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The effects of nasal irrigation with various solutions after endoscopic sinus surgery: systematic review and meta-analysis

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Review Article

Dr G Zhang takes responsibility for the integrity of the content of the paper

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Abstract

Background. Nasal irrigation is commonly performed in patients with chronic rhinosinusitis after functional endoscopic sinus surgery. This study systematically assessed the clinical efficacy of nasal irrigation from the medical literature.

Methods. The PubMed, Embase and Cochrane Central Register of Controlled Trials databases were searched using a comprehensive strategy, limited to English-language articles, published from October 1971 to March 2017, and comprising human subjects.

Results. A total of 824 trials were identified, 5 of which, involving 331 participants, were included in this systematic review. After selection, only three trials were eligible for inclusion in a meta-analysis. Nasal irrigation using normal saline and various solutions was found to be effective in reducing symptom scores and endoscopic scores for chronic rhinosinusitis patients after functional endoscopic sinus surgery. Comparison of outcome measures, such as eosinophil count reduction, revealed that various solutions are more effective than normal saline alone; however, no statistical significance was found in terms of reduced symptom or endoscopic scores.

Conclusion. Based on the current limited evidence, nasal irrigation is an effective therapy for chronic rhinosinusitis patients after functional endoscopic sinus surgery. However, when comparing various solutions with normal saline, no significant difference was found in symptom scores or endoscopic scores.

Introduction

Chronic rhinosinusitis is a common disease, characterised by inflammation of the nasal cavity and paranasal sinuses, with or without nasal polyps.[1] It is a heterogeneous, often refractory disease, with variable responses to medical therapies. It causes significant morbidity and negatively impacts on quality of life.[2] Functional endoscopic sinus surgery (FESS) is indicated for the treatment of chronic rhinosinusitis that is refractory to medical treatment.[1,3,4] As inflammatory processes continue to play a significant role in chronic rhinosinusitis patients after FESS, the continued use of medical therapy, especially topical treatment, is indispensable.[5] Nasal irrigation is a classic and powerful adjunctive method for the management of chronic rhinosinusitis after FESS.[6]

The mechanism of nasal irrigation remains unclear. Saline nasal irrigation may improve nasal mucosa function through several physiological effects, including: direct cleaning of mucus (mucus is a potential condition for bacteria to multiply; saline dilutes mucus and helps to clear it out); removal of antigens, bacterial biofilm or inflammatory mediators (thereby alleviating the inflammation); and improving mucociliary function.[7] A Cochrane review (2007) of nasal saline irrigations for chronic rhinosinusitis concluded that nasal saline irrigation was better than no irrigation for improving symptoms and quality of life.[8,9] Recent studies have shown that nasal irrigation with various topical medications can provide a high concentration of the drug and achieve better outcomes.[10,11]

Saline nasal irrigation in chronic rhinosinusitis after FESS has been proved to clean the nasal cavity and promote the restoration of mucosal function, and is widely used.[3,12] A number of studies have verified the efficacy of nasal irrigation with various solutions.[13–16] However, the value of various solutions in nasal irrigation remains controversial.[17] This study aimed to evaluate the efficacy of nasal irrigation with various solutions in order to treat chronic rhinosinusitis patients after FESS, and compare this with normal saline alone, in a systematic review and meta-analysis.

Materials and methods

Search methods

We searched the PubMed, Embase and Cochrane Central Register of Controlled Trials databases for original articles published in English from October 1971 to March 2017.

The search strategies used the following main keywords: nasal irrigations, saline irrigation, sinus irrigation, nasal rinsing, saline nasal washes, irrigations and chronic rhinosinusitis post endoscopic sinus surgery. Similar search words were used in each database.

Criteria for included studies

Types of participants

The study included research on adult patients with a clinical diagnosis of chronic rhinosinusitis, according to the European Position Paper on Rhinosinusitis and Nasal Polyps 2012 ('EPOS2012') guidelines,[1] who had recently undergone FESS.

Types of interventions

Those articles that compared various solutions plus normal saline with normal saline alone for nasal irrigations were included.

