Intranasal steroids for acute sinusitis (Review)
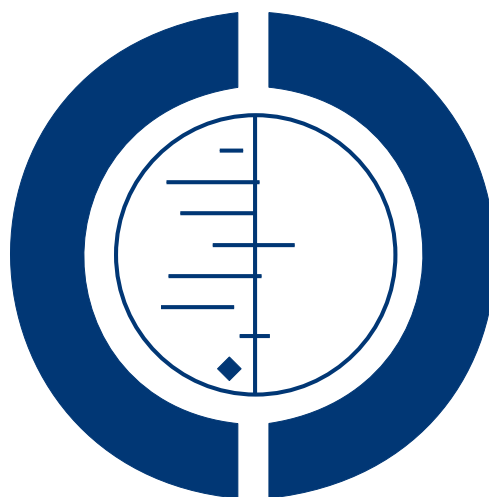
Zalmanovici Trestioreanu A, Yaphe J

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Intranasal steroids for acute sinusitis

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A B S T R A C T

Background

Acute sinusitis is a common reason for primary care visits. It causes significant symptoms and often results in time off work and school.

Objectives

We examined whether intranasal corticosteroids (INCS) are effective in relieving symptoms of acute sinusitis in adults and children.

Search methods

We searched CENTRAL 2013, Issue 4, MEDLINE (January 1966 to May week 2, 2013), EMBASE (1990 to May 2013) and bibliographies of included studies.

Selection criteria

Randomised controlled trials (RCTs) comparing INCS treatment to placebo or no intervention in adults and children with acute sinusitis. Acute sinusitis was defined by clinical diagnosis and confirmed by radiological evidence or by nasal endoscopy. The primary outcome was the proportion of participants with either resolution or improvement of symptoms. Secondary outcomes were any adverse events that required discontinuation of treatment, drop-outs before the end of the study, rates of relapse, complications and return to school or work.

Data collection and analysis

Two review authors independently extracted data, assessed trial quality and resolved discrepancies by consensus.

Main results

No new trials were found for inclusion in this update. Four studies involving 1943 participants with acute sinusitis met our inclusion criteria. The trials were well-designed and double-blind and studied INCS versus placebo or no intervention for 15 or 21 days. The rates of loss to follow-up were 7%, 11%, 41% and 10%. When we combined the results from the three trials included in the meta-analysis, participants receiving INCS were more likely to experience resolution or improvement in symptoms than those receiving placebo (73% versus 66.4%; risk ratio (RR) 1.11; 95% confidence interval (CI) 1.04 to 1.18). Higher doses of INCS had a stronger effect on improvement of symptoms or complete relief: for mometasone furoate 400 μg versus 200 μg (RR 1.10; 95% CI 1.02 to 1.18 versus RR 1.04; 95% CI 0.98 to 1.11). No significant adverse events were reported and there was no significant difference in the drop-out and recurrence rates for the two treatment groups and for groups receiving higher doses of INCS.

Authors' conclusions

Current evidence is limited for acute sinusitis confirmed by radiology or nasal endoscopy but supports the use of INCS as a monotherapy or as an adjuvant therapy to antibiotics. Clinicians should weigh the modest but clinically important benefits against possible minor adverse events when prescribing therapy.

PLAIN LANGUAGE SUMMARY

Steroids for acute sinusitis in adults and children

Acute sinusitis is a common reason for primary care visits; it is one of the 10 most common diagnoses in outpatient clinics, presenting with various symptoms and signs that include purulent nasal discharge and congestion and cough lasting beyond the typical seven to 10 days of a viral upper respiratory infection. There have been suggestions, based on studies of allergic rhinitis and chronic sinusitis, that intranasal corticosteroids (INCS) may relieve symptoms and hasten recovery in acute sinusitis due to their anti-inflammatory properties.

A critical systematic review of the literature found four well-conducted, randomised, placebo-controlled intervention studies, involving 1943 participants treated for 15 or 21 days. The results suggest that there may be a modest effect with INCS in the resolution or improvement of symptoms. Only minor adverse events such as epistaxis, headache and nasal itching were reported. Given the small number of studies included in this review, it is recommended that further randomised controlled trials be conducted. The evidence is up to date as of May 2013.

BACKGROUND

Description of the condition

Acute sinusitis is a common reason for primary care visits. It causes significant symptoms and often results in time off work and school. It is one of the 10 most common diagnoses in ambulatory practice and is the fifth most common diagnosis for which an antibiotic is prescribed. Primary care physicians tend to think of sinusitis as an acute bacterial infection and consequently prescribe antibiotics in 85% to 98% of cases. However, sinusitis is frequently caused by a viral infection. According to epidemiological estimates, only 0.2% to 2% of viral upper respiratory tract infections in adults are complicated by bacterial rhinosinusitis. It will often resolve in most patients without antibiotic treatment, even if it is bacterial in origin. Since no simple and accurate practice-based test exists for acute bacterial sinusitis, clinicians rely on clinical findings to make the diagnosis. Signs and symptoms of acute bacterial sinusitis and those of prolonged viral upper respiratory tract infection are very similar, resulting in frequent misclassification of viral cases (Snow 2001).

The common cold is associated with frequent and variable anatomical involvement of the upper airways, including occlusion and abnormalities in the sinus cavities (Gwaltney 1994). Rhinorrhoea, sinus tenderness, purulent secretions and a history of sinusitis were significant predictors for the diagnosis of sinusitis in a retrospective analysis (Little 2000). Acute sinusitis is defined as an inflammation of the sinuses with the symptom complex lasting less than eight weeks in adults and less than 12 weeks in children (Kaliner 1997).

Clinical diagnosis is made through the appearance of a characteristic constellation of symptoms and signs, including purulent nasal discharge and congestion and cough lasting beyond the typical seven to 10 days for a viral upper respiratory infection. Fever and facial pain may also occur. Diagnosis is often confirmed by sinus imaging; in this area, the use of computerised tomography (CT) scanning is gaining favour (Gwaltney 1995).

Inflammation of nasal mucosa plays an essential role in the development of sinusitis (Tutkun 1996). Sinusitis is invariably accompanied by inflammation of the contiguous nasal mucosa, therefore rhinosinusitis has become the preferred term (Snow 2001). The precipitating factor in acute sinusitis appears to be blockage of the sinus ostium. The obstruction, as well as mucus retention and infection, produce the characteristic signs and symptoms of rhinosinusitis. Although many conditions may lead to ostial closure, viral upper respiratory infections and allergic inflammation are by far the most frequent and important (Shapiro 1992).

Description of the intervention

Treatment of sinusitis is aimed at eliminating causative factors and controlling the inflammatory and infectious components (Becker 2003). It has been theorised that by decreasing the inflammatory response and reducing the mucosal swelling, a topical intranasal steroid would promote drainage and increase aeration of the sinuses, thus hastening the elimination of infectious organisms and decreasing the frequency and severity of recurrences (Mygind 1976). There is evidence that asthma, otitis media with effusion and acute sinusitis may all benefit from such therapy as well (Scadding 2000). A recent Cochrane review found that systemic corticosteroids as adjunctive to antibiotic treatment were effective for the short-term relief of symptoms in acute sinusitis; the authors mention that the data for this review are limited and there is a significant risk of bias (Venekamp 2011).

How the intervention might work

In addition to treating seasonal and perennial rhinitis (possible predisposing factors to the development of acute rhinosinusitis), intranasal corticosteroids (INCS) might be beneficial in reducing inflammation in the treatment of sinusitis and may help decrease secondary rhinovirus infections (Gawchik 2000). The mode of action of INCS is complex. It is not known whether INCS penetrate the nasal mucosa or act on target cells. However, their low systemic activity supports the concept of local action on nasal mucosa. This local effect can influence a variety of inflammatory cells and their mediators such as epithelial cells, lymphocytes, basophiles, mast cells and Langerhans cells. Corticosteroid-induced inhibition of the immunoglobulin E dependent release of histamine is a possible but unproven mode of action (Mygind 2001).

Why it is important to do this review

The management of rhinosinusitis depends on a number of variables related to the duration and severity of symptoms in the individual patient. Since there are a variety of conservative and pharmacological interventions available, the physician can find it difficult to develop a cohesive and logical approach to treatment (Benninger 1997). A small benefit for clinical outcomes was observed in patients treated with antibiotics for uncomplicated acute sinusitis; 80% of participants treated without antibiotics improved within two weeks (Ahovuo-Saloranta 2011). No clear evidence of efficacy of decongestants, antihistamines and nasal irrigations for acute sinusitis in children was found in a recent Cochrane Review (Shaikh 2012). Recent practice guidelines for the diagnosis and management of rhinosinusitis suggest considering the use of INCS as adjunctive therapy (Slavin 2005; Spector 1998). Although the guidelines reflect the belief of many clinicians that INCS are a valuable component of rhinosinusitis management, limited clinical data are available on their use in this disease. A

recent experimental prospective study on rabbits with surgically introduced sinusitis demonstrated no clear advantage of steroids in the treatment of sinus infections using this model (Cable 2000). The use of adjunctive medications for acute sinusitis such as antihistamines, decongestants and nasal steroids also remains controversial (Shrum 2001). Several recent studies tested the effectiveness of inhaled steroids for relieving symptoms in acute sinusitis in humans, concluding that this treatment is effective. A systematic review that addresses the effectiveness of this therapy will provide useful information to all primary care practitioners and could assist in formulating the best treatment plan for the individual patient.

OBJECTIVES

We examined whether intranasal corticosteroids (INCS) are effective in relieving symptoms of acute sinusitis in adults and children.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs) comparing topical intranasal steroids with placebo or no intervention.

Types of participants

1. Children and adults, irrespective of age, with acute sinusitis.
2. Acute sinusitis is defined by clinical diagnosis and nasal endoscopy or radiological evidence or nasal endoscopy.
3. We included trials including a mixed population of acute and non-acute sinusitis if outcomes were reported separately for these subgroups.

Types of interventions

Studies which used intranasal corticosteroids (INCS) - any preparation, dose or route of administration (for example, inhaled or drops) versus placebo or no intervention in the control group. We included trials reporting combined interventions only if the control arm received the same co-treatments as the intervention arm, except for topical steroids.

Types of outcome measures

Primary outcomes

1. Proportion of participants with resolution or improvement of symptoms.

Secondary outcomes

1. Any adverse event that necessitated discontinuation of treatment.
2. Proportion of participants that developed complications.
3. Drop-outs before the end of the study.
4. Rates of relapse in symptoms.
5. Proportion of participants that returned to school or work within a specific time frame.

Search methods for identification of studies

Electronic searches

For this update we searched the Cochrane Central Register of Controlled Trials (CENTRAL) 2013, Issue 4, part of *The Cochrane Library*, www.thecochranelibrary.com (accessed 22 May 2013), which contains the Cochrane Acute Respiratory Infections Group's Specialised Register; MEDLINE (April 2011 to May week 2, 2013) and EMBASE (April 2011 to May 2013). See Appendix 1 for details of previous searches.

