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Antibiotic Treatment for Acute Maxillary Sinusitis

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SYSTEMATIC REVIEW SOURCE

This is a systematic review abstract, a regular feature of the *Annals'* Evidence-Based Emergency Medicine (EBEM) series. Each features an abstract of a systematic review from the Cochrane Database of Systematic Reviews and a commentary by an emergency physician knowledgeable in the subject area.

The source for this systematic review abstract is: Williams JW, Aguilar C, Makela M, Cornell J, Hollman DR, Chiquette E, Simel DL. Antibiotics for acute maxillary sinusitis (Cochrane Review). In: *The Cochrane Library.* Issue 3. Oxford, United Kingdom: Update Software; 2002.

The *Annals'* EBEM editors helped prepare the abstract of this Cochrane systematic review as well as the Evidence-Based Medicine Teaching Points.

OBJECTIVE

To determine whether antibiotics are effective for acute maxillary sinusitis, and if so, whether any antibiotic class is superior.

DATA SOURCES

Trials were identified by MEDLINE and EMBASE searches through October 1998, requests to pharmaceutical companies for all published and unpublished trials, and bibliographies of included studies and previous systematic reviews.

STUDY SELECTION

Studies were included if they were randomized trials of 30 or more adults that compared antibiotic with placebo, or antibiotics from different classes, for acute maxillary sinusitis. The studies were required to confirm the diagnosis by radiography or sinus aspiration and report outcomes in terms of clinical cure or improvement.

DATA EXTRACTION

Two authors independently selected trials, extracted data, and assessed the quality of the trials. Primary outcomes were (1) clinical cure and (2) clinical cure or improvement. Secondary outcomes were radiographic improvement, relapse rates, and dropouts resulting from adverse effects.

MAIN RESULTS

Thirty-two trials, involving 7,330 patients, evaluated antibiotic treatment for acute maxillary sinusitis. Major comparisons were antibiotic versus control (n=5); newer, non-penicillin antibiotic versus penicillin class (n=10); and amoxicillin-clavulanate versus other extended spectrum antibiotics (n=10). Most trials were conducted in otolaryngology, non–emergency department settings. Of the 32 studies selected, 27 used conventional radiographs for diagnostic confirmation. Of these, 10 did not specify diagnostic criteria, 5 specified mucosal thickening as a minimal criteria, 5 specified greater than 5-mm mucosal thickening, and 7 specified sinus opacity or air-fluid level. Two studies used computed tomography (CT) of the sinus, and 3 used sinus aspiration with culture for diagnostic confirmation. Only 5 trials described adequate allocation and concealment procedures; 10 were double-blind. Compared with placebo, penicillin improved the rate of clinical cure (relative risk [RR] 1.72; 95% confidence interval [CI] 1.00 to 2.96). Treatment with amoxicillin did not significantly improve cure rate (RR 2.06; 95% CI 0.65 to 6.53), but there was significant variability among studies. Radiographic outcomes were improved by antibiotic treatment. There was no significant difference in cure rate between classes of antibiotics for the following comparisons: newer non-penicillin antibiotics versus penicillins (RR for cure: 1.07; 95% CI 0.99 to 1.17); newer non-penicillin antibiotics versus amoxicillin-clavulanate (RR for cure: 1.01; 95% CI 0.97 to 1.04). Dropouts caused by adverse effects were significantly higher with amoxicillin-clavulanate than cephalosporins. Relapse rates within 1 month of successful therapy were 5% and did not differ significantly between antibiotic classes.

CONCLUSIONS

For acute maxillary sinusitis confirmed radiographically or by aspiration, current evidence is limited but supports treatment with penicillin or amoxicillin for 7 to 14 days. Clinicians should weigh the moderate benefits of antibiotic treatment against the potential for adverse effects.

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COMMENTARY: CLINICAL IMPLICATION

Rhinosinusitis is 1 of the 10 most common diagnoses in ambulatory practice and is the fifth most common diagnosis for which antibiotics are prescribed.[1] However, it is estimated that up to 60% of such antibiotic prescriptions are unwarranted.[2] The overuse of antibiotics in rhinosinusitis, as in other respiratory infections, is thought to contribute to the problem of increasing antibiotic resistance. How might the results of the Cochrane Review improve our approach to this problem?

Antibiotics are only efficacious in bacterial sinusitis. Yet viral rhinosinusitis, which accounts for the majority of cases we evaluate, is similar to bacterial sinusitis both clinically and radiographically.[3] Therefore, the first issue to address is the role of diagnostic tests in differentiating bacterial from viral disease. Compared with the criterion standard of culture positive sinus aspirate, the specificity of diagnostic tests declines progressively from CT scan to plain radiograph to formal clinical criteria (using history and physical examination alone). Hence, the prevalence of bacterial sinusitis in patients with a positive result is roughly 70% by CT scan, 50% by plain films, and 40% by clinical criteria.[4,5] Because CT scan is too costly for routine evaluation and plain films add little to history and physical examination, Centers for Disease Control and Prevention (CDC) guidelines recommend that the diagnosis of acute nonsevere sinusitis be based on clinical criteria alone, without imaging. The clinical criteria, briefly summarized, are symptom duration greater than 7 days plus mucopurulent nasal discharge or signs of unilateral maxillary involvement (such as maxillary toothache).[2]

