



Is nasal saline irrigation all it is cracked up to be?

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ABSTRACT

Objective: This review examines the literature regarding nasal saline irrigation in the management of sinonasal disease. We explore the various properties of nasal irrigation solutions and their effects on nasal symptoms.

Data Sources: English-language studies identified from MEDLINE and the Cochrane Central Register of Controlled Trials through December 2011.

Study Selections: Randomized, controlled trials (RCTs), prospective controlled and comparative studies, and observational studies reporting on the indications, efficacy, and safety of nasal saline irrigation.

Results: Nasal saline irrigation has often been used as both a solo and an adjunctive treatment in sinonasal diseases, including allergic rhinitis and chronic rhinosinusitis. Nasal saline irrigation has contributed to a reduction of inflammation as well as relief of nasal symptoms. Identifying the optimal technique is hampered by the fact that studies have employed various delivery devices and saline compositions, which subsequently have demonstrated different effects on mucus clearance, ciliary beat activity, and inflammatory mediators.

Conclusion: Overall, the data appear to demonstrate some small clinical benefit to nasal saline irrigation. Nasal saline irrigation is well tolerated, with minimal side effects. Further definitive studies are needed to optimize efficacy.

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Introduction

Nasal saline irrigation (NSI) is common to both modern and traditional therapy regimens. Although NSI is frequently regarded as an adjunct to conventional treatment of sinonasal disease, it has demonstrated improvement in symptoms as well as reduction in the use of rescue medications such as systemic corticosteroids when used as an adjunct or as sole treatment. Although diverse, much of the literature regarding NSI is generally of low quality. In this review, we attempt to summarize the data that address the mechanism(s), efficacy, and safety of NSI in patients with sinonasal disease.

Epidemiology of sinonasal disease(s)

Sinonasal disease, which includes chronic rhinosinusitis, allergic rhinitis, and viral upper respiratory infections, is a significant cause of morbidity. Notably, chronic rhinosinusitis (CRS) is one of the most common chronic illnesses in Americans younger than 45 years of age, affecting nearly 13% of the US population.¹ Based on the US National Health Interview survey, the number of non-institutionalized adults with diagnosed sinusitis in 2009 was 29.3 million, and the number of ambulatory care visits with a primary diagnosis of chronic sinusitis in 2007 was nearly 12.5 million,¹

resulting in an annual treatment cost of sinusitis of close to \$3 billion.²

Medical therapy has been the basis for treating CRS and other sinonasal diseases. Medications include short- and long-term antibiotic therapy, topical and systemic steroids, topical and oral decongestants, oral antihistamines, and mucolytics. Surgery is another therapeutic option; however, it is generally relegated to disease that is refractory to medical therapy.

History/background

The origins of nasal irrigation are believed to be from the ancient Hindu practice of Ayurveda, whose roots are traced to the Vedas. Neti (or Hatha Yogi) is an important part of the yogic system of body cleansing techniques.³ It is intended mainly for the cleaning of the air passageways in the head, and it has been used for thousands of years to alleviate sinus and allergy symptoms. The two main variants of neti are jala neti, using water poured into 1 nostril such that it leaves through the other nostril, and the more advanced sutra neti. In sutra neti, a length of wet string or thin surgical tubing is inserted through the nose and into the mouth. The end is then pulled out of the mouth and while holding both ends at once, the string is alternately pulled in and out of the nose. Both techniques are used to flush out the nasal cavities by using gravity to draw the flow of saline water through nasal passages.³

Nasal saline irrigation has gained popularity amongst consumers as exemplified by media coverage on National Public Radio.^{4,5}

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Independent market data provided by A.C. Nielsen demonstrated that sales of saline irrigation products have doubled annually for the last few years.⁶ Apparently NSI has made a recent comeback, likely because it is a relatively inexpensive and easily administered therapy.

Mechanism of action

The exact mechanism(s) of action of NSI are not clearly understood. The mucus lining of the nasal cavity constitutes one of the body's first lines of defense against potential pathogenic organisms,⁷ and these organisms may subsequently become entrapped in the mucus. NSI may enhance the movement of mucus toward the nasopharynx, directly clean the nasal mucosa,⁸ and aid in thinning nasal secretions.^{9,10} It may promote clearance of inflammatory mediators such as histamine and prostaglandins,¹¹ prevent secondary infection, and promote mucosal healing.^{9,10} NSI is also thought to play an important role in the postoperative period, because it reduces the risk of adhesions and promotes ostiomeatal patency.¹² Finally, chronic sinonasal disease leads to a decline in mucociliary clearance (MCC), and this is presumed to be a result of osmotic changes in the mucus layer or reduction in the ciliary beat frequency (CBF).^{9,12} For these reasons, the physiological changes that theoretically occur with use of NSI make it an attractive therapy for many sinonasal conditions.