We searched MEDLINE and CENTRAL using the following search strategy. We combined the MEDLINE search with the Cochrane Highly Sensitive Search Strategy for identifying randomised trials in MEDLINE: sensitivity- and precision-maximising version (2008 revision); Ovid format (Lefebvre 2011). We adapted the strategy to search EMBASE (Appendix 2).

MEDLINE (OVID)

1 exp Sinusitis/
2 sinusit*.tw.
3 (rhinosinusit* or nasosinusit*).tw.
4 or/1-3
5 exp Steroids/
6 steroid*.tw.
7 exp Adrenal Cortex Hormones/
8 adrenal cortex hormone*.tw.
9 exp Anti-Inflammatory Agents/
10 anti-inflammat*.tw.
11 corticosteroid*.tw.
12 or/5-11
13 exp Administration, Intranasal/
14 exp Administration, Topical/

15 (nasal* or intranasal* or topical*).tw.
16 or/13-15
17 12 and 16
18 4 and 17

Searching other resources

We inspected the reference lists in all identified studies for further relevant studies. We also scrutinised the existing review literature (for example, Mucha 2003). We contacted trial authors for information about possible unpublished studies. There were no language or publication restrictions. We also searched the WHO ICTRP and ClinicalTrials.gov trials registries (14 May 2013) for completed and ongoing trials.

Data collection and analysis

Selection of studies

The two review authors independently reviewed the abstracts of potential studies to be included in the review. We obtained the full article and independently inspected it for relevance.

Data extraction and management

The two review authors independently extracted data from included trials. We documented disagreements and resolved them by discussion. We contacted the trial authors for clarification when necessary. We also documented justification for excluding studies from the review in the Characteristics of excluded studies table. We reported on the following domains.

1. Characteristics of trials: publication status, year, country of study, setting, design, inclusion and exclusion criteria, recruitment, methods, analysis, results.
2. Characteristics of participants: study population, number of participants in each group, age, gender, nationality, diagnostic criteria.
3. Characteristics of interventions: preparation used, dose, length of treatment and follow-up, compliance, co-interventions.
4. Outcomes: resolution of symptoms, improvement of symptoms, relapse, complications, return to school/work, adverse events related to the intervention, drop-outs before the end of the study and reasons for dropping out.

Assessment of risk of bias in included studies

The two review authors independently assessed the methodological quality of each study in the 'Risk of bias' tables, as outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011):
1. random sequence generation;

2. allocation concealment;
3. blinding of participants and personnel;
4. blinding of outcome assessment;
5. incomplete out come data;
6. selective reporting; and
7. other bias.

We included trials if they met the following criteria: randomisation method described that would not allow the investigator/participant to know or influence intervention group before the eligible participant entered in the study (low risk of bias) and randomisation stated but no information on method used is available (moderate risk of bias). There were no disagreements and we observed no selective reporting or other potential bias. We obtained additional information from the trial authors when the publications presented insufficient detail.

Measures of treatment effect

We analysed dichotomous data by calculating the risk ratio (RR) and risk difference (RD) for each trial with the uncertainty in each result being expressed as 95% confidence interval (CI). We expressed the results using the approach recommended in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We performed all analyses on the basis of intention-to-treat (ITT). We divided study data as far as possible from published and unpublished information into subgroups for children less than 18 years, adults and co-interventions. We planned subgroup analyses to assess the impact of these possible sources of heterogeneity. We used the fixed-effect model for combining studies in the absence of heterogeneity.

Unit of analysis issues

We included RCTs with standard designs and parallel groups in the review.

Dealing with missing data

We tried to contact study authors for missing data.

Assessment of heterogeneity

We assessed heterogeneity by inspection of the graphical presentations and I^2 statistic for heterogeneity.

Assessment of reporting biases

We did not have sufficient studies for performing funnel plot analysis to assess possible publication bias. We did not observe other reporting bias.

Data synthesis

We did not find any evidence of heterogeneity between studies as assessed by inspection of the graphical presentations; therefore we used the fixed-effect model for combining the studies.

Subgroup analysis and investigation of heterogeneity

We did not perform the planned subgroup analyses as the included studies did not report data for these subgroups.

Sensitivity analysis

We planned no sensitivity analyses in the absence of heterogeneity.

R E S U L T S

Description of studies

Results of the search

We did not identify any trials to include or exclude in this 2013 update from the 82 new references identified. In the previous review (Zalmanovici Trestioreanu 2011) 495 references were identified and the abstracts were inspected by the two review authors.

Included studies

Four studies with 1943 participants assigned to intranasal corticosteroids (INCS) or placebo met the inclusion criteria for this review. Three studies were multicentre trials; one was conducted at 22 sites - 12 primary care and 10 otolaryngology clinics (Dolor 2001), one study involved outpatients from 61 treatment centres in the USA (Nayak 2002), one study was conducted at 71 medical centres in 14 countries (Meltzer 2005) and one study involved participants from the Marmara University Hospital Pediatric Outpatient Clinic (Barlan 1997).
One trial had three treatment arms; two arms for different doses of INCS and one arm for placebo (Nayak 2002). One trial had four treatment arms; two arms for different doses of INCS, one arm for antibiotic and one arm for placebo (Meltzer 2005). We performed meta-analyses for treatment arms using different doses of INCS combined and separately.

Participants

Participants included in the trials were children and adults with a documented episode of acute sinusitis, confirmed by radiology or nasal endoscopy. The entry criteria in the trials were similar.

Intervention

All the studies used a placebo in the control group. Participants in the treatment groups in three studies received INCS for 21 days as fluticasone propionate two puffs daily in each nostril, giving a total dose of 200 μg (Dolor 2001), MFNS (mometasone furoate) twice daily giving a total dose of 400 μg or 800 μg (Nayak 2002) and budesonide 50 μg twice daily to each nostril as a nasal spray (Barlan 1997) as adjuvant therapy to antibiotics. One study used MFNS 200 μg and 400 μg total daily dose in the treatment arms for 15 days as monotherapy (Meltzer 2005). Other concomitant therapies were similar in all groups, in every study.

Outcomes

The included studies reported the proportion of participants with clinical success; the length of time until clinical success; difference over time in sinusitis symptoms; quality of life scores; relapse (Dolor 2001); improvement in total and individual symptoms scores; onset of relief and evaluation of changes in computerised tomography (CT) sinus scans (Nayak 2002); difference in weekly symptom scores as difference between groups or change from baseline (Barlan 1997); global response to treatment; time to onset of action; mean major symptom scores; mean total symptom scores; individual symptom scores; treatment failure and disease recurrence (Meltzer 2005). Information on adverse events that occurred during the trials is presented in Table 1. Drop-outs before the end of the study and the reasons for leaving were described in all the studies. One study did not report separate data for the groups for this outcome and the number of participants initially randomised in each group had a high drop-out rate. It reported results as medians of scores using non-parametric tests because a wide range of scores were without normal distribution; it was not included in the meta-analyses (Barlan 1997).

Excluded studies

We excluded 491 studies for one or more of the following reasons: not acute sinusitis; not randomised; observational studies; intervention of interest not used; no relevant outcomes reported; repeated reports of the same study; and review articles. Thirteen reports were considered potentially eligible for inclusion but after inspection of the full papers, we excluded nine (Bachert 2007; Gehanno 2000; Jurkiewicz 2004; Meltzer 1993; Meltzer 2000; Quarnberg 1992; Tutkun 1996; Williamson 2007; Yilmaz 2000) (see Characteristics of excluded studies table). In the first publication of this review (Zalmanovici 2007) two studies were awaiting further assessment for missing data (Meltzer 2000; Tutkun 1996). We excluded these studies in the first update (Zalmanovici 2009) as data were not made available from the trial authors, whom we contacted. The reasons for exclusion are added to the Characteristics of excluded studies table. In addition, for one study (Jurkiewicz 2004), no abstract or full paper was available.

Risk of bias in included studies

The studies were well-designed, randomised, double-blind, placebo-controlled trials. The overall risk of bias is presented graphically in Figure 1 and summarised in Figure 2.

Figure 1. 'Risk of bias' graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

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

Allocation

All four studies were RCTs. However, only two contained an adequate report of the generation of allocation sequence (Dolor 2001; Meltzer 2005) and one study reported concealment of allocation (Dolor 2001). The assessment for trial inclusion was based on allocation concealment.

Blinding

The trials were double-blinded and the method of blinding was adequate. One study did not describe the method of blinding (Barlan 1997).

Incomplete outcome data

Drop-outs before the end of the study and the reasons for leaving were described in the studies. The total loss to follow-up was 7% (Dolor 2001), 11% (Nayak 2002), 10% (Meltzer 2005) and 41% (Barlan 1997), respectively.

Selective reporting

The studies reported what was pre-stated in their protocol.

Other potential sources of bias

We identified no other sources of bias.

Effects of interventions

Four studies that included 1943 participants met our inclusion criteria (Barlan 1997; Dolor 2001; Meltzer 2005; Nayak 2002). Two studies had more than two arms, two treatment arms for different doses of intranasal corticosteroids (INCS), and we performed separate and combined dose meta-analyses (Meltzer 2005; Nayak 2002). One study was included in the review but not in the meta-analysis as it was not possible to extract data, non-parametric tests were used and it had a high drop-out rate (Barlan 1997).

Primary outcome

Proportion of participants with resolution or improvement of symptoms

Information on our primary outcome was found in three trials, assessed at 15 days in one study (Meltzer 2005) and at 21 days in two other studies (Dolor 2001; Nayak 2002). When combined using intention-to-treat (ITT) analysis, 73% of INCS-treated participants and 66.4% of controls had resolution or marked improvement of symptoms (for every 100 patients treated with INCS

seven additional patients had complete or marked symptom relief). Individuals treated with INCS (combined results for the 200 µg, 400 µg and 800 µg doses) were more likely to have complete relief or improvement than the placebo group (risk ratio (RR) 1.11; 95% confidence interval (CI) 1.04 to 1.18) (Analysis 1.3); (risk difference (RD) 0.07; 95% CI 0.03 to 0.11) and this result was statistically significant. When we performed separate meta-analyses for different doses of INCS, a stronger and statistically significant effect was obtained when patients were treated with 400 µg than 200 µg mometasone furoate (MFNS) total daily dose (RR 1.10; 95% CI 1.02 to 1.18 versus RR 1.04; 95% CI 0.98 to 1.11) (Analysis 1.1; Analysis 1.2); (RD 0.06; 95% CI 0.02 to 0.11 versus RD 0.04; CI 95% -0.02 to 0.09). The attributable risk percentage (AR%) calculated for the results that were statistically significant means that 8% (one in 12) of all patients who, having received the 400 µg dose of INCS, had resolution or improvement in symptoms could attribute that relief to the treatment. When calculated from results combined across all doses, the number is 9% (one in 11). One study that used in one of the treatment arms an 800 µg MFNS daily dose found a statistically significant effect for this dose (RR 1.21; 95% CI 1.05 to 1.39) (Nayak 2002).

