Systematic review of antimicrobial therapy in patients with acute rhinosinusitis

Rosenfeld R M, Singer M, Jones S

CRD summary
The authors concluded that improvement rates in otherwise healthy patients seen in primary care with uncomplicated, non-severe acute rhinosinusitis were high after 7 days with or without antibiotics. The review appears to support the authors' conclusions, but the reliability of the evidence may be weakened by the differences between the studies.

Authors' objectives
To evaluate the effect of antimicrobial therapy in patients with acute rhinosinusitis.

Searching
MEDLINE and the Cochrane CENTRAL Register were searched through February 2007; the search terms were reported. In addition, the reference lists in identified studies were screened. Only articles published in the English language were eligible.

Study selection

Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion in the review.

Specific interventions included in the review
Studies that compared systemic antibiotics with placebo were eligible for inclusion. The majority of studies were set in primary care. The included studies evaluated a variety of antibiotics; most evaluated amoxicillin, either alone or in combination with other antibiotics (dosages were not reported). Most of the studies allowed cointerventions such as analgesics and/or topical nasal decongestants. The median duration of treatment was 10 days.

Participants included in the review
Studies of patients aged 12 years or older, with a clinical condition defined as sinusitis, rhinosinusitis, sinusitis-like symptoms or rhinorrhea, were eligible for inclusion. Studies of patients with the 'common cold' or an 'upper respiratory tract infection', or who had had the disease for more than 30 days, were excluded. The included studies used a variety of inclusion and exclusion criteria for the patients (details were reported); most excluded patients with 'severe illness' and complicated sinusitis. The majority of based their diagnosis on clinical signs and symptoms or radiological criteria. The patients had a mean age of 36 years and in most studies the majority were female. Where reported, the median duration of illness was 8.1 days.

Outcomes assessed in the review
Studies that did not report patient-based outcomes were excluded. The review assessed 'cure' (defined as the absence or near absence of all presenting signs and symptoms of acute rhinosinusitis), 'improvement' (defined as partial or complete relief of presenting signs and symptoms) and adverse events.

How were decisions on the relevance of primary studies made?
Two reviewers independently selected the studies.

Assessment of study quality
Validity was assessed and scored using the Jadad scale, which considers randomisation, blinding and withdrawals. The maximum possible score was 5 points. The authors did not state how the validity assessment was performed.

Data extraction
Two reviewers independently extracted the data onto a standardised form and resolved any disagreements by discussion. The numbers of withdrawals and adverse events for each treatment group and outcomes of interest were extracted. Relative risks (RRs), rate differences (RDs) and the number-needed-to-harm (NNH) were calculated with 95% confidence intervals (CIs).
Methods of synthesis

How were the studies combined?
Pooled RRs and absolute RDs with 95% CIs were calculated using a random-effects model, weighted by the inverse of variance. Pooled clinical outcome rates were calculated for the placebo group alone (using pooled clinical outcome rates to ascertain the natural history of the condition) and for antibiotics versus placebo. Intention-to-treat analysis was used for all analyses, except for adverse events in which only data from patients who took the medication were used. For studies with more than one antibiotic treatment arms, only data from the amoxicillin treatment arms were used for the analysis of efficacy; all data were used for analyses of adverse events. The pooled NNH was reported for adverse events.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the I-squared statistic. Subgroup analysis was used to examine differences between heterogeneous studies with respect to diagnostic criteria (strictly clinical or imaging), diagnostic label (acute sinusitis or acute rhinorrhoea), duration of treatment (10 days or 3 to 7 days) and type of antibiotic (penicillin or amoxicillin).

Results of the review

Thirteen RCTs (n=3,159) were included.

All of the included studies were double-blinded and of a high quality (Jadad score 4 or 5). Most of the studies had high rates of follow-up (median 94%).

Natural history (placebo groups only).

The complete clinical cure rate was 8% (95% CI: 5, 14) at 3 to 5 days, rising to 35% (95% CI: 24, 48) at 7 to 12 days and 45% (95% CI: 23, 70) at 14 to 15 days.
The improvement rate was 30% (95% CI: 0, 99) at 3 to 5 days, rising to 73% (95% CI: 56, 85) at 7 to 12 days; this remained stable at 14 to 15 days.

Clinical cure.

There was no significant difference between antibiotics and placebo in the clinical cure rate at 3 to 5 days (3 homogeneous studies) or at 14 to 15 days (4 studies with low heterogeneity, I-squared 27%). At 7 to 12 days, antibiotics were associated with a significant increase in clinical cure rates compared with placebo (absolute RD 0.15, 95% CI: 0.04, 0.25, p=0.007), based on 9 studies with high heterogeneity (I-squared 80%).

Clinical improvement.

There was no significant difference between antibiotics and placebo in clinical improvement rates at 3 to 5 days (2 heterogeneous studies, I-squared 65%). Antibiotics were associated with a significant increase in clinical improvement rates compared with placebo at 7 to 12 days (absolute RD 0.14, 95% CI: 0.01, 0.28, p=0.037), based on 5 studies with high heterogeneity (I-squared 74%), and at 14 to 15 days (absolute RD 0.07, 95% CI: 0.02, 0.13, p=0.013), based on 3 studies with low heterogeneity (these reported results were taken from the tables, but the text stated that there was no significant difference between treatments at 14 or 15 days and that the results were based on 4 studies).

Adverse events.

Antibiotics were associated with a significant increase in any adverse event (absolute RD 0.11, 95% CI: 0.05, 0.16, p=0.001; NNH 9) and a significant increase in diarrhoea, which was the most commonly reported adverse event (absolute RD 0.05, 95% CI: 0.01, 0.09, p=0.027; NNH 20), compared with placebo. Other reported adverse events were skin rashes, vaginal discharges, headaches, dizziness and fatigue.

The results for various subgroup and sensitivity analyses were also reported.
Authors' conclusions
Improvement rates in otherwise healthy patients seen in primary care with uncomplicated, non-severe acute rhinosinusitis were high after 7 days with or without antibiotics.

CRD commentary
The review addressed a clear defined question. Limiting the search to English language publications listed in two databases or references might have resulted in the omission of other relevant studies; the authors acknowledged these limitations. Validity was assessed using specified criteria and, although only the composite score was presented, most studies met all of the validity criteria; readers can therefore assess the quality of the evidence presented. Methods were used to minimise reviewer error and bias when selecting the studies and extracting the data, but it was not clear whether similar steps were taken when assessing validity.

Statistical heterogeneity was assessed for analyses of antibiotics versus placebo and the studies were pooled using meta-analysis. Attempts were made to identify the sources of the significant heterogeneity found for most of the analyses. The authors discussed the problems of pooling heterogeneous data, but there were no comments about the heterogeneity among placebo arms used to support the conclusions about natural history. The authors also discussed the limited generalisability of the data to other populations. Overall, the data appear to support the authors’ conclusions, but the reliability of the evidence may be weakened by the differences between the studies.

Implications of the review for practice and research
The authors did not state any implications for practice or further research.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.