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 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

Received October 7, 2013; accepted October 9, 2013.

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. 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. 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.

In daily practice, nasal saline irrigation is often recommended in addition to topical corticosteroids in patients suffering from CRS. It has been suggested to improve sinonasal symptoms by enhancing mucociliary function, decreasing inflammatory mediators, reducing mucosal edema, and clearing mucus. A 2007 Cochrane review concluded that topical saline could be used as adjunctive therapy for symptom relief. 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 otosagepub.com) 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 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.

Table 1

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Classification</th>
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<tbody>
<tr>
<td>1. adults with CRS</td>
<td>High DoE</td>
</tr>
<tr>
<td>2. nasal saline irrigation</td>
<td>Moderate DoE</td>
</tr>
<tr>
<td>3. clinical cure or symptom relief</td>
<td>Low DoE</td>
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</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Study Characteristics</th>
<th>Directness of Evidence</th>
<th>Risk of Bias</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Domain</td>
<td>Treatment</td>
</tr>
<tr>
<td>Pynnonen et al.⁶</td>
<td>●</td>
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<tr>
<td>Heatley et al.⁷</td>
<td>❌</td>
<td>●</td>
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<tr>
<td>Rabago et al.⁸</td>
<td>○</td>
<td>●</td>
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<tr>
<td>Taccariello et al.⁹</td>
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**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.

*●*, satisfied; ❌, not satisfied; ○, insufficient information/unclear.
In an open-label randomized trial, Pynnonen et al \(^6\) randomly

Extraction of Study Data

We excluded 2 studies because of high RoB.\(^6,7\) One study

Assessing Studies

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Extraction of Study Data

In an open-label randomized trial, Pynnonen et al \(^6\) randomly

Duration of symptoms before enrollment varied from 3
to 12 months, with no differences between groups. Baseline

Comment

In this systematic review on the effectiveness of nasal saline

Figure 1. Flowchart of search strategy (March 26, 2013). CRS,

eligible, and their full texts were retrieved. No additional

Table 1

Table 2

25% in the spray group). Posttreatment

medication use between the groups. As such, the limited
treatment due to side effects, and compliance was

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

8 weeks, mean SNOT-20 scores of patients treated with nasal

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 dura-
tion of usual medical 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%.

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.

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Extracting 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 dry-
ness or crusting, nasal congestion, discolored nasal dis-
charge, 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.

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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. 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.

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, 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. 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.

**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.

**Acknowledgments**

We gratefully thank Bianca Kramer, medical information specialist at the Library of the Utrecht University and clinical librarian at the University Medical Center Utrecht, for her assistance and advice in searching and retrieval of studies and Renee L. Vroegop, Teun H. M. Gubbels, Sophie P. Kevenaar, Marjolein Peters, Jaqueline de Vries, and M. H. W. van Deurzen for their contribution to the pilot version of the study.

**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; 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; 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**

**Competing interests:** None.

**Sponsorships:** None.

**Funding source:** None.

**Supplemental Material**

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