Nasal saline irrigations for the symptoms of chronic rhinosinusitis (Review)

Harvey R, Hannan SA, Badia L, Scadding G

THE COCHRANE COLLABORATION®

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2009, Issue 1

http://www.thecochranelibrary.com

TABLE OF CONTENTS

HEADER . . . 1
ABSTRACT . . . 1
PLAIN LANGUAGE SUMMARY . . . 2
BACKGROUND . . . 2
OBJECTIVES . . . 4
METHODS . . . 4
RESULTS . . . 8
Figure 1. . . . 9
DISCUSSION . . . 13
AUTHORS' CONCLUSIONS . . . 13
REFERENCES . . . 14
CHARACTERISTICS OF STUDIES . . . 17
DATA AND ANALYSES . . . 32
Analysis 1.1. Comparison 1 A: Comparison of saline versus no treatment, Outcome 1 Symptom scores. . . . 33
Analysis 1.2. Comparison 1 A: Comparison of saline versus no treatment, Outcome 2 Quality of Life scores (disease specific). . . . 34
Analysis 1.3. Comparison 1 A: Comparison of saline versus no treatment, Outcome 3 Quality of Life scores (general). 34
Analysis 2.1. Comparison 2 B: Comparison of saline versus 'placebo', Outcome 1 Quality of Life scores (disease specific) Bulb. . . . 35
Analysis 2.2. Comparison 2 B: Comparison of saline versus 'placebo', Outcome 2 Quality of Life scores (disease specific) Pot. . . . 35
Analysis 3.1. Comparison 3 C: Saline versus standard therapy (intranasal steroid), Outcome 1 Quality of Life scores (disease specific) Isotonic. . . . 36
Analysis 3.2. Comparison 3 C: Saline versus standard therapy (intranasal steroid), Outcome 2 Quality of Life scores (disease specific) Hypertonic. . . . 36
Analysis 4.1. Comparison 4 E: Hypertonic versus isotonic saline, Outcome 1 Symptom scores. . . . 37
Analysis 4.2. Comparison 4 E: Hypertonic versus isotonic saline, Outcome 2 Radiologic scores. . . . 37
APPENDICES . . . 37
WHAT'S NEW . . . 40
HISTORY . . . 40
CONTRIBUTIONS OF AUTHORS . . . 40
DECLARATIONS OF INTEREST . . . 41
SOURCES OF SUPPORT . . . 41
INDEX TERMS . . . 41

[Intervention Review]

Nasal saline irrigations for the symptoms of chronic rhinosinusitis

Richard Harvey[1], Saiful Alam Hannan[2], Lydia Badia[3], Glenis Scadding[4]

[1]Otolaryngology, Head & Neck Surgery/Cochrane ENT Disorders Group, Royal National Throat Nose and Ear Hospital, London/John Radcliffe Hospital, Oxford, Oxford, UK. [2]ENT, Royal National Throat, Nose & Ear Hospital, London, UK. [3]ENT, Royal National Throat, Nose & Ear Hospital , London, UK. [4]Department of Rhinology, Royal National Throat, Nose & Ear Hospital, London, UK

Contact address: Richard Harvey, Otolaryngology, Head & Neck Surgery/Cochrane ENT Disorders Group, Royal National Throat Nose and Ear Hospital, London/John Radcliffe Hospital, Oxford, Level LG1 West Wing, John Radcliffe Hospital, Oxford, OX3 9DU, UK. richard@richardharvey.com.au.

Editorial group: Cochrane Ear, Nose and Throat Disorders Group.
Publication status and date: Edited (no change to conclusions), published in Issue 1, 2009.
Review content assessed as up-to-date: 16 November 2006.

Citation: Harvey R, Hannan SA, Badia L, Scadding G. Nasal saline irrigations for the symptoms of chronic rhinosinusitis. *Cochrane Database of Systematic Reviews* 2007, Issue 3. Art. No.: CD006394. DOI: 10.1002/14651858.CD006394.pub2.

ABSTRACT

Background

The use of nasal irrigation for the treatment of nose and sinus complaints has its foundations in yogic and homeopathic traditions. There has been increasing use of saline irrigation, douches, sprays and rinsing as an adjunct to the medical management of chronic rhinosinusitis. Treatment strategies often include the use of topical saline from once to more than four times a day. Considerable patient effort is often involved. Any additional benefit has been difficult to discern from other treatments.

Objectives

To evaluate the effectiveness and safety of topical saline in the management of chronic rhinosinusitis.

Search strategy

Our search included the Cochrane Ear, Nose and Throat Disorders Group Trials Register, the Cochrane Central Register of Controlled Trials (CENTRAL, *The Cochrane Library*, Issue 4 2006), MEDLINE (1950 to 2006) and EMBASE (1974 to 2006). The date of the last search was November 2006.

Selection criteria

Randomised controlled trials in which saline was evaluated in comparison with either no treatment, a placebo, as an adjunct to other treatments or against treatments. The comparison of hypertonic versus isotonic solutions was also compared.

Data collection and analysis

Trials were graded for methodological quality using the Cochrane approach (modification of Chalmers 1990). Only symptom scores from saline versus no treatment and symptom and radiological scores from the hypertonic versus isotonic group could be pooled for statistical analysis. A narrative overview of the remaining results is presented.

Main results

Eight trials were identified that satisfied the inclusion criteria. Three studies compared topical saline against no treatment, one against placebo, one as an adjunct to and one against an intranasal steroid spray. Two studies compared different hypertonic solutions against isotonic saline.

There is evidence that saline is beneficial in the treatment of the symptoms of chronic rhinosinusitis when used as the sole modality of treatment. Evidence also exists in favour of saline as a treatment adjunct. No superiority was seen when saline was compared against a reflexology 'placebo'. Saline is not as effective as an intranasal steroid. Some evidence suggests that hypertonic solutions improve objective measures but the impact on symptoms is less clear.

Authors' conclusions

Saline irrigations are well tolerated. Although minor side effects are common, the beneficial effect of saline appears to outweigh these drawbacks for the majority of patients. The use of topical saline could be included as a treatment adjunct for the symptoms of chronic rhinosinusitis.

PLAIN LANGUAGE SUMMARY

Nasal irrigation with saline (salt water) for the symptoms of chronic rhinosinusitis

The use of nasal irrigation for the treatment of nose and sinus complaints has its foundations in yogic and homeopathic traditions. It is often prescribed as an adjunct to other treatments such as intranasal steroids or antibiotics. However, there is significant effort involved in preparing and delivering the solutions. This review summarises the evidence for the effect of saline irrigations in the management of the symptoms of chronic rhinosinusitis. There is evidence that they relieve symptoms, help as an adjunct to treatment and are well tolerated by the majority of patients. While there is no evidence that saline is a replacement for standard therapies, the addition of topical nasal saline is likely to improve symptom control in patients with persistent sino-nasal disease. No recommendations can be made regarding specific solutions, dosage or delivery. There are no significant side-effects reported in trials.

BACKGROUND

Chronic rhinosinusitis (CRS) is a common disorder with a significant impact on the quality of life and health burden within the adult population (Gliklich 1995). Chronic rhinosinusitis is thought to affect between 5% and 15% of the population (Melen 1994). The diagnosis of rhinosinusitis is based on sino-nasal symptoms and is considered chronic when these have been present for 12 weeks or more (EPOS 2005). The recognition that rhinitis and sinusitis coexist and are concurrent in most individuals has allowed both these groups to evolve into the common terminology of rhinosinusitis (EPOS 2005). It is a diagnosis that is made by a wide variety of practitioners, including primary care physicians, otolaryngologists, immunologists, allergists and respiratory physicians. It is the principal diagnosis in nearly 2% of all patient visits to primary care (Schappert 1992). Medical therapy has been the basis for treating chronic rhinosinusitis. Short and long-term antibiotic therapy, topical and systemic steroids, topical and oral decongestants, oral antihistamines, mast cell stabilisers, anti-leukotriene agents, mucolytics, topical antibiotics, topical and systemic antimycotics, proton pump inhibitors, bacterial lysates, immunotherapy, phytotherapy and avoidance of environmental factors have all been used in the management of chronic rhinosinusitis (EPOS 2005). Surgery has an important, albeit evolving, role in the management of chronic rhinosinusitis (Smith 2005). Nasal irrigation is common to both modern and traditional therapy regimes. Delivered by bottle, spray, pump or nebuliser, the topical use of saline (salt water) has been included as a supplement to most treatment protocols.

Saline irrigations and sprays are, however, frequently regarded as a homeopathic adjunct in the treatment of sino-nasal disease. The nature of the benefit of saline is difficult to define physiologically.

The mechanical clearance of mucus is commonly proposed as the sole basis of its benefit. However, there is an increasing perception that saline has a contributory role in the resolution of inflammation and does not just relieve symptoms for mechanical reasons. Many theories exist for the potential beneficial physiological effects of topical saline. Improvement in mucus clearance, enhanced ciliary beat activity, removal of antigen, biofilm or inflammatory mediators and a protective role on sino-nasal mucosa have all been proposed.

Currently the medical literature includes recommendations for saline in a variety of sino-nasal complaints:

- Allergic rhinitis (IRMWS 1994)
- Pregnancy rhinitis (Ellegard 2006)
- Paediatric chronic sinusitis (Muntz 2004)
- Primary care recommendations (Seaton 1998)
- Sinonasal sarcoid (Long 2001)
- Wegener's granulomatosis (Tami 2005)
- Chronic rhinosinusitis (EPOS 2005)
- Post-operative care (Seppey 1996)
- Decontamination of radioactive material (Berger 2003)

Topical saline preparations vary from commercial single use and multi-use products to home-made solutions. Some of the common regimes are listed in Table 1.

Table 1. Common regimes

Study	Delivery	Routine	%NaCl	Recipe	Buffered
Rombago 2002	Pot	150 ml BD	2%	1 tsp salt, 1/2 tsp baking, 1 480ml water	Yes
Passali 2005	Atomiser	4 sprays QID	0.9%	Sea water	No
Tomooka 2000	Water-Pik	250 mls BD	1.6%	½ tsp salt, 250 ml water	No
Talbot 1997	Syringe/bulb	1 syringe or bulb BD/TDS	3%	2 to 3 tsp salt, 1 tsp baking soda in 950 ml water	Yes
Brown 2004	Bulb syringe	N/A	2.0%	950 ml boiled water and 1.5 tsp table salt	No

Table 1. Common regimes (*Continued*)

Wormald 2006	Squeeze bottle	200 ml each BD	0.9%	1 tsp salt, 1 tsp baking soda in 500 ml boiled water	Yes
Jala Neti 12th century	Neti pot or river	Approx 500 ml per nostril up to 4x/day	Adjusted to comfort	Tap water, room temperature	Optional
Other solutions			(1.1%) > 0.9%	EMS Dead Sea water	Yes

So ubiquitous is its use, the recommendation has also been made that saline should be used as a routine adjuvant to every treatment of acute or chronic rhinopathy (Passali 2005).

The direct clinical effectiveness of saline in treatment protocols is not clear. This review assesses the evidence for the clinical effectiveness of topical saline therapy in the management of the symptoms of chronic rhinosinusitis. The primary focus of the review is symptom relief. It includes assessment of trials where patients have conditions that produce chronic sino-nasal symptoms, not only those that fulfill a set of modern diagnostic criteria for chronic rhinosinusitis.

OBJECTIVES

To evaluate the effectiveness and safety of topical saline in the management of the symptoms of chronic rhinosinusitis.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials which fulfil the criteria outlined below. Controlled clinical trials were also identified by the search.

Types of participants

Adults and children with the symptoms of chronic rhinosinusitis. The pathologic classification of chronic rhinosinusitis is continually evolving and no attempt was made to redefine trials within current concepts of classification systems. The review focuses on the symptoms of persistent sino-nasal disease. This included patients suffering from rhinitis with seasonal exacerbations, perennial rhinitis, recurrent acute sinusitis in patients with ongoing symptoms between exacerbations and chronic rhinosinusitis (EPOS 2005). Endoscopic and CT evidence of sinusitis was not essential as recruitment was mainly from the primary care setting.

