Are amoxycillin and folate inhibitors as effective as other antibiotics for acute sinusitis: a meta-analysis

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Authors' objectives
To examine whether antibiotics are indicated in treating uncomplicated acute sinusitis and, if so, whether newer and more expensive antibiotics with broad spectra of antimicrobial activity are more effective than amoxycillin or folate inhibitors.

Searching
MEDLINE was searched up to May 1998 (start date unclear) using the terms of specific antibiotic classes and 'sinusitis'. The authors also scanned Excerpta Medicus, and recent abstracts from the American Society for Microbiology's programme of meetings and Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy (1993 to 1997). The references from all trials, review articles, and special issues were also examined for additional studies. Studies reported in any language were considered.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) and placebo-controlled trials were included.

Specific interventions included in the review
Any antibiotic versus placebo, and amoxycillin or folate inhibitors (co-trimoxazole, trimethoprim plus sulfametopyrazine, or brodimoprim) versus more expensive antibiotics. The more expensive antibiotics were co-amoxiclav, azithromycin, clarithromycin, ceflalexin, cefixime, cefpodoxime, cefuroxime, minocycline, cefalexin, doxycycline, tetracycline, pivampicillin, and roxithromycin.

Participants included in the review
Patients with acute sinusitis or acute exacerbation of chronic sinusitis. The mean ages of the patients ranged from 25 to 44 years, except in two trials that evaluated only paediatric patients.

Outcomes assessed in the review
Clinical cure (resolution of all signs and symptoms), improvement, and failure (signified by no change or worsening of signs and symptoms), as assessed within 48 hours of the end of the treatment.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
The trials were assessed for the following: blinded versus unblinded design; criteria for diagnosis of sinusitis; clinical outcomes; loss of patients to follow-up; and use of decongestants. In addition, the authors also used the scale developed by Jadad et al. (see Other Publications of Related Interest no.1) to assess the methodological quality of the trials. The authors do not state how the papers were assessed for validity, or how many of the authors performed the validity assessment.

Data extraction
The data were extracted independently by two authors.
Methods of synthesis
How were the studies combined?
The authors pooled the risk ratios (RR), risk differences, and event rates using both the Mantel-Haenszel fixed-effect model and the DerSimonian and Laird random-effects model (see Other Publications of Related Interest no.2). The 95% confidence intervals (CIs) were calculated. The authors also reported rates weighted by the inverse of their variance with random effects; only the random-effects calculations were reported in the results.

How were differences between studies investigated?
The authors conducted sensitivity analyses. They also assessed the heterogeneity between the studies using the chi-squared test, where a p-value of less than 0.01 indicated significance.

Results of the review
Twenty-seven RCTs met the inclusion criteria. Six were placebo-controlled (761 participants), 13 compared amoxycillin with other antibiotics (1,553 participants), and 8 compared a folate inhibitor with other antibiotics (410 participants).

There was no statistically-significant heterogeneity in the studies comparing antibiotics with placebo. There was no heterogeneity of treatment effects in the comparisons with amoxycillin. There was some evidence of heterogeneity in the studies comparing folate inhibitors with other antibiotics (p=0.09 and p=0.18 for clinical cure and clinical failure, respectively).

For antibiotic versus placebo, clinical cure favoured the use of antibiotics (RR 1.33, 95% CI: 1.02, 1.74) whilst clinical failure was reduced by antibiotic use (RR 0.54, 95% CI: 0.37, 0.79). The symptoms improved or disappeared in 69% of those patients who were not treated with antibiotics (95% CI: 57, 79).

For amoxycillin versus newer, more expensive antibiotics, there was no statistically-significant difference between amoxycillin and other antibiotics. The RR was 1.04 (95% CI: 0.98, 1.11) for clinical cure and 0.86 (95% CI: 0.62, 1.19) for clinical failure.

For folate inhibitors versus newer, more expensive antibiotics, there was no statistically-significant difference between folate inhibitors and other antibiotics. The RR was 1.01 (95% CI: 0.88, 1.17) for clinical cure and 1.01 (95% CI: 0.52, 1.97) for clinical failure.

Authors’ conclusions
Amoxycillin and folate inhibitors were essentially as effective as more expensive antibiotics for the initial treatment of uncomplicated acute sinusitis. Small differences in efficacy may exist, but these are unlikely to be clinically important.

CRD commentary
The authors clearly stated their research question and the inclusion and exclusion criteria. The study data were tabulated and discussed in the text, whilst the sensitivity analyses were also reported graphically. The literature search was good, searching for unpublished material and considering studies reported in any language. However, the authors limited the search to MEDLINE, which could have missed studies published outside of the USA. The authors assessed the methodological quality of the included trials, but it was not reported who selected the studies or assessed their quality.

The pooling of the data was appropriate and tests for heterogeneity were performed. In addition, sensitivity analyses were conducted. The conclusion that there is no current justification for the use of broad-spectrum antibiotics in the community, for treating uncomplicated acute sinusitis, follows from the review.

Implications of the review for practice and research
The authors state that their meta-analysis highlights the need to improve the quality of studies in the treatment of out-
patients with antibiotics. Future studies should include either radiographic findings or antral puncture and aspiration as criteria for study entry. Patients with chronic and subacute sinusitis should be studied separately, and the use of decongestants should be specified by the protocol. Patients with infection caused by drug-resistant organisms should not be excluded but should be investigated to determine whether antibiotic resistance is an important predictor of treatment failure.

The authors also state that in practice there is a need for accurate, inexpensive and noninvasive methods to diagnose acute bacterial sinusitis.

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Other publications of related interest

These additional published commentaries may also be of interest: Del Mar C. Review: amoxycillin and folate inhibitors are as effective as newer more expensive antibiotics for acute sinusitis. Evid Based Med 1999;4:77. Antibiotics for acute sinusitis in general practice [letters]. BMJ 1999;318:1623-4.

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