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Review Article

Nasal saline irrigation in pediatric rhinosinusitis: A systematic review

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ABSTRACT

Objective: To determine the efficacy of nasal saline irrigation (NSI) in reducing symptoms and improving quality of life in pediatric patients with acute (ARS) or chronic (CRS) rhinosinusitis.
Data sources: We searched the PubMed/MEDLINE and Embase electronic databases (indexed January, 1950 through April, 2017).
Review methods: Studies assessing the efficacy of NSI in pediatric patients with ARS or CRS were selected for analysis. Outcome measures, including symptom scores and parental surveys, were analyzed. Two independent reviewers evaluated each abstract and article.
Results: Of the 272 articles identified using our search strategy, only 1 study, focusing on the use of NSI in pediatric ARS, met all inclusion criteria. No studies investigating NSI in pediatric CRS were included for analysis. In general, studies demonstrated significant improvement of symptom scores with the use of NSI in pediatric rhinosinusitis; but, the use of varied outcome measures, control treatments, and NSI delivery made including studies and drawing conclusions difficult. No quantitative meta-analysis could be performed.
Conclusion: NSI may provide benefit for ARS in children; however, additional high-quality studies with defined outcome measures are needed to determine the quantitative efficacy of this therapy in the pediatric patients with rhinosinusitis—especially in pediatric CRS.

1. Introduction

1.1. Description of pediatric rhinosinusitis (pRS)

The pathogenesis of pediatric rhinosinusitis (pRS) is the subject of some debate and ongoing research [1]. The leading hypothesis is that pRS is a disease of mucociliary clearance beginning with a viral upper respiratory infection (URI) and ending with bacterial colonization of the paranasal sinuses [2]. The thought is that, during URIs, viruses induce inflammation that deranges normal mucociliary clearance. Thereafter, the typically sterile paranasal sinuses, being unable to properly drain, become inoculated with bacteria that colonize the nearby nasal mucosa and nasopharynx—resulting in rhinosinusitis.

pRS is a commonly encountered problem in pediatric otolaryngological practice: 0.5–10% of viral URIs progress to acute rhinosinusitis (ARS), and an undefined proportion advance to chronic rhinosinusitis (CRS) [3–5]. Similar to otitis media, Streptococcus pneumoniae, Haemophilus influenzae, and Moraxella catarrhalis account for more than 70% of the offending bacteria identified in pediatric ARS (pARS) [6]. The pathogens responsible for pediatric CRS (pCRS) differ somewhat but often include Haemophilus influenza, Streptococcus pneumonia, and *Staphylococcus aureus* [7]. While the literature is replete with studies showing favorable responses of rhinosinusitis to antibiotics (hence the leading bacterial etiology); in reality, there is likely a spectrum of pathophysiologies ranging from infectious to purely noninfectious inflammation that lead to the disorders [8].

1.2. Rationale for nasal saline irrigation (NSI) in the treatment of pRS

Antibiotics are the most commonly prescribed treatment for pRS. There have been multiple randomized controlled trials (RCTs) performed evaluating the efficacy of antibiotics, and meta-analyses show a significant reduction in symptoms and a higher rate of cure when compared to placebo in patients pARS [9]. As a result, current guidelines recommend that uncomplicated pARS should be treated with amoxicillin or, if extended spectrum is desired, amoxicillin-clavulanate or cephalosporins [10–12]. These agents have an acceptable safety profile and cover the majority of organisms commonly found in pARS (discussed above). In addition to antibiotic therapy, several modalities

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have been tested in pARS, including topical nasal steroid sprays, decongestant-antihistamines, mucolytic agents, and nasal saline irrigation (NSI), though the evidence is poor and consensus lacking for these agents [13].

Medical treatment for pCRS is more nuanced, owing to the temporally complex pathogenesis of the disease. While antimicrobial therapy has shown clear results with pARS, and although there is a large amount of evidence-based antibiotic treatment for adult CRS, there is not enough evidence for antibiotics to be recommended for use in pCRS [5,10,11]. Still, although no specific high-level evidence supports the effectiveness of broad-spectrum antibiotics in pCRS, their use is understandably widespread [14]. Interestingly, there is consensus that daily topical nasal steroid spray as well as daily NSI are beneficial adjunctive medical therapies, but the evidence appears minimal [5]. Beyond maximal medical therapy, adenoidectomy and endoscopic sinus surgery are commonly used in the treatment of pCRS [15].