Types of interventions

The use of saline, as an active treatment, delivered to the nose by any means (douche, irrigation, pulsed, spray or nebuliser) where treatment comparison groups include:

- Saline versus no saline
- Saline versus 'placebo'
- Standard therapy with saline versus standard therapy alone
- Saline alone versus active agent
- Hypertonic versus isotonic saline

The 'placebo' for nasal saline irrigation encompassed any intervention which has no known biological activity but provides a similar level of interaction within the setting of chronic disease. The aim of 'placebo' in this setting is to reduce the maintenance and performance bias of patients within trials. It is acknowledged that blinding the patients to nasal irrigation is extremely difficult. Standard therapy with saline versus standard therapy alone for chronic rhinosinusitis includes any commonly used agents as outlined in EPOS 2005, where the addition of saline has been used to assess directly the benefit of its addition. Trials that use saline as a placebo for other therapies, and not for therapeutic intent, were excluded. This was felt to be appropriate because trials that focus on the therapeutic effect of active agents delivered in spray bottles (fluticasone (Flonase®) and mometasone (Nasonex®)) have spray volumes of only 90 to 100 microlitres. The saline placebo sprays used in these trials have similar volumes. These were not considered as similar comparisons to higher volume delivery of saline often with an intended mechanical effect.

Types of outcome measures

Primary outcomes

- Validated quality of life measures, both generic and disease specific
- Symptom scores (visual analogue scores or Likert scores)

Secondary outcomes

- Adverse events
- Radiological scores (Lund and Mackay CT scores)
- Endoscopic scores (Lund or EPOS)

Search methods for identification of studies

Electronic searches

We searched the Cochrane Ear, Nose and Throat Disorders Group Trials Register, the Cochrane Central Register of Controlled Trials (CENTRAL, *The Cochrane Library*, Issue 4 2006), MEDLINE (1950 to 2006), EMBASE (1974 to 2006), CINAHL (Cumulative Index to Nursing and Allied Health Literature), *m*RCT (*meta*Register of Controlled Trials, including www.ClinicalTrials.gov), NRR (National Research Register), LILACS, KoreaMed, IndMED, PakMediNet, Scolio, Zetoc and ISI Proceedings. The date of the last search was November 2006. Search strategies for CENTRAL, MEDLINE, EMBASE and other databases can be found in Appendix 1.

Searching other resources

Reference lists from identified publications were scanned to identify further trials, and authors were contacted as necessary. A forward search was undertaken on the authors of the identified trials. We assessed non-English language publications if the translated abstract indicated that the study was a randomised controlled trial with the focus on saline use in the management of chronic rhinosinusitis.

Data collection and analysis

Selection of studies

The initial search results were scanned by one author to identify trials which loosely met the inclusion criteria. The full text articles of all the retrieved trials of possible relevance were reviewed by the two authors (RH and SAH) and the inclusion criteria applied independently. Any differences in opinion about which studies to include in the review were resolved by discussion.

Data extraction and management

Data from the studies were extracted by one author and rechecked by the other. Data extraction was performed using standardised forms which were structured to allow an intention-to-treat analysis. Where data were missing, attempts were made to request further information.

Assessment of risk of bias in included studies

The quality of all included trials was assessed independently by the two authors (RH and SAH) and any differences in opinion were resolved by discussion. A modification of the method used by Chalmers 1990 was used. The selected studies were assessed for the following characteristics:
1. The adequacy of the randomisation process;
2. The potential for selection bias after allocation to study group, i.e. losses to follow up and whether analysis was by intention-to-treat;
3. Quality of outcome assessment;
4. Blinding of the outcome assessment with the understanding that by the nature of the intervention, when the patients were the outcome assessors they could not be blinded to the therapy given.
Studies were graded A, B or C for their overall methodological quality:
A: Minimisation of bias in all four categories above, i.e. adequate randomisation; few losses to follow up and intention-to-treat analysis, high quality outcome assessment;
B: Each of the criteria in A partially met;
C: One or more of the criteria in A not met.
Study quality was not used for sensitivity analysis.
Adverse events were recorded in table form. This information was taken into consideration when writing the discussion. Further information on adverse events is presented in Table 2.

Table 2. Adverse reactions reported in trials

Study	n	Delivery	Adverse rates	Commonest complaint	Withdrawal rate	Comment
Bachmann 2000	40	Hypertonic (1.1% EMS) versus isotonic saline	Not declared	Rhinitis symptoms and nasal obstruction	10%	
Cordray 2005	15	Hypertonic (Dead Sea) versus isotonic saline versus steroid	9.5% (details not given)	Not declared	24% (6/21)	29% attrition only one disqualified
Garavello 2005a	44	Hypertonic (3%) via spray versus no saline	Not declared	Not declared	0%	
Garavello 2003	20	Hypertonic (3%) via 5 ml syringe versus no saline	Not declared	Not declared	0%	
Heatley 2001	150	Hypertonic (2.7%) via pot versus bulb versus reflexology	Not declared	Not declared	15%	70%+ Patients would recommend irrigation - no difference on delivery
Rabago 2002	76	2% buffered via pot versus no treatment	23% (in treatment group)	Burning, irritation, tearing, nose bleeds, headache, drainage	12% in treatment 4% in control	4 (9%) modified the irrigation
Rogkakou 2005	14	Cetirizine versus cetirizine and saline (Iperclean > 0.9%)	Not declared	Not declared	0%	
Shoseyov 1998	34	Hypertonic (3.5%) versus isotonic saline drops	12% (4/34) Hypertonic (3/18) Isotonic (1/16)	Nasal burning sensation	12%	3/4 ADRs in hypertonic group
Adam 1998	143	Hypertonic (3.0%) versus isotonic saline versus control	32% versus 13% nasal 'burning' irritation (P < 0.05) 21% versus 36% nasal dryness	Nasal burning and nausea	17% for hypertonic 6% for isotonic	44% and 47% would not use spray again
Friedman 2006	57	Hypertonic (DSS) versus 1.8% saline	Not declared	Non compliance reported	26% (15/57)	
Holmstrom 1997	45	0.9% spray	7% (3/45)	Rhinitis symptoms, epistaxis, sore throat	Not declared	83% wanted to continue post three weeks

Table 2. Adverse reactions reported in trials (*Continued*)

Johnsen 2001	79	Nozoil versus 0.9% buffered	8% Nozoil 5% isotonic	Rhinitis (Nozoil), Nose bleed (isotonic)	Not declared	
Keerl 1998	12	Isotonic saline via Rhinomer force	9%			
Keerl 1997	180	Ems versus isotonic saline douches	15.3%		46/180 did not complete questionnaire	
Michel 2005	66	Ems spray versus oxymetazoline 0.05%	0%	Not declared	Not declared	
Passali 2005	200	0.9% with atomiser versus syringe	Not declared	Not declared	Not declared	
Rabone 1999	46	Saline versus no saline via pot	Not declared	Problems with techniques and mixing fluid noted	22%	44% using at one year
Scheithauer 2006	50	Spray versus hand irrigation with saline			16%	Acceptance better in spray group
Seppey 1996	28	Sea water spray versus iodine bromide spray			7% (2/28)	Sea water subjectively preferred
Taccariello 1999	41	Sea water spray versus alkaline Douche versus no saline CRS treatment	Not declared	Not declared	12% (6/49)	3/6 in treatment group
Tano 2004	108	0.9% saline spray versus no treatment	Not declared	Not declared	36%	Only 60% compliance for most
Tomooka 2000	211	Hypertonic irrigation	24%	Nasal irritation, nasal discomfort, otalgia, or pooling of saline in paranasal sinuses with subsequent drainage	54% (114/211)	

Table 2. Adverse reactions reported in trials (*Continued*)

Wendeler 1997	38	Ems water versus water		Otitis media in controls and study discontinued		

Data synthesis

We attempted to analyse data by intention-to-treat. If data were comparable and of sufficient quality, an attempt was made to combine these to give a summary measure of effect. Standard mean differences (SMD) were obtained from the reported results in order to compare trials using outcome tools of different scales. Some of the raw data was extracted from graphs and tables. Some of the standard deviation (SD) results for the mean changes were derived or imputed from the confidence intervals or from SDs from the individual patient groups.

RESULTS

Description of studies

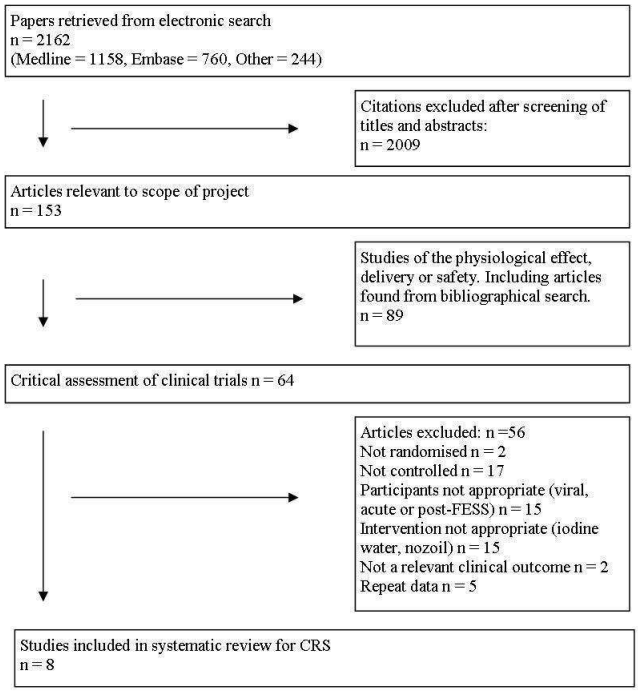
See: Characteristics of included studies; Characteristics of excluded studies.

Of the 2162 abstracts retrieved from our searches, the majority did not focus on the use of saline in treatment or were *in vitro* studies. Sixty-four clinical trials were identified from the search. One of these contained duplicate data along with observational follow up from a previous trial (Rabago 2005a; Rabago 2002). Seventeen of these studies were neither randomised nor controlled (Georgitis 1993; Georgitis 1994; Grossan 1974a; Grossan 1974b; Grossan 1974c; Keerl 1997; Keerl 1998; Kozlov 1997; Krayenbuhl 1995; Levine 2006; Muller-Sacks 1998; Neher 2005; Nuutinen 1986; Pagani 2001; Rabago 2005a; Shilenkova 1995; Traissac 1999). There were non-rhinologic controls in one study (Tomooka 2000). Case-control was employed in one study (Taccariello 1999). Acute upper respiratory tract symptom, postoperative care or other forms of rhinitis were the focus of 15 trials (Adam 1998; Holmstrom 1997; Johnsen 2001; Mack-Graesle 2004; Michel 2005; Pal'chun 2004; Passali 2005; Pigret 1996; Pinto 2006; Rabone 1999; Scheithauer 2006; Seppey 1996; Tano 2004; Unal 2001; Wiikmann 1996). The interventions (15) or primary outcomes (2) were not met in a further 17 studies (Barbieri 2002; Friedman 2006; Hartog 1996; Hartog 1997a; Hartog 1997b; Johannssen 1996; LaForce 2004; Liu 2000; Mora 2002; Passali 2003; Polasek 1987; Pynnonen 2006; Rabago 2006; Shaikh 1995; Shaikh 1996; Subiza 1999; Wendeler 1997). Repetition of data was present in five studies (Angrisano 2003; Garavello 2005b; Heatley 2000; Seaton 1998; Slawson 1998).

The remaining eight trials satisfied the inclusion criteria (Bachmann 2000; Cordray 2005; Garavello 2003; Garavello 2005b; Heatley 2001; Rabago 2002; Rogkakou 2005; Shoseyov 1998). The methods, participants, interventions and outcomes of the included studies are listed in the table of 'Characteristics of Included Studies'. There were a wide range of delivery techniques and solutions used in these studies and the duration of treatment varied between seven days and six months. It was not always possible to determine accurately the volume of saline given.

A flow chart of study retrieval and selection is provided in Figure 1.

Figure 1.



Studies are divided into five types for ease of comparison:
A: Comparison of saline versus no treatment;
B: Comparison of saline versus 'placebo';
C: Standard therapy with saline versus standard therapy alone;
D: Saline alone versus active agent;
E: Hypertonic versus isotonic saline.

A: Comparison of saline versus no treatment

Garavello 2003

This randomised controlled trial sought to evaluate the change in symptom scores of children with rhinitis by the use of saline irrigation. Twenty children from a rhinological service in secondary care in Italy were divided into a saline treatment group and a control group. No other active treatments were included in the study protocol. However, patients were allowed to use antihistamines as required and record their use in a diary. A 3.0% hypertonic saline solution was delivered by syringe with a volume of 2.5 cc to each nose three times a day. The control group received no topical solution. The patients and parents recorded daily symptom scores. A mean daily symptom score was developed along with antihistamine use. No other validated questionnaire or objective outcome was used. No patients were lost to follow up.

