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Limited Evidence: Higher Efficacy of Nasal Saline Irrigation over Nasal Saline Spray in Chronic Rhinosinusitis—An Update and Reanalysis of the Evidence Base

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Abstract

Objective. To assess the effectiveness of nasal saline irrigation in adult patients with chronic rhinosinusitis.

Data Sources. PubMed, EMBASE, the Cochrane Library.

Review Methods. A comprehensive search was performed, and 2 authors independently screened publications. The design of selected studies was assessed on directness of evidence and risk of bias.

Results. Of 1596 publications, 1 open-label randomized trial with high directness of evidence and moderate risk of bias was included. In this study, 127 patients were randomly allocated to isotonic nasal saline irrigation or isotonic nasal saline spray, as added to their usual medication. The mean 20-Item Sinonasal Outcome Test (SNOT-20) scores of those treated with nasal irrigation improved more than those allocated to nasal spray. While the authors consider an improvement of 16 or more to be clinically meaningful, the changes from baseline in mean SNOT-20 scores of those treated with irrigation (and the differences with those treated with nasal spray) at 2, 4, and 8 weeks were 12.2 (difference 5.5, [95% confidence interval −0.04 to 11.0]), 16.2 (difference 8.8 [3.2 to 14.4]), and 15.0 (difference 6.5 [0.4 to 12.6]), respectively. Side effects of posttreatment nasal dripping were common but minor and did not lead to discontinuation of treatment.

Conclusion and Recommendation. It should be explained to adult patients with chronic rhinosinusitis that there is limited information on the relative effect of nasal saline irrigation and nasal saline spray on subjective symptom improvement, since there is only 1 trial available with a moderate risk of bias showing limited benefit of irrigation over spray.

Keywords

chronic rhinosinusitis, nasal saline irrigation, nasal saline spray, treatment, evidence-based medicine

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Clinical Scenario

A 33-year-old man visits your ear-nose-throat outpatient clinic with complaints of reduced smell, facial pain, and nasal discharge, lasting for 4 months. Besides purulent discharge in the middle meatus on both sides, nasal endoscopic findings were normal. Computed tomography (CT) scanning of the paranasal sinuses shows mucosal thickening in the maxillary sinuses. Based on these examinations, you conclude that the patient suffers from chronic rhinosinusitis (CRS) without nasal polyposis, and you wonder whether to advise nasal saline irrigation to relieve his complaints.

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Background

CRS is very common, affecting approximately 5% to 15% of the adult population in both Europe and the United States.[1] Its impact on patient quality of life is considerable, equaling other chronic conditions such as chronic back pain, congestive heart disease, and chronic obstructive pulmonary disease.[2] CRS is defined by the American Association of Otolaryngology—Head and Neck Surgery 2007 practice guideline as the presence of at least 2 of the following symptoms for a minimum of 12 weeks: nasal congestion, nasal discharge, facial pain/pressure, and hyposmia. In addition, inflammation should be documented by purulence or polyps at the middle meatus or radiographic imaging of the paranasal sinuses.[3]

In daily practice, nasal saline irrigation is often recommended in addition to topical corticosteroids in patients suffering from CRS.[1,4] It has been suggested to improve sinonasal symptoms by enhancing mucociliary function, decreasing inflammatory mediators, reducing mucosal edema, and clearing mucus.[5] A 2007 Cochrane review concluded that topical saline could be used as adjunctive therapy for symptom relief.[4] However, in this review, clinical heterogeneity between studies was substantial as the authors included trials in children and adults with chronic sinus disease as well as trials in patients with allergic rhinitis. The most recent study included in this review was published in 2006. As new evidence may have become available over time, an updated search is warranted. The aim of this systematic review is therefore to provide an update and reanalysis of the available evidence on the effectiveness of nasal saline irrigation in adult patients with CRS.

Searching for Evidence

We systematically reviewed the evidence base to answer our research question: What is the effectiveness of nasal saline irrigation in adult patients with CRS, in terms of time to clinical cure, symptom relief, and side effects?