The rationale for the use of NSI in pRS (both acute and chronic) relates to the hypothesis that pRS is a disorder of altered mucociliary clearance. NSI treatment is thought to work by several mechanisms including direct cleansing of mucus (mucus is a potential medium for bacterial growth; saline thins mucus and helps to clear it out) and removal of antigens, biofilm or inflammatory mediators (thereby resolving inflammation). However, NSI is primarily believe to work by improving mucociliary function (as suggested by increased ciliary beat frequency) [16]. While any type of nasal irrigation could potentially perform this function, NSI has been adopted based on the presumption that it is safe, cheap, and widely available.

1.3. Rationale for conducting this systematic review

One of the main hurdles in the effective treatment of pRS is the proper and systematic deployment of the large arsenal of available pharmacotherapy. As discussed above, there is evidence that analgesics, antibiotics, decongestants, steroids, mucolytics, and antihistamines are effective in alleviating the symptoms of pRS [13]. Unfortunately, the quality of this evidence is rather poor, and the side effects from these agents not insignificant [17]. As such, in the spirit of non-maleficence, many providers have turned to watchful waiting or the use of safe non-medical therapy for symptomatic management of pARS and pCRS—such as NSI [18]. Interestingly, while the majority of pediatric otolaryngologists recommend NSI when treating patients with pARS and pCRS, it is not clear where the evidence for this use of NSI comes from Ref. [14].

The goal of this review is to evaluate the evidence for the efficacy of NSI in reducing symptoms and improving quality of life in pARS and pCRS. To meet this goal, a comprehensive systematic literature review was performed with the assistance of a reference librarian and the studies analyzed by the authors. The results are discussed, below, and situated among the currently accepted pathophysiology, presentation, diagnosis, and treatment of pARS and pCRS.

2. Methods

2.1. General study design

The study was designed per the recommendations of the Centre for Reviews and Dissemination's Guidance for Undertaking Reviews in Health Care [19] and is being reported in adherence with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [20]. The review was organized and accomplished using Covidence software.

2.2. Study search and registration

Before undertaking the review, we checked whether there existed similar or ongoing reviews by searching the Database of Abstracts of Reviews of Effects (DARE), the Cochrane Database of Systematic Reviews (CDSR), and the Prospective Register of Systematic Reviews (PROSPERO). We found a series of studies examining the evidence for decongestants, antihistamines, and NSI for ARS in children [13]; but, we were unable to find similar studies in pediatric CRS. No systematic reviews existed examining the (particular/sole) use of NSI in ARS and CRS in children at the beginning of this work. The study was not eligible for registration in PROSPERO as study screening, data extraction, and the research protocol were altered prior to PROSPERO enrollment.

2.3. Information sources

A comprehensive and systematic literature review was performed, with the assistance of a research librarian, using the PubMed/MEDLINE and Embase databases (indexed January, 1950 through April, 2017).

2.4. Search strategy

The literature search was completed in April, 2017 primarily using the Medical Subject Heading (MeSH) term ‘nasal lavage’. Other key search terms included ‘sodium chloride,’ ‘sinusitis,’ and ‘pediatric.’ The exact search queries for each database are outlined in Table 1. Studies from January 1950 through April 2017 were included in the search, but language was limited to English language studies only.

2.5. Inclusion and exclusion criteria

Studies were screened by the authors and included/excluded based the criteria outlined in Table 2 and detailed below.

2.5.1. Types of participants

We included studies of children, aged 0–18 years, with ARS or CRS. In general, and for the purposes of this review, pARS is used to describe clinically diagnosed rhinosinusitis of less than 4 weeks' duration in a pediatric patient [10]. pARS, here, was used as a catchall for both viral and bacterial ARS in children—though it must be noted that most

Table 1
Search strategies used for electronic database searches.
PubMed/MEDLINE and Embase electronic databases were searched with the exact search queries detailed in the table in April, 2017 and again in August, 2017 to asses study performance. The PubMed/MEDLINE search yielded 207 studies and the Embase search yielded 267 studies.