Indications

NSI is recommended for a variety of sinonasal conditions, including allergic rhinitis (AR), atrophic rhinitis, rhinitis of pregnancy, viral upper respiratory tract infections (URTIs), CRS, acute rhinosinusitis, sinonasal sarcoidosis, Wegener's granulomatosis, and as a postoperative adjunct after functional endoscopic sinus surgery (FESS).¹⁰ Although there are very few absolute contraindications for NSI, patients with incompletely healed facial trauma, those suffering from conditions associated with an increased risk for aspiration (such as neuromuscular disorders), or those who cannot perform the procedure should avoid this modality.¹³

Efficacy

Few comparative, prospective and reproducible studies consistently demonstrate NSI's efficacy. We summarize the literature regarding NSI stratified by sinonasal disease as follows:

Sinusitis

Rabago et al¹⁴ investigated the benefit of NSI in 76 adults with chronic sinusitis or recurrent acute sinusitis. In this randomized controlled trial (RCT), 52 subjects received 150 mL per nostril daily of 2.0% buffered saline (with baking soda) delivered via SinuCleanse Nasal Cup (Med-Systems, Inc., Madison, Wisconsin) for 6 months. Twenty-four subjects as part of the control group received no topical therapy. The primary outcomes were quality of life (QOL) scores from 2 validated questionnaires: the general health assessment Medical Outcomes Survey (MOS) Short Form12 (SF12)¹⁵ and the Rhinosinusitis Disability Index (RSDI),¹⁶ a disease-specific instrument assessing QOL in emotional, functional, and physical domains. The investigators also measured overall sinus symptoms severity with a Single-Item Symptom Severity Assessment (SIA). The SIA measures global sinus symptom severity, with higher SIA scores indicating increased severity.¹⁴ Antibiotic use, compliance, and adverse events were secondary outcomes. At 6 months, RSDI improvement was 24.7% (−14.4, $P < .05$), and SIA improvement was 41% (−1.6; $P < .05$) in active treatment compared with the control group. The SF-12 did not show a statistically significant improvement. Subjects randomized to active therapy also reported fewer 2-week periods with sinus-related symptoms ($P < .05$) and used fewer antibiotics ($p < .05$).¹⁴ Notably, in a 12-month fol-

low-up to this study, the investigators found sustained improvement in both the RSDI ($P < .001$) and SIA scores ($P = .01$).¹⁷

In contrast, Heatley et al¹⁸ compared the efficacy of NSI with that of “control” treatment in an RCT and found equivalence between these modalities. In this crossover study, 150 adult subjects with CRS were randomized to receive 2.7% hypertonic NSI via a bulb syringe, 2.7% hypertonic NSI via nasal irrigation pot or to receive reflexology massage as a “placebo” for 2 weeks each. QOL scores from two validated surveys—the Medical Outcomes Survey Short Form 36-Item Health Survey (SF36)¹⁹ and the 31-Item Rhinosinusitis Outcomes Measures (RSOM31)²⁰—were used as primary end-points. Significant but equivalent improvement in RSOM31 score occurred after 2 weeks of intervention in all 3 groups ($P < .01$), and 35% of all subjects using irrigation or reflexology reported decreased use of sinus medications, with no measurable difference between the 3 groups.¹⁸

Both strengths and limitations are worth noting in these studies. The attrition rate was significant, with 9% (7 of 76) of subjects in the Rabago¹⁴ and 15% (22 of 150) in the Heatley study¹⁸ failing to complete the study. Both studies used validated questionnaires; however, blinding was not addressed in the Heatley trial. The Rabago study examined outcomes via a prolonged 6-month study, whereas Heatley's study was limited to only 2 weeks of treatment.^{14,18}

In a Cochrane meta-analysis by Harvey et al,²¹ the authors found that NSI was beneficial in the treatment of CRS and could be included as a sole treatment or treatment adjunct for CRS. In this meta-analysis, 8 trials were identified that satisfied the inclusion criteria. Three studies compared topical saline with no treatment, 1 against placebo, 1 as an adjunct to, and 1 compared NSI with intranasal steroids. Furthermore, 2 studies compared different hypertonic solutions versus isotonic saline. From these studies, NSI was concluded to be beneficial in the treatment of the symptoms of CRS when used as the sole modality of treatment. Evidence also exists in favor of saline as a treatment adjunct. However, NSI was not found to be as effective as an intranasal steroid.²¹

Allergic rhinitis

Garavellos et al²² investigated the efficacy of NSI using hypertonic saline as an adjunctive treatment in the prevention of seasonal allergic rhinitis (SAR) related symptoms in children. In this RCT, 20 children with SAR to *Parietaria*²³ were randomized to receive daily NSI with 3% hypertonic saline delivered by syringe with a volume of 2.5 mL to each nostril three times per day during the season (6 weeks) or no topical solution. Subjects were allowed to use rescue antihistamines. The main outcome was the “mean daily rhinitis score,” which was based on the following symptoms: (1) nasal itching; (2) rhinorrhea; (3) nasal obstruction; and (4) wheezing. Intensity of each of these 4 symptoms was rated on a scale of 0 to 4. In subjects allocated to NSI, the “mean daily rhinitis score” significantly improved in the 3rd, 4th, and 5th weeks of therapy ($P < .05$) compared with the control group. Furthermore, a significant decrease occurred in oral antihistamine rescue ($P < .05$) during the 3rd, 4th, and 6th weeks of treatment. No patients were lost to follow-up in this study.²²