Types of outcome measures

These included: findings of biopsies (of the anterior ethmoid sinus) conducted to assess eosinophil counts; paranasal sinus computed tomography (CT) scores; 20- or 22-item Sino-Nasal Outcome Test (SNOT-20 or SNOT-22) scores; visual analogue scale (VAS) scores; mucociliary clearance assessment; endoscopic scores; and adverse events.

Study selection, data extraction and quality assessment

Studies were identified with the search strategy by two independent reviewers. Where there was uncertainty regarding eligibility, any difficulties were resolved by discussion and consensus. The Cochrane Risk of Bias Tool was used to assess the included studies.[18] The quality assessment was performed by the independent reviewers, and a third reviewer was consulted for any uncertainties. Analytical data missing from the primary reports were requested from the relevant authors.

Statistical analysis

Data suitable for meta-analysis were entered into the software package Review Manager (RevMan), version 5.3.[19] Differences were expressed as weighted mean difference with 95 per cent confidence intervals (CIs) for change from baseline symptom scores. Statistical heterogeneity across trials was assessed with the chi-square statistic ($p < 0.1$) and the I^2 statistic. As a guide, I^2 values of 25, 50 and 75 per cent correspond to low, medium and high levels of heterogeneity, respectively.[20,21] When a significant heterogeneity was found, a random-effects model was used to examine the pooled results and 95 per cent CI. Otherwise, a fixed-effects model was applied. Publication bias was assessed by visually inspecting funnel plots.[22] A p value of less than 0.05 was considered statistically significant. We intended to carry out sensitivity analyses to assess the robustness of the conclusions, if sufficient studies were available.

Results

Results of search

A total of 824 studies were identified; 741 of these were removed after screening the title and abstract, and 43 articles were removed after full text assessment. Five studies were included for systematic review. A flowchart of study search and selection is shown in Figure 1.

Characteristics of included studies

The 5 included studies, published between 2008 and 2015, comprised 331 patients aged 18–73 years.[23–27] The five trials investigated nasal irrigation using various solutions, such as sulphurous-arsenical-ferruginous thermal water, Ringer's lactate solution, electrolysed acid water, amphotericin B saline, and hyaluronan plus saline. The characteristics of the included studies are showed in Table 1.

The duration of treatment time ranged from six weeks to six months. Several outcome measures were used, including paranasal sinus CT scores, SNOT-20 or SNOT-22 scores, VAS scores, mucociliary clearance assessment, and endoscopic scores (Lund–Kennedy scores). The primary outcome measure was symptom scores (SNOT-20 or SNOT-22, and VAS scores). The secondary outcome measure was nasal endoscopic scores. The outcomes assessed in the study by Staffieri *et al.* were based on findings of biopsies (of the anterior ethmoid sinus), which included eosinophil counts, and there were no other outcome measures.[27] The study by Macchi *et al.* lacked sufficient data for analysis.[25] Finally, three studies had sufficient discrete data for inclusion in a formal meta-analysis.[23,24,26]

Risk of bias assessment

Risk of bias in the included studies was assessed using the Cochrane Collaboration Tool for Assessing Risk of Bias. Figure 2 provides the methodological details for each trial. The included studies were randomised trials, but only one trial was a randomised controlled trial with an adequate description of intervention methods.[26]

Eosinophil counts

Nasal irrigation with thermal water solution locally reduces the eosinophil count. This may limit the eosinophil-mediated production of cytokines and inflammatory molecules, which damage nasal mucosa and lead to oedema and sinonasal inflammation.[27] Staffieri *et al.* showed that eosinophil counts were significantly decreased after thermal water solution irrigation ($p = 0.04$).[27] On the contrary, Macchi *et al.* found that the eosinophil counts were not significantly different after hyaluronan plus saline solution irrigation when compared with normal saline ($p = 0.249$).[25] Neither of these studies could provide sufficient data for inclusion in a meta-analysis.