Database	Search query
PubMed/MEDLINE	("Sodium Chloride" [Mesh] OR “sodium chloride” [tiab] OR saline [tiab] OR ″nasal rinse" [tiab] OR ″nasal irrigation" [tiab] OR ″Nasal Lavage" [Mesh] OR ″nasal lavage" [tiab] OR ″nasal lavages" [tiab]) AND ("Sinusitis" [Mesh] OR sinusitis [tiab] OR rhinosinusitis [tiab]) AND ("infant" [MeSH Terms] OR ″child" [MeSH Terms] OR ″adolescent" [MeSH Terms] OR pediatric [tiab] OR child [tiab] OR infant [tiab] OR children [tiab] OR teens [tiab] OR adolescent [tiab] OR adolescents [tiab] OR adolescence [tiab] OR childhood [tiab] OR baby [tiab] OR infants [tiab] OR teenager [tiab] OR teenagers [tiab])
Embase	(exp sinusitis/OR sinusitis.mp. OR rhinosinusitis.mp.) AND (nasal irrigation.mp. OR saline rinse.mp. OR saline irrigation.mp. OR nasal lavage.mp. OR nasal saline.mp. OR nasal irrigations.mp. OR saline rinses.mp. OR saline irrigations.mp. OR nasal lavages.mp. OR exp sodium chloride/OR nasal lavage/) AND (child/OR adolescent/OR infant/OR pediatrics/OR children.mp. OR child.mp. OR adolescent.mp. OR adolescents.mp. OR infant.mp. OR infants.mp. OR teens.mp. OR teenagers.mp.)

Table 2
Inclusion/exclusion criteria for studies.
Defined inclusion and exclusion criteria used to screen study abstracts and used to include eligible full-text studies.

Criteria	Inclusion	Exclusion
Participants	• pediatric patients; ≤ 18 years old • clinical diagnosis of rhinosinusitis (acute or chronic)	• adult patients; > 18 years old • patients with diseases that have confounding symptoms (atopy, cystic fibrosis, primary ciliary dyskinesia, etc.) • patients recovering from surgery
Intervention	• nasal saline irrigation with or without other oral treatments	• treatments not explicitly detailed (in terms of dose, schedule, etc.) • non-saline nasal irrigation (nasal sprays, nasal steroids, nasal antibiotics, etc.)
Comparators	• comparator that allowed for (isolated) the determination of the efficacy of NSI	• each study arm having a different form of nasal irrigation • comparator that confounded the efficacy of NSI
Outcomes	• symptom resolution as measured by symptom scores or parental surveys	• N/A
Study type	• randomized controlled trials • prospective comparative cohort trials • case control studies • retrospective cohort studies • full-length studies/manuscripts • English language • peer-reviewed	• reviews • clinical guidelines • consensus statements • epidemiological studies • diagnostic studies • molecular/laboratory studies • observational studies • case studies • abstracts

research in children has focused on pediatric acute bacterial rhinosinusitis (pABRS). Due to the lack of guidelines with regards to the diagnosis of the chronic disease, pCRS, here, was used as a catchall to describe CRS (rhinosinusitis of greater than 12 weeks' duration) in pediatric patients without underlying conditions (such as cystic fibrosis, primary ciliary dyskinesia, and others) [5,21,22]. Because the pathogenesis of rhinosinusitis in children with these and other chronic illnesses is of a different etiology [23,24], they have been excluded from this review.

2.5.2. Types of interventions and comparators

We considered studies examining the use of NSI in at least one arm of the study. We considered the ideal intervention and comparator to be NSI vs. standard of care (e.g. antibiotics for pARS); but, given the complexities and ethics involved in pediatric trials, we allowed the use of other concurrent medications, such as antibiotics, antipyretics, steroids, decongestants, and anti-histamines. Because of the proposed mechanism of the intervention (namely, mechanical removal of material from the nasal cavities), we excluded studies comparing two different types of nasal solutions, sprays, or irrigation—such studies could not be used to determine the efficacy of NSI; rather, they would point to an efficacy of nasal irrigation in general (see discussion above).