In a later study, Garavello et al²⁴ evaluated the effect of topical 3% hypertonic saline administered via a nasal atomizer spray in children with rhinoconjunctivitis symptoms. In this RCT, 44 children (<16 years of age) with SAR were randomized to receive hypertonic saline or no topical treatment for 7 weeks. Antihistamine use was permitted for rescue and its use recorded. The main outcome was the “mean weekly rhinoconjunctivitis score” based on the presence of 4 symptoms: (1) nasal discharge; (2) nasal obstruction; (3) ocular reddening; and (4) ocular pruritis. The degree of severity of each symptom was recorded on a scale of 0 to 3 [0 = none; 1 = mild; 2 = moderate; 3 = severe]. A total score

representing the sum of the scores of these 4 symptoms was then used to calculate a mean daily rhinitis score per patient per week. The mean weekly rhinoconjunctivitis score in the active group was numerically improved throughout the entire pollen season, and this difference became statistically significant in the 6th and 7th week ($P < .05$). A statistically significant reduction in intake of oral antihistamine rescue also was found in 5 of the 7 weeks ($P < .05$). Four patients (2 from each group) did not complete the study.²⁴

Although both studies described adequate randomization and concealment procedures, neither study described the blinding process, nor did either rely on a validated questionnaire or objective outcomes. One also must question whether 3 times per day use of NSI would be a reasonable expectation in a pediatric population.

Upper respiratory tract infections

In a two-phase, multicenter, parallel group, open, and randomized comparison trial,²⁵ 390 children, ages 6 through 10, with URTIs were randomized to receive either standard medications (antipyretics, nasal decongestants, mucolytics, and $\pm$ systemic antibiotics) plus isotonic NSI (Atlantic Ocean seawater, Physiomer; Goemar Laboratoire de la Mer, Saint Malo, France) via either medium jet flow (9 mL of liquid each nostril) or fine spray (3 mL per nostril) or standard medications alone. They were followed for 3 weeks during the “acute illness phase” (continuing to use the assigned treatment regimen 6 times per day) and then for an additional 9 weeks during the prevention phase (using the assigned treatment regimen 3 times per day). The primary efficacy end-points were nasal symptom resolution during an acute illness (visits 1 and 2) and during the preventive phase (visits 3 and 4), the reappearance of symptoms, additional medication usage, complications, days of missed school, and reported days of illness. Composite ‘rhinologic scores’ were measured on a 4-point numeric scale (‘1’ indicated no symptoms, and ‘4’ indicated severe symptoms). The parameters assessed included nasal secretion and its type, nasal obstruction, sore throat, cough and expectoration, sneezing, itching, and loss of senses of smell and taste. In both phases, the NSI delivery groups demonstrated equally and statistically significant improvement in nasal secretions and obstruction compared with control (mean scores versus non-saline group during treatment phase, 1.79 vs 2.10 and 1.25 vs 1.58, respectively, $P < .05$ for both). During the “prevention phase,” subjects stratified to the saline group showed significant improvement in symptoms of sore throat, cough, nasal obstruction and secretion ($P < .05$ for all).²⁵

In contrast, Adam et al²⁶ conducted a three-arm randomized controlled trial, enrolling 143 adults with viral URTIs randomized to receive hypertonic 2% buffered spray NSI, normal saline (0.9%) NSI, or ‘no treatment.’ The main outcomes were the nasal symptom score (NSS) on day 3 and time to symptom resolution. The NSS consisted of the sum of scores for nasal congestion, rhinorrhea, and headache, with each score rated on a 4-point severity score (0, no symptoms; 1, mild symptoms; 2, moderate symptoms; and 3, severe symptoms). The day 3 mean nasal symptom score was 3.8 (95% CI, 3.0–4.5) for the group randomized to hypertonic saline, 3.7 (95% CI, 2.9–4.5) for the normal saline group, and 4.1 (95% CI, 3.5–4.7) for the no treatment group. Ultimately, no significant differences were found with respect to the primary outcome measures when hypertonic saline was compared with normal saline or no-treatment groups, and neither active treatment resulted in a diminution of the duration or severity of nasal symptoms compared with control.²⁶

In a Cochrane meta-analysis, Kassel et al²⁷ evaluated the efficacy of NSI in treating the symptoms of acute URTIs in children and adults. Three RCTs (618 participants) comparing topical nasal saline treatment with other interventions in adults and children with clinically diagnosed acute URTIs were included. Most outcomes examined demonstrated no difference between nasal saline treat-

ment and control. There was limited evidence of benefit with NSI in adults. One study showed a mean difference of 0.3 day (out of 8 days) for symptom resolution, but this was not significant. The authors conclude that the included trials were too small and had too high a risk of bias to be confident about the possible benefits of NSI in acute URTIs.

Discussion

There are notable limitations in the previous studies. These studies generally involved only a small number of subjects, most examined subjects with CRS, subjects were allowed to take other medications (including oral antihistamines and antibiotics), follow-up was limited, attrition was significant, and blinding was often not addressed. Significant heterogeneity existed between the study designs, including duration of treatment, outcome measures, as well as variables regarding NSI itself, such as device and salinity. Based on such limited data, NSI appears to have a small benefit compared with ‘no treatment’ for subjective parameters such as symptoms and disease-specific quality of life scores. Although it is understandable that blinding subjects to a physical therapy such as NSI is difficult, further placebo-controlled and comparative studies are necessary. These trials are summarized in Table 1.

Comparative studies of interventions/variables

Little consensus has been reached regarding the best approach for NSI administration. Options available for NSI include a multitude of different volumes, delivery vehicles, tonicities, buffering, and additives, which are reviewed in the following sections.

Device.

Topical delivery of nasal medications involves direct contact with mucosa, ideally leading to higher local concentrations and less systemic effects when compared with oral administration.²⁸ The efficacy of a topical medication, however, depends on its ability to reach the target tissue, and thus disparity may be seen with various delivery techniques. Saline can be delivered to the nose by several methods, including cupped hand, spray, aerosolized, positive-pressure devices (squeeze bottles), negative pressure (sniffing/inhaling/gravity pots solution), and motorized devices.

