, by Study Population Size[44-46,54-60]

Study	Cited in guidelines and key reviews	Patient population	Study treatment	Administration protocol	Treatment duration	Safety results	Efficacy results
Snidvongs et al,[45] 2012	Bernstein et al. *AAAAI*. 2019; Orlandi, et al. *ICAR*. 2021; Fokkens, et al. *EPOS*. 2020: Yoon et al,[44] 2018	N = 111 Adults, ages (mean ± SD) 50.1 ± 13.5 y, diagnosed with CRSwNP or CRSsNP, requiring endoscopic sinus surgery after failing medical therapy	After sinus surgery, patients irrigated with either 1 mg micronized budesonide or micronized betamethasone dissolved in 240 mL saline solution.	Patients irrigated the nose once daily. No patient reduced their use in the first 3 months. Afterward, patients self-tapered to alternate days or twice weekly as dictated by disease control.	No limit to maximum duration; mean follow-up was 55.5 ± 33.9 weeks	None measured	Baseline vs posttreatment for all patients (mean ± SD): • Symptom score (2.6 ± 1.1 vs 1.2 ± 1.0), SNOT−22 score (2.2 ± 1.1 vs 1.0 ± 0.8), and LKS (6.7 ± 3.0 vs 2.5 ± 2.0) were significantly improved with CSI • Change from baseline showed significant improvement for all patients ($P < .001$)
Soudry et al,[55] 2016	Bernstein et al. *AAAAI*. 2019; Grayson et al. *IFAR*. 2019; Yoon et al,[44] 2018; Tan et al. 2019; Lee et al. *Immunol Allergy Clin North Am*. 2020; Marcias-Valle et al. *Ear Nose Throat J*. 2020	N = 48 Adults, mean age of 54.5 y, diagnosed with CRS, postendoscopic sinus surgery, and undergoing cortisol and IOP testing	Patients irrigated with 0.5 mg micronized budesonide in 240 mL saline solution.	Patients were instructed to irrigate the nose once daily or twice daily, for ≥ 6 mo.	Mean duration: 22 mo	IOP was within normal limits in all patients; stimulated cortisol levels were abnormally low in 11 patients (23%); further analysis showed that concomitant use of standard INCS and pulmonary corticosteroid inhalers with BNI was significantly associated with HPA suppression ($P = .02$).	None measured
Smith et al,[56] 2016	Bernstein et al. *AAAAI*. 2019; Grayson, et al. *IFAR*. 2019; Yoon et al,[44] 2018; Lee et al. *Immunol Allergy Clin North Am*. 2020; Marcias-Valle et al. *Ear Nose Throat J*. 2020; Tan et al. *Curr Opin Otolaryngol Head Neck Surg*. 2019.	N = 35 Adults, mean age of 49.5 y, diagnosed with CRSwNP or CRSsNP, post- endoscopic sinus surgery, who were using BNI for ≥ 12 mo	Patients irrigated with micronized budesonide mixed in saline solution (concentration of 1 mg per irrigation twice daily; total daily dosage of 2 mg).	Patients began BNI 1 wk postoperatively. Patients performed irrigation twice daily for ≥ 12 mo.	Mean duration: 38.2 mo	Mean morning serum cortisol results were within normal limits. There was no evidence of HPA-axis suppression.	SNOT-22 score (mean ± SD) at baseline was 49.1 ± 21.9; SNOT-22 score at time of HPA-axis testing was 20.5 ± 16.9. Results were not tested for statistical significance.
Man et al,[57] *Int* 2013	Bernstein et al. *AAAAI*. 2019; Grayson et al. *IFAR*. 2019; Yoon et al,[44] 2018	N = 23 Adults, age of 53.3 ± 13.7 y (mean ± SD), diagnosed with CRS (with or without polyps) and who had previously undergone bilateral endoscopic sinus surgery	Patients irrigated with 3 mg micronized fluticasone propionate in 240 mL saline solution.	Patients performed CSI twice daily for 6 wk.	6 wk	Salivary cortisol levels were within normal limits before and after treatment, with no evidence of HPA suppression. There was no clinical or statistical difference in mean pre- and post-IOP. No patients developed posterior subcapsular cataracts.	None measured
Bhalla et al,[58] 2008	Bernstein et al. *AAAAI*. 2019; Yoon et al,[44] 2018, Lee et al. *Immunol Allergy Clin North Am*. 2020	N = 18 Adults with CRSwNP refractory to conservative medical therapy	Patients irrigated with 1 mg micronized budesonide dissolved in 240 mL of saline solution.	Patients dissolved budesonide suspension in saline and irrigated 60 mL in each nostril twice daily using a commercially available saline rinse kit. Patients were required to perform uninterrupted treatment for ≥ 8 wk.	8 wk for pre- and posttreatment morning cortisol levels; 9-23 wk for adrenocorticotropic hormone stimulation testing	There was no evidence of HPA-axis suppression ($P = .42$). No adverse effects were reported.	None measured
Seiberling et al,[59] 2013	Bernstein et al. *AAAAI*. 2019; Grayson et al. *IFAR*. 2019; Yoon et al,[44] 2018	N = 18 Adults, mean age of 57.2 y, diagnosed with CRSwNP who failed conventional treatment and sinus surgery	Patients were divided into 2 groups: • Group A: had been using micronized BNI ≥ 1 mo before enrollment • Group B: started micronized BNI on enrollment • Patients irrigated with 1 mL of micronized budesonide dissolved in 240 mL saline	Patients were prescribed budesonide ampules and were instructed to dissolve 1 mL of micronized budesonide in 240 mL saline solution. Patients performed CSI twice daily for ≥ 1 mo.	Mean duration: • Group A: 6.3 mo • Group B: 5.89 wk	• Group A: 1 patient had a single IOP measurement > 21 mm Hg; it was not clear whether this was an adverse effect of INCS. • Group B: no patients had a significant change in IOP or IOP > 21 mm Hg.	None measured