2.5.3. Types of outcomes

We focused the review on outcomes of importance to patients. Accordingly, we examined both symptom resolution (improvement in symptom score from enrolment to the end of therapy) and overall symptom burden (as measured by parents). For secondary outcomes, we considered the time to cure, proportion of adverse events, and adherence to therapy.

2.5.4. Types of studies

As the goal of the study was to investigate the efficacy of NSI, we searched for randomize controlled trials. Still, we considered evidence from levels I–III of the Oxford Centre for Evidence-based Medicine rating system [25], which includes: properly powered and conducted randomized clinical trial; well-designed controlled trials without randomization; prospective comparative cohort trials; case-control studies; and retrospective cohort studies. Observational studies and case series cannot draw conclusions about the efficacy of an intervention and were excluded.

2.6. Process for assessing bias

Study quality, validity, and bias were assessed independently by 2 reviewers (J.G. and F.W.V). The quality of evidence for individual studies was scored according to modified Jadad scoring [26] and validity scored with a quantified adaptation of the Cochrane Risk of Bias Tool [27] (Table 3). Studies were scored using Covidence software. Each study was rated independently by the authors and agreement on scores determined by a majority consensus; there were no disagreements on ratings after discussion amongst the authors.

2.7. Process for data abstraction

Data extraction and analysis were performed independently by 2 reviewers (J.G. and F.W.V). The use of two authors was also used as a gauge of the review's overall performance. Variables collected included participants, interventions, comparators, outcomes, and general study details. Variables were collected using Covidence software.

2.8. Statistical methods

No meta analysis or statistical tests were performed. However, we had planned on normalizing symptom scores (by dividing them by the maximum score for each system), calculate risk ratios (RR), 95% confidence intervals, deriving a summary measure, and plotting the results on a forest plot. Heterogeneity was to be assessed using the chi-squared test for heterogeneity.

3. Results

3.1. Study selection

A dual database search yielded 272 unique results linked to our search queries (Table 1). Titles and abstracts were screened for inclusion/exclusion based on preset criteria (Table 2), yielding 27 studies for full text review. After full text review, additional studies were excluded, yielding 1 study that is quantitatively analyzed and discussed below (Fig. 1).

3.2. Study characteristics

3.2.1. NSI in pediatric chronic rhinosinusitis

While the systematic search and review identified 5 evaluable

Table 3
Modified rating systems used to score study quality, validity, and bias.
Study quality, validity, and bias were assessed using a modified version of the Jadad scoring scale [26] and a modified version of the Cochrane Risk of Bias Tool (CRBT) [27].

	Modified Jadad scoring	Modified CRBT scoring
Scoring details	• Was the study described as randomized? yes = +1; no = 0 • Was the method of randomization appropriate? yes = +1; no = −1; not described = 0 • Was the study described as blinding? yes = +1; no = 0 • Was the method of blinding appropriate? yes = +1; no = −1; not described = 0 • Was there a description of withdrawals and dropouts? yes = +1; no = 0 • Was there a clear description of inclusion/exclusion criteria? yes = +1; no = 0 • Was the method used to assess adverse effects described? yes = +1; no = 0 • Was the method of statistical analysis described? yes = +1; no = 0	• Random sequence generation (selection bias) low risk = +1; unclear risk = 0; high risk = −1 • Allocation concealment (selection bias) low risk = +1; unclear risk = 0; high risk = −1 • Blinding (performance bias and detection bias) low risk = +1; unclear risk = 0; high risk = −1 • Incomplete outcome data (attrition bias) low risk = +1; unclear risk = 0; high risk = −1 • Selective reporting (reporting bias) low risk = +1; unclear risk = 0; high risk = −1 • Other bias low risk = +1; unclear risk = 0; high risk = −1
Highest possible score	8 points	6 points