Garavello 2005b

This randomised trial of children with rhinoconjunctivitis symptoms for at least one year assessed the effect of topical saline to treat both nasal and ocular symptoms. Forty-four children (<16 years) were recruited from secondary care and divided into two groups. One group of twenty-two patients received 3.0% saline via a nasal atomiser spray with three sprays (150 ul) per nostril, three times a day. The control group received no topical treatment. Treatment lasted seven weeks. Antihistamine use was allowed as required and recorded in a diary. The outcome measures were daily symptom scores, antihistamine use and adverse events. Four patients (two from each group) did not complete the study either declining to continue or being lost to follow up.

Rabago 2002

Seventy-six adults with the symptoms of chronic sinusitis or recurrent acute sinusitis were recruited mainly from primary care (70 patients). The remaining six patients were from secondary care. The participants were divided in a 2:1 block randomisation. One group (n = 52)) received 2.0% buffered saline delivered via SinuCleanse® Nasal Cup. The treatment consisted of 150 ml per nostril daily for six months. The remaining control group (n = 24) received no topical treatment. No other therapy was part of the treatment protocol. The primary outcomes were Quality of Life scores from Short Form 12 (SF-12) and Rhinosinusitis Disability Index (RSDI) along with a single-item symptoms severity assessment (SIA). Antibiotic use, compliance and adverse events were also recorded. Six treatment patients and one control patient did not complete the trial.

B: Comparison of saline versus 'placebo'

Heatley 2001

This randomised controlled trial sought to determine the effect of saline delivered by different techniques and 'placebo' on the Quality of Life scores of chronic sinusitis patients. One hundred and fifty people from primary care in the USA were divided randomly into three groups for comparison. Group 1 (n = 50) were given nasal irrigation with a bulb syringe, Group 2 used nasal irrigation via an irrigation pot and Group 3 were given reflexology as a 'placebo'. Participants used 2.7% saline solutions used in unspecified volumes daily for two weeks. Quality of Life scores from Short Form 36 (SF36) and Rhinosinusitis Outcomes Measure (RSOM31) questionnaires were used as primary endpoints. Medication use was also recorded in diaries. There was an 85% completion rate with attrition numbers of 7, 11 and 4 within groups 1, 2 and 3 respectively.

C: Standard therapy with saline versus standard therapy alone

Rogkakou 2005

A randomised controlled trial of adults with chronic rhinitis to assess the effect of saline added to antihistamine therapy. Fourteen patients were randomised to two groups. One group (n = 7) received cetrizine 10 mg daily with saline spray for four weeks. The other group (n = 7) received cetrizine only with no local therapy. The background of the patients was not specified but both groups had similar characteristics. Unspecified volume of Iperclean® hypertonic saline spray was delivered four times a day. The outcomes measured included day and night symptom scores, Rhinasthma® questionnaire and acoustic rhinometry.

D: Saline alone versus active agent

Cordray 2005

Twenty-one adult patients from primary care in the United States were recruited to assess the effect of hypertonic saline spray versus triamcinolone versus isotonic saline spray. All participants had persistent nasal symptoms of rhinitis. The patients were randomly divided into three groups within a single blinded study design. No other treatment was allowed during the treatment period of seven days. Of the original 21 patients, only 15 completed the study. This represented five within each group. Two patients withdrew because of adverse reactions, two were lost to follow up and one for antihistamine use. The details of which groups the losses came from were not included in the publication. The Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) was the primary endpoint.

E: Hypertonic versus isotonic saline

Bachmann 2000

Forty adult patients attending a secondary centre in Germany participated in the trial. Inclusion criteria included presence of symptoms for six months and no use of nasal sprays. All patients were randomly divided into two groups, one receiving hypertonic Ems saline (from mineral springs Bad Ems, Germany) and the other isotonic saline. Double blinding was obtained for patients and physicians. Both groups used a Rhinocare® irrigator with 200 ml of solution twice a day for one week. Four patients withdrew from the study (one from Ems group and three from the isotonic

group). Only one patient withdrew because of an adverse event. The group from which they were randomised was not declared. The outcomes included symptom, endoscopic and radiological scores, mucociliary clearance, rhinomanometry and olfactometry scores.

Shoseyov 1998

Paediatric patients from an Israeli hospital contributed to this study. Thirty-four children from three to 16 years were recruited. It is not clear if they all came from secondary care. They were randomised to two groups receiving 10 drops (1 ml) of either 3.5% or isotonic saline three times a day for four weeks. The trial used '10 drops (or approximately 1 ml) three times a day' in children. This still represents a 15 to 30 magnitude of volume that is delivered to nose if compared to a normal child nasal drug dosage of one spray per nostril per day. Based on this calculation we felt that this was still appropriate for inclusion. Four patients withdrew (three hypertonic, one isotonic) due to nasal burning sensations. Despite similar pre-treatment characteristics, adequate randomisation is unlikely with equal numbers in each group despite uneven attrition. Primary outcomes were symptom and radiological scores. Parents were used to record some of the symptom data.

Risk of bias in included studies

All randomised controlled trials were subjected to a critical review of their methodology by the two authors and were graded for their overall methodological quality according to the stated criteria. Methodological quality varied between studies with scores of included studies being either A (one trial), B (five trials) or C (two trials). Although all were randomised trial designs, only four described adequate randomisation and concealment procedures (Rabago 2002; Garavello 2003; Garavello 2005b; Rogkakou 2005).

Baseline comparative data were given in all studies. However, there was a substantial pre-treatment difference in the group from Cordray 2005. The control, or saline group, had a Rhinoconjunctivitis Quality of Life Questionnaire score of 2.60 compared to 3.38 and 3.24 in the hypertonic and corticosteroid groups respectively. No statistical assessment was made. No other study demonstrated significant differences between baseline groups.

Attrition was significant, with the following failure to complete numbers: Cordray 2005 29% (6 of 21); Heatley 2001 15% (22 of 150); Bachmann 2000 10% (4 of 40); Rabago 2002 9% (7 of 76); Shoseyov 1998 12% (4 of 34) and Garavello 2005b 3% (1 of 40). Garavello 2003 had no losses and Rogkakou 2005 did not comment. Discussion or tabulated data on patients who did not complete were available in all trials. However, statistical assessment was only discussed in Rabago 2002 and an intention-to-treat analysis was not undertaken in any study.

Four trials used validated questionnaire data in their assessment: Rogkakou 2005 (Rhinasthma); Cordray 2005 (Rhinoconjunctivitis Quality of Life Questionnaire); Heatley 2001 (RSOM31, SNOT 20 and SF36); Rabago 2002 (RSDI and SF12). The SF-36 data was used in Heatley 2001 for baseline assessment but no further post intervention SF36 data was provided. Blinding was not addressed in four trials (Rogkakou 2005; Garavello 2003; Garavello 2005b; Heatley 2001). Although inherently difficult to blind patients to interventions, such as nasal irrigation, Rabago 2002 had used investigator blinding combined with blinding of patients to previous data to minimise bias. Single-blinded structure was similarly used in Cordray 2005. Double blinding was achieved in both studies investigating hypertonic versus isotonic solutions (Bachmann 2000; Shoseyov 1998).

Only the hypertonic versus isotonic saline studies addressed secondary outcome measures or objective surrogates for rhinosinusitis.

Effects of interventions

There was significant variability in the tools used for outcome assessment. No trial centres used the same questionnaire or symptom scale. Heterogeneity also existed between participants with some classified as chronic rhinosinusitis and others as perennial allergic rhinosinusitis or recurrent sinusitis but with persistent symptoms. Data on total numbers demonstrating improvement were not available from the information published. An attempt was made to assess the standardised mean difference of the different outcome measures for intra group comparison. Only symptom scores from Group A (saline versus no treatment) and symptom and radiological scores from Group E (hypertonic versus isotonic group) could be pooled for analysis. Any other meta-analysis was either impossible or not considered appropriate because of the heterogeneity of the treatments, treatment amounts and durations, trial procedures and scoring systems. A narrative overview of the remaining results is therefore presented. The pooled results for groups A and E are presented in the tables of 'Comparisons and data'.

A: Comparison of saline versus no treatment

Summary

Saline better than no treatment for improving symptoms and disease specific quality of life scores.

Symptom scores: combined SMD 1.42 (1.01 to 1.84). with an overall effect P < 0.00001. The I^2 = 86.7% suggesting heterogeneity.

Disease specific quality of life: SMD 1.36 (0.80 to 1.91) with an overall effect P < 0.00001.

General quality of life: SMD 0.47 (-0.04 to 0.97) with overall effect P = 0.07.

Rabago 2002

Primary outcome measure

The saline group demonstrated improved Rhinosinusitis Disability Index (RSDI) and Single-item Symptom Severity Index Assessment (SIA) scores compared to controls. Six-month RSDI improvement was 24.7% (-14.4) and SIA of 41% (-1.6). These were statistically significant and above the proposed minimally important clinical difference for the RSDI. The SF12 did not show a

statistically significant improvement.

Garavello 2003

Primary outcome measure

The combined symptom scores did not show a significant improvement at six weeks. There were statistically significant improvements at 3, 4 and 5 weeks in favour of the saline group but not at the completion of study.

Garavello 2005b

Primary outcome measure

The combined occulo-nasal symptom score was better during the pollen season in the saline group at the completion of study. The control group had mean symptom scores of (0 to 16) 10.25 compared to 3.75 in the saline patients at the end of the study. This was a significant outcome favouring the saline group.

The pooled results for group A are presented in the tables of 'Comparisons and data'.

B: Comparison of saline versus 'placebo'

Summary

Saline did not improve disease specific quality of life scores over a reflexology control.

Disease specific quality of life: SMD -0.53 (-0.96 to -0.11) with an overall effect P = 0.01 for bulb and SMD -24 (-43.93 to -4.07) with and overall effect P = 0.02 for pot.

Heatley 2001

Primary outcome measure

All groups (pot, bulb and reflexology) had improvements on RSOM31 and SNOT20 scores. The mean improvements were 25.5%, 20.4% and 35.1% in the groups 1, 2 and 3 respectively. Percentages of individuals improved were 72%, 74% and 78%. There was no significant difference between groups and control. Inter-group assessment was not provided. Our analysis of the mean change and imputed SD of mean change suggested there may have been an outcome in favour of the control group. The 'placebo' group was as efficacious as both saline uses. SF-36 analysis was omitted from the post-intervention results.

C: Standard therapy with saline versus standard therapy alone

Summary

Saline improves disease specific quality of life scores as an addition to oral antihistamine therapy.

Rogkakou 2005

Primary outcome measure

The Rhinasthma questionnaire showed a 92.4% and 86% improvement on the upper airway and global indices respectively. These outcomes showed a significant effect (upper airway P = 0.02, global P = 0.001) favouring the combined saline therapy group. Standard deviations were not available for independent analysis.

D: Saline alone versus active agent

Summary

Isotonic or hypertonic saline did not improve disease specific quality of life scores over intra-nasal steroid.

Disease specific quality of life: SMD -3.29 (-5.51 to -1.06) with an overall effect P = 0.004 for isotonic solutions and SMD -2.88 (-4.92 to -0.84) with an overall effect P = 0.006 for hypertonic saline.

Cordray 2005

Primary outcome measure

The Rhinoconjunctivitis Quality of Life Questionnaire improvements were 68.2%, 40.2% and 6.2% for the corticosteroid, hypertonic (Dead Sea) saline and isotonic saline groups. The isotonic improvement was not statistically significant. The other interventions demonstrated a significant improvement . The study was not powered sufficiently to compare Dead Sea salt with corticosteroid. The three-way comparison also showed a treatment effect favouring hypertonic compared to isotonic saline. This result is included in the pooled analysis for Group E.

E. Hypertonic versus isotonic solutions

Summary

No difference was found in comparison of isotonic to hypertonic saline.

Symptom scores: SMD 0.34 (-0.11 to 0.80) with an overall effect P = 0.14. I^2 = 51.2%.

Radiology scores: SMD 0.39 (-0.20 to 0.97) with an overall effect P = 0.19. I^2 = 97.6% suggesting heterogeneity.

Bachmann 2000

Primary outcome measure

There was no significant difference between symptom scores from each group. Both improved relative to baseline. The mean symptoms score change was 0.6 and 0.7 for the isotonic saline and hypertonic (Ems) group respectively (scale 1 to 6). The Student's t test P value was > 0.05.