Nasal symptoms scores

Data on total and individual nasal symptom scores were available for meta-analysis in three trials.[23,24,26] Low *et al.* compared Ringer's lactate solution with normal saline, and found that Ringer's lactate solution could dramatically improve nasal symptoms, such as nasal blockage, nasal congestion, headache, facial pain and nasal discharge.[26] In chronic rhinosinusitis patients who received nasal irrigation with electrolysed acid water or amphotericin B saline after FESS,[23,24] the SNOT-20 or SNOT-22 scores were significantly lower than the scores before FESS. However, there were no significant differences among the electrolysed acid water and amphotericin B saline groups compared with the normal saline irrigation (control) group.[23,24] Pooled results failed to show a

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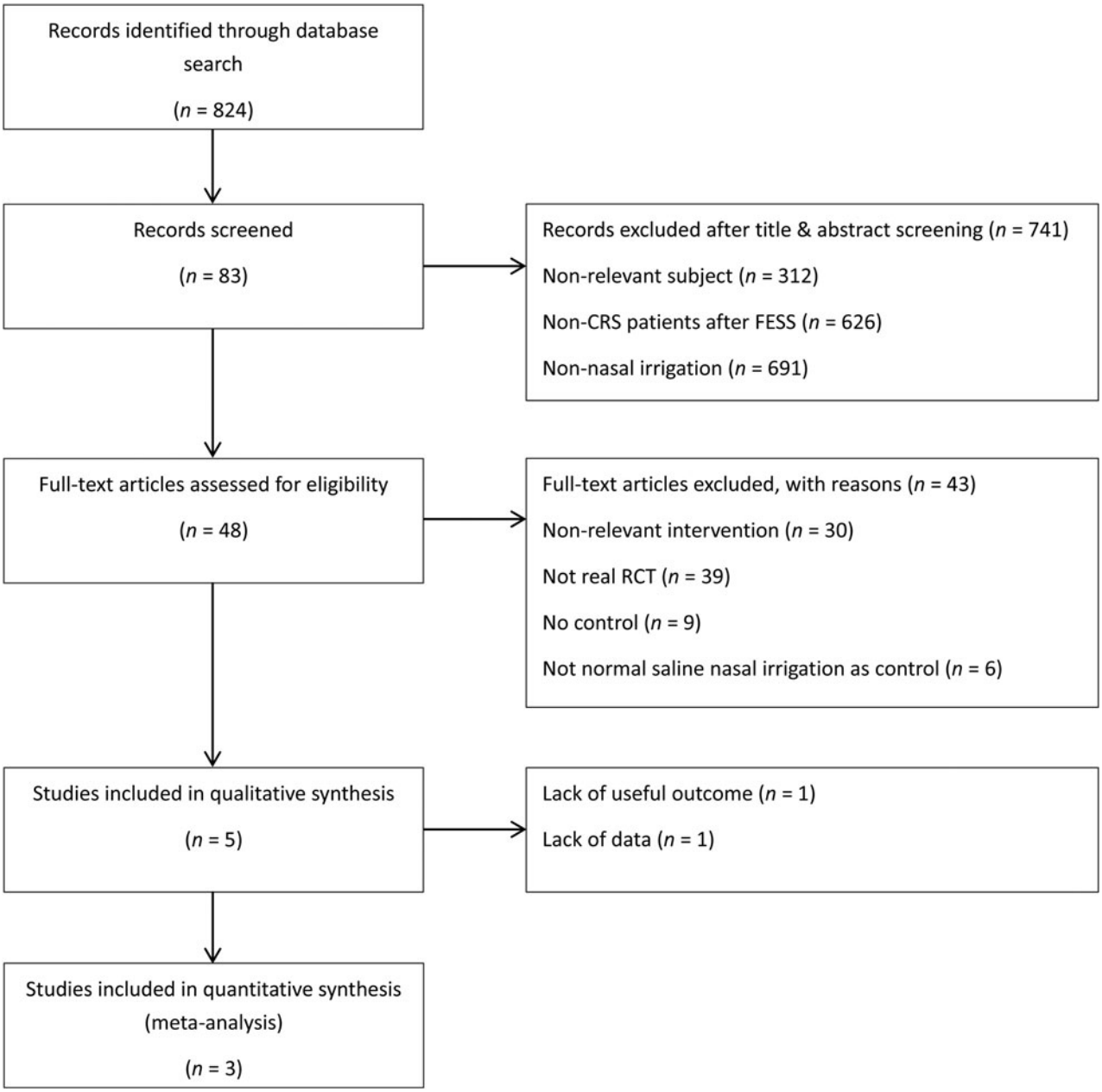

Fig. 1. Flowchart of study search and selection. CRS = chronic rhinosinusitis; FESS = functional endoscopic sinus surgery; RCT = randomised controlled trial

significant difference in nasal symptoms when various solutions were compared with normal saline alone (weighted mean difference = 2.84, 95 per cent CI −1.87 to 7.54, p = 0.24; p for heterogeneity = 0.25, I^2 = 28 per cent; Figure 3). Sensitivity analysis could not be carried out because of the small number of included studies.