Pynnonen et al²⁹ investigated whether isotonic NSI delivered via positive pressure was more effective than isotonic NSI via nasal sprays at improving quality of life and decreasing medication use. In this prospective RCT, 127 adults with acute or CRS (defined as chronic nasal and sinus symptoms for 2–4 weeks) were randomized to NSI with 240 mL isotonic sodium chloride/sodium bicarbonate mixture (via Sinus Rinse irrigations from NeilMed Pharmaceuticals, Santa Rosa, California) twice daily or isotonic saline spray twice daily (via Deep Sea nasal spray by Major Pharmaceuticals, Livonia, Michigan) for 8 weeks. The main outcome measure was the change in the mean 20-Item Sino-Nasal Outcome Test, (SNOT-20),³⁰ a disease-specific health related QOL measure score, with secondary outcomes including rescue medication use. Throughout the 8 weeks of this investigation, the irrigation group achieved lower SNOT-20 compared with the spray group ($P = .002$). Forty percent of subjects in the irrigation group reported symptoms “often or always” at 8 weeks compared with 61% in the spray group, with an absolute risk reduction of 0.2; 95% CI, 0.02–0.38 ($P = .01$). Despite this difference in SNOT-20, no significant difference was seen between groups in rescue medication use. Limitations in this study include that it could not be blinded, did not have adequate power to evaluate patients with AR, and did not address adherence.²⁹

To better understand potential differences in delivery between nasal irrigation delivery devices, Miller et al³¹ conducted a prospective, descriptive analysis. The investigators selected 7 adult patients with CRS who were 6 weeks or more post FESS, to assess the

Table 1
Summary of efficacy trials

Study	Design	Subjects	Intervention	Delivery	Routine	Solution	Primary Outcomes	Secondary Outcomes	Results
Rabago ¹⁴ (2002)	RCT	Adults (n = 76) w/ CRS or recurrent ARS	NSI vs. no Tx (control group)	SinuCleanse Nasal Cup ^a (pot)	150 mL per nostril daily for 6 months	2% buffered saline (with baking soda)	RSDI, SIA, SF12 at 1.5, 3, 6 months	RMU	- Improved RSDI (58.4 ± 2.0 to 72.8 ± 2.2, P ≤ .05) c/w control - SIA score improved (3.9 ± 0.1 to 2.4 ± 0.1, P ≤ .05) c/w control - No improvement in SF-12 - Improvement in RSDI score after 2 weeks in all Tx group (P < .001) - 35% of subjects reported decreased use of sinus medications - 70% of subjects would recommend irrigation - no differences on delivery
Heatley ¹⁸ (2001)	Prospective, RCT	Adults (n = 150) w/CRS	- Group 1 (n = 50) used NSI with bulb syringe vs. - Group 2 used NSI with irrigation pot vs. - Group 3, 'placebo' performed reflexology massage daily for 2 weeks	bulb syringe, nasal irrigation pot or reflexology massage	Daily for 2 weeks	2.7% NaCl	SF36, RSDI	RMU	- Reduction in mean daily rhinitis score during 5 weeks of study w/statistical significance in 3 rd , 4 th , 5 th weeks of Tx (P < .05) - Decrease in oral AH use which became statistically significant during 3 rd , 4 th , 6 th weeks (P < .05) - Reduction in mean weekly RCS during whole pollen season which was statistically significant in weeks 6 & 7 (P < .05) - reduction in oral AH use which was statistically significant in 5 of 7 weeks (P < .05)
Garavellio ²² (2003)	Prospective, RCT	Children (n = 20) ages 6–12 w/SAR to Parietaria	Group 1 (n = 10) HS (3%) vs. Group 2 (n = 10) no saline	5 mL syringe	2.5 mL each nostril TID for 6 weeks (pollen season)	3.0% NaCl	Mean daily rhinitis score, oral AH use		
Garavellio ²⁴ (2005)	Prospective RCT	Children (n = 44); age < 16 w/SAR to Parietaria	Group 1 (n = 22) w/3% HS vial nasal atomizer spray with 3 sprays each nostril TID vs no topical Tx (control group)	Nebulized/bottle with atomizer	3 sprays (50uL) per nostril TID x pollen season or 7 weeks	3% NaCl pH 7.45	Mean weekly RCS, oral AH use	RMU	
Slapak ²⁵ (2008)	Prospective, parallel-group, open, RCT	Children (n = 401); ages 6–10, with uncomplicated cold or influenza Acute phase – up to 2 weeks (visits 1 & 2) Prevention phase (visits 3, 4, 8 weeks after study entry)	Group 1: standard medications alone Saline groups Group 2: NSI plus standard medications via medium jet flow (n = 100) Group 3: NSI via fine spray plus standard medication, (n = 100) Group 4 NSI via wash for eye and nose plus standard medications, (n = 100)	Jet flow, fine spray bottle, dual wash	6 times a day during acute illness 3 times a day during prevention phase 12 weeks For the medium jet flow (group 1) 9 mL of saline was administered per application and per nostril; for both other sprays the volume was 3 mL per application and per nostril.	Modified seawater solution (Atlantic Ocean) ^b	Nasal Sx resolution during acute illness and reappearance of cold or flu	RMU complications, days off school, reported days of illness during following weeks	- At visit 2, subjects in saline group achieved Sx resolution in nasal secretion and obstruction (mean scores vs. non-saline group 1.79 vs. 2.10 and 1.25 vs. 1.58 respectively, P < .05) - During prevention phase, subjects in saline group showed significantly lower scores in cough, nasal obstruction and secretion (P = .05) - By visit 3, subjects in saline group had fewer RMU (P < .05), fewer illness days (31% vs 75%), school absences (17% vs 35%), and complications (8% vs 32%) (P < .05)
Adam ²⁶ (1998)	RCT with 2 controls	Adults, (n = 143) with cold or sinus infection (pts w/AR, Sx > 3 weeks, excluded)	3% HS vs. IS vs control (three groups)	Via 2 oz. spray bottle	2 squirts per nostril TID for 1 week	HS (3 tsp of canning salt + 1 tsp of baking soda in 1 quart of tap water)	- NSS on day 3 - NSS on day of well-being (day of symptom resolution) - RMU	Days of work or school missed, compliance in nasal spray use, nasal spray side effects	- No difference in NSS - Mean day of well being was 8.3 (95% CI, 6.9–9.7, 9.2 (95% CI, 6.9–11.43) and 8.0 (95% CI, 6.7–9.3) days in HS, NS and observation groups - Day 3 mean NSS was 3.8 (95% CI, 3.0–4.5) for HS, 3.7 (95% CI, 2.9–4.5) for NS and 4.1 (95% CI, 3.5–4.7) for observation