Secondary outcome measure

Endoscopic or radiological scores did not differ between the two groups. Significant improvement was seen in all but the isotonic secretion score and frontal radiological score. The mean endoscopic scores were 1.23 (redness), 1.0 (swelling) and 0.35 (secretion) for the isotonic group and 1.05, 1.15 and 0.74 respectively for the hypertonic group (scale 1 to 6). Radiological mean change scores were 0.18 (frontal), 0.76 (maxillary) and 1.06 (ethmoid) for the isotonic groups and 0.42, 0.63 and 0.84 respectively for the hypertonic group (scale 1 to 6). Ethmoid and maxillary scores had similar outcomes and were chosen for pooled analysis as these reflected similar scoring to Shoseyov 1998.

Shoseyov 1998

Primary outcome measure

There was a significant outcome in the cough score favouring the hypertonic group (reduction of score HS 56% versus NS 6%, P < 0.05). Other nasal symptom scores were similar.

Secondary outcome measure

Radiological scores favoured the hypertonic group (reduction in score HS 67% versus NS 3%, P < 0.05).

The pooled results for group E are presented in the tables of 'Com-

parisons and data'.

Adverse events

Nasal burning, irritation and nausea were the most frequently recorded adverse effects. No major adverse events were recorded in the 1659 patients using isotonic or hypertonic saline from 22 trials. Wendeler 1997 used tap water and concluded early due to a high rate of otitis media. The use of hypotonic water in the control group was thought to be responsible. The reported adverse events in both included and selected excluded studies are shown in Table 2.

DISCUSSION

The included studies were of modest quality and several contained only small numbers of patients. Rabago 2002 provides the strongest support for the use of saline as an adjunct to the management of the symptoms of chronic rhinosinusitis. It also has the strongest methodology, assessment and use of validated questionnaires.

Primary care populations were the most commonly studied groups. The majority of recommendations for saline use are likely to be given within this group. Many of these patients will not have had endoscopic or CT scan confirmation of their pathology. Thus the inclusion of both chronic (perennial) allergic and chronic inflammatory sinus disease (EPOS 2005) was deemed practical.

The effect size (that is, the degree to which symptoms or quality of life scores are improved) is likely to be modest. However, the use of saline can be provided with low cost and good tolerability. On balance it seems to be beneficial to include topical saline use in the symptom control for persistent sino-nasal disease.

There was no evidence presented in these studies of any significant harmful side effects of saline use. However, minor complaints and non-compliance were reported. Nasal burning, irritation and nausea were the most frequently recorded adverse effects. Even though the highest adverse event rate was reported in Rabago 2002 (23%), all 44 treatment group patients completing the study would recommend nasal irrigation to family and friends with sinus problems.

Heatley 2001 reported on patient opinion with saline use. Over 70% of patients reported that saline was helpful and would continue to use or would recommend the use of saline for further symptoms. The follow-up observational study of Rabago 2005a reported that 95% of patients would continue to use saline for their nasal complaints. However, the majority (55%) did so intermittently and reported frequencies of only 2.3 times per week.

AUTHORS' CONCLUSIONS

Implications for practice

The beneficial effect of saline appears to outweigh the drawbacks for the majority of patients. Topical saline could be included as a treatment adjunct for managing the symptoms of chronic rhinosinusitis and conditions producing chronic sino-nasal symptoms. The is no evidence that saline is more effective than active agents. There is evidence that hypertonic solutions improve mucociliary clearance (Talbot 1997; Bachmann 2000) . The effect on symptoms is less evident. There may be some added clinical benefit but it is balanced against patient tolerance. No information can be provided regarding the delivery type, dosage frequency or volume.

Implications for research

There is tremendous variability in the tools used for outcome assessment in rhinosinusitis. Epistemological work into the most commonly used and appropriate outcome measures is required. The dissemination of this knowledge will encourage their use in trials and allow comparison between studies. Validated and accurate patient centred outcome tools should always be preferred over ad hoc or customised questionnaires. Examples of these questionnaires include SNOT20, CSS and SF-36. Recently published guidelines (Meltzer 2006) provide a framework for making assessments in future studies. A review of evidence for the physiological impact of saline that might explain the beneficial effect, most appropriate delivery technique, tonicity, frequency and volume of topical nasal saline is also required.

REFERENCES

References to studies included in this review

Bachmann 2000 *{published data only}*
Bachmann G, Hommel G, Michel O. Effect of irrigation of the nose with isotonic salt solution on adult patients with chronic paranasal sinus disease. *European Archives of Oto-Rhino-Laryngology* 2000;**257**(10):537–41. [: 0937–4477]

Cordray 2005 *{published data only}*
Cordray S, Harjo JB, Miner L. Comparison of intranasal hypertonic Dead Sea saline spray and intranasal aqueous triamcinolone spray in seasonal allergic rhinitis. *Ear, Nose and Throat Journal* 2005;**84**(7):426–30. [: 0145–5613]

Garavello 2003 *{published data only}*
Garavello W, Romagnoli M, Sordo L, Gaini RM, Di Berardino C, Angrisano A. Hypersaline nasal irrigation in children with symptomatic seasonal allergic rhinitis: A randomized study. *Pediatric Allergy and Immunology* 2003;**14**(2):140–3. [: 0905–6157]

Garavello 2005a *{published data only}*
Garavello W, Di Berardino F, Romagnoli M, Sambataro G, Gaini RM. Nasal rinsing with hypertonic solution: An adjunctive treatment for pediatric seasonal allergic rhinoconjunctivitis. *International Archives of Allergy and Immunology* 2005;**137**(4): 310–4. [: 1018–2438]

Heatley 2001 *{published data only}*
* Heatley DG, McConnell KE, Kille TL, Leverson GE, Heatley DG, McConnell KE, Kille TL, Leverson GE. Nasal irrigation for the alleviation of sinonasal symptoms. *Otolaryngology - Head and Neck Surgery* 2001;**125**(1):44–8. [: 0194–5998]

Rabago 2002 *{published data only}*
Rabago D, Zgierska A, Mundt M, Barrett B, Bobula J, Maberry R. Efficacy of daily hypertonic saline nasal irrigation among patients with sinusitis: A randomized controlled trial. *Journal of Family Practice* 2002;**51**(12):1049–55. [: 0094–3509]

Rogkakou 2005 *{published data only}*
Rogkakou A, Guerra L, Massacane P, Baiardini I, Baena-Cagnani R, Zanella C, Canonica GW, Passalacqua G. Effects on symptoms and quality of life of hypertonic saline nasal spray added to antihistamine in persistent allergic rhinitis - A randomized controlled study. *Allergie et Immunologie* 2005;**37**(9):353–6. [: 0397–9148]

Shoseyov 1998 *{published data only}*
Shoseyov D, Bibi H, Shai P, Shoseyov N, Shazberg G, Hurvitz H. Treatment with hypertonic saline versus normal saline nasal wash of pediatric chronic sinusitis. *Journal of Allergy and Clinical Immunology* 1998;**101**(5):602–5. [: 0091–6749]

References to studies excluded from this review

Adam 1998 *{published data only}*
Adam P, Stiffman M, Blake RL Jr. A clinical trial of hypertonic saline nasal spray in subjects with the common cold or rhinosinusitis [see comment]. *Archives of Family Medicine* 1998;**7** (1):39–43. [MEDLINE: PARTICIPANTS; : 1063–3987]

Angrisano 2003 *{published data only}*
Angrisano A. Hypertonic saline nasal wash: effect on grass pollen rhinitis in children. *Allergy and Clinical Immunology International* 2003;**1**:(Supplement 1): Abstract no. P-16-47. [MEDLINE: REPEAT DATA; : CN–00526358]

Barbieri 2002 *{published data only}*
Barbieri M, Salami A, Mora F, Casazza A, Sovatzis A, Teglia R, Cordone MP, Mora R. Behaviour of Serum IgE and IgA in patients with allergic rhinitis treated with iodine bromide thermal water. *Acta Otorhinolaryngologica Italica* 2002;**22**(4):215–9. [MEDLINE: iNTERVENTIONS]

Friedman 2006 *{published data only}*
Friedman M, Vidyasagar R, Joseph N. A randomized, prospective, double-blind study on the efficacy of Dead Sea salt nasal irrigations. *Laryngoscope* 2006;**116**(6):878–82. [MEDLINE: iNTERVENTIONS; : 0023–852X]

Garavello 2005b *{published data only}*
* Garavello W, Sordo L, Romagnoli M, Giannobi P, Gaini RM, Di Berardino C. Seasonal allergic rhinitis and hypersaline nasal irrigation in children: a randomized study. XVIII IFOS World Congress, Rome Italy, 25-30 June 2005. 2005. [MEDLINE: REPEAT DATA]

Georgitis 1993 *{published data only}*
Georgitis JW. Local hyperthermia and nasal irrigation for perennial allergic rhinitis: Effect on symptoms and nasal airflow. *Annals of Allergy* 1993;**71**(4):385–9. [MEDLINE: ALLOCATION - case series; : 0003–4738]

Georgitis 1994 *{published data only}*
Georgitis JW. Nasal hyperthermia and simple irrigation for perennial rhinitis: Changes in inflammatory mediators. *Chest* 1994;**106**(5):1487–92. [MEDLINE: ALLOCATION - case series; : 0012–3692]

Grossan 1974a *{published data only}*
Grossan M. A device for nasal irrigation. *Transactions - American Academy of Ophthalmology and Otolaryngology* 1974;**78**(4): ORL279–80. [MEDLINE: ALLOCATION - case series; : 0002–7154]

Grossan 1974b *{published data only}*
Grossan M. Irrigation of the child's nose. *Clinical Pediatrics* 1974; **13**(3):229–31. [MEDLINE: ALLOCATION - case series; : 0009–9228]

Grossan 1974c *{published data only}*
Grossan M. A new nasal irrigator device. *Eye, Ear, Nose and Throat Monthly* 1974;**53**(3):87–90. [MEDLINE: ALLOCATION - case series; : 0014–5491]

Hartog 1996 *{published data only}*
Hartog B, Van Benthem PP, Prins LC, Hordijk GJ. The efficacy of sinus irrigation versus sinus irrigation followed by functional endoscopic sinus surgery. A randomised prospective trial in patients with chronic maxillary sinusitis. XVI Congress of the European Rhinologic Society. XV ISIAN. VIII Congress of the International Rhinologic Society. 1996.

Hartog 1997a *{published data only}*

* Hartog B, van Benthem PP, Hordijk GJ. The efficacy of sinus irrigation versus sinus irrigation followed by functional endoscopic sinus surgery: a randomized prospective trial in patients with chronic maxillary sinusitis. *Clinical Otolaryngology and Allied Sciences* 1997;**106**(9):759–66. [MEDLINE: iNTERVENTIONS]

Hartog 1997b *{published data only}*

Hartog B, van Benthem PP, Prins LC, Hordijk GJ, Hartog B, van Benthem PP, Prins LC, Hordijk GJ. Efficacy of sinus irrigation versus sinus irrigation followed by functional endoscopic sinus surgery. *Annals of Otology, Rhinology and Laryngology* 1997;**106**(9): 759–66.

Heatley 2000 *{published data only}*

Heatley D, McConnell KE, Kilie T, Leverson GA. Nasal irrigation for the alleviation of sinonasal symptoms. *Otolaryngology - Head and Neck Surgery* 2000;**123**(2):78–9.