Endoscopic scores

Data on endoscopic scores were available for meta-analysis in two trials.[23,24] In chronic rhinosinusitis patients who received nasal irrigation with electrolysed acid water or amphotericin B saline, the endoscopic scores dramatically decreased after FESS. However, when electrolysed acid water or amphotericin B saline were compared with normal saline alone, there were no significant differences in endoscopic scores for chronic rhinosinusitis patients after FESS (weighted mean difference = −0.20, 95 per cent CI −0.71 to 0.31, p = 0.45; p for heterogeneity = 0.09, I^2 = 65 per cent; Figure 4).[24,28] There was a medium degree of heterogeneity between the studies when combined in the meta-analysis (p = 0.45, I^2 = 65 per cent), which was associated with a non-significant trend in favour of the various solutions groups. It suggested that the various solutions were no more effective than nasal irrigation with normal saline alone. Sensitivity analysis could not be carried out because of the small number of included studies.

Publication bias

A funnel plot of Ringer's lactate solution, electrolysed acid water and amphotericin B saline irrigations showed that the included studies[23,24,26] were distributed near the centre of the plot, suggesting minimal publication bias (Figure 5).

Safety

Five trials reported some adverse events.[23–27] The adverse events mainly included hyposmia, headache, nasal discharge,

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Table 1. Characteristics of included studies

Study (year)	Study type	Groups (number of patients)	Interventions	Treatment duration	Outcome measures
Staffieri *et al.*[27] (2008)	Randomised trial	Thermal water (40); normal saline (40)	– Thermal water: sulphurous-arsenical-ferruginous – Normal saline: thermal water isotonic sodium chloride solution	6 months	Mean counts of inflammatory cells in ethmoid biopsies
Macchi *et al.*[25] (2013)	Randomised trial	Hyaluronan + saline (23); normal saline (23)	– Hyaluronan + saline: 9 mg sodium hyaluronate + 3 ml normal saline – Normal saline: 6 ml (nebulise & wash)	3 months	Endoscopic score, VAS score, ciliary motility, presence of mycetes
Low *et al.*[26] (2014)	Double-blind randomised controlled trial	Normal saline (20); hypertonic saline (21); Ringer's lactate solution (22)	– Not mentioned	6 weeks	SNOT-20, VAS score, endoscopic score, mucociliary clearance, paranasal sinus CT score
Jiang *et al.*[24] (2014)	Randomised trial	Electrolysed acid water (44); normal saline (42)	– Electrolysed acid water: 250 ml – Normal saline: 250 ml	2 months	SNOT-20, saccharine transit time, endoscopic score, bacterial culture rate, smell threshold
Jiang *et al.*[23] (2015)	Randomised trial	Amphotericin B saline (38); normal saline (39)	– Amphotericin B saline: 4 ml (amphotericin B) + 200 ml (normal saline) – Normal saline: 4 ml (normal saline) + 200 ml (normal saline)	2 months	Taiwanese SNOT-22, endoscopic score, acoustic rhinometry, smell test, saccharine transit test

VAS = visual analogue scale; SNOT-20/22 = 20/22-item Sino-Nasal Outcome Test; CT = computed tomography