Secondary outcomes

Any adverse event that necessitated discontinuation of treatment

This outcome was reported in two studies (Meltzer 2005; Nayak 2002). No separate data for each treatment arm were available in one study (Nayak 2002) and the participants were equally distributed among the three arms. One study reported a drop-out rate from treatment of 1%, 3%, 2% and 2% because of adverse events in the INCS 200 µg, 400 µg, antibiotic and placebo arms (Meltzer 2005) (Table 1).

Proportion of participants that developed complications

No studies reported this outcome.

Drop-outs before the end of the study

This outcome is reported in three studies (Dolor 2001; Meltzer 2005; Nayak 2002). No statistically significant difference could be found for participants that were lost to follow-up in the two groups (RR 0.85; 95% CI 0.64 to 1.12) (Analysis 1.6). Using a higher dose of INCS did not change the results (RR 0.86; 95% CI 0.61 to 1.20) (Analysis 1.4) for MFNS 400 µg versus MFNS 200 µg (RR 0.75; 95% CI 0.46 to 1.21) (Analysis 1.5).

Rates of relapse in symptoms

Two studies reported data for this outcome (Dolor 2001; Meltzer 2005). No statistically significant differences could be found between groups; 6.3% and 10% had relapse in the INCS and placebo groups (RR 0.71; 95% CI 0.44 to 1.15) (Analysis 1.7). The median time to first recurrence was three days earlier in the placebo group (22 versus 25 days) in one study (Dolor 2001). One study did not find significant differences between groups for different doses of INCS (Meltzer 2005).

Proportion of participants that returned to school or work within a specific time frame

No studies reported this outcome. One study (Dolor 2001) reported a higher subjective level of work performance that was significantly different on day 21 (P value = 0.009) in the INCS treatment group versus placebo. The difference between groups with respect to the total number of hours missed from work was not significant (P value = 0.40).

DISCUSSION

Acute sinusitis is typically first seen as an upper respiratory tract infection that has persisted beyond five to seven days. The diagnosis of sinusitis is based on a combination of clinical history with physical examination, nasal cytology or imaging studies (or both). Factors that may predispose to sinusitis include allergic or occupational rhinitis, vasomotor rhinitis, nasal polyps, rhinitis medicamentosa and immunodeficiency (Spector 1998). Although acute sinusitis is an infectious disease in which several bacterial species play a major aetiological role, there is an important interaction between respiratory viruses (for example, common cold viruses) and bacteria in the pathogenesis of acute community-acquired sinusitis (Winther 1990). Upper respiratory tract infections and allergic inflammation are recognised as the important risk factors for acute sinusitis, with upper respiratory tract infection being the most common (Wald 1988).

Summary of main results

Four studies met the inclusion criteria in our review. They were well-conducted and produced results that suggest a clinically relevant, earlier resolution of symptoms in participants treated with intranasal corticosteroids (INCS), without the risk of severe adverse events, even when higher doses in the therapeutic range were used. All four of the trials reached statistical significance for this outcome. One in 12 of all patients who having received the 400 μg dose had resolution or improvement in symptoms could attribute that relief to the treatment. Across all doses, the number is one in 11. No statistically significant difference in the relapse

rate between groups was found. One study (Barlan 1997) found that INCS may be a useful ancillary treatment to antibiotics in childhood sinusitis and effective in reducing the cough and nasal discharge earlier in the course of acute sinusitis. Clinical signs and symptoms decreased significantly in both groups in comparison to baseline (P < 0.01) and in the intervention group when compared to placebo in the scores for cough and nasal discharge at the end of the second week (P < 0.05). This study was not included in the meta-analyses as it had a high drop-out rate (41%), drop-outs were not described separately for both groups, outcomes were reported as weekly scores using non-parametric tests and it was not possible to extract data for our outcomes. One of the included studies (Nayak 2002) found a significant improvement in the total symptom score and in individual symptom scores during the treatment period.

The mean change in the score from computerised tomography (CT) scans of the sinuses from baseline to day 21 was not statistically significant between the treatment and control groups. One other included study (Dolor 2001) found the median number of days to clinical success in those treated with INCS was six days compared to nine and a half days in those treated with a placebo. The subjective level of work performance at 21 days was significantly better in the treatment group. Improvement in sinusitis symptoms scores, sinusitis-related quality of life and the total number of hours of work missed were not significantly different in the two groups. Mometasone furoate (MFNS) 400 μg daily demonstrated significant superiority over MFNS 200 μg daily in nasal congestion/stuffiness score (P = 0.013) and global response to treatment (P = 0.002) was more consistently superior across the endpoints and over amoxicillin in one study (Meltzer 2005), suggesting that higher doses are needed. Also, this study found significant improvement in the major symptom score (P < 0.001), total symptom score (P < 0.001), global response to treatment (P = 0.001) and individual symptom scores (rhinorrhoea, nasal congestion/stuffiness, sinus headache, facial pain) for MFNS 400 μg over placebo.

The results of these studies and reviews support the current clinical rationale of adding an INCS to antibiotic therapy for acute episodes of rhinosinusitis and suggest that higher doses are needed; effectiveness as monotherapy remains to be demonstrated by further studies. The included studies enrolled adults and children and the samples were representative of participants that physicians would recognise as common in their practice. Clinical improvement was assessed by patient-derived (subjective) symptom reports and this outcome met one of our study goals: evaluating alleviation of symptoms together with possible adverse events.

Overall completeness and applicability of evidence

It is important that the mucous membranes and ciliary function are restored to normal as soon as possible, to avoid recurrence or

development of chronic sinusitis (Quarnberg 1992). Two surveys of primary care and specialty physicians suggested considerable variability in approaches to treatment (Piccirillo 2001; Williams 1993). Recommendations for appropriate treatment for acute sinusitis range from symptomatic treatment alone (Snow 2001) to a prolonged course of antibiotic therapy (Winther 1990). A variety of ancillary treatments aimed at improving nasal and sinus ostial patency (antihistamines, decongestants, INCS and nasal irrigation) might be helpful in the treatment of sinusitis but there are few controlled studies to support or deny their effectiveness (Zeiger 1992). Numerous clinical trials attest to the efficacy of topical corticosteroids in controlling symptoms of allergic rhinitis (Juniper 1990; Seigel 1988). The similarity of the respiratory epithelium in the nose and paranasal sinuses, as well as the contiguity of these areas, would lead one to expect that sinusitis might also be treatable with inhaled corticosteroids.

Whether nasal steroid therapy can sufficiently decrease nasal inflammation and improve mucociliary transport to the point where the ostiomeatal complex becomes competent is unknown. Topical corticosteroids offer the theoretical advantage of a localised therapeutic action in nasal tissues, without the occurrence of undesirable systemic effects (Sahay 1980). Inhaled corticosteroids have been used safely in patients with allergic rhinitis or asthma. There exists a theoretical concern regarding the potential spread of infection in acute sinusitis. However, this does not occur when topical corticosteroids are administered concurrently with antibiotics (Druce 1990; Druce 1991). Investigations of whether INCS promotes resolution of symptoms and prevents recurrences of sinusitis have yielded conflicting results (Meltzer 1993; Quarnberg 1992).

Acute sinusitis is a very common infection in childhood but its management remains a controversial issue. A considerable proportion of children, especially those with mild or improving symptoms, may not have to be treated at all (Contopoulos 2003). Management of acute sinusitis usually includes an oral antibiotic. However, it has been estimated that about 45% of cases will resolve without antibiotics (Spector 1998).

Considering the host of symptoms associated with acute rhinosinusitis, recovery can take time and be of substantial discomfort to the affected patient. The burden of affected individuals in terms of decreased productivity, absenteeism from the workplace and diminished quality of life, when added to the cost of care and the growing public health menace of antibiotic-resistant bacteria, makes rhinosinusitis a serious disease that warrants a precise diagnosis and effective therapy. Recognised pitfalls in acute rhinosinusitis management are the injudicious use of antibiotics and antihistamines (Winstead 2003). The decision on the best treatment for the specific patient should be based on the severity of symptoms, adapted individually, taking in consideration the existing evidence and the patient's preferences.

Most clinicians diagnose acute sinusitis using only clinical symptoms, without additional diagnostic tests. Over-diagnosis of acute bacterial rhinosinusitis is not surprising, considering the lack of specific clinical features that distinguish it from non-bacterial upper respiratory tract infections. Often, patients and physicians believe that an upper respiratory tract infection has gone on too long and that antibiotic treatment is therefore needed. Symptomatic treatment and reassurance are the preferred initial management strategy for patients with mild symptoms. Antibiotic therapy should be reserved for patients with severe symptoms who meet the criteria for the clinical diagnosis of acute bacterial rhinosinusitis, regardless of the duration of the illness. The greatest barrier to efficient antibiotic treatment of acute bacterial rhinosinusitis is the lack of a simple and accurate diagnostic test. Until a better test is widely available in clinical practice, the primary diagnosis of acute bacterial rhinosinusitis will remain imprecise (Snow 2001).

Quality of the evidence

Currently, nasal steroid therapy has become an acceptable adjunct in treating both acute and chronic sinusitis. Several intranasal steroids are now available: flunisolide, beclomethasone, triamcinolone, fluticasone, budesonide and mometasone. Each of these has proven to be effective in the treatment of allergic rhinitis and may be a useful addition in sinus disease (Spector 1998). The *International Consensus Conference Proceedings on Rhinitis* recommends the use of INCS as a first-line therapy, since they have been found to be well-tolerated and effective with minimal adverse events (Gawchik 2000).

The evidence available suggests that some intranasal steroids, such as beclomethasone dipropionate, may slow growth when used regularly for prolonged periods (Allen 2000). Studies of MFNS in adults and children with allergic rhinitis showed a lack of hypothalamic-pituitary axis suppression, no childhood growth suppression and were consistent with extremely low bioavailability of MFNS after intranasal administration (Brannan 1997; Davies 1997; Schenkel 2000). Reducing the systemic activity of nasal corticosteroids to the lowest possible level is desirable. Pharmacologically, newer drugs such as MFNS and fluticasone propionate appear to have substantially higher topical potencies, higher lipid solubilities and lower systemic bioavailabilities than older compounds. With respect to adverse events, emerging data suggest that MFNS and fluticasone may have less potential for systemic effects during prolonged use, particularly in children (Corren 1999). For short-term therapy of one to two months, the first-generation INCS (beclomethasone, triamcinolone, budesonide and flunisolide) could be used and MFNS and fluticasone (second-generation drugs) could be considered for long-term therapy. With the exception of fluticasone for children aged four years and older and MFNS for those aged three years and older, the other INCS including beclomethasone, triamcinolone, budesonide and flunisolide are approved for children six years and older. All are effective, so the major considerations are cost and safety (Galant 2001).

The decision on the best treatment for the specific patient should be based on the severity of symptoms, adapted individually, taking in consideration the existing evidence and the patient's preferences.

Potential biases in the review process

A small number of studies were included in this review and not all reported an adequate concealment of allocation to treatment.

Agreements and disagreements with other studies or reviews

The minor effects of inhaled corticosteroids for acute sinusitis observed in this review are supported by other existing evidence, including the evidence mentioned here.