Holmstrom 1997 *{published data only}*

Holmstrom M, Rosen G, Wahlander L, Holmstrom M, Rosen G, Wahlander L. Effect of nasal lavage on nasal symptoms and physiology in wood industry workers. *Rhinology* 1997;**35**(3): 108–12. [MEDLINE: PARTICIPANTS; : 0300–0729]

Johannssen 1996 *{published data only}*

Johannssen V, Maune S, Erichsen H, Hedderich H, Werner JA. [Effect of postoperative endonasal mucous membrane care on nasal bacterial flora: prospective study of 2 irrigation methods with NaCl solution after paranasal sinus surgery]. *Laryngo-Rhino-Otologie* 1996;**75**(10):580–3. [MEDLINE: iNTERVENTIONS; : 0935–8943]

Johnsen 2001 *{published data only}*

* Johnsen J, Bratt BM, Michel-Barron O, Glennow C, Petruson B, Johnsen J, Bratt BM, Michel-Barron O, Glennow C, Petruson B. Pure sesame oil vs isotonic sodium chloride solution as treatment for dry nasal mucosa. *Archives of Otolaryngology - Head and Neck Surgery* 2001;**127**(11):1353–6. [MEDLINE: PARTICIPANTS; : 0886–4470]

Keerl 1997 *{published data only}*

Keerl R, Weber R, Muller C, Schick B. [Efficiency and acceptance of nasal irrigation after endonasal sinus surgery]. *Laryngo-Rhino-Otologie* 1997;**76**(3):137–41. [MEDLINE: ALLOCATION - case series; : 0935–8943]

Keerl 1998 *{published data only}*

Keerl R, Weber R, Draf W, Dshambazov K. [Tolerance, subjective complaints and mucociliary clearance in rhinitis sicca before and after nasal irrigation with Rhinomer Force 1]. *Laryngo-Rhino-Otologie* 1998;**77**(4):196–200. [MEDLINE: ALLOCATION - case series; : 0935–8943]

Kozlov 1997 *{published data only}*

Kozlov VS. [Controlled irrigation using sinus catheter IaMIK-5 in the treatment of chronic sinusitis]. *Vestnik Otorinolaringologii* 1997; **3**:35–7. [MEDLINE: ALLOCATION - case series; : 0042–4668]

Krayenbuhl 1995 *{published data only}*

Krayenbuhl M, Seppey M. [Efficacy of Rhinomer Force 3 in the postoperative course of endonasal surgery]. *Revue Medicale de la Suisse Romande* 1995;**115**(3):249–52. [MEDLINE: ALLOCATION - case series; : 0035–3655]

LaForce 2004 *{published data only}*

LaForce CF, Corren J, Wheeler WJ, Berger WE, Rhinitis Study Group. Efficacy of azelastine nasal spray in seasonal allergic rhinitis patients who remain symptomatic after treatment with fexofenadine. *Annals of Allergy, Asthma and Immunology* 2004;**93** (2):154–9. [MEDLINE: iNTERVENTIONS; : 1081–1206]

Levine 2006 *{published data only}*

Levine HL, Cordray S, Miner LA. Use of Dead Sea salt solution for chronic rhinitis and rhinosinusitis. *Operative Techniques in Otolaryngology - Head and Neck Surgery* 2006;**17**(2):147–50. [MEDLINE: ALLOCATION - case series; : 1043–1810]

Liu 2000 *{published data only}*

Liu Z, Li F, Zhang S. [Preliminary clinical observation on treatment of chronic rhinitis with rhinitis spray]. *Zhongguo Zhong Xi Yi Jie He Za Zhi [Chinese Journal of Integrated Traditional and Western Medicine]* 2000;**20**(5):330–1. [MEDLINE: iNTERVENTIONS]

Mack-Graesle 2004 *{published data only}*

Mack-Graesle B. [Physiological saline for nasal irrigation in the prevention of common cold]. *Deutsche Apotheker Zeitung* 2004;**144** (7):50–3. [MEDLINE: PARTICIPANTS; : 0011–9857]

Michel 2005 *{published data only}*

Michel O, Essers S, Heppt WJ, Johannssen V, Reuter W, Hommel G. The value of Ems Mineral Salts in the treatment of rhinosinusitis in children: Prospective study on the efficacy of mineral salts versus xylometazoline in the topical nasal treatment of children. *International Journal of Pediatric Otorhinolaryngology* 2005;**69**(10): 1359–65. [MEDLINE: PARTICIPANTS; : 0165–5876]

Mora 2002 *{published data only}*

Mora R, Chiarlone M, Crippa B, Mora F, Barbieri M. Nasal irrigations with sulphurea water in the treatment of the oral allergy syndrome. *Medicina Clinica e Termale* 2002;**14**(48):287–90. [MEDLINE: iNTERVENTIONS]

Muller-Sacks 1998 *{published data only}*

Muller-Sacks E, Bode V. [Sea salt containing nose spray in rhinitis sicca. Results of an observational study]. *Deutsche Apotheker Zeitung* 1998;**138**(20):73–6. [MEDLINE: ALLOCATION - case series; : 0011–9857]

Neher 2005 *{published data only}*

Neher A, Fischer H, Appenroth E, Lass-Florl C, Mayr A, Gschwendtner A, Ulmer H, Gotwald TF, Gstottner M, Kozlov V, Nagl M. Tolerability of N-chlorotaurine in chronic rhinosinusitis applied via yamik catheter. *Auris, Nasus, Larynx* 2005;**32**(4): 359–64. [MEDLINE: ALLOCATION - case series; : 0385–8146]

Nuutinen 1986 *{published data only}*

Nuutinen J, Holopainen E, Haahtela T, et al.Balanced physiological saline in the treatment of chronic rhinitis. *Rhinology* 1986;**24**(4): 265–9. [MEDLINE: ALLOCATION - case series; : 0300–0729]

Pagani 2001 *{published data only}*

Pagani J, Villa MP, Paggi B, Natale N, Mecchia A, Massa F, et al.Efficacy of nasal wash with saline solution 2% Na-chloride in children with high nasal resistance. *European Respiratory Journal* 2001;**18**(Suppl 33):1s–120s. [MEDLINE: ALLOCATION - case series]

Pal'chun 2004 *{published data only}*

Pal'chun VT, Beliakova LV, Luchikhina LA, Kononova NA. [Efficacy of physiomer spray after endonasal surgical interventions].

Vestnik Otorinolaringologii 2004;**3**:45–7. [MEDLINE: PARTICIPANTS; : 0042–4668]

Passali 2003 ***{published data only}***

Passali D, Salerni L, D'Aco L, Gaudini E, Passali FM. [The effects of bicarbonate-sulphate-alkaline-carbonic waters ('santissima water' of Chianciano Thermae) in catarrhal diseases of upper respiratory ways]. *Rivista Italiana di Otorinolaringologia Audiologia e Foniatria* 2003;**23**(1):39–49. [MEDLINE: iNTERVENTIONS; : 0392–1360]

Passali 2005 ***{published data only}***

Passali D, Damiani V, Passali FM, Passali GC, Bellussi L. Atomized nasal douche vs nasal lavage in acute viral rhinitis. *Archives of Otolaryngology - Head and Neck Surgery* 2005;**131**(9):788–90. [MEDLINE: PARTICIPANTS; : 0886–4470]

Pigret 1996 ***{published data only}***

Pigret D, Jankowski R. Management of post-ethmoidectomy crust formation: randomized single-blind clinical trial comparing pressurized seawater versus antiseptic/mucolytic saline. *Rhinology* 1996;**34**(1):38–40. [MEDLINE: PARTICIPANTS; : 0300–0729]

Pinto 2006 ***{published data only}***

Pinto JM, Elwany S, Baroody FM, Naclerio RM. Effects of saline sprays on symptoms after endoscopic sinus surgery. *American Journal of Rhinology* 2006;**20**(2):191–6. [MEDLINE: PARTICIPANTS; : 1050–6586]

Polasek 1987 ***{published data only}***

Polasek O, Haudenschild P. [Double blind study and cross-over of the effect of nasal lavage with Prorhinel in chronic rhinitis]. *Therapeutische Umschau* 1987;**44**(12):978–81. [MEDLINE: iNTERVENTIONS; : 0040–5930]

Pynnonen 2006 ***{published data only}***

Pynnonen MA. Study of nasal irrigation versus nasal spray for chronic nasal and sinus symptoms 2005/06. In: ClinicalTrials.gov [Internet] 2006 [cited date]. [: NCT00318006]

Rabago 2005a ***{published data only}***

Rabago D, Pasic T, Zgierska A, Mundt M, Barrett B, Maberry R. The efficacy of hypertonic saline nasal irrigation for chronic sinonasal symptoms. *Otolaryngology - Head and Neck Surgery* 2005; **133**(1):3–8. [MEDLINE: ALLOCATION - case series; : 0194–5998]

Rabago 2006 ***{published data only}***

Rabago D, Barrett B, Marchand L, Maberry R, Mundt M. Qualitative aspects of nasal irrigation use by patients with chronic sinus disease in a multimethod study. *Annals of Family Medicine* 2006;**4**(4):295–301. [MEDLINE: OUTCOME; : 1544–1709]

Rabone 1999 ***{published data only}***

Rabone SJ, Saraswati SB. Acceptance and effects of nasal lavage in volunteer woodworkers [see comment]. *Occupational Medicine* 1999;**49**(6):365–9. [MEDLINE: PARTICIPANTS; : 0962–7480]

Scheithauer 2006 ***{published data only}***

Scheithauer MO, Scheithauer I, Klocker N, Verse T. [Comparison of two application forms for isotonic sodium-chloride solution in postoperative sinus-surgery wound care]. *Laryngo-Rhino-Otologie* 2006;**85**(1):14–9. [MEDLINE: PARTICIPANTS; : 0935–8943]

Seaton 1998 ***{published data only}***

Seaton TL. Hypertonic saline for chronic sinusitis. *Journal of Family Practice* 1998;**47**(2):94. [MEDLINE: REPEAT DATA; : 0094–3509]

Seppey 1996 ***{published data only}***

Seppey M, Schweri T, Hausler R. Comparative randomised clinical study of tolerability and efficacy of Rhinomer Force 3 versus a reference product in post-operative care of the nasal fossae after endonasal surgery. *ORL; Journal of Oto-Rhino-Laryngology and its Related Specialties* 1996;**58**(2):87–92. [MEDLINE: PARTICIPANTS; : 0301–1569]

Shaikh 1995 ***{published data only}***

Shaikh WA. Ephedrine-saline nasal wash in allergic rhinitis. *Journal of Allergy and Clinical Immunology* 1995;**96**(5 Pt 1):597–600. [MEDLINE: iNTERVENTIONS; : 0091–6749]

Shaikh 1996 ***{published data only}***

Shaikh WA. Ephedrine-saline nasal wash in allergic rhinitis. *The Journal of the Association of Physicians of India* 1996;**44**(4):289. [MEDLINE: iNTERVENTIONS]

Shilenkova 1995 ***{published data only}***

Shilenkova VV, Shilenkov AA, Markov GI. [Use of sinus catheter "Iamik" in children]. *Vestnik Otorinolaringologii* 1995;**2**:19–21. [MEDLINE: ALLOCATION - case series; : 0042–4668]

Slawson 1998 ***{published data only}***

Slawson D. Is hypertonic saline wash effective in the treatment of pediatric chronic sinusitis?. *Evidence-Based Practice* 1998;**1**(8):6. [MEDLINE: REPEAT DATA]

Subiza 1999 ***{published data only}***

Subiza JL, Subiza J, Barjau MC, Rodriguez R, Gavilan MJ. Inhibition of the seasonal IgE increase to Dactylis glomerata by daily sodium chloride nasal-sinus irrigation during the grass pollen season. *Journal of Allergy and Clinical Immunology* 1999;**104**(3 Pt 1):711–2. [MEDLINE: OUTCOME; : 0091–6749]

Taccariello 1999 ***{published data only}***

Taccariello M, Parikh A, Darby Y, Scadding G. Nasal douching as a valuable adjunct in the management of chronic rhinosinusitis. *Rhinology* 1999;**37**(1):29–32. [MEDLINE: ALLOCATION - case control; : 0300–0729]

Tano 2004 ***{published data only}***

Tano L, Tano K. A daily nasal spray with saline prevents symptoms of rhinitis. *Acta Oto-Laryngologica* 2004;**124**(9):1059–62. [MEDLINE: PARTICIPANTS; : 0001–6489]

Tomooka 2000 ***{published data only}***

Tomooka LT, Murphy C, Davidson TM. Clinical study and literature review of nasal irrigation. *Laryngoscope* 2000;**110**(7): 1189–93. [MEDLINE: ALLOCATION - case control; : 0023–852X]

Traissac 1999 ***{published data only}***

Traissac L, Ohayon-Courtes C, Dufour P, Bordenave L. [Nasal washing with Physiomer... The first 10 years (1988-1998)]. *Revue de Laryngologie Otologie Rhinologie* 1999;**120**(2):133–5. [MEDLINE: ALLOCATION - case series; : 0035–1334]

Unal 2001 ***{published data only}***

Unal M, Gorur K, Ozcan C. Ringer-lactate solution versus isotonic saline solution on mucociliary function after nasal septal surgery.

Journal of Laryngology and Otology 2001;**115**(10):796–7. [MEDLINE: PARTICIPANTS; : 0022–2151]

Wendeler 1997 ***{published data only}***

Wendeler HM, Muller J, Dieler R, Helms J. Nasal irrigation using isotonic Emser salt solution in patients with chronic rhinosinusitis [Nasenspulung mit isotoner emser–salz–losung bei chronischer rhinosinusitis]. *Oto-Rhino-Laryngologia Nova* 1997;**7**(5-6):254–8.

Wiikmann 1996 ***{published data only}***

Wiikmann C, Chung D, Lorenzetti F, Lessa M, Voegels R. Use of saline solutions in post operatory care for FESS: Buffered hypertonic saline promotes a faster improvement than normal saline. 19th Congress of the European Rhinologic Society, Germany Ulm, 16-19 June. 2006. [MEDLINE: PARTICIPANTS]

Additional references

Berger 2003

Berger ME, Jones OW, Ricks RC, Garrett S. Decontaminating the nasal passages. *Health Physics* 2003;**84**(5 Supp):80–2.