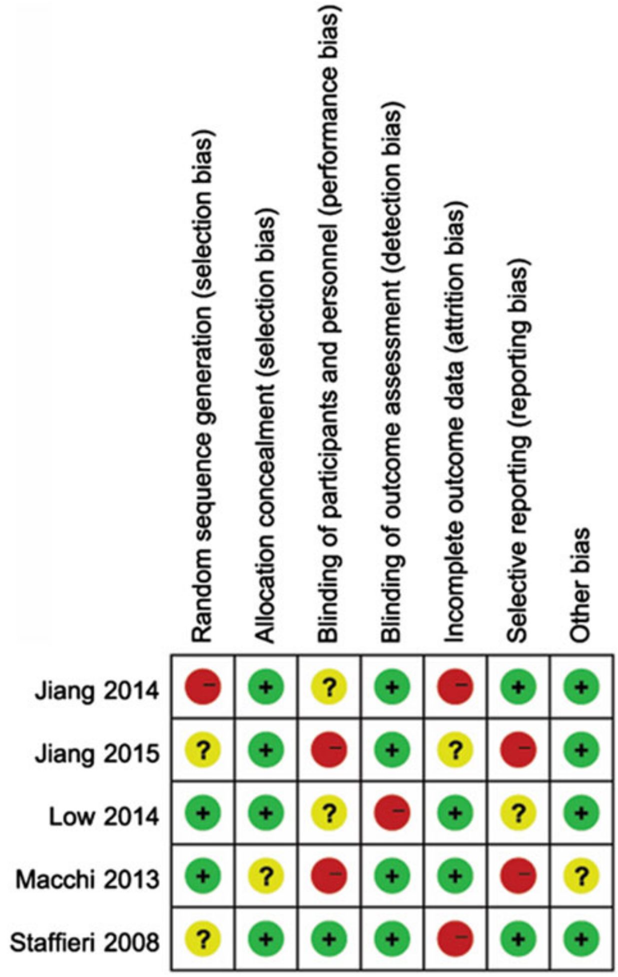

Fig. 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

rhinorrhagia and so on.[29] The occurrence of adverse events in those who underwent nasal irrigation using various solutions was not significantly different compared with the normal saline irrigation group.[30] There were no occurrences of a therapy-related serious systemic reaction that required treatment in the hospital.

Discussion

Nasal saline irrigation is a common adjuvant therapy for chronic rhinosinusitis patients.[12] Clinical studies and meta-analysis have shown nasal irrigation to be an effective therapy for decreasing chronic rhinosinusitis symptoms and nasal endoscopic scores, both pre- and post-operatively. It is safe, with no systemic pharmaceutical absorption risks.[31] Patients' acceptance means it is suitable for long-term topical therapy management.[32] Furthermore, nasal irrigation is an inexpensive treatment that can be used alone or in conjunction with other interventions for chronic rhinosinusitis patients pre- or post-operation.[17] Topical nasal irrigation is an effective treatment because a high concentration of the drug can be applied locally, with minimal systemic side effects.[33] Side effects of saline irrigation might include local irritation, ear pain, nose bleeds, headache, nasal burning, nasal drainage, bottle contamination and hyposmia.[29,34] However, these effects are rare and not severe, and patients can decide to stop nasal irrigation treatment at any time.[32]

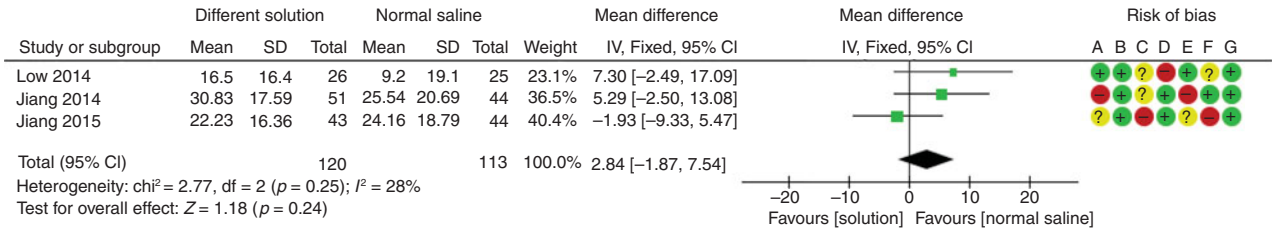

Fig. 3. Forest plot showing meta-analysis of the trials comparing symptom scores for various solutions versus normal saline. Risk of bias key: A = random sequence generation (selection bias); B = allocation concealment (selection bias); C = blinding of participants and personnel (performance bias); D = blinding of outcome assessment (detection bias); E = incomplete outcome data (attrition bias); F = selective reporting (reporting bias); and G = other bias. SD = standard deviation; IV = inverse variance; CI = confidence interval