studies [28–32] exploring the use of NSI in pCRS, none met all inclusion criteria. These studies were excluded due to their design (2/5 were retrospective case series [29,30]) and comparators (3/5 studies compared two different forms of nasal irrigation [28,31,32]). The main gap in the evidence concerns the latter—the lack of an appropriate control arm in all current studies of NSI in pCRS. While all 5 studies demonstrate efficacy or non-inferiority of nasal irrigation, it is unclear whether NSI or nasal irrigation, in general, is beneficial. An example of this confounding effect, and, perhaps, the best evidence for the efficacy of NSI in pCRS comes from Wei and colleagues [30,32]. The group demonstrated significant improvement in both quality of life and CT Lund-Mackay scores after 6 weeks of once-daily NSI [32] as well as long-term efficacy with NSI as a first-line treatment in pCRS [30]. Unfortunately, the use of antibiotic nasal irrigation in the comparator arm prevents inclusion of this study for analysis given that the effect of NSI (as opposed to antibiotics or irrigation) cannot properly be abstracted.

In their first study [32], Wei and colleagues randomized 40 pCRS patients to either 0.9% NSI or 0.9% NSI and intranasal gentamicin irrigation daily for 6 weeks. The primary outcome was symptom resolution as measured by the well-validated Sinus and Nasal Quality-of-Life Survey (SN-5) [33] and CT improvement as measured by the Lund-Mackay scoring system [34]. Outcomes were measured at baseline, after three weeks of treatment, and at the conclusion of the study. After three weeks of intranasal irrigation with either NSI or intranasal gentamicin and NSI, SN-5 scores were significantly improved. Lund-Mackay scores were significantly improved at the endpoint. Notably, there was no difference between treatments, suggesting that intranasal irrigation (with either NSI or antibiotic solution and NSI) is effective in pCRS. While the study was an appropriately controlled and double-blinded RCT, it is not possible to say whether NSI is efficacious in pCRS due to the antibiotic irrigation used in the control arm.

In a follow-up study [30], Wei and colleagues retrospectively analyzed 144 pCRS patients that had used 0.9% NSI daily for 6 weeks. There was no comparator. The primary outcome was Lund-Mackay scores and parental surveys at the 6-week endpoint. After 6 weeks of daily NSI, the authors noted significant improvement in Lund-MacKay scores and that 66% of parents reported complete symptom resolution. As this was a retrospective cohort study with significant potential for bias, it is not an appropriate source for determining the efficacy of NSI in pCRS and was not included in our analysis.

The relatively scarce evidence for the effectiveness of NSI in pCRS is surprising given its widespread use by pediatric otolaryngologists in this setting [5,14]. It is fair to say that the evidence for the use of NSI in pCRS rests on the two studies from Wei and colleagues [30,32]. Perhaps provider confidence is buoyed by the evidence for the safety and efficacy of NSI in adult patients with CRS [35]. Still, there is a clear space for further well designed, sufficiently large, and well-conducted studies comparing NSI to an appropriate control in pCRS. Given the lack of clarity for effectively treating pediatric pCRS, the low cost of NSI, the safety of NSI, and the yearly expense of treating pCRS, such research is likely to be impactful.

3.2.2. NSI in pediatric acute rhinosinusitis

The systematic search and review identified 8 evaluable studies detailing the treatment of pediatric ARS patients with NSI [36–43]. Of these 8 studies, 5 were excluded due to poor detailing of the treatment procedures [36,37,41–43] (i.e. specific drug or delivery method was omitted or inconsistent) and 2 were excluded because of the use of other nasal saline regimens as comparators [38,40]. One study met all our criteria for inclusion, is broken down in Table 4, and scrutinized below. Overall, that more studies met our initial screening criteria for pARS than pCRS was surprising, given that NSI is routinely recommended for use in the treatment of pCRS but not pARS [5,10]. Further, most studies included in the review demonstrated significant improvement in a measurement in the treatment arm that included NSI. However, as with the pCRS studies above, most were plagued with poor comparators that prevented identifying the efficacy of NSI. The main gap in the evidence is scarcity of studies comparing the standard of care (antibiotics) with NSI in pARS. That being said, there is one single such study, which represents the best evidence for the use of NSI in pARS [39].