Abbreviations: AH, anti-histamine; ARS, acute rhinosinusitis; CRS, chronic rhinosinusitis; HS, hypertonic saline; IS, isotonic saline; NaCl, sodium chloride; NSI, nasal saline irrigation; NSS, nasal symptom score- sum of scores for nasal congestion, rhinorrhea, and headache; RCS, rhinoconjunctivitis score; RCT, randomized controlled trial; RSDI, Rhinosinusitis Disability Index; RSDI31, Rhinosinusitis Outcomes Measure; RMU, routine medication use; SAR, seasonal allergic rhinitis; SF-12, Survey Short Form; SF36, Quality of Life scores from Short Form 36; Single-Item Sinus Symptom Severity Assessment, SIA; Sx, symptoms; TID, three times a day; Tx, treatment.

^aSinuCleanse Nasal Cup (Med-Systems, Inc., Madison, Wisconsin).

^bAtlantic Ocean seawater, Physiomer; Goemar Laboratoire de la Mer, Saint Malo, France.

effectiveness of 4 topical delivery systems (a 45-mL spray bottle, atomizer, nebulizer, or 3-oz. bulb syringe), by relying on a blue dye solution as a marker of deposition. Blinded observers rated the anatomic distribution of dye via fiberoptic endoscopy and found the bulb syringe was statistically superior to the nebulizer in all sinonasal sites ($P < .05$) and statistically superior to the atomizer or spray bottle in the ethmoidal region ($P < .05$). Of note, different quantities of each solution were administered with each technique, and although endoscopically the bulb syringe demonstrated greater deposition, how this translates clinically is still unclear. Additionally, the study population was small and only included postoperative subjects. Thus, we are not sure whether these results can be translated to patients with CRS who have not undergone sinus surgery.³¹

In another study, Olson et al³² compared the intranasal distribution of solution delivered via positive pressure (Sinus Rinse irrigations from NeilMed Pharmaceuticals), negative pressure (via cup hand and sniffed), or nebulizer device (delivering droplet particles in the 20–30 μ m range). In this prospective, controlled trial, 8 healthy adults each received nasal irrigation with 40 mL of isotonic contrast material via the 3 methods. For each subject, coronal computed tomography guided imaging of paranasal sinuses was performed immediately after administration of the solution to compare the volume of distribution achieved by each method. Of the 3 methods, positive-pressure and negative-pressure irrigation distributed contrast solution widely to the ethmoid and maxillary sinuses, with distribution more uniform using positive-pressure irrigation, whereas the nebulization method resulted in a significantly lower volume of retained contrast solution ($P < .05$).³²

Several specialized irrigation devices rely on administering nasal saline via a motorized device. Most of these devices deliver a pulsating, nonsteady stream of saline at a low predetermined fixed cyclic rate. This rate may stimulate the nasal cilia and promote better sinus health, while reducing the severity of inflammation.³³ Although motorized pump irrigators have demonstrated efficacy in diseases such as cystic fibrosis,³⁴ the data exploring its use in other sinonasal disease are superficial, and no head-to-head evaluations comparing non-motorized mechanical pressure NSI methods with standard NSI devices in sinonasal disease are available. Given the lack of substantial data regarding motorized NSI devices, we summarize the prospective, observational trial mentioned above³³ in addition to the data from the aforementioned trials in Table 2.

In conclusion, when comparing delivery devices for NSI, the literature is quite limited and heterogeneous. The investigations examined a small number of subjects, evaluated different sinonasal diseases, and relied on disparate endpoints. Understanding the limitations of these few, non-randomized and non-blinded studies, it would appear that a higher volume of saline delivered via a positive-pressure system is likely needed to attain maximal efficacy with NSI. Further randomized controlled trials, particularly those comparing pulsatile nasal irrigation with other devices, are needed to determine the best device for delivery.