Retrieving Studies

Assisted by our clinical librarian, we retrieved relevant publications from PubMed, EMBASE, and the Cochrane Library (up to March 26, 2013). We used the terms *rhinosinusitis* and *nasal irrigation* and relevant synonyms. Appendix 1 (available at otojournal.org) includes our search strategy.

Two authors (J.W.G.B., L.M.N.) independently retrieved publications and removed duplicates. They selected articles based on title and abstract screening. Articles that assessed nasal saline irrigation (either as monotherapy or as an adjunct to medical treatment) were included. Further, articles had to compare nasal saline irrigation to either no treatment, placebo, or an active agent. Animal or in vitro studies, studies in children and patients with allergic rhinitis and immunocompromised patients, case reports, reviews, and opinion papers were excluded.

For final selection, the same 2 authors screened full texts of potentially eligible articles for absolute risks for nasal saline irrigation and control treatment or their risk differences. The article retrieval was completed by cross-reference checking in Scopus and Web of Science for selected articles, while citations of related reviews, meta-analyses, and guidelines were screened to identify additional eligible trials. The similar procedure was followed to check for eligibility of articles that were thereby retrieved. Initial disagreements on eligibility and selection of articles between authors were solved by discussion; therefore, the selection is based on full consensus.

Assessing Studies

Based on predefined criteria, three authors (J.W.G.B, L.M.N., and N.M.K.) independently evaluated the design of included studies on directness of evidence (DoE) and risk of bias (RoB). They resolved initial disagreements by discussion. When item information for the assessment of a DoE or RoB was not or not clearly reported, we rated it as insufficient and considered it as not satisfied. When the reporting allowed assessment, we rated it as either satisfied or not satisfied.

Assessment of the DoE involved evaluation of patients, notably (1) adults with CRS; treatment comparison, notably (2) nasal saline irrigation; and the outcomes, notably (3) clinical cure or symptom relief. Studies were classified as high directness if they satisfied all the aspects of our 3-part question, moderate directness if they satisfied 2, and or low DoE if they satisfied only 1.

Assessment of the RoB involved evaluation of selection bias, notably the study design characteristics treatment assignment by (1) random and (2) concealed allocation, and information bias, notably standardization of (3) treatments and (4) outcome assessments, (5) blinding of outcome assessment, and (6) completeness of reported data (**Table 1**). Studies were classified as low RoB if they satisfied criteria 1 and 2 plus all other study design features, moderate RoB if they satisfied criteria 1 and 2 but failed on 1 or 2 of the other 4 features, and the remainder were classified as high RoB.

We aimed to include studies for data extraction with a high and moderate DoE and low and moderate RoB.

Extraction of Study Data

From selected articles, three authors (J.W.G.B., L.M.N., and N.M.K.) independently extracted data. We aimed to extract and report absolute risks for nasal saline irrigation and control treatment, plus their risk difference with accompanying 95% confidence intervals. If they were not provided or could not be calculated, we presented the findings as reported in the original article.

Results

Retrieving Studies

Our initial search yielded 4917 articles. Removing duplicates left 1596 unique articles for screening on title and abstract. Of these, 33 articles were considered potentially

Table 1. Study Assessment.[a]

	Directness of Evidence					Risk of Bias						
Study Characteristics	Domain	Treatment	Outcome	Follow-up	DoE Score	Randomization	Concealed Allocation	Treatment Standardization	Outcome Standardization	Blinding of Outcome	Complete Data	RoB score
Pynnonen et al.[6]	●	●	●	●	H	●	●	○	●	○	●	M
Heatley et al.[7]	⊠	●	●	●	M	○	○	○	●	○	●	H
Rabago et al.[8]	○	●	●	●	M	●	●	○	●	○	●	M
Taccariello et al.[9]	○	●	●	●	M	○	○	○	●	○	●	H

	Directness of Evidence
Domain	Patients aged 18 years and older with rhinosinusitis symptoms for at least 12 weeks, no previous sinus surgery
Treatment	Isotonic or hypertonic nasal saline irrigation (at least once daily)
Outcome	Clinical cure or symptom relieve
Follow up	At least 2 weeks
	Risk of Bias
Randomization	Method of randomization adequately described
Concealed allocation	Concealment of allocation (treatment allocation was independent from selection) adequately described
Treatment standardization	Standardization of co-treatment
Outcome standardization	Protocolled, uniform assessment of outcome
Blinding of outcome	Outcome is documented without knowledge of the treatment status
Complete data	Adequate reporting of all included patients

Abbreviations: DoE, directness of evidence; RoB, risk of bias; M, moderate; H, high.
[a]●, satisfied; ○, not satisfied; ⊠, insufficient information/unclear.