(*continued*)

Table 2 (*Continued*)

Study	Cited in guidelines and key reviews	Patient population	Study treatment	Administration protocol	Treatment duration	Safety results	Efficacy results
			solution twice daily (0.5 mg/d)				
Kosugi et al,[60] 2016	Bernstein et al. *AAAAI*. 2019; Grayson et al. *IFAR*. 2019; Yoon et al,[44] 2018; Tan et al. *Curr Opin Otolaryngol Head Neck Surg*. 2019	N = 16 Adults, mean age of 50.9 y, diagnosed with CRSwNP or CRSsNP who met criteria for difficult-to-treat CRS	Patients irrigated with 1 mg micronized budesonide into 500 mL saline solution.	A glycerol solution of 1% budesonide was prepared by a pharmacy. Patients were instructed to dilute 2 drops of 1% budesonide (1 mg) into 500 mL of saline. Patients irrigated both nostrils with 250 mL solution once daily using a 20-mL syringe.	3 mo	None measured	After high-volume micronized BNI, 75% of patients had improved SNOT-22 scores, and 75% had improved LKS. SNOT-22 mean scores (baseline, 50.2 [SD, 19.3]; poststudy, 29.6 [20.4]; $P = .006$), and LK mean scores (8.8 [SD, 3.3]; 5.1 [4.4]; $P = .01$) improved significantly.
Welch et al,[61] 2010	Bernstein et al. *AAAAI*. 2019; Yoon et al,[44] 2018	N = 10 Adults ≥ 18 y of age who had undergone endoscopic sinus surgery, had recurrent polyposis, and were not taking systemic corticosteroids for ≥ 3 mo	Patients irrigated twice daily with 0.5 mg/2 mL micronized budesonide dissolved in 240 mL saline solution.	Patients instructed to perform irrigation twice daily using budesonide mixed in saline that was prepared (1 L distilled water, 1 tsp of noniodinated salt, and 1 tsp of baking soda).	6 wk	Average serum cortisol and 24-h urinary cortisol results fell within normal limits. No HPA suppression was detected.	None measured
Sachanandani et al,[46] *i*2009	Bernstein et al. *AAAAI*. 2019; Orlandi et al. *ICAR*. 2021; Fokkens et al. *EPOS*. 2020	N = 9 Adult, mean age of 54.5 y, with CRSwNP or CRSsNP	Patients irrigated each nostril once daily with 0.25 mg micronized budesonide ampules, dissolved in 5 mL saline solution.	Patients were instructed to empty 1 budesonide respule in a container and mix 5 mL of saline solution using a 5-mL syringe. Patients irrigated 5 mL into each nostril while performing 3 positions: head down and back or head down and forward (Mygind's or Mecca position), head in downward position (Ragan's position), and head-back position (in a 45° angle). The patients were to hold their head in each position for 2-3 min and to sit up and rest between each position. Patients completed this process on 1 side and then repeated the process for the opposite nostril.	30 d	None of the patients' poststimulation cortisol levels were below the critical level of 18-20 μg/dL. No HPA suppression was detected.	Mean difference in SNOT-20 scores was −1 (95% CI, −1.77 to −0.23; $P = .02$), indicating clinically significant improvement after therapy.
Steinke et al,[47] 2009	Bernstein et al. *AAAAI*. 2019; Orlandi et al. *ICAR*. 2021; Fokkens, et al. *EPOS*. 2020	N = 8 Adults with chronic hyperplastic eosinophilic sinusitis or aspirin-exacerbated respiratory disease who failed previous medical therapy	Patients irrigated twice daily with micronized BNI 500 μg resuspended in > 100 mL saline.	Patients were instructed to dilute budesonide suspension in saline. Patients who performed CSI for ≥ 3 mo were included in the analysis.	≥ 3 mo	None measured	Median Sinus CT score before treatment was 15 (maximum, 30) and improved to 5 ($P < .05$) after treatment. Significant improvement (mean ± SD) in sense of smell (visual analog scale), from 1.1 ± 0.7 to 3.6 ± 0.8 ($P < .05$) was observed. Five of 6 participants who had prerhinoscopy and postrhinoscopy showed improvement after treatment; 3 of 4 patients had complete resolution of nasal polyps.