AUTHORS' CONCLUSIONS

Implications for practice

Current evidence supports the use of intranasal corticosteroids for relief or improvement in clinical outcomes in acute uncomplicated sinusitis, although data are limited and modest effects were observed. There is no evidence that their use as a monotherapy or as an adjuvant therapy would be detrimental in therapeutic doses. The study population included in this review was diagnosed both clinically and by radiology or endoscopy and is not necessarily identical to the participants from the clinical practice where the diagnosis is usually based on clinical signs and symptoms alone.

Implications for research

Given the small number of trials, additional large, randomised, placebo-controlled trials are needed to evaluate the efficacy of intranasal corticosteroids for acute sinusitis. These trials should describe adequate allocation and concealment procedures, be double-blinded and include outcomes on work performance, return to work and functional status, as well as assessment of different doses of INCS, the optimal duration of treatment and the risk-benefit ratio. Studies on participants with milder forms of acute sinusitis receiving symptomatic treatment including INCS and without antibiotic therapy could also be conducted, taking into consideration the emergence of resistant organisms and adverse events that result from the irrational use of antibiotics.

REFERENCES

References to studies included in this review

Barlan 1997 *{published data only}*
Barlan IB, Erkan E, Bakir M, Berrak S, Basaran MM. Intranasal budesonide spray as an adjunct to oral antibiotic therapy for acute sinusitis in children. *Annals of Allergy, Asthma & Immunology* 1997;**78**:598–601.

Dolor 2001 *{published data only}*
Dolor RJ, Witsell DL, Hellkamp AS, Williams JW, Califf RM, Simel DL. Comparison of cefuroxime with or without intranasal fluticasone for the treatment of rhinosinusitis. The CAFFS Trial: a randomized controlled trial. *JAMA* 2001;**286**:3097–105.

Meltzer 2005 *{published data only}*
Meltzer EO, Bachert C, Staudinger H. Treating acute rhinosinusitis: comparing efficacy and safety of mometasone furoate nasal spray, amoxicillin and placebo. *Journal of Allergy and Clinical Immunology* 2005;**116**(6):1289–95.

Nayak 2002 *{published data only}*
Nayak AS, Settipane GA, Pedinoff A, Charous BL, Meltzer EO, Busse WW, et al.Effective dose range of mometasone furoate nasal spray in the treatment of acute rhinosinusitis. *Annals of Allergy, Asthma & Immunology* 2002;**89**:271–8.

References to studies excluded from this review

Bachert 2007 *{published data only}*
Bachert C, Meltzer EO. Effect of mometasone furoate nasal spray on quality of life of patients with acute rhinosinusitis. *Rhinology* 2007;**45**(3):190–6.

Gehanno 2000 *{published data only}*
Gehanno P, Beauvillain C, Bobin S, Chobaut JC, Desaulty A, Dubreuil C, et al.Short therapy with amoxicillin-clavulanate and corticosteroids in acute sinusitis: results of a multicentre study in adults. *Scandinavian Journal of Infectious Diseases* 2000;**32**:679–84.

Jurkiewicz 2004 *{published data only}*

Jurkiewicz D, Zielnik-Jurkiewicz B. Intranasal corticosteroid in the treatment of acute sinusitis. *5th European Congress of Oto-Rhino-Laryngology Head and Neck Surgery (EUFOS)*. 2004.

Meltzer 1993 *{published data only}*

Meltzer EO, Orgel HA, Backhaus JW, Busse WW, Druce HM, Metzger J, et al.Intranasal flunisolide spray as an adjunct to oral antibiotic therapy for sinusitis. *Journal of Allergy and Clinical Immunology* 1993;**92**:812–23.

Meltzer 2000 *{published data only}*

Meltzer EO, Charous BL, Busse WW, Zinreich SJ, Lorber RR, Danzig MR, et al.Added relief in the treatment of acute recurrent sinusitis with adjunctive mometasone furoate nasal spray. *Journal of Allergy and Clinical Immunology* 2000;**106**:630–7.

Quarnberg 1992 *{published data only}*

Quarnberg Y, Kantola O, Salo J, Toivanen M, Valtonen H, Vuori E. Influence of topical steroid treatment on maxillary sinusitis. *Rhinology* 1992;**30**:103–12.

Tutkun 1996 *{published data only}*

Tutkun A, Inanli S, Batman C, Uneri C, Sehitoglu MA. The impact of intranasal steroid as an adjunct to therapy for sinusitis. *Marmara Medical Journal* 1996;**9**(1):11–4.

Williamson 2007 *{published data only}*

Williamson IG, Rumsby K, Benge S, Moore M, Smith PW, Cross M, et al.Antibiotics and topical nasal steroid for treatment of acute maxillary sinusitis. *JAMA* 2007;**298**(21): 2487–96.

Yilmaz 2000 *{published data only}*

Yilmaz G, Varan B, Yilmaz T, Gurakan B. Intranasal budesonide spray as an adjunct to oral antibiotic therapy for acute sinusitis in children. *European Archives of Oto-rhino-laryngology* 2000;**257**(5):256–9.

Additional references

Ahovuo-Saloranta 2011

Ahovuo-Saloranta A, Rautakorpi UM, Borisenko OV, Liira H, Williams Jr JW, Makela M. Antibiotics for acute maxillary sinusitis. *Cochrane Database of Systematic Reviews* 2011, Issue 3. [DOI: 10.1002/14651858.CD000243.pub2]

Allen 2000

Allen DB. Do intranasal corticosteroids affect childhood growth?. *Allergy* 2000;**55**(Suppl 62):15–8.

Becker 2003

Becker DG. Medical treatment of sinusitis. *Journal of Long-term Effects of Medical Implants* 2003;**13**(3):195–205.

Benninger 1997

Benninger MS, Anon J, Mabry RL. The medical management of rhinosinusitis. *Otolaryngology - Head and Neck Surgery* 1997;**117**(3 Pt 2):S41–9.

Brannan 1997

Brannan MD, Herron JM, Affrime MB. Safety and tolerability of once-daily mometasone furoate aqueous nasal spray in children. *Clinical Therapeutics* 1997;**19**:1330–9.

Cable 2000

Cable BB, Wassmuth Z, Mann EA, Hommer D, Connely G, Klem C, et al.The effect of corticosteroids in the treatment of experimental sinusitis. *American Journal of Rhinology* 2000;**14**(4):217–22.

Contopoulos 2003

Contopoulos-Ioannidis DG, Ioannidis JP, Lau J. Acute sinusitis in children: current treatment strategies. *Paediatric Drugs* 2003;**5**(2):71–80.

Corren 1999

Corren J. Intranasal corticosteroids for allergic rhinitis: how do different agents compare?. *Journal of Allergy and Clinical Immunology* 1999;**104**(4 Pt 1):S144–9.

Davies 1997

Davies RJ, Nelson HS. Once-daily mometasone furoate nasal spray: efficacy and safety of a new intranasal glucocorticoid for allergic rhinitis. *Clinical Therapeutics* 1997;**19**:27–38.

Druce 1990

Druce HM. Adjuncts to medical management of sinusitis. *Otolaryngology - Head and Neck Surgery* 1990;**103**:880–3.

Druce 1991

Druce HM, Slavin RG. Sinusitis: critical need for further study. *Journal of Allergy and Clinical Immunology* 1991;**88**: 675–7.

Galant 2001

Galant SP, Wilkinson R. Clinical prescribing of allergic rhinitis medication in the preschool and young school-age child: what are the options?. *BioDrugs: Clinical Immunotherapeutics, Biopharmaceuticals and Gene Therapy* 2001;**15**(7):453–63.

Gawchik 2000

Gawchik SM, Saccar CL. A risk-benefit assessment of intranasal triamcinolone acetonide in allergic rhinitis. *Drug Safety* 2000;**23**(4):309–22.

Gwaltney 1994

Gwaltney JM, Phillips CD, Miller RD, Riker DK. Computed tomographic study of the common cold. *New England Journal of Medicine* 1994;**330**(1):25–30.

Gwaltney 1995

Gwaltney JM Jr, Jones JG, Kennedy DW. Medical management of sinusitis: educational goals and management guidelines: the International Conference on Sinus Disease. *Annals of Otology, Rhinology and Laryngology Supplement* 1995;**167**:22–30.

Higgins 2011

Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org. Chichester, UK: Wiley–Blackwell.

Juniper 1990

Juniper EF, Guyatt GH, O'Byrne PM, Viveiros M. Aqueous beclomethasone dipropionate nasal spray: regular versus "as required" use in the treatment of seasonal allergic rhinitis. *Journal of Allergy and Clinical Immunology* 1990;**86**:380–6.

Kaliner 1997

Kaliner MA, Osguthorpe JD, Fireman P, Anon J, Georgitis J, Davis ML, et al.Sinusitis: bench to bedside. Current findings, future directions. *Journal of Allergy and Clinical Immunology* 1997;**99**(Suppl):829–48.

Lefebvre 2011

Lefebvre C, Manheimer E, Glanville J. Chapter 6: Searching for studies. In: Higgins JPT, Green S editor(s). *Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0 [updated March 2011]. The Cochrane Collaboration. Available from www.cochrane-handbook.org*. Chichester: Wiley-Blackwell, 2011.

Little 2000

Little DR, Mann BL, Godbout CJ. How family physicians distinguish acute sinusitis from upper respiratory tract infections: a retrospective analysis. *Journal of the American Board of Family Practice* 2000;**13**(2):101–6.

Mucha 2003

Mucha SM, Baroody FM. Sinusitis update. *Current Opinion in Allergy and Clinical Immunology* 2003;**3**(1):33–8.

Mygind 1976

Mygind N, Prytz S, Sorensen H, Pedersen CB. Long term treatment of nasal polyps with beclomethasone dipropionate aerosol. Treatment and rationale. *Acta Otolaryngologica (Stockholm)* 1976;**82**:252–5.

Mygind 2001

Mygind N, Nielsen LP, Hoffmann HJ, Shukla A, Blumberga G, Dahl R, et al.Mode of action of intranasal corticosteroids. *Journal of Allergy and Clinical Immunology* 2001;**108**(Suppl 1):16–25.

Piccirillo 2001

Piccirillo JF, Mager D, Frisse M, Brophy RH, Goggin A. Impact of first-line vs. second-line antibiotics for the treatment of acute uncomplicated sinusitis. *JAMA* 2001; **286**(15):1849–56.

RevMan 2012

The Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager (RevMan). 5.2. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2012.

Sahay 1980

Sahay JN, Ibrahim NBN, Chatterjee SS, Nassar WY, Lodge KV, Jones CW. Long term study of flunisolide treatment in perennial rhinitis with special reference to nasal mucosal histology and morphology. *Clinical Allergy* 1980;**10**:451–7.

Scadding 2000

Scadding GK. Other anti-inflammatory uses of intranasal corticosteroids in upper respiratory inflammatory diseases. *Allergy* 2000;**55**(Suppl 62):19–23.