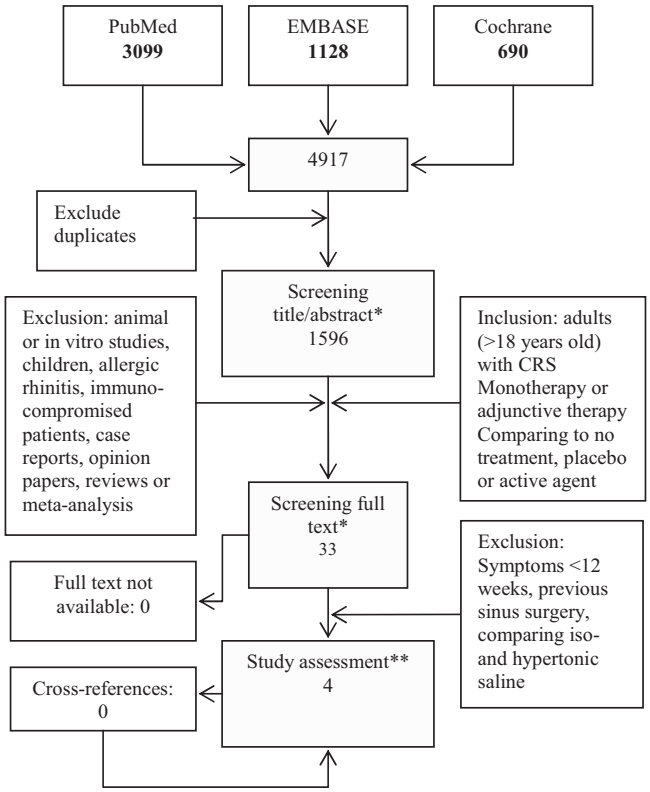

Figure 1. Flowchart of search strategy (March 26, 2013). CRS, chronic rhinosinusitis. *Based on agreement among 2 independent authors (J.W.G.B., L.M.N.). **Based on agreement among 3 independent authors (J.W.G.B., L.M.N., and N.M.K.).

eligible, and their full texts were retrieved. No additional studies were found following our iterative cross-reference checking process. Based on full-text evaluation, 4 studies were included for study assessment (**Figure 1**).

Assessing Studies

We excluded 2 studies because of high RoB.[6,7] One study with moderate RoB included a majority of patients (77%) that underwent previous sinus surgery and was therefore excluded from further analysis.[8] As such, 1 study with high DoE and moderate RoB remained for data extraction (**Table 1**).[9]

Extraction of Study Data

In an open-label randomized trial, Pynnonen et al[6] randomly allocated 127 patients aged 18 years and older with 1 or more of the following symptoms: nasal stuffiness, nasal dryness or crusting, nasal congestion, discolored nasal discharge, or thick nasal discharge to either nasal irrigation with an isotonic saline solution (n = 64) or isotonic saline nasal spray (n = 63), twice daily for 8 weeks. Participants were allowed to continue their usual medications. Patients who underwent previous sinus surgery were excluded. Medication use and 20-Item Sinonasal Outcome Test (SNOT-20) scores[10] were recorded for 8 weeks. Time to resolution of symptoms was not assessed.