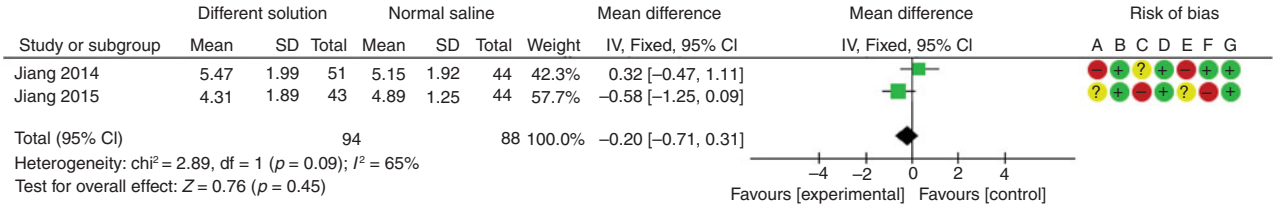

Fig. 4. Forest plot showing meta-analysis of the trials comparing endoscopic scores for various solutions versus normal saline. Risk of bias key: A = random sequence generation (selection bias); B = allocation concealment (selection bias); C = blinding of participants and personnel (performance bias); D = blinding of outcome assessment (detection bias); E = incomplete outcome data (attrition bias); F = selective reporting (reporting bias); and G = other bias. SD = standard deviation; IV = inverse variance; CI = confidence interval

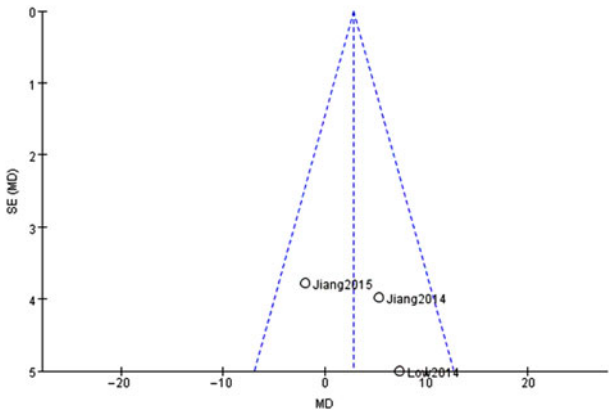

Fig. 5. Funnel plot for publication bias, which shows that the three studies (circles) are spread around the midline of the pyramid. SE = standard error; MD = mean difference

For some patients with recalcitrant chronic rhinosinusitis, increasing saline irrigation along with the use of a topical substance have been recommended.[17] Solutions that can be used for nasal irrigation are: normal or hypertonic saline, with the addition of an antibiotic, corticosteroid, antifungal or surfactant.[17] In addition, the volume (low or high), pressure (passive or active), frequency and duration of nasal irrigations are variable.[7] Their volume ranges from around 30 to 500 ml, and is considered appropriate by adult patients.[35]

Some studies have verified the efficacy of nasal irrigation with various solutions. Farag *et al.* found no significant differences in chronic rhinosinusitis symptoms post-FESS between surfactant and hypertonic saline irrigation.[13] Chiu *et al.* concluded that baby shampoo nasal irrigation was an inexpensive, tolerable adjuvant to conventional medical therapies for symptomatic patients after FESS.[14] Its greatest benefit may be in improving symptoms of thickened nasal discharge and postnasal drainage. Kim *et al.* found that maxillary sinus saline irrigation may be effective in the prevention of poor prognostic factors, such as persistent purulent discharge, at the early stages after FESS.[15] A number of authority system reviews have already been published.[16]

However, there are limited data on nasal irrigation using various solutions for chronic rhinosinusitis patients post-FESS. In this study, we attempted to identify all of the reviews on chronic rhinosinusitis patients who underwent nasal irrigation as adjuvant therapy after FESS.[8] We subsequently selected five trials for a systematic review.[23–27]

This systematic review evaluated and compared the outcomes of 5 studies involving 331 chronic rhinosinusitis patients post-FESS, who received nasal irrigation with various solutions or normal saline alone. The solutions used may be a useful adjuvant treatment following FESS for chronic rhinosinusitis, but are not significantly different compared with normal saline irrigation.