Schenkel 2000

Schenkel EJ, Skoner DP, Bronsky EA, Miller SD, Pearlman DS, Rooklin A. Absence of growth retardation in children with perennial allergic rhinitis after one year of treatment with mometasone furoate aqueous nasal spray. *Pediatrics* 2000;**105**:E22.

Seigel 1988

Seigel SC. Topical intranasal corticosteroid therapy in rhinitis. *Journal of Allergy and Clinical Immunology* 1988; **81**:984–91.

Shaikh 2012

Shaikh N, Wald ER, Pi M. Decongestants, antihistamines and nasal irrigation for acute sinusitis in children. *Cochrane Database of Systematic Reviews* 2012, Issue 9. [DOI: 10.1002/14651858.CD007909.pub3]

Shapiro 1992

Shapiro GG, Rachelefski GS. Introduction and definition of sinusitis. *Journal of Allergy and Clinical Immunology* 1992; **90**:417–8.

Shrum 2001

Shrum KM, Grogg SE, Barton P, Shaw HH, Dyer RR. Sinusitis in children: the importance of diagnosis and treatment. *Journal of the American Osteopathic Association* 2001;**101**(Suppl 5):8–13.

Slavin 2005

Slavin RG, Spector SL, Bernstein IL, Kaliner MA, Kennedy DW, Virant FS, et al.The diagnosis and management of sinusitis: a practice parameter update. *Journal of Allergy and Clinical Immunology* 2005;**116**(Suppl 6):13–47.

Snow 2001

Snow V, Mottur-Pilson C, Hickner JM. Principles of appropriate antibiotic use for acute sinusitis in adults. *Annals of International Medicine* 2001;**134**(6):495–7.

Spector 1998

Spector SL, Bernstein IL, Li JT, Berger WE, Kaliner MA, Schuller DE, et al.Parameters for the diagnosis and management of sinusitis. *Journal of Allergy and Clinical Immunology* 1998;**102**(Suppl):107–44.

Venekamp 2011

Venekamp RP, Thompson MJ, Hayward G, Heneghan CJ, Del Mar CB, Perera R, et al.Systemic corticosteroids for acute sinusitis. *Cochrane Database of Systematic Reviews* 2011, Issue 12. [DOI: 10.1002/14651858.CD008115.pub2]

Wald 1988

Wald ER. Sinusitis in children. *Pediatric Infectious Disease Journal* 1988;**7**(Suppl 11):150–3.

Williams 1993

Williams JW Jr, Simel DL. Practice variation for managing acute sinusitis. *Clinical Research* 1993;**41**:566A.

Winstead 2003

Winstead W. Rhinosinusitis. *Primary Care* 2003;**30**(1): 137–54.

Winther 1990

Winther B, Gwaltney JM Jr. Therapeutic approach to sinusitis: antiinfectious therapy as the baseline of

management. *Otolaryngology - Head and Neck Surgery* 1990;
103(5 (Pt 2)):876–9.

Zeiger 1992
Zeiger RS. Prospects for ancillary treatment of sinusitis in
the 1990s. *Journal of Allergy and Clinical Immunology* 1992;
90:478–95.

References to other published versions of this review

Zalmanovici 2007
Zalmanovici A, Yaphe J. Steroids for acute sinusitis.
Cochrane Database of Systematic Reviews 2007, Issue 2.

[DOI: 10.1002/14651858.CD005149.pub2]

Zalmanovici 2009
Zalmanovici A, Yaphe J. Intranasal steroids for acute
sinusitis. *Cochrane Database of Systematic Reviews* 2009,
Issue 4. [DOI: 10.1002/14651858.CD005149.pub3]

Zalmanovici Trestioreanu 2011
Zalmanovici Trestioreanu A, Yaphe J. Intranasal
steroids for acute sinusitis. *Cochrane Database of
Systematic Reviews* 2011, Issue 8. [DOI: 10.1002/
14651858.CD005149.pub3]

* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

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

Barlan 1997

Methods	Randomised: method of randomisation not mentioned Allocation concealment not mentioned Double-blind: yes Intention-to-treat not mentioned Follow-up described 151 recruited; 89 (59%) completed study; 41% drop-out Design: parallel
Participants	N = 89; 42 male, 47 female Age 1 to 15 years Inclusion criteria: 2 of 3 major criteria - purulent nasal discharge, cough, purulent pharyngeal drainage or 1 major and 2 minor criteria: facial pain, periorbital oedema, earache, tooth pain, sore throat, headache, increased wheeze, fever, foul breath for more than 7 days and Rx criteria Water radiographs at the beginning of study positive if complete opacification or maxillary mucoperiosteal thickening more than 4 mm. 79 participants had positive Rx Exclusion criteria: history of allergic rhinitis, asthma, recurrent/chronic sinusitis Baseline characteristics: similar in both groups, no significant differences Patients maintained daily symptom cards and were examined by the same physician each week. Symptom scores were evaluated by a scale from 0 to 3
Interventions	Tx group: budesonide 50 µg bid nasal spray to each nostril, N = 43 C group: placebo nasal spray bid, N = 46 All participants in both groups received amoxicillin-clavulanate potassium 40 mg/kg/day tid Duration: 3 weeks
Outcomes	Difference in weekly symptom scores for cough and nasal discharge in the first, second and third week of the study in both groups, as difference between groups or change from baseline Relapse: results were reported as medians of scores using non-parametric tests because a wide range of scores without normal distribution
Notes	Marmara University Hospital Outpatient Clinic patients enrolled from November 1993 to October 1994 Informed consent signed by all parents. 151 patients enrolled, 89 completed study, 62 dropped out, no separate data for both groups Reasons for drop-outs: non-compliance with weekly visits or not recording daily symptoms

Risk of bias

Bias	Authors' judgement	Support for judgement

Barlan 1997 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Randomised, method not mentioned
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No separate data for groups, ITT not mentioned
Selective reporting (reporting bias)	Low risk	No evidence of reporting bias
Other bias	Unclear risk	-
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	-

Dolor 2001

Methods	Multicentre randomisation - permuted blocks scheme stratified by site with a block size of 4 generated using SAS version 6.12 Allocation concealment - study kits administered sequentially by blinding site personnel to block size Blinding: yes Intention-to-treat: yes Follow-up described: yes 88 (93%) completed study Design: parallel
Participants	N = 95; 30 men, 65 women Age 30 to 50; median age 39 years Inclusion criteria: older than 18 years, history of recurrent sinusitis or chronic rhinitis and clinical evidence of acute sinusitis confirmed Rx or by nasal endoscopy Diagnosis of acute sinusitis: clinical criteria - participants with 2 of the 5 following symptoms present were enrolled: headache, facial pain, nasal congestion, thick coloured nasal discharge, olfactory disturbance Rx criteria: air-fluid level, mucosal thickening or opacification of sinus Exclusion criteria: previous sinus surgery, sinus lavage in the past 7 days, nasal polyposis, recurrent epistaxis, chronic bacterial sinusitis with failure of antibiotic therapy, INCS use within past 14 days, chronic use of corticosteroids or immunosuppressives, immunocompromised, allergy to penicillin/cephalosporins, participants without a telephone, pregnant, nursing women Baseline characteristics - similar in both groups, no significant differences Participants assessed at baseline, 10, 21, 56 days by diary records and telephone follow-up

Dolor 2001 *(Continued)*

Interventions	Tx group: nasal spray fluticasone propionate 2 puffs (total dose 200 μg) once daily in each nostril; N = 47
	C group: nasal spray placebo 2 puffs once daily in each nostril; N = 48
	All participants in both groups received 2 puffs xylometazoline hydrochloride in each nostril twice daily 10 minutes before the study nasal spray and 250 mg cefuroxime axetil twice daily for 10 days
	Duration of study: 21 days
	Follow-up: 8 weeks
	Allowed to continue: NSAIDs, analgesics, immunotherapy for allergies, orally inhaled corticosteroids
	Not permitted during study: oral decongestants, mucolytics, corticosteroids oral or parenteral, antihistamines, immunosuppressives
	Sinus lavage or sinus surgery was discouraged during the first 3 weeks of the trial, antibiotic use in the past 7 days or 21 days if longer half-life was not permitted
	Compliance with Tx: assessed by a standardised form given to patients for recording daily symptoms, Tx, adverse events, work attendance. 94% completed study Tx without difference between groups
Outcomes	Proportion of patients with clinical success (cured or much improved) at 10, 21, 56 days on telephone follow-up
	Time to clinical success differences over time in sinusitis and quality of life scores
	Level of work performance
	Total number of hours lost from work
	Recurrences
Notes	Study conducted between October 1998 to April 2000 at 22 sites (12 primary care and 10 otolaryngology)
	Equal proportions of participants from primary care and otolaryngology practices in both treatment arms
	All study sites received standardised instructions for conducting the study
	Study progress monitored by a research associate
	Patients assessed symptoms on numeric scales and received booklets with specific instructions for use of nasal spray
	High agreement between patient-recorded and interviewer-obtained symptoms
	Drop-outs:
	Tx group: 1 - rash, 1 - unknown, 1 - lost to follow-up
	44 completed 21-day Tx and telephone follow-up, 36 completed diary, 46 included in primary analysis
	C group: 1 - withdrew, 2 - switched to different antibiotics
	45 completed 21-day Tx, 44 completed telephone follow-up, 32 completed diary, 46 included in primary analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	See methods

Dolor 2001 (*Continued*)

Allocation concealment (selection bias)	Low risk	See methods
Incomplete outcome data (attrition bias) All outcomes	Low risk	See methods
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting
Other bias	Low risk	-
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	See methods
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	-

Meltzer 2005

Methods	Multicentre randomisation 1:1:1:1 ratio to 1 of 4 arms by computer-generated code Allocation concealment: not mentioned Double-blind: yes Intention-to-treat: yes Follow-up described 10% drop-out in Tx phase, 95% completed follow-up phase Design: parallel
Participants	N = 981; 338 men, 643 women Age 12 to 76 years Inclusion criteria: age more than 12 years with clinical criteria for acute sinusitis; MSS more than 5 but less than 12 at baseline, assessed by participant and investigator and no more than 3/5 symptoms rated severe (rhinorrhoea, PND nasal congestion, stuffiness, sinus headache and facial pain on pressure) adding cough to the TSS Exclusion criteria: fulminant bacterial rhinosinusitis, chronic rhinosinusitis, nasal/sinus surgery within the last 6 months for this condition, otitis, atrophic rhinitis, nasal polyps, symptomatic seasonal allergic rhinitis, allergy to corticosteroids Asthmatic participants needed to be stable last 30 days and FEV1 more than 65% last 3 months before screening Rhinoscopic examination was performed at all visits Participants were assessed at baseline days 8, 15, 29 and monitored by telephone on days 3 to 4. Response to Tx evaluated by participant and investigator as scores for symptoms on a scale from 0 to 3 Baseline characteristics similar for all the arms
Interventions	4 groups Tx groups: 1. MFNS 200 µg once daily nasal spray + placebo nasal spray once daily + placebo capsules tid; N = 243

Meltzer 2005 (*Continued*)