Duration of symptoms before enrollment varied from 3 to 12 months, with no differences between groups. Baseline mean SNOT-20 scores were similar for both groups (37.6 for irrigation and 35.5 for spray). Of the 127 randomized patients, 120 (94%), 117 (92%), and 114 (90%) were analyzed at 2, 6, and 8 weeks, respectively. At 2, 6, and 8 weeks, mean SNOT-20 scores of patients treated with nasal saline irrigation improved more than of those receiving nasal saline spray (**Table 2**). The authors also calculated the proportion of patients in both treatment groups with a clinically significant improved SNOT-20 score (defined as a reduction of 16 points or more) and found an absolute risk reduction of 15% for treatment with nasal saline irrigation, corresponding with a number needed to treat of 7. During follow-up, there was no difference in the number and duration of usual medication use between groups. Medication type and dosage were, however, not reported. Minor side effects were frequently reported in both groups (42% in the irrigation group, 25% in the spray group). Posttreatment nasal saline dripping, an expected side effect, was most commonly reported in both groups (n = 14). No patients discontinued treatment due to side effects, and compliance was about 80%.

Comment

In this systematic review on the effectiveness of nasal saline irrigation in adult patients with CRS, we identified 1 trial that assessed nasal saline irrigation versus nasal saline spray as an adjunct to usual medical treatment. This trial, with high DoE and moderate RoB, found a larger improvement in subjective symptoms, as measured by the change from baseline in mean SNOT-20 scores, for nasal saline irrigation as compared with nasal saline spray. The absolute benefit of nasal saline irrigation over nasal spray was, however, modest.

We did not identify new trials since the 2007 Cochrane review was published. Because we excluded trials in children, patients with allergic rhinitis, and those who underwent previous sinus surgery, we included only 1 of the studies that were included in the 2007 Cochrane review.[4]

Some aspects of our findings need further consideration.

First, the trial included patients based on symptoms,[6] while in daily practice, additional diagnostic procedures (ie, nasal endoscopy and/or CT scanning) are usually performed.[1,3] The effects of nasal saline irrigation may vary across patients with clinically diagnosed CRS, like in this trial, and those in which the diagnosis is confirmed by nasal endoscopy and/or CT scanning as recommended by current clinical guidelines.[1,3] As such, our findings are limited to patients with clinically diagnosed CRS.

Second, patients in both treatment groups were allowed to use their usual medication. Although detailed information regarding medication type, duration of use, and dosage was lacking in the study, no differences were reported in overall medication use between the groups. As such, the limited benefit of nasal saline irrigation over nasal saline spray

Table 2. Reduction in mean SNOT-20 scores from baseline at 2, 4, and 8 weeks.

	Nasal Saline Irrigation (Baseline Mean Score 37.6)		Nasal Saline Spray (Baseline Mean Score 35.5)		
Week	n	Reduction	n	Reduction	Δ (95% CI)
2	59	12.2	61	6.7	5.5 (–0.04; 11.0)
4	57	16.2	60	7.4	8.8 (3.2; 14.4)
8	55	15.0	59	8.5	6.5 (0.4; 12.6)

Abbreviations: SNOT-20, 20-Item Sinonasal Outcome Test[10]; CI, confidence interval; Δ, difference.

regarding symptom improvement may not necessarily result in reduced use of co-medication.

Third, the trial included in our review used an isotonic saline solution.[6] Currently, it has not been established whether the effects differ for isotonic or hypertonic nasal solution. Also, the optimal type of delivery, frequency, and volume of delivery are not yet established, and future studies on this topic are therefore needed.[4]

Fourth, Pynnonen et al found the reduction in mean SNOT-20 score for nasal irrigation to be 5.5 to 8.8 points larger than for nasal saline spray. As the authors considered a change in SNOT-20 score of 16 points clinical meaningful,[6,10] the difference between nasal irrigation and nasal spray is, although statistically significant, less relevant from a clinical point of view.

Finally, we take into consideration that treatment with nasal saline irrigation causes only minor side effects. Furthermore, treatment adherence as measured in clinical trials is moderate to high.[5] Reliable information regarding treatment adherence in daily clinical practice is, however, lacking. Costs of nasal saline irrigation vary but are generally low, especially when patients are instructed to make the saline solution themselves.[5]

Conclusion and Recommendation

Our systematic review identified 1 open-label randomized trial comparing the effects of nasal saline irrigation to saline nasal spray as an adjunct to co-medication in adult patients with clinically diagnosed CRS. This trial indicates that nasal saline irrigation may provide subjective symptom improvement over nasal saline spray. Although minor side effects such as posttreatment nasal saline dripping were common, no patients in this trial discontinued treatment due to such side effects. However, these results should be interpreted with caution, because RoB was judged moderate. Further methodologically sound trials are needed to draw more definitive conclusions on its use.