The various solutions for nasal irrigation all have their own characteristics. Ringer's lactate solution resulted in improved nasal symptoms such as nasal blockage or congestion, headache, facial pain, and nasal discharge.[26] Nasal irrigation with electrolysed acid water[24] and hyaluronan plus saline[25] can improve symptom scores and endoscopic scores, but are not significantly different to normal saline irrigation. Nasal irrigation with electrolysed acid water can make chronic rhinosinusitis patients feel more uncomfortable than irrigation with normal saline. Nasal irrigation with amphotericin B saline can decrease chronic rhinosinusitis recurrence.[23,24] Nasal irrigation with thermal water can decrease eosinophil counts and thus relieve nasal inflammation and oedema.[27] Overall, these various solutions can be effective for chronic rhinosinusitis patients after FESS. Solutions such as thermal water, Ringer's lactate solution, electrolysed acid water, amphotericin B saline, and hyaluronan plus saline may be a useful adjunct to nasal irrigation following FESS for chronic rhinosinusitis patients, based on decreased endoscopic scores and symptom scores.[23–27]

Because of differences in outcome measures and insufficient data, only three studies could be included in a meta-analysis. Regarding the two studies that were not

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included, the investigation by Staffieri *et al.*[27] lacked outcome measures other than biopsy findings, and the study by Macchi *et al.*[25] had insufficient data.

The remaining three studies included in the meta-analysis[23,24,26] used the same symptom and endoscopic scoring systems, and calculated the change from baseline to the endpoint. Therefore, we combined the mean differences weighted on the precision of estimates (weighted mean difference), rather than using a standardised mean difference, which is typically used to evaluate outcomes.

Comparison of Ringer's lactate solution, electrolysed acid water and amphotericin B saline with normal saline irrigation revealed a weighted mean difference of 2.84 (95 per cent CI −1.87 to 7.54, $p = 0.24$), with low heterogeneity ($p = 0.25$, $I^2 = 28$ per cent). Comparison of electrolysed acid water and amphotericin B saline with normal saline irrigation revealed a weighted mean difference of −0.20 (95 per cent CI −0.71 to 0.31, $p = 0.45$), with medium heterogeneity ($p = 0.09$, $I^2 = 65$ per cent). However, sensitivity analysis could not be carried out because of the small number of included studies. Furthermore, a funnel plot of Ringer's lactate solution, electrolysed acid water and amphotericin B saline irrigations, indicated that the studies were distributed near the centre of the plot, suggesting minimal publication bias.

- This study systematically assessed the clinical efficacy of nasal irrigation from the medical literature
- Nasal irrigation with saline and various solutions reduced symptom and endoscopic scores in chronic rhinosinusitis patients after functional endoscopic sinus surgery
- Irrigation using various solutions was more effective in reducing the eosinophil count than normal saline
- However, there was no statistically significant reduction in symptom or endoscopic scores between various solutions and normal saline

The present study findings indicate that nasal irrigation with various solutions is more effective than normal saline alone for chronic rhinosinusitis patients after FESS, although the differences were not significant. The various solutions and doses of nasal irrigation, the diverse scoring systems, and the different treatment durations may potentially affect our results. Moreover, the small sizes of the studies and the lack of clinical randomised controlled trials made our analysis unsatisfactory. More clinical trials are needed to compare the effectiveness of nasal irrigation with various solutions for chronic rhinosinusitis post-FESS and help guide clinical practice.

Conclusion

To our knowledge, this is the first meta-analysis to assess the effects of nasal irrigation with various solutions and compare these with normal saline alone for chronic rhinosinusitis post-FESS. Nasal irrigation was an effective therapy for chronic rhinosinusitis patients after FESS. However, when comparing various solutions with normal saline, no significant differences were found in terms of symptom scores and endoscopic scores. Future studies addressing the long-term effects and moderator variables of various solutions will overcome the present limitations, and contribute additional clinical information.

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Competing interests. None declared

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