Salinity and additives

NSI may help remove debris, increase clearance of secretions, and thin the mucus.³⁵ Solutions with a greater hypertonicity or alkalinity may actually reduce edema through diffusion of osmolar gradients, improve MCC, CBF, and patency of sinus ostia.¹² Because of a dearth of well-designed studies, we summarize the data in the following section and in Table 3.

Ciliary beat frequency

CBF is an important defense mechanism of the respiratory tract, and its impairment is associated with respiratory diseases such as sinusitis.³⁶ In vitro models showed that varying tonicities may have an impact on the magnitude of change in CBF.^{37,38} In these studies,

isotonic and hypotonic solutions produced little to no ciliary slowing. However, ciliostasis was observed at 3.0%, 7.0%, and 14.0% solution. In a study by Boek et al,³⁷ a 7% solution led to ciliostasis within 5 minutes, although the effect was reversible, whereas a 14.4% solution had an irreversible ciliostatic effect. Further in vitro investigation in subjects without sinonasal disease demonstrated that increased tonicity led to ciliostasis in the normal human sinus epithelium,³⁷ but the effect is temporary.³⁹ Based on these few in vitro studies, a higher tonicity may be less efficacious or even deleterious to CBF/MCC; thus, a tonicity above 7% should possibly be avoided.

Mucociliary clearance. Limited data support the role of sodium chloride irrigation solutions on enhanced MCC. For example, a double-blind RCT by Ural et al³⁵ demonstrated that sodium chloride (isotonic or hypertonic) improved MCC in 87 subjects with sinonasal disease (AR or CRS), by demonstrating a reduction in saccharine clearance time (SCT).⁴⁰ The degree of hypertonicity also may play a role in enhanced MCC. In a randomized, double-blind, cross-over study, Homer et al⁹ demonstrated a significant improvement in MCC (measured by SCT) in 38 healthy subjects with 5% saline versus 0.9% saline ($P = .005$) and versus 3% saline ($P = .04$). Notably, no difference was seen in SCTs between normal saline or 3% saline administration ($P = .64$). Furthermore, Talbott et al¹² demonstrated that a buffered hypertonic 3% NSI improved the MCC via SCT, whereas buffered normal saline (0.9%) had no such effect in 21 healthy subjects (in-between group difference of $P = .0013$). Because these 2 studies recruited only healthy subjects, we are still left to question whether such a difference in efficacy exists in patients with sinonasal disease. Additionally, whether a reduction in SCT translates to clinical improvement in CRS, AR, or other sinonasal disease has yet to be determined.

The enhanced clinical efficacy of hypertonic versus isotonic saline was demonstrated, however, in 1 small study. In a double-blind RCT, Shoseyov et al⁴¹ compared the effectiveness of 3.5% saline with that of isotonic saline in 34 children with CRS. Significant improvement was found in predefined cough and radiologic scores, favoring the hypertonic group compared with the isotonic group ($P < .05$ for both scores). Several potential drawbacks to this study deserve mention, including a high attrition rate of 12% (or 4/34), the lack of use of a validated questionnaire, and the likely poor adherence rate of using saline lavage 3 times per day in children.⁴¹

Additive agents. The rationale to create buffered, alkaline nasal solutions is derived from the fact that the nasal mucosa becomes slightly more alkaline in patients with rhinitis.^{42,43} Thus, optimally buffering a NSI solution (possibly with bicarbonate) to a target pH should in theory improve the absorption of NSI across the nasal epithelia.⁴³ Several studies in patients with and without sinonasal symptoms have examined the effect of buffered solutions on SCT and MCC⁴⁴ as well as clinical symptoms and radiographic scores.⁴⁵ Essentially, there were no between-group (between buffered vs non-buffered sodium chloride solutions at various tonicities) differences in SCT, radiographic scores, or clinical symptom improvement.^{44,45}

In conclusion, several variables may have an impact on the efficacy of NSI, including device, tonicity, and buffering agents. Although hypertonic solutions appear to improve MCC, whether this translates to clinical effect is unknown. Furthermore, although some added clinical benefit may occur from differences in tonicity and the addition of buffering agents, these modifications must be balanced against patient tolerance. Finally, further research in subjects with sinonasal disease is needed, because most of the published studies were performed in healthy subjects. Given the limi-