	2. MFNS 200 µg nasal spray bid + placebo capsules tid; N = 235 3. amoxicillin 500 mg tid for 10 days + placebo nasal spray bid; N = 251 C group: placebo nasal spray bid + placebo capsules tid; N = 252 Duration of study: 15 days Capsules given for 10 days Follow-up: 14 days Not allowed during study: nasal saline, nasal cromolyn sodium, ipratropium bromide, corticosteroids (excluding oral inhaled corticosteroids for mild/moderate asthma), antihistamines, decongestants, leukotriene pathway modificants, analgesics, NSAID Compliance assessed at days 8 and 15 by questioning whether drug had been taken Each participant received at least 1 dose of study drug
Outcomes	Mean MSS Mean TSS Individual scores Time to onset of action Global response to Tx Adverse events Disease recurrence Tx failure (worsening or not improvement in symptoms during the Tx phase)
Notes	Study conducted at 71 medical centres in 14 countries from January to September 2003 Drop-outs: during the Tx phase in the 200 µg, 400 µg MFNS, amoxicillin, placebo were 9%, 9%, 8%, 13% Reasons for discontinuation: adverse events, Tx failure, loss to follow-up, did not wish to continue, non-compliance with protocol, did not meet protocol criteria for entry

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	See methods
Allocation concealment (selection bias)	Unclear risk	See methods
Incomplete outcome data (attrition bias) All outcomes	Low risk	See methods
Selective reporting (reporting bias)	Low risk	-
Other bias	Unclear risk	-
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	See methods

Meltzer 2005 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	-

Nayak 2002

Methods	Multicentre, randomised; method of randomisation not mentioned Allocation concealment not mentioned Double-blind: yes Follow-up described: yes 864 (89%) participants included in the primary efficacy analysis Design: parallel
Participants	N = 967; 402 men, 565 women Age 8 to 78 years Inclusion criteria: acute episode of rhinosinusitis, at least 1 moderate/severe nasal symptom (these may include purulent rhinorrhoea, stuffiness/congestion, post-nasal drip, sinus headache, facial pain, cough), purulent rhinorrhoea present, sinusitis confirmed by a CT scan, which is read by a radiologist at each study site at baseline, a total symptom score more than 6 Exclusion criteria: nasal polyps, cystic fibrosis, Kartagener syndrome, expected immediate sinus or nasal surgery, glaucoma, history of subcapsular cataracts, clinical significant diseases Symptoms evaluated at baseline (day 1) and day 21 by patient and investigator by scales. Patients evaluated at baseline, 15, 21 days CT scans of paranasal sinuses at baseline and 21 days evaluated by an independent blinded radiologist Similar baseline characteristics and baseline symptoms scores in all 3 groups Patients recorded symptom scores, adverse events and use of medication twice daily
Interventions	3 groups Tx groups: 1 MFNS 400 µg nasal spray twice daily; N = 324 2 MFNS 200 µg nasal spray twice daily; N = 318 C group: Matching placebo nasal spray twice daily; N = 325 All participants in all groups received amoxicillin-clavulanate potassium 875 mg twice daily for 21 days Not allowed during study: any form of corticosteroid, nasal decongestants, antihistamines Washout period before the baseline visit for previous use of antibiotics, intranasal or systemic corticosteroids, decongestants Adherence to therapy assessed by weighing the nasal spray dosing containers without patients' knowledge
Outcomes	Improvement in total symptoms score Improvement in individual symptom score Overall response to treatment: proportion of participants with complete or marked relief Onset of relief

Nayak 2002 *(Continued)*

	Evaluation of changes in CT scans of sinuses Adverse events
Notes	Outpatients from 61 Tx centres in the US 967 participants randomised, 103 participants (11%) not included in analysis because CT did not confirm sinusitis and excluded post-randomisation, diary data not available, less than 80% compliance with Tx, less than 7 days Tx (32, 36, 35 in the MFNS 400, 200 µg and placebo groups) Reasons for exclusion or discontinuation were evenly distributed among the groups Physician evaluation of symptoms at day 21 was consistent with patient-recorded evaluation

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	See methods
Allocation concealment (selection bias)	Unclear risk	See methods
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	See notes
Selective reporting (reporting bias)	Unclear risk	-
Other bias	Unclear risk	-
Blinding of participants and personnel (performance bias) All outcomes	Low risk	See methods
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	-

bid: twice daily
C: control
CT: computed tomography
FEV1: forced expiratory volume in one second
INCS: intranasal corticosteroid
ITT: intention-to-treat
MFNS: mometasone furoate
MSS: major symptom score
NSAID: non-steroidal anti-inflammatory drugs
PND: post-nasal drip
Rx: radiological
tid: three times daily
TSS: total symptom score

Tx: treatment

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

Study	Reason for exclusion
Bachert 2007	Study on quality of life. Outcome for a subset of patients from one of the included studies (Meltzer 2005)
Gehanno 2000	Allocation: randomised, parallel Participants: N = 433 adults with confirmed acute sinusitis Intervention: amoxicillin-clavulanate and methylprednisolone or placebo per oral administration No intranasal steroids used
Jurkiewicz 2004	Abstract and full paper not available
Meltzer 1993	Allocation: randomised, parallel Participants: N = 175 participants 14 years or older with confirmed acute or chronic sinusitis Intervention: amoxicillin-clavulanate potassium combined with nasal spray of either flunisolide or placebo No separate arms for acute and chronic sinusitis reported
Meltzer 2000	Missing data - number randomised, numbers included in analyses, drop-outs and reasons for drop-out. The numbers reported do not add up to 100%. An email was sent to the author but there was no reply
Quarnberg 1992	Allocation: randomised, parallel Participants: N = 40 participants 16 years or older with confirmed recurrent or chronic sinusitis Intervention: erythromycin and either budesonide or placebo aerosol Separate arms for acute recurrent and chronic sinusitis were not reported
Tutkun 1996	Missing data - not mentioned acute/chronic sinusitis, diagnostic criteria not reported, drop-outs not reported. Email was sent to the author but there was no reply
Williamson 2007	Inclusion criteria for the review were not met
Yilmaz 2000	Allocation: randomised, parallel Participants: 52 children with confirmed acute sinusitis Intervention: cefaclor and either oral pseudoephedrine or intranasal budesonide No placebo used in the control group

D A T A   A N D   A N A L Y S E S

Comparison 1.   Intranasal corticosteroids versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Proportion of participants with resolution of symptoms or improved (MFNS 400 μg daily)	2	1130	Risk Ratio (M-H, Fixed, 95% CI)	1.10 [1.02, 1.18]
2 Proportion of participants with resolution of symptoms or improved (MFNS 200 μg daily)	2	590	Risk Ratio (M-H, Fixed, 95% CI)	1.04 [0.98, 1.11]
3 Proportion of participants with resolution of symptoms or improved (combined MFNS 200, 400 and 800 μg daily)	3	1792	Risk Ratio (M-H, Fixed, 95% CI)	1.11 [1.04, 1.18]
4 Number of participants that dropped out from the study (MFNS 400 μg daily)	2	1130	Risk Ratio (M-H, Fixed, 95% CI)	0.86 [0.61, 1.20]
5 Number of participants that dropped out from the study (MFNS 200 μg daily)	2	590	Risk Ratio (M-H, Fixed, 95% CI)	0.75 [0.46, 1.21]
6 Number of participants that dropped out from the study (combined MFNS 200, 400 and 800 μg daily)	3	1792	Risk Ratio (M-H, Fixed, 95% CI)	0.85 [0.64, 1.12]
7 Relapse (combined 200 and 400 μg daily)	2	825	Risk Ratio (M-H, Fixed, 95% CI)	0.71 [0.44, 1.15]

Analysis 1.1. Comparison 1 Intranasal corticosteroids versus placebo, Outcome 1 Proportion of participants with resolution of symptoms or improved (MFNS 400 µg daily).

Review: Intranasal steroids for acute sinusitis

Comparison: 1 Intranasal corticosteroids versus placebo

Outcome: 1 Proportion of participants with resolution of symptoms or improved (MFNS 400 g daily)

Study or subgroup	MFNS 400 g n/N	Placebo n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Meltzer 2005	224/235	225/252	■	57.8 %	1.07 [1.01, 1.12]
Nayak 2002	178/318	160/325	■	42.2 %	1.14 [0.98, 1.32]
Total (95% CI)	**553**	**577**		**100.0 %**	**1.10 [1.02, 1.18]**

Total events: 402 (MFNS 400 g), 385 (Placebo)
Heterogeneity: Chi² = 1.30, df = 1 (P = 0.25); I² =23%
Test for overall effect: Z = 2.60 (P = 0.0093)
Test for subgroup differences: Not applicable

```
          0.001 0.01  0.1    1    10  100  1000
          Favours placebo    Favours MFNS 400  g
```
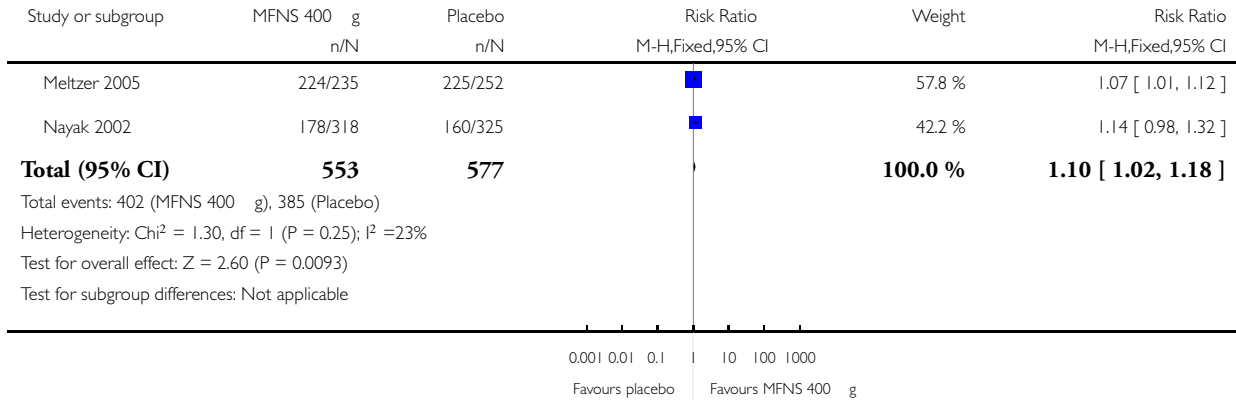
Analysis 1.2. Comparison 1 Intranasal corticosteroids versus placebo, Outcome 2 Proportion of participants with resolution of symptoms or improved (MFNS 200 µg daily).

