Comparison of antibiotics with placebo for treatment of acute sinusitis: a meta-analysis of randomised controlled trials
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CRD summary
The review concluded that use of antibiotics for acute sinusitis conferred a small therapeutic benefit over placebo and a corresponding rise in adverse events. The authors’ conclusions were supported by the evidence presented, but limitations in the reporting of review process should be taken into consideration when interpreting these results.

Authors’ objectives
To investigate the effectiveness and safety of antibiotics compared with placebo for acute sinusitis.

Searching
PubMed and Scopus databases were searched up to May 2008; search terms were reported. Bibliographic references of all relevant articles were handsearched. Papers published in languages other than English, Spanish, French, Italian and German or presented as conference abstracts were excluded.

Study selection
Double-blinded, randomised controlled trials (RCTs) that compared antibiotic treatment with placebo for patients of any age with acute sinusitis (of any location) were eligible for inclusion. Diagnosis of acute sinusitis was required to be determined by either clinical criteria or positive radiological, microbiological or laboratory tests. Trials that included patients with mixed types of sinusitis or mixed types of respiratory tract infections were included only if data on the subgroup of patients with acute sinusitis were reported separately or if a clinical diagnosis of acute sinusitis was supported for more than two thirds of the study population.

The most commonly compared antibiotic was amoxicillin, other antibiotics included phenoxymethyl-penicillin, amoxicillin-clavulanic acid, doxycycline, azithromycin, cefuroxime and ciclacillin. All study medications were administered orally. Use of concomitant ancillary treatments was not allowed in two trials. Included participants were outpatients with suspected acute sinusitis, (uncomplicated) acute maxillary sinusitis, acute bacterial sinusitis, suspected and acute rhinosinusitis. Diagnostic inclusion criteria included clinical criteria alone (this varied across trials), bacteriological methods and laboratory methods as well as imaging studies. Where reported, mean symptom duration before start of treatment ranged from 8.1 days to 2.2 weeks. Mean age of participants ranged from 5.6 to 43 years. Trials were conducted in Europe, Canada and USA.

The authors did not state how papers were selected for the review.

Assessment of study quality
Study quality was assessed according to the Jadad scale; a score of 5 represented the highest quality study.

The authors did not state how many reviewers performed the quality assessment.

Data extraction
Data were extracted to calculate odds ratios (ORs) together with 95% confidence intervals (CI). Two reviewers independently extracted data. Any disagreements were resolved through discussion.

Methods of synthesis
Summary odds ratios and their associated 95% CIs were calculated using the DerSimonian and Laird random-effects model. Heterogeneity was assessed using $X^2$ and the $I^2$ statistic. Publication bias was assessed based on visual inspection of a funnel plot. Subgroup analyses were performed (age group, diagnostic criteria, timing of assessment and year of publication). Differences between subgroups were assessed on the basis of the $X^2$ statistic.
Results of the review
Seventeen double-blinded placebo-controlled RCTs (n=3,291 outpatients: 2,915 adults and 376 children) were included in the meta-analyses. All trials had a Jadad score of 4 or 5.

A greater number of patients were cured or improved with any antibiotic treatment when compared with placebo (OR 1.64, 95% CI 1.35 to 2.00, I²=3.2%; 16 RCTs). No evidence of statistical heterogeneity was found. There were no significant differences between treatments when studies were classified by age group, diagnostic criteria, timing of assessment or year of publication. Trials that reported cure separately found a significant effect in favour of antibiotic treatment (OR 1.82, 95% CI 1.34 to 2.46, I²=49.6%; 12 RCTs). Cure or improvement was more likely with amoxicillin alone compared with placebo (OR 1.48, 95% CI 1.17 to 1.89; 10 RCTs). No between-group differences were found for disease complications or disease recurrence.

A significantly greater number of patients experienced adverse events with antibiotic treatment compared with placebo (OR 1.87, 95% CI 1.21 to 2.90, I²=63.3%; 12 RCTs). In particular there was a greater incidence of diarrhoea or other gastrointestinal disturbances (OR 2.28, 95% CI 1.24 to 4.21; 14 RCTs). No between-group differences were found in the number of patients who withdrew from treatment due to adverse events.

Authors' conclusions
Use of antibiotics for acute sinusitis conferred a small therapeutic benefit over placebo and a corresponding rise in adverse events.

CRD commentary
The review addressed a focused question and inclusion criteria were clearly defined. The literature search was adequate, but restriction to full papers published in specific languages meant that there was a possibility of publication bias. Appropriate steps were taken to minimise the likelihood of error and bias during data extraction; it was unclear whether similar steps were taken at study selection or assessment of study validity. Study quality was formally assessed using relevant criteria; although only summary scores were reported all studies were deemed to be of good quality. Standard meta-analytic methods were used to pool data. Heterogeneity was assessed, although this was not consistently reported. The authors made some attempts to investigate potential sources of heterogeneity.

The authors’ conclusions reflected the evidence presented, but due to potential bias in the review process the reliability of the conclusions is unclear.

Implications of the review for practice and research
Practice: The authors suggested that antibiotics should be reserved for carefully selected patients with a higher probability of bacterial disease.

Research: The authors suggested that further studies were required that aimed to better identify the characteristics of patients with a greater likelihood of bacterial disease.

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