Table 2
Summary of device trials

Study	Design	Subjects	Intervention	Primary Outcome(s)	Results
Pynnonen ²⁹ (2007)	Prospective, RCT	Adults (<i>n</i> = 127) w/CRS	240 mL isotonic NaCl/NaHCO ₃ irrigation via low positive pressure (NeilMed Sinus Rinse) ^a twice daily (<i>n</i> = 64) vs isotonic saline spray twice daily via Deep Sea spray ^b (<i>n</i> = 63) for 8 weeks	Mean SNOT-20 score, change in symptom frequency, change in medications	- Irrigation group achieved lower SNOT-20 scores than the spray throughout (<i>P</i> < .05) - 40% of subjects in the irrigation group reported symptoms "often or always" at 8 weeks vs 61% in the spray group (absolute risk reduction, 0.2; 95% CI, 0.02–0.38 (<i>P</i> = .01) - No significant differences in sinus medication use were seen between group
Toomooka ³³ (2000)	Prospective, controlled clinical trial	Adults (<i>n</i> = 211) with sinonasal disease (AR, atrophic rhinitis, aging rhinitis and post-nasal drip) and 20 control subjects	250 mL lukewarm tap water with ½ tsp tablet salt twice daily via Water Pik ^c and Grossan nasal adapter ^d for 3 to 6 weeks	Change in QWB questionnaire score	- In NSI group, improvement in 23 of 30 nasal symptoms queried after 6 weeks (<i>P</i> < .05) compared with baseline - In NSI improvement in global health status measure on QWB vs baseline (<i>P</i> = .036) but not in control subjects vs baseline (<i>P</i> = .9705)
Olson ³² (2002)	Prospective, controlled comparative study	Healthy Adults (<i>n</i> = 8)	- 40 mL of isotonic, nonionic iodine-based contrast solution at strength of 140mg/mL via hand/sniffing vs. - 40 mL of isotonic, nonionic iodine-based contrast solution at strength of 140 mg/mL via positive pressure vs. - 40 mL of isotonic, nonionic iodine-based contrast solution at strength of 140 mg/mL via nebulizer	Volume and distribution of solution on coronal CT	- Positive pressure & negative-pressure irrigation distributed contrast solution widely to ethmoid and maxillary sinuses - Distribution of contrast solution was more uniform using positive-pressure irrigation than negative-pressure irrigation - Nebulizer distributed contrast solution poorly and resulted in a significantly lower volume of retained contrast solution (<i>P</i> < .05)
Miller ³¹ (2004)	Prospective, descriptive comparative study	Adults (<i>n</i> = 7) w/CRS 6 weeks post FESS	- 4 topical delivery systemic (spray bottle, atomizer, nebulizer and bulb syringe) independently applied to subjects	Anatomical distributions videotaped during endoscopy	- No statistical difference between the atomizer and spray bottle - Bulb syringe was statistically superior to the nebulizer in all sinonasal sites (<i>P</i> < .0011) - Bulb syringe was statistically superior to the atomizer and spray bottle in the ethmoidal region. (<i>P</i> < .0002)

Abbreviations: AR, allergic rhinitis; CRS, chronic rhinosinusitis; CT, computed tomography; FESS, functional endoscopic sinus surgery; NaCl/NaHCO₃, Sodium Chloride/Sodium Bicarbonate; NSI, nasal saline irrigation; QWB, quality of well being questionnaire; RCT, randomized controlled trial; SNOT-20, 20-Item Sino-nasal outcome test.

^aSinus Rinse irrigations from NeilMed Pharmaceuticals, Santa Rosa, California.

^bDeep Sea nasal spray by Major Pharmaceuticals, Livonia, Michigan.

^cTeledyne Water Pik (Fort Collins, Colorado) available from Anthony Products (Indianapolis, Indiana), and Ethicare Products (Fort Lauderdale, Florida).

^dGrossan nasal adapter from HydroMed (Los Angeles, California) and Kenwood Therapeutics (Fairfield, New Jersey).

tations in these studies, interpreting the data or drawing convincing conclusions is difficult.

Adverse effects. Despite their frequent use, there may be potential harm from NSI. Fortunately, NSI has been associated with rare and generally mild side effects. These include ear fullness, burning or stinging of the nasal mucosa, and epistaxis.^{14,29,33} Also, NSI devices could become contaminated with bacteria, and these infected devices could play a role in potentiating recalcitrant infections.

Whether the bacteria in the nasal mucosa came first or possibly were the consequence of contaminated irrigation fluid is not clear.

Bacteria may form biofilms, and these biofilms may facilitate attachment of the bacteria to the surfaces of the nasal mucosa as well as possibly an inert surface such as nasal irrigation devices. The biofilm-producing bacteria adopt the biofilm form when they become associated with inert surfaces, resulting in firm