As detailed in Table 4, Ragab and colleagues randomized 84 patients to receive either 100 mg/kg oral amoxicillin +0.9% NSI or placebo +0.9% NSI daily for two weeks to determine the efficacy of NSI in the setting of pARS [39]. The primary outcomes were symptom resolution as determined by a validated total symptom score [11], quality of life ratings measured per the Pediatric Rhinoconjunctivitis Quality of Life Questionnaire (PRQLQ) [44], and bacterial growth as measured by middle meatus (MM) cultures [45]. Secondary outcomes included measurement of adverse effects, parental satisfaction, and self-reported treatment compliance. Outcomes were measured at baseline, after one and two weeks of treatment, and at the conclusion of the study.

Ragab and colleagues demonstrated that, after two weeks of daily NSI with/without amoxicillin, there were significant improvements in all primary outcomes (TSS, PRQLQ, MM cultures) at endpoint—but no difference with/without antibiotics. The data suggest that NSI can be used alone to treat pARS as efficaciously as antibiotics. The results, when evaluated on an intent-to-treat basis show that clinical cure in the amoxicillin group was insignificantly different (84%) in comparison to

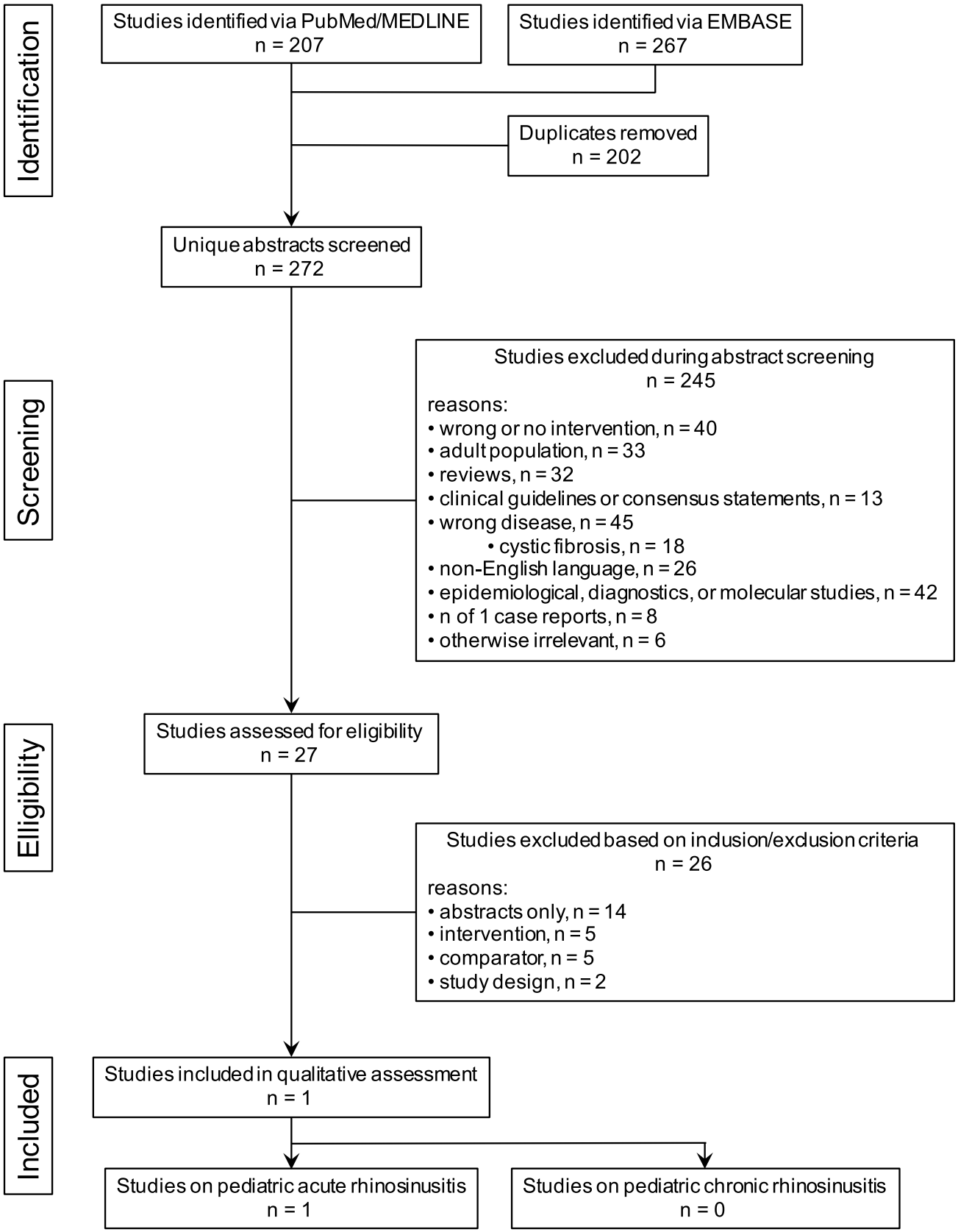

Fig. 1. Diagram of systematic review.
PRISMA-style [20] flow diagram summarizing the results of the literature search and the numbers of studies identified, screened, eligible, and included in the final review. Also included: reasons for study exclusion at the various stages of the systematic review.

Table 4
Characteristics of Ragab and colleagues' study on NSI in pARS
URI = upper respiratory infection; MM = middle meatus; TSS = total symptom score; PRQLQ = pediatric rhinoconjunctivitis quality of life questionnaire; CRBT = Cochrane Risk of Bias Tool.

Participants		• 84 children (less than 18 years old) with a clinical diagnosis of ARS o URI great than 10 days' duration but shorter than 28 days' length o at least 3 of the following symptoms - discolored discharge - purulent secretion in MM - severe local pain - fever (> 38.8 °C) - double sickening (i.e. a deterioration after an initial milder phase of illness) • 62 patients contributed to analysis o 31 in intervention group; 31 in comparator group o 33M, 29F, mean age ± SD = 5.01 ± 2.13 o no sex/age/disease severity difference between groups • Study conducted in Shebeen El-Kom, Egypt