Abbreviations: BNI, budesonide nasal irrigation; CI, confidence interval; CRSsNP, chronic rhinosinusitis without nasal polyps; CRSwNP, chronic rhinosinusitis with nasal polyps; CSI, corticosteroid irrigation; CT, computed tomography; HPA, hypothalamic–pituitary–adrenal; INCS, intranasal corticosteroid spray; IOP, intraocular pressure; LKS, Lund-Kennedy score; SNOT, Sino-Nasal Outcome Test; tsp, teaspoon.

suppression was detected.[61] Seiberling et al.[59] reported that for patients with CRSwNP who had failed sinus surgery, 1 of 10 patients who used budesonide CSI (0.5 mg/d) for a mean of 6.3 months had elevated IOP (> 20 mm Hg). In this group, baseline IOP was not measured before starting budesonide CSI. In a different group of patients with CRSwNP (n = 8), no changes in IOP were observed over a mean of 5.89 weeks of budesonide CSI.[59] Bhalla et al.[58] conducted a retrospective study in 14 patients with recalcitrant CRSwNP and a history of sinus surgery who received 120 mL of budesonide CSI (1 mg dissolved in 240 mL saline) twice daily for 8 weeks. Morning cortisol levels were evaluated before and after treatment, and ACTH stimulation testing was conducted for those patients who continued treatment for 9 to 23 weeks. Testing revealed no evidence of HPA axis suppression.[58] A 6-week study by Man et al.[57] evaluating the effect of 120 mL fluticasone CSI per nostril twice daily (3 mg dissolved in 240 mL saline) in 23 patients with CRS (with or without polyps) and history of sinus surgery found no evidence of HPA suppression, no clinical or statistical changes in IOP, and no development in posterior subcapsular cataracts.

Limitations of Current Evidence for Corticosteroid Irrigation

It is difficult to compare or summarize conclusions from published studies of CSI because they used varied solution volumes (60 mL to 125 mL per nostril),[37–43] therapeutic agents (budesonide, betamethasone, mometasone, or fluticasone), and doses (Tables 1 and 2). Their preparation protocols (by compounding pharmacy or by patient) and administration (frequency, time of day, body positioning) also varied. Because most studies were small, showed marginal benefits, and rarely included safety assessments, it is difficult to determine which parameters, if any, influenced clinical effects.

Evidence for the benefit and safety of corticosteroid-containing nasal irrigation is limited. To date, no CSI studies have shown statistically significant differences in a type-I error–controlled primary end point over any comparator, owing to design limitations and small sample sizes. Several studies, such as those by Rotenberg et al.[38] (n = 20 per group), Rawal et al.[42] (n = 25 per group), and Tait et al.[37] (n = 40 per group), failed to reveal statistically a significant benefit of CSI over standard saline irrigation, suggesting that the addition of corticosteroid does not provide additional benefit to saline irrigation. Harvey et al.[40] suggested benefits for CSI compared with standard INCS, and their study has been referenced as showing benefits of CSI. That study enrolled a highly select subset of patients scheduled for surgery because only 44 of 950 patients (5%) assessed for eligibility agreed to participate. These patients initiated treatment at the time of surgery and used 2 mg of INCS, which is 5 times the dose indicated for treatment of nasal polyps.[51] Some outcome measures reached nominal statistical significance; however, the study did not control for multiplicity, for example, using a statistical method to adjust for the increased risk of a type-1 error (false-positive finding) when multiple hypotheses are tested, and therefore, these findings may represent chance occurrence.[40,62]

The lack of efficiency of CSI is concerning. One irrigation study performed on nasal casts found that surgical procedures, such as Draf III, could cause irrigation fluid to spill prematurely across the resected septum, thus reducing the effect of irrigation to other sinuses.[63]

Additional safety data for CSI are needed because studies to date have been underpowered and of insufficient duration to adequately assess important AEs, including assessment of ocular and systemic adverse effects. In addition, all these studies have reported conflicting results regarding HPA axis suppression.[38,46,55,58] Many of these studies measured random cortisol levels, which is not recommended for assessing HPA axis suppression, rather than measuring cosyntropin stimulation using the validated ACTH test, considered the reference standard for primary adrenal insufficiency.[52,64] Therefore, results from studies not using ACTH testing should be reconsidered owing to this limitation. In addition, most studies reported no safety findings (Tables 1 and 2); however, many were too short in duration, with small sample sizes, making it impractical to detect certain corticosteroid AEs of interest, such as cataract formation.