Table 3
Summary of salinity trials

Study	Design	Subjects	Intervention	Delivery	Routine	Solution	Primary Outcomes	Results
Shoseyov ⁴¹ (1998)	RCT, double blind	Children (<i>n</i> = 34), ages 3–16, w/CRS	HS (3.5%) vs. NS (0.9%)	Drop bottle	- 10 drops (1 mL) of 3.5% (HS) saline TID for 4 weeks vs. - 10 drops (1 mL) of NS (0.9%) TID for 4 weeks	NS: 0.9% (0.9% wt/vol NaCl/H ₂ O) HS: 3.5% (wt/vol NaCl/H ₂ O)	Change in symptom and radiological scores	- The HS group improved in all scores vs. baseline - The NS group showed improvement only in 'Post nasal drip score' vs. baseline - Significant difference in radiology score (HS: 2.13 ± 1.76 vs. NS = 7.86 ± 1.4) and cough scores (HS = 1.6 ± 0.74 vs. NS = 3.33 ± 0.49) <i>P</i> < .0001 for both - No clinical change in end of the study in both groups - SCT w/5% saline significantly reduced vs. 0.9% (<i>P</i> = .005) and 3% saline (<i>P</i> = .04) - No difference between 0.9% and 3% saline
Homer ⁹ (2000)	Randomized, double-blind, crossover trial	Healthy adults (<i>n</i> = 38)	0.9% NS, vs. 3% saline vs. 5% saline	"Plastic squeeze bottle nebulizer"	1. Measure SCT, 2. administration of four sprays of solution; 3. Sniff. 4. Wait 1 min. 5. Blow nose. 6. Wait 1 min before recording SCT	Saline douching of 0.9% NS, 3% saline and 5% saline	MCC via SCT after douching with three solutions	- SCT w/5% saline significantly reduced vs. 0.9% (<i>P</i> = .005) and 3% saline (<i>P</i> = .04) - No difference between 0.9% and 3% saline
Talbott ¹² (1997)	Observational	Healthy adults (<i>n</i> = 21)	NS (0.9%) vs. HS (3%)	Atomized nasal spray	1. Baseline SCT; 2. 10 sprays of one concentration in each nostril separated by 1 minute; 3. Repeat SCT after 10 minutes; 4. Repeat same procedure on separate day with opposite concentration than used initially	0.9% NS buffered to pH of 7.6 vs. 3% HS buffered to pH of 7.6	Change in SCT, measurement of MCC	- No significant difference in control values between the solutions (<i>P</i> = .27) - Transit time decreased from baseline in the HS trials by 17% (<i>P</i> = .007) compared with a 2% decrease (<i>P</i> = .71) for NS - The difference between the percent changes was statistically significant, with a (<i>P</i> = .013) - HS produced a mean improvement of 3.1 minutes (SD = 4.4; <i>P</i> = .002) vs. 0.14 minutes in the NS group (SD = 7.0; <i>P</i> = .69). - Difference of changes was statistically significant (<i>P</i> = .02).
Ural ³⁵ (2009)	RCT	Adults (<i>n</i> = 132): 45 controls 21 w/PAR 24 w/AS 42 w/CRS	HS vs. NS	Disposable syringe filled with 8 mL solution (4 mL per nostril)	1. Baseline SCT; 2. 10 day application of either IS or HS saline; 3. At end of 10d irrigation period, SCT was repeated	HS (3% at pH of 7.6) vs. IS (0.9% at pH of 7.6)	MCC as measured by SCT	- Irrigation with HS restored impaired MCC in CRS patients (<i>P</i> = .05) - Isotonic saline improved MCC in AR and AS patients (<i>P</i> = .05)
Bachmann ⁴⁵ (2000)	Prospective, RCT, double-blind	Adults (<i>n</i> = 40) w/CRS	HS (1.1% EMS ^b) vs. IS (0.9%)	Rhinocare irrigator ^a	Endonasal irrigation of 200 mL solution BID for 1 week	EMS ^b (1.1%) vs. NaCl 0.9%	Symptom, endoscopic and radiological scores, MCC, rhinomanometry and olfactometry scores	- Subjective complaints, endonasal endoscopy and radiography results improved in both groups vs. baseline (<i>P</i> = .0001) - Two groups not significantly different in outcome

Abbreviations: AS, acute sinusitis; BID, twice daily; CRS, chronic rhinosinusitis; EMS, EMS Mineral Salts, includes other ions in trace amounts in addition to Na⁺ and Cl⁻; also with HCO₃-ions; HS, hypertonic saline; IS, isotonic saline; MCC, mucociliary clearance; NaCl, sodium chloride; NS, normal saline; PAR, perennial allergic rhinitis; SCT, saccharine clearance test; TID, three times daily.

^aRhinoCare, Siemens & Co. GmbH & Co. KG.

^bEMS salt solution (Siemens & Co., Bad Ems, Germany).

bacterial adhesion and greater difficulty in eradication.⁴⁶ Biofilms have been demonstrated on the sinonasal mucosa of CRS patients⁴⁷ and have been shown to be present particularly in CRS patients who have required revision surgery.⁴⁸ Bacteria existing in this form are able to evade host defenses, and the changes assumed in adopting this mode of growth reduce their susceptibility to antibiotic therapy.⁴⁹

Welch et al⁵⁰ investigated whether irrigation bottles used after FESS could become colonized. Twenty adult patients were enrolled and examined at 1, 2, and 4 weeks after FESS. Overall, 29% of all bottles (15/51) demonstrated bacterial growth, with 25% (10/40) demonstrating growth within 2 weeks. Forty-five percent of bottles demonstrated bacterial growth in the last collection period. Concerns in this study include a high attrition rate (45%) and the fact that none of the subjects were evaluated clinically for infection.⁵⁰

Subsequently, in a prospective, observational trial, Keen et al⁵¹ demonstrated high rates of bacterial contamination of nasal irrigation bottles, which they postulate may contribute to resistant nasal/sinus infections. Eleven adult patients with recalcitrant CRS (who had not had prior sinus surgery) using NSI were examined every 2 weeks for a total of 6 weeks. At each visit, a culture was taken from their irrigation bottle and middle meatus. Also, 6 irrigation bottles were examined with scanning electron microscopy to detect potential biofilm formation. Overall, 42 of 43 (97%) bottles demonstrated bacterial growth, primarily *S.aureus*. Furthermore, bacterial biofilms were found on the inner surface of 4 of the 6 irrigation bottles analyzed via scanning electron microscopy. This study suggested the dynamic 2-way flow of bacteria between the nose and the bottle—again leading to the question of which was the primary source of infection. Notably, treatment with Milton's solution (1% NaOCl plus 19% NaCl) and microwaving were found to be effective methods for sterilizing the bottles in this study.⁵¹

Conclusion

NSI is a frequent component of treatment of sinonasal disease and is usually well tolerated. Overall the data demonstrate some small clinical benefit. Surprisingly, despite the fact that NSI has been used since ancient yoga times, data supporting its use currently are nominal. Given the disparity in various pathological conditions, future studies should focus on specific phenotypes of sinonasal diseases. Present data also reinforce the importance of well-designed studies with robust subject numbers and focused examination of delivery method, salinity, and buffering.

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