Intervention		• NSI + placebo o NSI (15–20 mL) delivered via syringe 1–3 times daily o placebo (of similar appearance and taste) q8h orally
Comparator		• NSI + amoxicillin o NSI (15–20 mL) delivered via syringe 1–3 times daily o amoxicillin 100 mg/kg/day divided into three doses q8h orally
Outcome measures		• Primary: measurements at baseline, day 7, and day 14 o TSS o nasal endoscopy and MM swabs o PRQLQ o Time to symptomatic resolution/clinical improvement or failure • Secondary o Adverse effects o Parental satisfaction o Self-reported treatment compliance o Blinding assessment
Study design		• Triple blind randomized control trial
Risk of bias/study quality Jadad score	8/8	• Was the study described as randomized? o yes, + 1 • Was the method of randomization appropriate? o yes, +1, computer-generated blocked randomization • Was the study described as blinding? o yes, +1 • Was the method of blinding appropriate? o yes, +1, triple blind with assessment of blinding • Was there a description of withdrawals and dropouts? o yes, +1 • Was there a clear description of inclusion/exclusion criteria? o yes, +1 • Was the method used to assess adverse effects described? o yes, +1 • Was the method of statistical analysis described? o yes, +1
CRBT score	6/6	• Random sequence generation (selection bias) o low risk, +1, computer-generated blocked randomization • Allocation concealment (selection bias) o low risk, +1, sequentially numbered treatment packages • Blinding (performance bias and detection bias) o low risk, +1, triple blind with assessment of blinding • Incomplete outcome data (attrition bias) o low risk, +1, balanced and reported attrition • Selective reporting (reporting bias) o low risk, +1, all primary outcome measures reported • Other bias o low risk, +1, no other sources of bias identified

patients in the placebo group (71%). Moreover, no serious side effects were observed in either treatment group; but, significantly more side effects (notably, diarrhea) were observed in the group treated with amoxicillin. Finally, compliance with irrigation was high (≥80%) in both groups. The clear reporting of these results and unbiased study design earned this study a perfect Jadad and CRBT scores (Table 4).