The Cochrane meta-analysis quantifies the benefit of penicillin in sinusitis as relative risk of cure compared with placebo. The relative risk of 1.24 translates to a number needed to treat of 7, meaning 7 patients with radiographic sinusitis must be treated with antibiotics to achieve clinical cure in 1 additional patient. The limited efficacy of antibiotics is due in large part to the high spontaneous cure or improvement rate in the placebo groups (62% to 69%), which in turn reflects the poor specificity of radiography for identifying bacterial sinusitis. In emergency medicine practice, if the diagnosis of sinusitis is based on clinical criteria alone, the prevalence of bacterial sinusitis in the target population will be somewhat lower than in clinical trials that used radiography for diagnosis. The anticipated treatment effect will thus be diluted, and the number needed to treat will be somewhat greater than 7. Indeed, a recent large trial of antibiotics for sinusitis, in which the diagnosis was made by history and physical examination alone,

found no statistically significant benefit to antibiotics.[6]

Because the benefit of antibiotics in acute sinusitis is small, most cases resolve without antibiotics, and complications of untreated bacterial disease are rare, the CDC recommends as an initial strategy prescribing decongestants alone and reserving antibiotics for cases that fail to resolve in 7 days.[7] Patients with signs or symptoms of severe disease deserve immediate antibiotic treatment. The predominant pathogen in acute bacterial sinusitis is *Streptococcus pneumoniae*; knowledge of local *S pneumoniae* resistance should guide antibiotic selection. Standard-dose amoxicillin is the recommended first-line antibiotic, despite the fact that the Cochrane meta-analysis found a statistical benefit for penicillin only. High-dose amoxicillin and broader spectrum antibiotics such as amoxicillin/clavulanate or respiratory fluoroquinolones should be considered only if penicillin-resistant *S pneumoniae* is a major concern and for treatment failures.

TAKE HOME MESSAGE

Treatment of acute maxillary sinusitis with narrow spectrum antibiotics such as amoxicillin is supported by current evidence. However, benefit from antibiotics will be realized in clinical practice only if the target population has a similar prevalence of bacterial disease as in clinical trials, suggesting that treatment should be limited to patients who fulfill strict clinical criteria. Use of more expensive, broader spectrum antibiotics is not warranted for initial therapy.

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EVIDENCE-BASED MEDICINE TEACHING POINTS

Publication bias. Systematic reviews combine the results of several trials, often using meta-analyses, to calculate a summary treatment effect. In an ideal systematic review, all relevant, methodologically sound studies on the topic are included; however, this is not always the case. A major potential source of error in systematic reviews is publication bias. Publication bias arises when studies are performed but not published, and therefore not included in the review. Research has shown that these unpublished trials tend to be those with negative results and tend to be small studies that lack the power required to make firm conclusions.[8] Failure to be published may be related to sponsorship, author fatigue, editorial rejection, or a combination of these factors.

An assessment of potential publication bias is now performed and reported with some meta-analyses. A common method used to estimate the influence of publication bias is to prepare a funnel plot. Funnel plots are scatterplots of the individual studies in the analysis, where treatment effect (RR or odds ratio) on the x axis is plotted against the study sample size on the y axis. Ideally, a vertical line drawn through the summary treatment effect forms the center of the inverted funnel, with large studies arrayed close to this line at the apex and small studies scattered more widely at the base. Publication bias is suggested by an asymmetric appearance to the funnel (although there are other causes of asymmetry in funnel plots[9]). In this hypothetical example (Figure), a lack of studies in the right lower corner of the plot suggests that small studies with negative results were not included in the analyses. Systematic reviews in which funnel plot asymmetry is substantial should be interpreted with caution and viewed as possibly overestimating the treatment effect.

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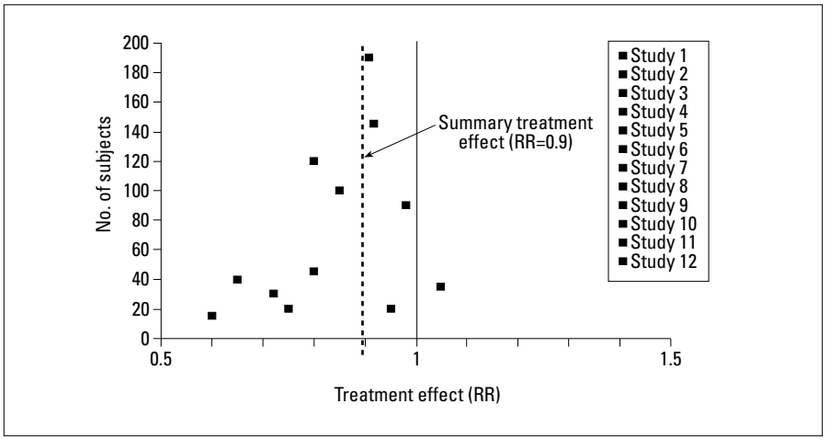
Figure.
Funnel plot.



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