Antimicrobial treatment in acute maxillary sinusitis: a meta-analysis


Authors' objectives
To assess which antibiotic is most effective in the treatment of acute maxillary sinusitis in otherwise healthy adults and adolescents, and which has the fewest side effects.

Searching
A computerised search of MEDLINE (1984-Aug 1995) was carried out using the key terms 'sinusitis and drug therapy' or 'maxillary sinusitis and drug therapy', and by exploding the MeSH terms. The search was limited to studies published in English, French, German, Dutch, Danish and Swedish. Additional studies were located by checking the bibliographies of retrieved articles, a recent Dutch Ph.D. thesis on maxillary sinusitis, and the reference list accompanying the Dutch general practitioners guideline on acute sinusitis. The Excerpta Medica was also reviewed.

Study selection
Study designs of evaluations included in the review
Randomised blinded comparative studies.

Specific interventions included in the review
Antibiotics (penicillins, cephalosporins, tetracyclines, macrolids and sulphonamides) including co-trimoxazole, amoxicillin, clarithromycin, cefaclor, amoxicillin and clavulanic acid, clarithromycin, doxycyclin, loracarbef, cefuroxim-axetil, azithromycin, cefpodoxim-proxetil, bacampicillin, cyclacillin, co-tetroxazin. Various dose regimens were used.

Participants included in the review
Otherwise healthy adults (aged 13 years or over) with acute maxillary sinusitis.

Outcomes assessed in the review
Clinical cure (defined as complete recovery with absence of all signs and symptoms), clinical success (defined as either clinical cure or clinical improvement, i.e. there was no need for an additional follow-up treatment) and adverse events. Minor adverse events were not included in the analyses and antibiotics were considered to be 'not tolerated' when adverse events were severe enough to lead to cessation 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 authors do not state that they assessed quality.

Data extraction
Two authors extracted the data independently onto a pre-structured questionnaire. Any disagreements were subsequently resolved by the two authors reviewing the paper together. Only data within the publications were considered and authors were not contacted for additional information. The following information was extracted from the publications: type and properties of the antibiotic, outcome details, study setting (primary care/secondary care), prescription of local decongestants (no/yes), treatment dose (prescribed daily dose/antibiotic divided by daily dose (DDD) as defined by the WHO) (1 or less/greater than 1), duration of treatment (less than 10 days/10 days or more), basis for the diagnosis (clinical signs/clinical signs plus ultrasound/radiograph/aspiration plus culture), geographical area of population (Northern Europe/Southern Europe/United States), and year of publication (1990 or before/after 1990).
Methods of synthesis
How were the studies combined?
Odds ratios (OR) with confidence intervals (95% CIs) were calculated for each of the study outcomes. Data were then pooled and contingency tables constructed on the basis of the type and properties of the antibiotics, and the outcomes. Associations (OR, 95%CI) were estimated from the contingency tables by means of a Mantel-Haenszel procedure.

How were differences between studies investigated?
Unstratified (assuming that the base rates of clinical cure did not differ between the studies, given a specific type or property of antibiotics) and stratified (on the basis of study) OR were calculated. For all of the clinically significant OR, studies with similar background characteristics were clustered in order to increase the power of the analyses. The following background characteristics were considered as potential confounders: setting, prescription of local decongestants, treatment, dose, duration of treatment, basis for the diagnosis, geographical area and year of publication. Clinical significance was defined using an arbitrary cut off point of \( p>1.50 \) or \( p<0.67 \). Clustering of the studies was considered to be justified if the OR adjusted for a background characteristic did not differ from the OR stratified by study for more than 15% and the OR did not vary across strata (ie the OR per stratum did not differ from the OR per combined stratum for more than 15%). If this was not the case a confounding or effect modification by unmeasured background characteristics was judged to be present.

Results of the review
Sixteen blinded RCTs involving 3,310 participants who received antimicrobial treatment, were included.

Individual studies:
When analysed individually only two studies showed statistically significant differences in their outcome measures: doxycyclin versus loracarbef, clinical success OR=3.95 (95%CI: 1.08, 14.44); cefaclor versus cefpodoxim-proxetil OR=2.45 (95%CI: 1.32, 4.55).

Unstratified analyses:
Overall clinical cure rate after antimicrobial therapy was 69% (1234/1794), overall clinical success rate was 92% (1971/2151), and the overall adverse events rate was 2.4% (81/3310). Sulphonamides vs penicillins (OR=2.13, 95% CI: 1.36, 3.40); macrolids vs penicillins (OR=2.06, 95% CI: 1.08, 4.24); broad-spectrum vs narrow-spectrum antimicrobials (OR=1.84, 95% CI: 1.00, 3.69); bactericidal vs bacteriostatic antimicrobials (OR=1.36, 95% CI: 1.07, 1.72).

Stratification by study:
These analyses yielded clinically significant (<0.67 or >1.50) for five contingency tables: beta-lactamase inhibition regarding clinical cure; type of antibiotic (penicillins, macrolids) regarding clinical success; spectrum regarding clinical success; type of antibiotic (penicillins, cephalosporins) regarding adverse events; and type of antibiotic (penicillins, tetracyclines) regarding adverse events. Only the clinical cure rate of antimicrobials with no beta-lactamase inhibition (n=114 patients) vs beta lactamase inhibition (n=122 patients) was found to be significant (OR=2.44, 95% CI: 1.27, 4.81). Stratification by background characteristics:

In all except four of the contingency tables, clustering of the studies appeared to be not justified because the OR adjusted for the background characteristics changed by 15% or more as compared with the OR stratified by study. The four stable OR were: penicillins vs cephalosporins, stratified for geographical area (adverse events OR=0.51, 95% CI: 0.26, 0.95); penicillins vs macrolids, stratified for diagnosis (clinical success OR=1.57, 95% CI: 0.77, 3.42); broad vs narrow spectrum antimicrobials, stratified for diagnosis (clinical success OR=1.69, 95% CI: 0.91, 3.42); broad vs narrow spectrum antimicrobials, stratified for treatment dose (clinical success OR=1.51, 95% CI: 0.79, 3.16).

Authors’ conclusions
Differences in outcome between antimicrobial treatments of acute sinusitis in otherwise healthy adults and adolescents appear to be small. Therefore, the cheapest antimicrobial treatment can be selected.
CRD commentary
This is a very clearly presented study with detailed analyses. However, the authors failed to state how decisions on the relevance of studies were made and it appears that the quality of the included studies was not assessed. The literature search focused on only one electronic database although attempts were made to locate other studies through searching bibliographies and Excerpta Medica. However, relevant information may have been omitted through limiting the language of publication. In addition, the possibility of publication bias cannot be ruled out as no specific attempts were made to locate unpublished data. This is, however, acknowledged by the authors and the potential impact this may have had on their findings is discussed. In acknowledgement of the potential sources of heterogeneity between the included studies, the authors incorporated both unstratified and stratified (by study and by a variety of background characteristics) analyses. In view of the factors highlighted above, the evidence presented would appear to support the authors' conclusions.

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

Research: The authors stated that 'there is a strong need for placebo controlled randomised studies on antimicrobial treatment (antibiotics with beta-lactamase inhibition) with short-term outcomes and diagnostic strategies comparable with those in other trials. Moreover, the nearly total lack of knowledge on the long-term effects of antimicrobial treatment in acute maxillary sinusitis stresses the need for additional long term studies'.

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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.