Chalmers 1990

Chalmers I, Adams M, Dickersin K, Hetherington J, Tarnow-Mordi W, Meinert C, et al.A cohort study of summary reports of controlled trials. *Journal of the American Medical Association* 1990; **263**:1401–5.

Ellegard 2006

Ellegard EK. Pregnancy Rhinitis. *Immunology and Allergy Clinics of North America* 2006;**26**(1):119–35.

EPOS 2005

European Academy of Allergology and Clinical Immunology. European position paper on rhinosinusitis and nasal polyps. *Rhinology* 2005;**18**(1):1–87.

Gliklich 1995

Gliklich RE, Metson R. The health impact of chronic sinusitis in patients seeking otolaryngologic care. *Otolaryngology - Head and Neck Surgery* 1995;**113**:104–9.

IRMWS 1994

International Rhinitis Management Working Group. Report on the diagnosis and management of rhinitis: International Rhinitis Management Working Group. *Allergy* 1994;**49 (suppl)**:1–34.

Long 2001

Long CM, Smith TL, Loehrl TA, Komorowski RA, Toohill RJ. Sinonasal disease in patients with sarcoidosis. *American Journal of Rhinology* 2001;**15**(3):211–5.

Melen 1994

Melen I. Chronic Sinusitis: Clinical and pathophysiological aspects. *Acta Otolaryngolgica* 1994;**515**:45–8.

Meltzer 2006

Meltzer EO, Hamilos DL, Hadley JA, Lanza DC, Marple BF, Nicklas RA, et al.Rhinosinusitis: Developing guidance for clinical trials. *Otolaryngology - Head and Neck Surgery* 2006;**135**(5): S31–S80.

Muntz 2004

Muntz H. Pediatric chronic rhinosinusitis. *Current Opinion in Otolaryngology - Head and Neck Surgery* 2004;**12**(6):505–8.

Schappert 1992

Schappert SM. National ambulatory medical care survey: 1991 summary. National Center for Health Statistics 1992.

Smith 2005

Simth TL, Batra PS, Seiden AM, Hannley M. Evidence supporting endoscopic sinus surgery in the management of adult chronic rhinosinusitis: a systematic review. *American Journal of Rhinology* 2005;**19**(6):537–43.

Talbot 1997

Talbot AR, Herr TM, Parsons DS. Mucociliary clearance and buffered hypertonic saline solution. *Laryngoscope* 1997;**107**(4): 500–3. [: 0023–852X]

Tami 2005

Tami TA. Granulomatous diseases and chronic rhinosinusitis. *Otolaryngologic Clinics of North America* 2005;**38**(6):1267–78.

* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Bachmann 2000

Methods	RCT
Participants	Setting: Not declared Country: Germany Mean Age: 43 years % Female: 33% Duration: 7 days Number randomised: 40
Interventions	Hypertonic 'Ems' versus isotonic saline irrigation
Outcomes	Symptom, endoscopic and radiological scores SCT, Rhinomanometry Olfactometry
Notes	Quality Score: B

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Cordray 2005

Methods	RCT
Participants	Setting: Primary care Country: US Mean Age: 35 years % Female: 80% Duration: 7 days Number randomised: 15
Interventions	Hypertonic spray versus isotonic spray versus aqueous triamcinolone spray
Outcomes	RQLQ
Notes	Quality Score: C

Risk of bias

Item	Authors' judgement	Description

Cordray 2005 (*Continued*)

Allocation concealment?	Unclear	B - Unclear

Garavello 2003

Methods	RCT
Participants	Setting: Secondary care Country: Italy Mean Age: 6 to 12 years % Female: 60% Duration: 6 weeks Number randomised: 20
Interventions	Hypertonic saline via syringe versus no saline
Outcomes	Patient and parent recorded symptom scores
Notes	Quality Score: B

Risk of bias

Item	**Authors' judgement**	**Description**
Allocation concealment?	Yes	A - Adequate

Garavello 2005a

Methods	RCT
Participants	Setting: Secondary care Country: Italy Mean Age: 9 years % Female: 63% Duration: 7 weeks Number randomised: 40
Interventions	Hypertonic saline via atomiser versus no saline
Outcomes	Patient and parent recorded symptom scores
Notes	Quality Score: B

Risk of bias

Item	**Authors' judgement**	**Description**

Garavello 2005a (*Continued*)

Allocation concealment?	Yes	A - Adequate

Heatley 2001

Methods	RCT
Participants	Setting: Primary care Country: US Mean Age: 49 years % Female: 62% Duration: 14 days Number randomised: 150
Interventions	Bulb syringe versus Neti Pot versus reflexology
Outcomes	RSOM31; SF-36
Notes	Quality Score: B

Risk of bias

Item	**Authors' judgement**	**Description**
Allocation concealment?	Unclear	B - Unclear

Rabago 2002

Methods	RCT
Participants	Setting: Primary and secondary care Country: US Mean Age: 42 years % Female: 72% Duration: 6 months Number randomised: 76
Interventions	Hypertonic saline with SinuCleanse nasal cup versus no saline
Outcomes	SF-12; RSDI; SIA
Notes	Quality Score: A

Risk of bias

Item	**Authors' judgement**	**Description**

Rabago 2002 (*Continued*)

Allocation concealment?	Yes	A - Adequate

Rogkakou 2005

Methods	RCT
Participants	Setting: Not disclosed Country: Italy Mean Age: 32 years % Female: 57% Duration: 4 weeks Number randomised: 14
Interventions	Cetirizine versus Cetrizine with hypertonic saline spray
Outcomes	Rhinasthma questionaire Symptom scores
Notes	Quality Score: B

Risk of bias

Item	**Authors' judgement**	**Description**
Allocation concealment?	Yes	A - Adequate

Shoseyov 1998

Methods	RCT
Participants	Setting: Not disclosed Country: Israel Mean Age: 9 years % Female: 43% Duration: 4 weeks Number randomised: 34
Interventions	Hypertonic (3.5%) versus isotonic saline drops
Outcomes	Symptom scores Plain X-ray radiological scores
Notes	Quality Score: C

Risk of bias

Shoseyov 1998 (*Continued*)

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Characteristics of excluded studies *[ordered by study ID]*

Adam 1998	ALLOCATION Randomised, blinded PARTICIPANTS (excluded) 143 adults with viral upper respiratory tract infection INTERVENTIONS (excluded) Isotonic versus hypertonic saline spray versus no saline OUTCOMES Nasal symptom scores
Angrisano 2003	ALLOCATION Randomised, blinded (potentially part of (Garavello, Sordo et al. 2005)) PARTICIPANTS 20 children with chronic rhinitis INTERVENTIONS (excluded) Hypertonic saline spray versus no saline OUTCOMES Nasal symptom scores antihistamine use
Barbieri 2002	ALLOCATION Randomised, blinded PARTICIPANTS 80 adults with chronic rhinitis INTERVENTIONS (excluded) Iodine bromide versus Nozoil drops OUTCOMES Symptom scores, IgA,M,G, endoscopic score, rhinomanometry, SCT
Friedman 2006	ALLOCATION Randomised, blinded PARTICIPANTS 57 adults with chronic rhinosinusitis INTERVENTIONS (excluded) Hypertonic saline (Dead Sea) irrigation versus isotonic saline OUTCOMES Symptom scores, RQLQ
Garavello 2005b	See Garavello 2005a
Georgitis 1993	ALLOCATION Non-randomised, cross-over PARTICIPANTS 30 adults with chronic rhinitis INTERVENTIONS (excluded) Heated water vapour nebulised versus vapour versus nasal water irrigation OUTCOMES Symptom score Nasal airflow

(*Continued*)

Georgitis 1994	ALLOCATION Non-randomised, cross-over PARTICIPANTS 30 adults with chronic rhinitis INTERVENTIONS (excluded) Heated water vapour nebulised versus vapour versus nasal water irrigation OUTCOMES (excluded) Histamine, prostaglandin D2, and leukotriene C4
Grossan 1974a	ALLOCATION (excluded) Not a trial - clinical note and case reports. Informal case series. PARTICIPANTS Children with rhinosinusitis
Grossan 1974b	ALLOCATION (excluded) Not a trial - clinical note and case reports. Informal case series. PARTICIPANTS Children with rhinosinusitis
Grossan 1974c	ALLOCATION (excluded) Not a trial - clinical note and case reports. Informal case series. PARTICIPANTS Children with rhinosinusitis
Hartog 1996	ALLOCATION Randomised, blinded PARTICIPANTS 30 adults with chronic rhinosinusitis INTERVENTIONS (excluded) Antrostomy irrigation - not a study of saline irrigations
Hartog 1997a	ALLOCATION Randomised, blinded PARTICIPANTS 30 adults with chronic rhinosinusitis INTERVENTIONS (excluded) Antrostomy irrigation - not a study of saline irrigations
Hartog 1997b	ALLOCATION Randomised, blinded PARTICIPANTS 30 adults with chronic rhinosinusitis INTERVENTIONS (excluded) Antrostomy irrigation - not a study of saline irrigations
Heatley 2000	See Heatley 2001

(*Continued*)

Holmstrom 1997	ALLOCATION (excluded) Case series PARTICIPANTS 45 adults with chronic rhinitis (occupational) INTERVENTIONS Isotonic saline OUTCOMES Symptom scores Symptoms NPIF SCT
Johannssen 1996	ALLOCATION (excluded) Prospective cohort PARTICIPANTS (excluded) 36 adults post-FESS INTERVENTIONS (excluded) Hypertonic (Ems salt) container douche versus hand douche OUTCOMES (excluded) Microbiological swabs Endoscopic wound score
Johnsen 2001	ALLOCATION Randomised, cross-over PARTICIPANTS (excluded) 79 adults with nasal mucosa dryness INTERVENTIONS (excluded) Nozoil (pure sesame oil) versus isotonic saline OUTCOMES Symptom scores
Keerl 1997	ALLOCATION (excluded) Case series PARTICIPANTS 12 adults with chronic rhinitis INTERVENTIONS Isotonic saline OUTCOMES Symptom scores, SCT, acceptance questionnaire
Keerl 1998	ALLOCATION (excluded) Retrospective cohort PARTICIPANTS (excluded) 180 adults post-FESS INTERVENTIONS (excluded) Hypertonic (Ems) saline douche versus isotonic saline OUTCOMES Performance, effectiveness and acceptance questionnaire

(*Continued*)

Kozlov 1997	ALLOCATION (excluded) Case series PARTICIPANTS 6 adults with chronic rhinitis INTERVENTIONS (excluded) Sinus catheter RMNK-5
Krayenbuhl 1995	ALLOCATION (excluded) Case series PARTICIPANTS (excluded) Adults post-FESS INTERVENTIONS Rhinomer Force 3
LaForce 2004	ALLOCATION Randomised, blinded PARTICIPANTS 344 adults with chronic rhinitis INTERVENTIONS (excluded) Azelastine spray (AS) versus AS plus fexofenadine versus saline spray and placebo (saline not used as therapy) OUTCOMES Symptom scores
Levine 2006	ALLOCATION (excluded) Case series PARTICIPANTS 31 adults with chronic rhinosinusitis INTERVENTIONS (excluded) Dead Sea salt OUTCOMES CSS and SF36
Liu 2000	INTERVENTIONS (excluded) Rhinitis Spray (RS) - Not a saline nasal spray
Mack-Graesle 2004	PARTICIPANTS (excluded) Common cold
Michel 2005	ALLOCATION Randomised, blinded PARTICIPANTS (excluded) 66 children with viral/acute rhinosinusitis INTERVENTIONS (excluded) Hypertonic (Ems) saline versus oxymetazoline 0.05% OUTCOMES Symptom scores, rhinoscopy, otoscopy, audiometry

(*Continued*)

Mora 2002	ALLOCATION Randomised, blinded PARTICIPANTS 50 adults with chronic rhinitis INTERVENTIONS (excluded) Sulphurea water versus water
Muller-Sacks 1998	ALLOCATION (excluded) Case series PARTICIPANTS Adults with chronic rhinitis INTERVENTIONS Sea salt aqueous spray
Neher 2005	ALLOCATION (excluded) Case series PARTICIPANTS 12 adults with chronic rhinosinusitis INTERVENTIONS (excluded) N-Chlorotaurine 1% via YAMIK
Nuutinen 1986	ALLOCATION (excluded) Case series PARTICIPANTS 93 adults with chronic rhinitis/rhinosinusitis INTERVENTIONS Isotonic saline
Pagani 2001	ALLOCATION (excluded) Case series PARTICIPANTS Children with chronic rhinitis INTERVENTIONS (excluded) Hypertonic (2%) saline
Pal'chun 2004	ALLOCATION Randomised, blinded PARTICIPANTS (excluded) Adults post-FESS INTERVENTIONS (excluded) Physiomer spray
Passali 2003	ALLOCATION Randomised, blinded PARTICIPANTS 50 adults with chronic rhinitis INTERVENTIONS (excluded) Santissima water versus isotonic spray OUTCOMES