Considerations for Off-label Use of Corticosteroids in Nasal Irrigation

A major limitation for use of CSI is the lack of oversight from regulatory bodies because no FDA–approved CSI product exists. Health care providers may prescribe off-label use of budesonide ampules that are indicated for nebulized treatment of asthma, or they may order CSI solutions prepared by a compounding pharmacy.

The lack of uniformity and quality control for CSI is concerning. Pharmaceutical products must abide by current Good Manufacturing Practice regulations,[65] and drug compounding typically receives oversight from official organizations such as the Pharmacy Compounding Accreditation Board.[65] Patient preparation of a corticosteroid and saline solution, in which saline is mixed with corticosteroid powder or single-dose ampules (intended for inhalation), may not be homogenous. Moreover, the amount of medication that patients self-prepare and administer on a daily basis to their sinonasal cavities, may be inconsistent. Differences in administration techniques may also contribute to an inconsistent distribution of medication. Patient adherence to irrigation instructions can also affect dosing because 1 study noted that older patients and nonnative English speakers had lower rates of adherence than patients who have previously had surgery or irrigation experience.[66]

It is important to note that saline irrigation using contaminated tap water has been associated with primary amebic meningoencephalitis deaths. The Centers for Disease Control and Prevention showed that adding salt mixture to tap water for saline irrigation does not inactivate pathogens such as *Naegleria fowleri*.[67] Therefore, patients may be at risk of becoming infected with contaminated water if they do not ensure that the water used to create nasal irrigation solutions is properly distilled, previously boiled, or filtered using a filter with an absolute pore size of ≤ 1 μg.[67] Nasal irrigation bottles are also commonly contaminated by strains of bacteria, most often with *Staphylococcus aureus*.[68,69] Thus, bottle contamination can lead to reinfection unless patients are educated and adhere to proper sterilization techniques (eg, using boiling water, detergents, Milton's solution, or microwave disinfection).[68]

Considerations for Future Corticosteroid Irrigation Trials

Limitations of trials reviewed here highlight important challenges for future CSI trials to address. Before developing a phase 3 registration-quality trial, phase 1 or 2 dose-ranging studies would need to be conducted. It would be useful to standardize an irrigation technique that ensures adequate distribution of irrigation fluid to target nasal sites and to use imaging techniques (eg, gamma scintigraphy) to determine drug distribution patterns. Patient-training protocols would be required for preparing and administering irrigation solutions and on accurately monitoring adherence. Decisions to exclude or stratify patients based on symptom severity, disease duration, previous surgery, response to previous therapy, or presence of nasal polyps would also be important. Selection of prespecified efficacy end points and rigorous statistical methods to control for type-I errors are also critical. Furthermore, although several objective and subjective outcome measures, such as polyp grade, nasal symptom scores, and SNOT-22 score, have been evaluated in registration trials for CRSwNP treatments, standardized methods for assessing treatment response in CRSsNP have yet to be established. Systematic safety assessments, including adrenal function and ocular examinations in an adequately sized population, should be performed over a sufficient duration of treatment to detect AEs that

might be experienced during long-term management of this chronic inflammatory disease.

Conclusion

Although CSI is frequently prescribed for CRS, very limited clinical evidence supports the safety and efficacy of this treatment modality. Notably, no corticosteroid products have been reviewed or approved by the FDA for use in nasal irrigation. Trials evaluating CSI have mainly been conducted in small numbers of patients after surgery, limiting generalizability to the broader population of patients with CRS. These study designs, in addition to protocols in current clinical use, vary widely in dosing and administration parameters. In contrast, FDA–approved drug-device combination products for treatment of NP (ie, mometasone nasal spray, EDS-FLU, and sinus-eluting stents) are supported by robust evidence from registered clinical trials, manufactured with strict quality controls, and subject to ongoing postmarketing safety monitoring. Designing more robust clinical trials will help determine whether CSI is a valid treatment option. Because the long-term safety of these CSI compounded preparations has not been rigorously established, longitudinal safety monitoring studies for CSI should also be prioritized. Until more robust evidence is developed to support CSI use, providers should strongly consider limiting treatment to drug and device products approved as safe and effective by the FDA.

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