As opposed to adult CRS, in the setting of adult ARS, NSI is not recommended for symptomatic relief [11,18]. Perhaps as a result of these clinical recommendations, there have been few studies in pARS of NSI. Still, the study by Ragab and colleagues [39] is promising and warrants further investigation of NSI as a first-line treatment for pARS. Additional studies are important to solidify Ragab and colleagues' findings given recent emphases on antibiotic stewardship [46].

3.3. Summary of data

Five full length studies examining the efficacy of NSI in pCRS were identified. None of the five studies met all criteria for inclusion; but, all studies demonstrated efficacy or non-inferiority of NSI. However, it remains unclear whether NSI or nasal irrigation, in general, is beneficial in pCRS.

Eight full length studies examining the efficacy of NSI in pARS were identified. One of the studies [39] met all criteria for inclusion and demonstrated significant improvement in all measured outcomes with the use of NSI—notably showing no difference with/without antibiotics. Due to a scarcity of studies, no meta analysis could be performed.

4. Discussion

4.1. Clinical practice guidelines and key findings from this systematic review

The most recent clinical consensus statement for pCRS [5] recommends the use of NSI as adjunctive treatment, and the most recent clinical guidelines for pARS [10] give no recommendation on the use of NSI due to the paucity of quality evidence [13]. Data from our systematic review demonstrate that the quality of evidence is better for NSI in the setting of pARS than pCRS. There are no data that demonstrate the efficacy of NSI in pCRS (as opposed to nasal irrigation in general). On the other hand, data support the use of NSI in pARS as the treatment is safe, adhered-to, and efficacious.

4.2. Clinical inferences and data interpretation

In light of the total available evidence, and based on the validity of the studies, NSI could be used as a first-line treatment in the setting of uncomplicated pARS. The study by Ragab and colleagues demonstrates that NSI is efficacious, safer than antibiotics, and well adhered-to. In general, NSI is a safe treatment that may be beneficial to some pARS or pCRS patients, though the existing evidence is too limited to support recommendations for or against its role as a standard intervention in the setting of pCRS.

4.3. Potential biases

The main limitations of our study have to do with our inclusion/exclusion criteria. First, by limiting ourselves to English language only studies, we omitted a significant literature on the efficacy NSI in

treating pRS that exists in the Arabic and East Asian languages/cultures. Second, by excluding studies that compared the efficacy of NSI to general nasal irrigation, we omitted a significant amount of literature. However, it is our belief that such studies cannot be used to determine the specific effectiveness of NSI; but, rather, point to the efficacy of nasal irrigation in general.

4.4. The ideal NSI efficacy trial in pRS

An excellent trial to address the efficacy of NSI in pRS should have the following elements: a well defined study population (pediatric patients with guideline-defined pARS or pCRS), a simple intervention and comparator (one arm with nasal saline; the other arm with the standard of care), defined outcome measures (validated symptom scores such as the SN-5 [33]), and a randomized controlled design (as this is the only way to determine efficacy of a treatment). We included similar criteria to include studies in this review; but, we could not find any study meeting all criteria—likely due to intrinsic challenges in conducting trials in children.

4.5. Challenges to NSI trials in pRS

There are clear challenges to NSI trials in pRS. The two largest barriers have to do with the study population and the intervention & comparator. Pediatric trials are difficult to conduct due to the subjects' vulnerability—requiring additional protections for minors. Compounding this problem are the myriad definitions of pARS and pCRS (including those of non-infectious etiologies) and the lack of a standard pharmacological treatment for pCRS (not to mention surgical approaches). The intervention also poses challenges, namely with regards to NSI's formulation, delivery, and adherence—this last point warranting a systematic review onto its own. Given the findings of this review, it may be wise to leverage the non-inferiority of NSI in pARS and propose similar trials for pCRS.

5. Conclusions

Previous systematic reviews found no appropriately designed studies to determine the effectiveness of NSI in pARS [13]. Here, we find that the evidence base for the effectiveness of NSI in symptomatic relief of pARS is better than the evidence in pCRS and that NSI may provide benefit in the first line setting for pARS. However, additional high-quality studies with defined outcome measures are needed to determine the effectiveness of this therapy as compared to the standard of care in pCRS.

Disclosures

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