(*Continued*)

	Symptom score Examination score SCT Rhinometry Audiometry
Passali 2005	ALLOCATION Randomised, blinded PARTICIPANTS (excluded) 200 adults with viral acute rhinosinusitis INTERVENTIONS (excluded) Isotonic spray versus atomiser OUTCOMES (excluded) Rhinometry and SCT
Pigret 1996	ALLOCATION Randomised, blinded PARTICIPANTS (excluded) 20 adults post-FESS INTERVENTIONS (excluded) Antiseptic plus mucolytic versus sea water spray OUTCOMES Symptom scores Crust weight
Pinto 2006	ALLOCATION Randomised, blinded PARTICIPANTS (excluded) 50 adults post-FESS INTERVENTIONS Hypertonic versus isotonic versus no saline OUTCOMES Symptom scores Pain medication
Polasek 1987	ALLOCATION Randomised cross-over PARTICIPANTS Adults with chronic rhinitis INTERVENTIONS (excluded) Iodine bromide water (Prorhinel)versus no treatment
Pynnonen 2006	ALLOCATION Randomised, blinded PARTICIPANTS 150 adults with chronic rhinitis and rhinosinusitis INTERVENTIONS (excluded) Nasal spray versus irrigation OUTCOMES

(*Continued*)

	SNOT-20 and medication use
Rabago 2005a	ALLOCATION (excluded) Case series PARTICIPANTS Follow-up observational study from Rabago 2002 INTERVENTIONS Hypertonic (2%) saline OUTCOMES Symptom scores, usage patterns
Rabago 2006	ALLOCATION (excluded) Case series PARTICIPANTS Adults with chronic rhinosinusitis INTERVENTIONS Hypertonic (2%) saline OUTCOMES (excluded) Qualitative research
Rabone 1999	ALLOCATION Randomised cross-over PARTICIPANTS (excluded) 46 adults with chronic rhinitis (occupational) INTERVENTIONS Isotonic saline versus no saline OUTCOMES Symptom scores, Quality of Life
Scheithauer 2006	ALLOCATION Randomised, blinded PARTICIPANTS (excluded) 50 adults post-FESS INTERVENTIONS (excluded) Spray versus hand irrigation with saline OUTCOMES (excluded) Video assessment of crust, usage questionnaire
Seaton 1998	See Shoseyov 1998
Seppey 1996	ALLOCATION Randomised, blinded PARTICIPANTS (excluded) 28 adults post FESS INTERVENTIONS (excluded) Sea water spray versus iodine bromide spray OUTCOMES Symptom scores Endoscopic scores

(*Continued*)

Shaikh 1995	ALLOCATION Randomised, blinded PARTICIPANTS 150 adults with chronic rhinitis INTERVENTIONS (excluded) 1% ephedrine versus isotonic saline OUTCOMES Symptom scores, nasal flow
Shaikh 1996	See Shaikh 1995
Shilenkova 1995	ALLOCATION (excluded) Case series PARTICIPANTS 44 children with chronic rhinosinusitis INTERVENTIONS (excluded) Use of IaMIK irrigation
Slawson 1998	See Shoseyov 1998
Subiza 1999	ALLOCATION Randomised, blinded PARTICIPANTS 25 adults with chronic rhinitis INTERVENTIONS Isotonic saline versus no saline OUTCOMES (excluded) Specific systemic IgE
Taccariello 1999	ALLOCATION Randomised, blinded PARTICIPANTS 41 adults with chronic rhinosinusitis INTERVENTIONS (excluded) Sea water spray versus isotonic douche (case controlled with no saline controls) OUTCOMES Symptom scores, endoscopic scores, Quality of Life scores
Tano 2004	ALLOCATION Randomised cross-over (excluded) PARTICIPANTS 108 normal adults INTERVENTIONS Isotonic saline versus no saline OUTCOMES Symptom scores, antibiotic use

(*Continued*)

Tomooka 2000	ALLOCATION (excluded) Case series (non rhinologic controls) PARTICIPANTS 211 adults with chronic rhinitis and rhinosinusitis INTERVENTIONS Hypertonic saline OUTCOMES Symptom scores, Quality of Well Being score
Traissac 1999	ALLOCATION (excluded) Case series PARTICIPANTS (excluded) 344 patients with nasal complaints and post-FESS INTERVENTIONS Sea water spray
Unal 2001	ALLOCATION Randomised, blinded PARTICIPANTS (excluded) 32 adults post septoplasty INTERVENTIONS (excluded) Ringers lactate versus isotonic saline OUTCOMES (excluded) SCT
Wendeler 1997	ALLOCATION Randomised, blinded PARTICIPANTS 38 adults with chronic rhinosinusitis INTERVENTIONS (excluded) Hypertonic (Ems) versus water (discontinued due to acute otitis media rates in water group)
Wiikmann 1996	ALLOCATION Unobtainable PARTICIPANTS (excluded) Adults post-FESS INTERVENTIONS (excluded) Hypertonic versus isotonic saline

DATA AND ANALYSES

Comparison 1. A: Comparison of saline versus no treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Symptom scores	3	129	Std. Mean Difference (IV, Fixed, 95% CI)	1.42 [1.01, 1.84]
2 Quality of Life scores (disease specific)	1	69	Std. Mean Difference (IV, Fixed, 95% CI)	1.36 [0.80, 1.91]
3 Quality of Life scores (general)	1	69	Std. Mean Difference (IV, Fixed, 95% CI)	0.47 [-0.04, 0.97]

Comparison 2. B: Comparison of saline versus 'placebo'

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Quality of Life scores (disease specific) Bulb	1	89	Std. Mean Difference (IV, Fixed, 95% CI)	-0.53 [-0.96, -0.11]
2 Quality of Life scores (disease specific) Pot	1	85	Mean Difference (IV, Fixed, 95% CI)	-24.0 [-43.93, -4.07]

Comparison 3. C: Saline versus standard therapy (intranasal steroid)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Quality of Life scores (disease specific) Isotonic	1	10	Std. Mean Difference (IV, Fixed, 95% CI)	-3.29 [-5.51, -1.06]
2 Quality of Life scores (disease specific) Hypertonic	1	10	Std. Mean Difference (IV, Fixed, 95% CI)	-2.88 [-4.92, -0.84]

Comparison 4. E: Hypertonic versus isotonic saline

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Symptom scores	3	80	Std. Mean Difference (IV, Fixed, 95% CI)	0.34 [-0.11, 0.80]
2 Radiologic scores	2	70	Std. Mean Difference (IV, Fixed, 95% CI)	0.39 [-0.20, 0.97]

Analysis 1.1. Comparison 1 A: Comparison of saline versus no treatment, Outcome 1 Symptom scores.

Review: Nasal saline irrigations for the symptoms of chronic rhinosinusitis

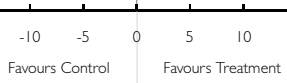
Comparison: 1 A: Comparison of saline versus no treatment

Outcome: 1 Symptom scores

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Fixed,95% CI	Weight	Std. Mean Difference IV,Fixed,95% CI
Garavello 2003	10	-0.5 (5.36)	10	-3 (5.36)		21.7 %	0.45 [-0.44, 1.34]
Garavello 2005a	20	1.5 (2.62)	20	-7 (3.11)		20.7 %	2.90 [1.99, 3.81]
Rabago 2002	46	1.6 (1.36)	23	0.01 (0.96)		57.7 %	1.26 [0.72, 1.81]
Total (95% CI)	**76**		**53**			**100.0 %**	**1.42 [1.01, 1.84]**

Heterogeneity: Chi^2 = 14.99, df = 2 (P = 0.00056); I^2 =87%

Test for overall effect: Z = 6.74 (P < 0.00001)



Analysis 1.2. Comparison 1 A: Comparison of saline versus no treatment, Outcome 2 Quality of Life scores (disease specific).

Review: Nasal saline irrigations for the symptoms of chronic rhinosinusitis

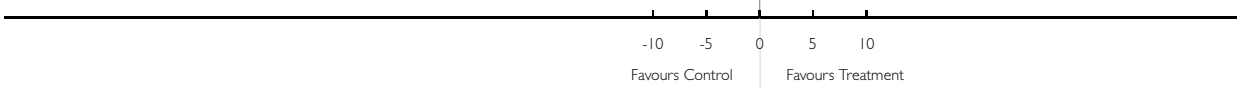
Comparison: 1 A: Comparison of saline versus no treatment

Outcome: 2 Quality of Life scores (disease specific)

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Fixed,95% CI	Weight	Std. Mean Difference IV,Fixed,95% CI
Rabago 2002	46	14.4 (11.53)	23	0.9 (4.8)		100.0 %	1.36 [0.80, 1.91]
Total (95% CI)	**46**		**23**			**100.0 %**	**1.36 [0.80, 1.91]**

Heterogeneity: not applicable

Test for overall effect: Z = 4.81 (P < 0.00001)



Analysis 1.3. Comparison 1 A: Comparison of saline versus no treatment, Outcome 3 Quality of Life scores (general).

Review: Nasal saline irrigations for the symptoms of chronic rhinosinusitis

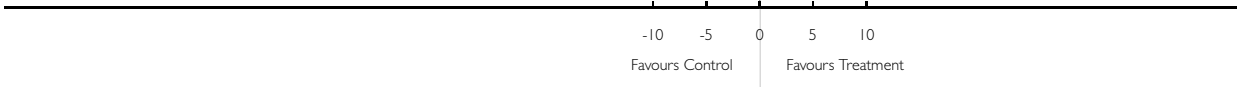
Comparison: 1 A: Comparison of saline versus no treatment

Outcome: 3 Quality of Life scores (general)

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Fixed,95% CI	Weight	Std. Mean Difference IV,Fixed,95% CI
Rabago 2002	46	12.7 (24.42)	23	2.2 (16.79)		100.0 %	0.47 [-0.04, 0.97]
Total (95% CI)	**46**		**23**			**100.0 %**	**0.47 [-0.04, 0.97]**

Heterogeneity: not applicable

Test for overall effect: Z = 1.81 (P = 0.071)



Analysis 2.1. Comparison 2 B: Comparison of saline versus 'placebo', Outcome 1 Quality of Life scores (disease specific) Bulb.

Review: Nasal saline irrigations for the symptoms of chronic rhinosinusitis

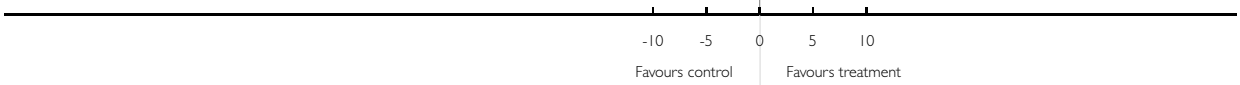
Comparison: 2 B: Comparison of saline versus 'placebo'

Outcome: 1 Quality of Life scores (disease specific) Bulb

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Fixed,95% CI	Weight	Std. Mean Difference IV,Fixed,95% CI
Heatley 2001	43	38 (36.53)	46	61 (47.78)		100.0 %	-0.53 [-0.96, -0.11]
Total (95% CI)	**43**		**46**			**100.0 %**	**-0.53 [-0.96, -0.11]**

Heterogeneity: not applicable

Test for overall effect: Z = 2.47 (P = 0.013)



Analysis 2.2. Comparison 2 B: Comparison of saline versus 'placebo', Outcome 2 Quality of Life scores (disease specific) Pot.

Review: Nasal saline irrigations for the symptoms of chronic rhinosinusitis

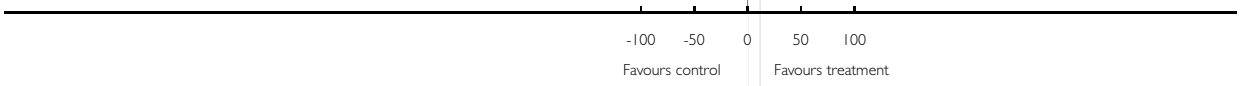
Comparison: 2 B: Comparison of saline versus 'placebo'

Outcome: 2 Quality of Life scores (disease specific) Pot

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Heatley 2001	39	37 (45.8)	46	61 (47.78)		100.0 %	-24.00 [-43.93, -4.07]
Total (95% CI)	**39**		**46**			**100.0 %**	**-24.00 [-43.93, -4.07]**

Heterogeneity: not applicable

Test for overall effect: Z = 2.36 (P = 0.018)



Analysis 3.1. Comparison 3 C: Saline versus standard therapy (intranasal steroid), Outcome 1 Quality of Life scores (disease specific) Isotonic.