Translating Evidence into Practice

We informed our patient with CRS that nasal saline irrigation may provide some improvement for his symptoms. We explained to him that current evidence on the relative effect of nasal saline irrigation and nasal saline spray on the improvement of subjective symptoms is very limited, since there is only 1 trial with a moderate RoB available showing limited benefit of irrigation over spray, against little risk of (minor) side effects.

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Author Contributions

Jelle W. G. van den Berg, construction of the search strategy, retrieval of articles, selection of relevant articles, assessment of study quality, extraction of study data, analysis and interpretation of data, drafting figures and tables, drafting manuscript, revision of the manuscript, final approval of the version to be published; **Linden M. de Nier**, construction of the search strategy, retrieval of articles, selection of relevant articles, assessment of study quality, extraction of study data, analysis and interpretation of data, drafting figures and tables, drafting manuscript, revision of the manuscript, final approval of the version to be published; **Nina M. Kaper**, formulating clinical question, selection of relevant articles, assessment of study quality, extraction of study data, analysis and interpretation of data, drafting figures and tables, drafting manuscript, revision of the manuscript, final approval of the version to be published; **Anne G. M. Schilder**, analysis and interpretation of data, revision of the manuscript, final approval of the version to be published; **Roderick P. Venekamp**, formulating clinical question, analysis and interpretation of data, drafting figures and tables, drafting manuscript, revision of the manuscript, final approval of the version to be published; **Wilko Grolman**, analysis and interpretation of data, revision of the manuscript, final approval of the version to be published; **Geert J. M. G. van der Heijden**, design of study, analysis and interpretation of data, revision of the manuscript, final approval of the version to be published, supervision of study.

Disclosures

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Supplemental Material

Additional supporting information may be found at http://oto.sagepub.com/content/by/supplemental-data

References

1. Fokkens W, Lund V, Mullol J, et al. European position paper on rhinosinusitis and nasal polyps 2012. *Rhinol Suppl*. 2012: 1-298.
2. Glicklich RE, Metson R. The health impact of chronic sinusitis in patients seeking otolaryngologic care. *Otolaryngol Head Neck Surg*. 1995;113:104-109.
3. Rosenfeld RM, Andes D, Bhattacharyya N, et al. Clinical practice guideline: adult sinusitis. *Otolaryngol Head Neck Surg*. 2007;137(suppl 3):S1-S31.
4. Harvey R, Hannan SA, Badia L, Scadding G. Nasal saline irrigations for the symptoms of chronic rhinosinusitis. *Cochrane Database Syst Rev*. 2007(3):CD006394.
5. Tomooka LT, Murphy C, Davidson TM. Clinical study and literature review of nasal irrigation. *Laryngoscope*. 2000;110: 1189-1193.
6. Pynnonen MA, Mukerji SS, Kim HM, Adams ME, Terrel JE. Nasal saline for chronic sinonasal symptoms, a randomized controlled trial. *Arch Otolaryngol Head Neck Surg*. 2007;133: 1115-1120.
7. Heatley DG, McConnel KE, Kille TL, Leverson GE. Nasal irrigation for the alleviation of sinonasal symptoms. *Otolaryngol Head Neck Surg*. 2001;125:44-48.
8. Rabago D, Pasic T, Zgierska A, Mundt M, Barrett B, Maberry R. The efficacy of hypertonic saline nasal irrigation for chronic sinonasal symptoms. *J Fam Pract*. 2002;51:1049-1055.
9. Taccariello M, Darby Y, Scadding G. Nasal douching as a valuable adjunct in the management of chronic rhinosinusitis. *Rhinology* 1999;37:29-32.
10. Piccirillo JF, Merritt MG, Richard ML. Psychometric and clinimetric validity of the 20-Item Sino-Nasal Outcome test (SNOT-20). *Otolaryngol Head Neck Surg*. 2002;126:41-47.