Review: Intranasal steroids for acute sinusitis

Comparison: 1 Intranasal corticosteroids versus placebo

Outcome: 2 Proportion of participants with resolution of symptoms or improved (MFNS 200 g daily)

Study or subgroup	MFNS 200 g n/N	Placebo n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Dolor 2001	39/47	30/48	■	11.8 %	1.33 [1.03, 1.71]
Meltzer 2005	218/243	225/252	■	88.2 %	1.00 [0.95, 1.07]
Total (95% CI)	**290**	**300**		**100.0 %**	**1.04 [0.98, 1.11]**

Total events: 257 (MFNS 200 g), 255 (Placebo)
Heterogeneity: Chi² = 4.92, df = 1 (P = 0.03); I² =80%
Test for overall effect: Z = 1.32 (P = 0.19)
Test for subgroup differences: Not applicable

```
          0.001 0.01  0.1    1    10  100  1000
          Favours placebo    Favours MFNS 200  g
```
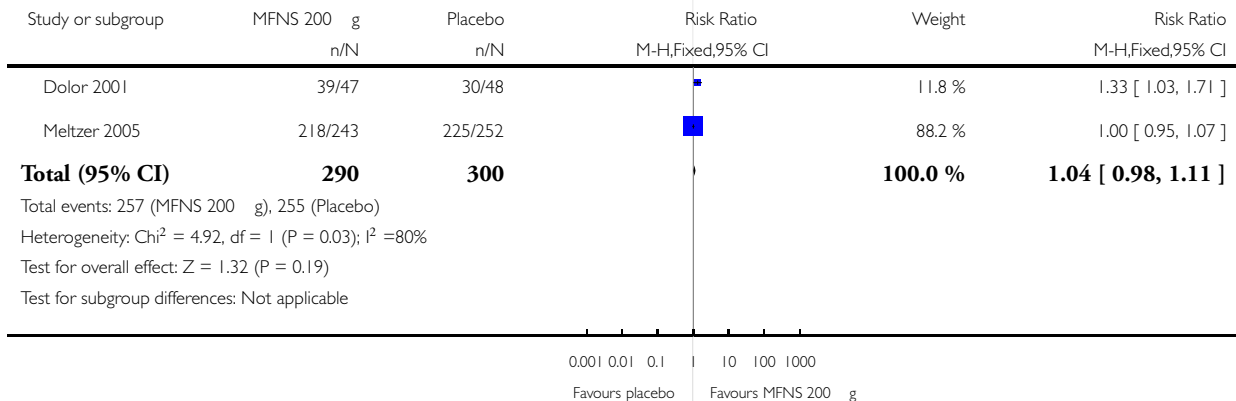
Analysis 1.3. Comparison 1 Intranasal corticosteroids versus placebo, Outcome 3 Proportion of participants with resolution of symptoms or improved (combined MFNS 200, 400 and 800 µg daily).

Review: Intranasal steroids for acute sinusitis

Comparison: 1 Intranasal corticosteroids versus placebo

Outcome: 3 Proportion of participants with resolution of symptoms or improved (combined MFNS 200, 400 and 800   g daily)

Study or subgroup	MFNS combined 200,400,800 n/N	Placebo n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Dolor 2001	39/47	30/48		5.5 %	1.33 [1.03, 1.71]
Meltzer 2005	442/478	225/252		54.9 %	1.04 [0.99, 1.09]
Nayak 2002	371/642	160/325		39.6 %	1.17 [1.03, 1.34]
Total (95% CI)	**1167**	**625**		**100.0 %**	**1.11 [1.04, 1.18]**

Total events: 852 (MFNS combined 200,400,800), 415 (Placebo)

Heterogeneity: Chi² = 9.55, df = 2 (P = 0.01); I² =79%

Test for overall effect: Z = 3.26 (P = 0.0011)

Test for subgroup differences: Not applicable

```
       0.001 0.01  0.1    I    10  100  1000
          Favours placebo      Favours MFNS 200,400,800
```

Analysis 1.4. Comparison 1 Intranasal corticosteroids versus placebo, Outcome 4 Number of participants that dropped out from the study (MFNS 400 µg daily).

Review: Intranasal steroids for acute sinusitis

Comparison: 1 Intranasal corticosteroids versus placebo

Outcome: 4 Number of participants that dropped out from the study (MFNS 400 g daily)

Study or subgroup	MFNS 400 g n/N	Placebo n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Meltzer 2005	20/235	33/252		47.9 %	0.65 [0.38, 1.10]
Nayak 2002	36/318	35/325		52.1 %	1.05 [0.68, 1.63]
Total (95% CI)	**553**	**577**		**100.0 %**	**0.86 [0.61, 1.20]**

Total events: 56 (MFNS 400 g), 68 (Placebo)

Heterogeneity: Chi² = 1.89, df = 1 (P = 0.17); I² =47%

Test for overall effect: Z = 0.89 (P = 0.37)

Test for subgroup differences: Not applicable

```
       0.1  0.2  0.5   1    2    5   10
    Favours MFNS 400  g      Favours placebo
```
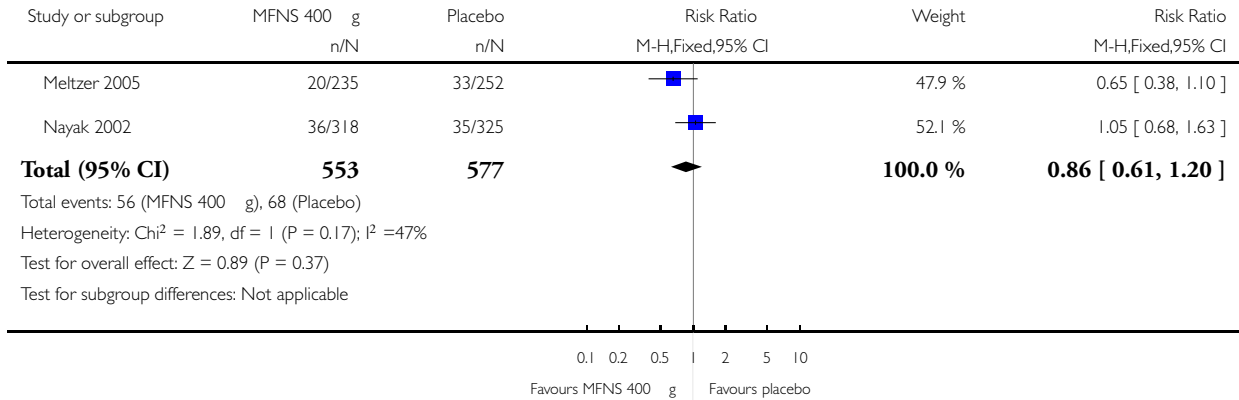
Analysis 1.5. Comparison 1 Intranasal corticosteroids versus placebo, Outcome 5 Number of participants that dropped out from the study (MFNS 200 µg daily).

Review: Intranasal steroids for acute sinusitis

Comparison: 1 Intranasal corticosteroids versus placebo

Outcome: 5 Number of participants that dropped out from the study (MFNS 200 g daily)

Study or subgroup	MFNS 200 g n/N	Placebo n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Dolor 2001	3/47	3/48		8.4 %	1.02 [0.22, 4.81]
Meltzer 2005	23/243	33/252		91.6 %	0.72 [0.44, 1.19]
Total (95% CI)	**290**	**300**		**100.0 %**	**0.75 [0.46, 1.21]**

Total events: 26 (MFNS 200 g), 36 (Placebo)

Heterogeneity: Chi² = 0.17, df = 1 (P = 0.68); I² =0.0%

Test for overall effect: Z = 1.19 (P = 0.23)

Test for subgroup differences: Not applicable

```
       0.1  0.2  0.5   1    2    5   10
    Favours MFNS 200  g      Favours placebo
```

Analysis 1.6. Comparison 1 Intranasal corticosteroids versus placebo, Outcome 6 Number of participants that dropped out from the study (combined MFNS 200, 400 and 800 µg daily).

Review: Intranasal steroids for acute sinusitis

Comparison: 1 Intranasal corticosteroids versus placebo

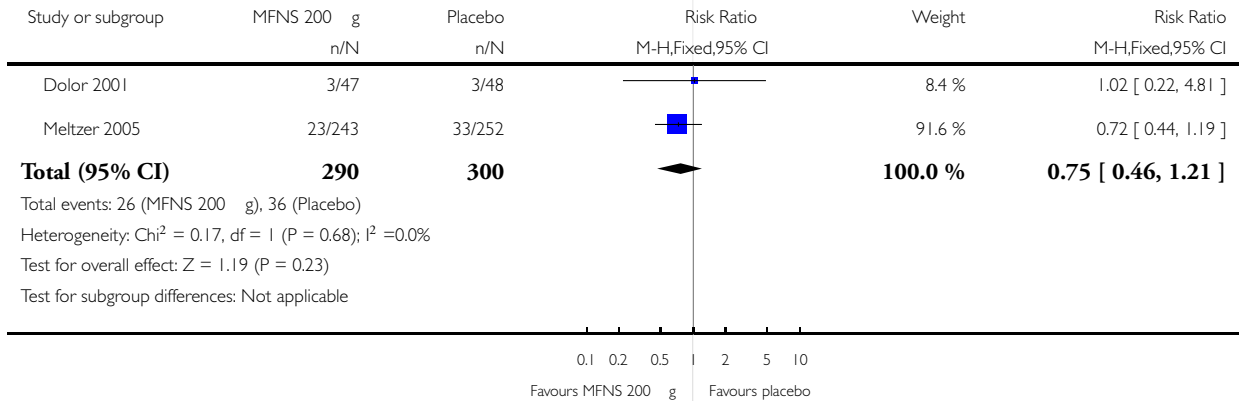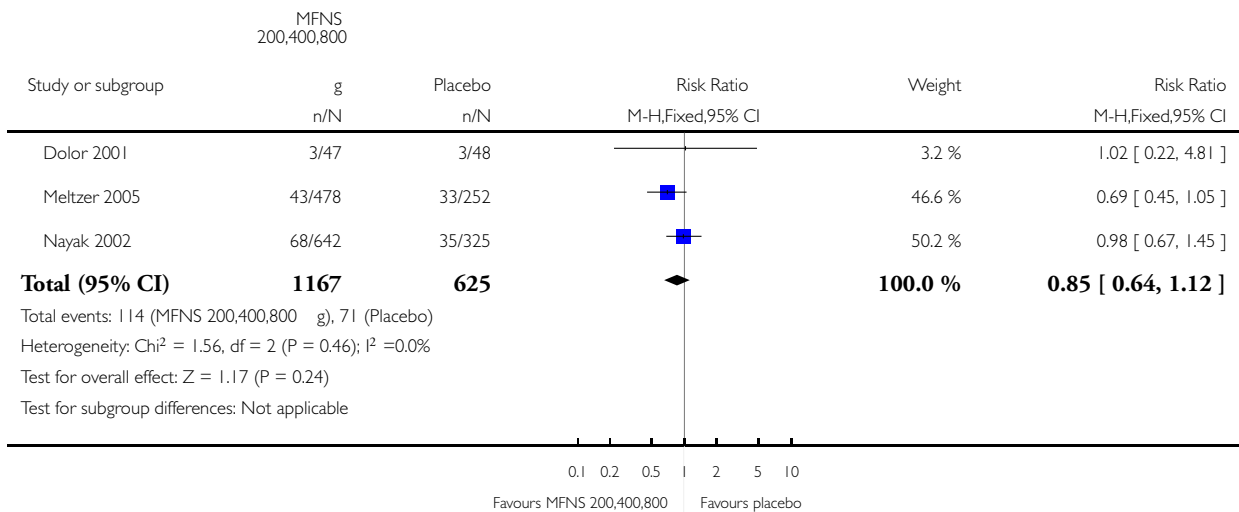Outcome: 6 Number of participants that dropped out from the study (combined MFNS 200, 400 and 800 g daily)