Review: Nasal saline irrigations for the symptoms of chronic rhinosinusitis

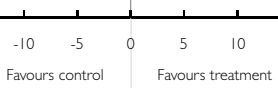
Comparison: 3 C: Saline versus standard therapy (intranasal steroid)

Outcome: 1 Quality of Life scores (disease specific) Isotonic

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Fixed,95% CI	Weight	Std. Mean Difference IV,Fixed,95% CI
Cordray 2005	5	0.16 (0.73)	5	2.21 (0.32)		100.0 %	-3.29 [-5.51, -1.06]
Total (95% CI)	**5**		**5**			**100.0 %**	**-3.29 [-5.51, -1.06]**

Heterogeneity: not applicable

Test for overall effect: Z = 2.89 (P = 0.0038)



Analysis 3.2. Comparison 3 C: Saline versus standard therapy (intranasal steroid), Outcome 2 Quality of Life scores (disease specific) Hypertonic.

Review: Nasal saline irrigations for the symptoms of chronic rhinosinusitis

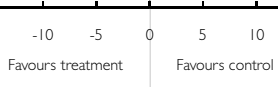
Comparison: 3 C: Saline versus standard therapy (intranasal steroid)

Outcome: 2 Quality of Life scores (disease specific) Hypertonic

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Fixed,95% CI	Weight	Std. Mean Difference IV,Fixed,95% CI
Cordray 2005	5	1.36 (0.2)	5	2.21 (0.32)		100.0 %	-2.88 [-4.92, -0.84]
Total (95% CI)	**5**		**5**			**100.0 %**	**-2.88 [-4.92, -0.84]**

Heterogeneity: not applicable

Test for overall effect: Z = 2.76 (P = 0.0057)



Analysis 4.1. Comparison 4 E: Hypertonic versus isotonic saline, Outcome 1 Symptom scores.

Review: Nasal saline irrigations for the symptoms of chronic rhinosinusitis

Comparison: 4 E: Hypertonic versus isotonic saline

Outcome: 1 Symptom scores

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Fixed,95% CI	Weight	Std. Mean Difference IV,Fixed,95% CI
Bachmann 2000	20	0.7 (0.5)	20	0.6 (0.46)		53.1 %	0.20 [-0.42, 0.83]
Cordray 2005	5	1.36 (0.2)	5	0.16 (0.73)		7.2 %	2.03 [0.34, 3.71]
Shoseyov 1998	15	1.26 (0.52)	15	1.13 (0.59)		39.7 %	0.23 [-0.49, 0.95]
Total (95% CI)	**40**		**40**			**100.0 %**	**0.34 [-0.11, 0.80]**

Heterogeneity: Chi^2 = 4.12, df = 2 (P = 0.13); I^2 =51%

Test for overall effect: Z = 1.49 (P = 0.14)

Analysis 4.2. Comparison 4 E: Hypertonic versus isotonic saline, Outcome 2 Radiologic scores.

Review: Nasal saline irrigations for the symptoms of chronic rhinosinusitis

Comparison: 4 E: Hypertonic versus isotonic saline

Outcome: 2 Radiologic scores

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Fixed,95% CI	Weight	Std. Mean Difference IV,Fixed,95% CI
Bachmann 2000	20	0.72 (0.73)	20	1.11 (1.34)		87.0 %	-0.35 [-0.98, 0.27]
Shoseyov 1998	15	5.4 (0.96)	15	0.27 (0.91)		13.0 %	5.34 [3.72, 6.95]
Total (95% CI)	**35**		**35**			**100.0 %**	**0.39 [-0.20, 0.97]**

Heterogeneity: Chi^2 = 41.44, df = 1 (P<0.00001); I^2 =98%

Test for overall effect: Z = 1.30 (P = 0.19)

APPENDICES

Appendix 1. Search strategies for electronic databases

CENTRAL
#1 NOSE single term (MeSH)
#2 NASAL CAVITY single term (MeSH)
#3 NASAL MUCOSA single term (MeSH)
#4 PARANASAL SINUSES single term (MeSH)
#5 PARANASAL SINUS DISEASES single term (MeSH)
#6 exp SINUSITIS single term (MeSH)
#7 exp RHINITIS single term (MeSH)
#8 NASAL POLYPS single term (MeSH)
#9 NASAL OBSTRUCTION single term (MeSH)
#10 nose OR nasal* OR sinus* OR rhinosinus* OR paranasal* OR rhinitis* OR nasosinus* OR pansinus*
#11 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10
#12 HYPERTONIC SOLUTIONS single term (MeSH)
#13 SOLUTIONS single term (MeSH)
#14 SALINE SOLUTION HYPERTONIC single term (MeSH)
#15 SODIUM CHLORIDE single term (MeSH)
#16 saline OR sodium chloride OR salt water OR hypertonic* OR isotonic*
#17 #12 OR #13 OR #14 OR #15 OR #16
#18 douch* OR spray* OR wash* OR rinse* OR rinsing OR irrigat*
#19 #17 AND #18
#20 IRRIGATION single term (MeSH)
#21 irrigation
#22 #19 OR #20 OR #21
#23 #11 AND #22
MEDLINE (OVID)
1. NOSE/
2. NASAL CAVITY/
3. NASAL MUCOSA/
4. PARANASAL SINUSES/
5. PARANASAL SINUS DISEASES/
6. exp SINUSITIS/
7. exp RHINITIS/
8. NASAL POLYPS/
9. NASAL OBSTRUCTION/
10. (nose OR nasal$ OR sinus$ OR rhinosinus$ OR paranasal$ OR rhiniti$ OR nasosinus$ OR pansinus$).ti,ab.
11. OR/1-10
12. HYPERTONIC SOLUTIONS/
13. SOLUTIONS/
14. SALINE SOLUTION HYPERTONIC/
15. SODIUM CHLORIDE/
16. (saline OR sodium chloride OR salt water OR hypertonic$ OR isotonic$).ti,ab.
17. OR/12-16
18. (douch$ OR spray$ OR wash$ OR rinse$ OR rinsing OR irrigat$).ti,ab.
19. 17 and 18
20. irrigation.mp.
21. 19 OR 20
22. 11 and 21
EMBASE (OVID)
1. NOSE/

2. NOSE CAVITY/
3. exp NOSE MUCOSA/
4. exp PARANASAL SINUS/
5. PARANASAL SINUS DISEASE/
6. exp SINUSITIS/
7. exp RHINITIS/
8. NOSE POLYP/
9. NOSE OBSTRUCTION/
10. (nose OR nasal$ OR sinus$ OR rhinosinus$ OR paranasal$ OR rhiniti$ OR nasosinus$ OR pansinus$).ti,ab.
11. OR/1-10
12. HYPERTONIC SOLUTION/
13. SODIUM CHLORIDE/
14. (saline OR sodium chloride OR salt water OR hypertonic$ OR isotonic$).ti,ab.
15. OR/12-14
16. (douch$ OR spray$ OR wash$ OR rinse$ OR rinsing OR irrigat$).ti,ab.
17. 15 AND 16
18. irrigation.mp.
19. 17 OR 18
20. 11 AND 19

CINAHL (1982 onwards)

1.NOSE.DE.
2.NASAL-CAVITY.DE.
3.NASAL-MUCOSA.DE.
4. PARANASAL-SINUSES#.DE.
5.NOSE-DISEASES.DE.
6.PARANASAL-SINUS-DISEASES#.DE.
7. RHINITIS.DE.
8.NASAL-POLYPS.DE.
9.NASAL-OBSTRUCTION.DE.
10.(nose OR nasal$ OR sinus$ OR ethmoid$ OR rhinosinus$ OR paranasal$ OR rhiniti$ OR nasosinus$ OR pansinus$).TI,AB.
11.OR/1-10
12.HYPERTONIC-SOLUTIONS#.DE.
13.ISOTONIC-SOLUTIONS#.DE.
14.HYPOTONIC-SOLUTIONS.DE.
15.SOLUTIONS.DE.
16.SODIUM CHLORIDE.DE.
17.(saline OR sodium chloride OR salt water OR saltwater OR hypertonic$ OR isotonic$ OR hypotonic$).TI,AB.
18.OR/12-17
19. (douch$ OR spray$ OR lavag$ OR wash$ OR rinse$ OR rinsing OR irrigat$).TI,AB.
20. 18 and 19
21. irrigation$1
22. 20 OR 21
23. 11 and 22

INDMED

nose OR nasal$ OR sinus$ OR ethmoid$ OR rhinosinus$ OR paranasal$ OR rhinitis$ OR nasosinus$ OR pansinus$
AND
saline OR sodium chloride OR salt water OR saltwater OR hypertonic$ OR isotonic$
OR hypotonic$
AND
douch$ OR spray$ OR lavag$ OR wash$ OR rinse$ OR rinsing OR irrigat$

LILACS

nose OR nasal$ OR sinus$ OR ethmoid$ OR rhinosinus$ OR paranasal$ OR rhinitis$ OR nasosinus$ OR pansinus$
AND

saline OR sodium chloride OR salt water OR saltwater OR hypertonic$ OR isotonic$ OR hypotonic$ OR douch$ OR spray$ OR lavag$ OR wash$ OR rinse$ OR rinsing OR irrigat$

mRCT

(nose OR nasal% OR sinus% OR ethmoid% OR rhinosinus% OR paranasal% OR rhinitis% OR nasosinus% OR pansinus%) AND (saline OR sodium chloride OR salt water OR saltwater OR hypertonic% OR isotonic% OR hypotonic%)

(nose OR nasal% OR sinus% OR ethmoid% OR rhinosinus% OR paranasal% OR rhinitis% OR nasosinus% OR pansinus%) AND (douch% OR spray% OR lavag% OR wash% OR rinse% OR rinsing OR irrigat%)

ISI Proceedings

(TS=nose OR TS=nasal* OR TS=sinus* OR TS=ethmoid* OR TS=rhinosinus* OR TS=paranasal* OR TS=rhinitis* OR TS=nasosinus* OR TS=pansinus* OR TI=nose OR TI=nasal* OR TI=sinus* OR TI=ethmoid* OR TI=rhinosinus* OR TI=paranasal* OR TI=rhinitis* OR TI=nasosinus* OR TI=pansinus*
AND
TS=saline OR TS=sodium chloride OR TS=salt water OR TS=saltwater OR TS=hypertonic* OR TS=ypotonic* OR TS=isotonic* OR TI=saline OR TI=sodium chloride OR TI=salt water OR TI=saltwater OR TI=hypertonic* OR TI=hypotonic* OR TI=isotonic*
AND
TS=douch* OR TS=spray* OR TS=lavag* OR TS=wash* OR TS=rinse* OR TS=rinsing OR TS=irrigat* OR TI=douch* OR TI=spray* OR TI=lavag* OR TI=wash* OR TI=rinse* OR TI=rinsing OR TI=irrigat*)
OR
TS=NASAL IRRIGATION OR TI=NASAL IRRIGATION

WHAT'S NEW

Last assessed as up-to-date: 16 November 2006.

26 October 2008	Amended	Converted to new review format.

HISTORY

Protocol first published: Issue 1, 2007

Review first published: Issue 3, 2007

23 May 2007	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

Richard Harvey

Searching for trials, quality assessment of trials, design of data extraction form, data extraction, data analysis, input at all other stages of review.

S. Alam Hannan

Searching for trials, quality assessment of trials, design of data extraction form, data extraction, data analysis, input at all other stages of review.

Lydia Badia

Proposal development, content expertise and supervision of review process.

Glenis K Scadding

Proposal development, content expertise and supervision of review process.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- Oxford Nuffield Medical Fellowship, UK.

INDEX TERMS

Medical Subject Headings (MeSH)

Chronic Disease; Conjunctivitis [therapy]; Irrigation; Isotonic Solutions [administration & dosage]; Randomized Controlled Trials as Topic; Rhinitis [*therapy]; Saline Solution, Hypertonic [administration & dosage]; Sinusitis [*therapy]; Sodium Chloride [*administration & dosage]

MeSH check words

Adult; Child; Humans