Study or subgroup	MFNS 200,400,800 g n/N	Placebo n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Dolor 2001	3/47	3/48		3.2 %	1.02 [0.22, 4.81]
Meltzer 2005	43/478	33/252		46.6 %	0.69 [0.45, 1.05]
Nayak 2002	68/642	35/325		50.2 %	0.98 [0.67, 1.45]
Total (95% CI)	**1167**	**625**		**100.0 %**	**0.85 [0.64, 1.12]**

Total events: 114 (MFNS 200,400,800 g), 71 (Placebo)

Heterogeneity: Chi² = 1.56, df = 2 (P = 0.46); I² =0.0%

Test for overall effect: Z = 1.17 (P = 0.24)

Test for subgroup differences: Not applicable

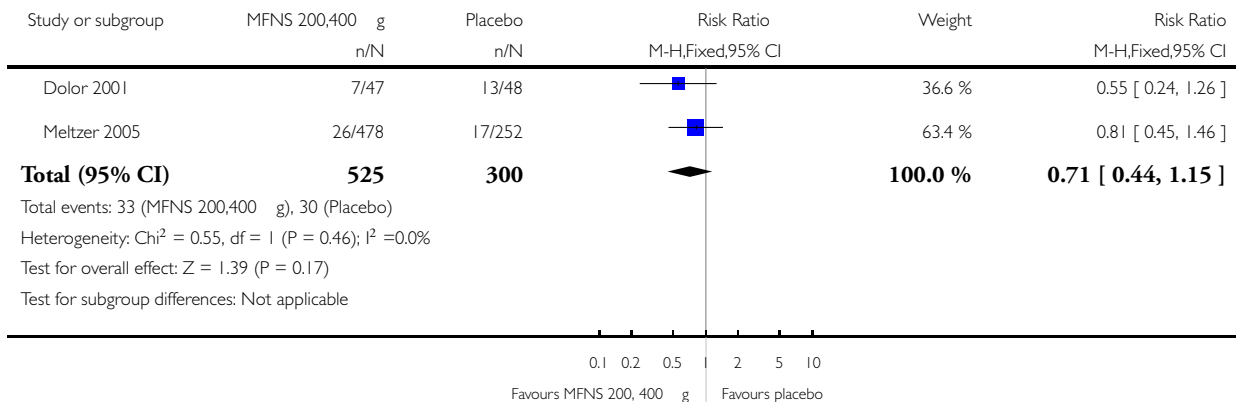0.1 0.2 0.5 1 2 5 10

Favours MFNS 200,400,800   Favours placebo

Analysis 1.7. Comparison 1 Intranasal corticosteroids versus placebo, Outcome 7 Relapse (combined 200 and 400 μg daily).

Study or subgroup	MFNS 200,400 g n/N	Placebo n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Dolor 2001	7/47	13/48		36.6 %	0.55 [0.24, 1.26]
Meltzer 2005	26/478	17/252		63.4 %	0.81 [0.45, 1.46]
Total (95% CI)	**525**	**300**		**100.0 %**	**0.71 [0.44, 1.15]**

Total events: 33 (MFNS 200,400 g), 30 (Placebo)
Heterogeneity: Chi^2 = 0.55, df = 1 (P = 0.46); I^2 =0.0%
Test for overall effect: Z = 1.39 (P = 0.17)
Test for subgroup differences: Not applicable

0.1 0.2 0.5 1 2 5 10
Favours MFNS 200, 400 g   Favours placebo

ADDITIONAL TABLES

Table 1. Adverse events

Study	Intervention	Side effects	Comments
Dolor 2001	Fluticasone propionate 2 puffs - total dose 200 μg or placebo nasal spray once daily in addition to 250 mg cefuroxime axetil orally twice daily and 2 puffs of xylometazoline hydrochloride twice daily	Headache, bloody nose, vaginal itching, yeast infection, nausea, stomach irritation, diarrhoea, increased congestion, hay fever, light-headed, sore throat, thirsty, itching, rash, cough, fatigue, metallic taste, felt dried out, nasal tissue felt inflamed	No serious unexpected adverse events reported Any adverse event - 37% in the fluticasone group versus 20% in the placebo group (P value = 0.7) no statistical significant difference Adverse events could be attributed also to the co-treatment
Nayak 2002	Amoxicillin-clavulanate potassium 875 mg twice daily orally and MFNS 200, 400 μg or placebo nasal spray twice daily	Epistaxis was the most frequently reported adverse event Nasal burning, irritation and headache occurred in less than 2% of any treatment group	Treatment well-tolerated, adverse events similar for all 3 arms of mild/moderate intensity: 12%, 15%, 15% in the MFNS 400, 800 μg and placebo arms 50 patients discontinued treatment

Table 1. Adverse events *(Continued)*

			because of adverse events, most commonly diarrhoea and nausea due to the antibiotic and were equally distributed among groups. Epistaxis, nasal burning, irritation or infection were not a cause for discontinuation of treatment
Barlan 1997	Budesonide 50 μg or placebo nasal spray to each nostril bid in addition to amoxicillin clavulanate potassium 40 mg/kg/day tid	Rash after 1 week attributed to the antibiotic in 1 subject that was switched to cefaclor	No specific adverse events related to the INCS use were reported
Meltzer 2005	MFNS 200 μg once daily or twice daily nasal spray Amoxicillin 500 mg tid Placebo nasal spray and capsules	Headache and epistaxis were most common reported	Most adverse events were mild or moderate with a similar incidence among treatment groups: 36.2%, 35.4%, 33.5% and 38.1% with MFNS 200 μg, 400 μg, amoxicillin and placebo 1%, 3%, 2% and 2% of participants discontinued treatment because of adverse events in the 200 μg, 400 μg INCS, antibiotic and placebo arms

bid: twice daily
INCS: intranasal corticosteroid
MFNS: mometasone furoate
tid: three times daily

APPENDICES

Appendix 1. Previous search strategy

For this update we searched the Cochrane Central Register of Controlled Trials (CENTRAL) 2011, Issue 2, part of *The Cochrane Library*, www.thecochranelibrary.com (accessed 25 May 2011), which contains the Cochrane Acute Respiratory Infections Group's Specialised Register; MEDLINE (September 2008 to May week 2, 2011) and Embase.com (October 2008 to May 2011). See Appendix 1 for details of previous searches.

Previously we searched the Cochrane Central Register of Controlled Trials (*The Cochrane Library* 2008, Issue 4) which contains the Cochrane Acute Respiratory Infections Group's Specialised Register, MEDLINE (January 1966 to October 2008), EMBASE (1990 to October 2008) and bibliographies of included studies.

MEDLINE was searched using the following keywords and MeSH terms in conjunction with the highly sensitive search strategy designed by The Cochrane Collaboration for identifying randomised controlled trials (Lefebvre 2008). The same strategy was used to search CENTRAL and adapted to search EMBASE.

MEDLINE (OVID)
1 exp SINUSITIS/

2 sinusit*.tw.
3 rhinosinusit*.tw.
4 or/1-3
5 exp STEROIDS/
6 steroid*.tw.
7 exp Adrenal Cortex Hormones/
8 adrenal cortex hormone*.tw.
9 exp Anti-Inflammatory Agents/
10 anti-inflammat*.tw.
11 corticosteroid*.tw.
12 or/5-11
13 exp Administration, Intranasal/
14 exp Administration, Topical/
15 (nasal* or intranasal* or topical*).tw.
16 or/13-15
17 12 and 16
18 4 and 17

Appendix 2. Embase.com search strategy

#24 #16 AND #23
#23 #22 NOT #21
#22 #17 OR #18
#21 #19 NOT #20
#20 'human'/de
#19 'animal'/de OR 'nonhuman'/de OR 'animal experiment'/de
#18 random*:ab,ti OR placebo*:ab,ti OR crossover*:ab,ti OR 'cross over':ab,ti OR allocat*:ab,ti OR trial:ti OR ((doubl* OR singl*) NEAR/1 blind*):ab,ti
#17 'randomized controlled trial'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp
#16 #4 AND #11 AND #15
#15 #12 OR #13 OR #14
#14 nasal*:ab,ti OR intranasal*:ab,ti OR topical*:ab,ti
#13 'topical drug administration'/de
#12 'intranasal drug administration'/de
#11 #5 OR #6 OR #7 OR #8 OR #9 OR #10
#10 'adrenal cortex hormone':ab,ti OR 'adrenal cortex hormones':ab,ti
#9 'anti-inflammatory':ab,ti OR 'anti-inflammatories':ab,ti OR antiinflammat*:ab,ti OR 'anti inflammatory':ab,ti OR 'anti inflammatories':ab,ti
#8 'antiinflammatory agent'/exp
#7 'corticosteroid'/exp
#6 steroid*:ab,ti
#5 'steroid'/exp
#4 #1 OR #2 OR #3
#3 rhinosinusit*:ab,ti OR nasosinusit*:ab,ti
#2 sinusit*:ab,ti
#1 'sinusitis'/exp

WHAT'S NEW

Last assessed as up-to-date: 22 May 2013.

Date	Event	Description
22 May 2013	New citation required but conclusions have not changed	Our conclusions remain unchanged.
22 May 2013	New search has been performed	Searches updated. No new trials were identified in this update

HISTORY

Protocol first published: Issue 1, 2005

Review first published: Issue 2, 2007

Date	Event	Description
25 May 2011	New citation required but conclusions have not changed	Searches updated. No new studies found for inclusion or exclusion. The conclusions remain unchanged
3 June 2010	Amended	Contact details updated.
28 October 2008	New citation required but conclusions have not changed	Two trials identified in the updated search and three trials for which data are not available were added to the excluded studies list (Bachert 2007; Jurkiewicz 2004; Meltzer 2000; Tutkun 1996; Williamson 2007).
28 October 2008	New search has been performed	Searches conducted.

CONTRIBUTIONS OF AUTHORS

Dr Anca Zalmanovici wrote the review, searched the literature, selected the studies to be included, assessed their quality, entered the data into RevMan 2012, wrote the methods, results and discussion sections and updated the review.

Dr John Yaphe searched the literature, was an independent assessor in selecting trials to be included, assessed the quality of the trials, wrote the discussion section and edited the review.

DECLARATIONS OF INTEREST

None known.

NOTES

INDEX TERMS
Medical Subject Headings (MeSH)

Acute Disease; Administration, Intranasal; Adrenal Cortex Hormones [*administration & dosage]; Randomized Controlled Trials as Topic; Sinusitis [*drug therapy]

MeSH check words

Adult; Child; Humans