Should Sore Throats Be Treated With Antibiotics?

EBEM Commentators
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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: Del Mar CB, Glasziou PP, Spinks AB. Should sore throats be treated with antibiotics? (Cochrane Review). In: *The Cochrane Library.* Issue 3. Chichester, United Kingdom: John Wiley & Sons, Ltd.; 2004.

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

OBJECTIVE

To determine whether antibiotics should be given to patients with sore throat.

DATA SOURCES

The authors searched MEDLINE (1966 to 2003), the Cochrane Central Register of Controlled Trials (2003), EMBASE (1990 to 2003), and the reference sections of the articles found. The search is considered updated to 2003.

STUDY SELECTION

Inclusion criteria were: randomized or quasirandomized controlled trials comparing antibiotics with placebo, and trials with measures of the typical symptoms (throat pain, headache, or fever) or complications (suppurative and nonsuppurative) of sore throat.

DATA EXTRACTION

Criteria for judging the methodological quality and for assigning allocation concealment scores were not described. Furthermore, the patient populations studied were almost exclusively from western Europe and the midwestern United States. Outcome data were extracted by reading from tables and graphs and, in some cases, by contacting the authors directly. Patient-relevant outcomes included throat pain, headache, fever, and occurrence of rheumatic fever, glomerulonephritis, otitis media, sinusitis, and peritonsillar abscess. No mention was made of intra-observer agreement anywhere in the review.

Because clinicians often have difficulties applying odds ratio (OR) results directly to their patients, for this analysis of the Cochrane Review, number needed to treat and/or number needed to harm are reported. The calculation of number needed to treat and number needed to harm was completed using the summary data in the graphs and an online number needed to treat calculator (http://www.nntonline.net) and includes 95% confidence intervals (CIs). (For these computations, the control event rate was calculated by weighting the contributions of each individual study according to the weighting factors reported in the graphs.) This method produces results that only approximate the actual exact treatment effect; however, the benefit to clinicians is a much better understanding of the summary measures. When the result was not statistically significant, the OR is reported. Whenever the OR result was significant, the number needed to treat/number needed to harm is reported.

MAIN RESULTS

Of the 26 included studies, many were of poor quality. Only 17 were double blinded. Randomization in early studies was sometimes performed in ways that may have introduced bias. Only 13 studies clearly concealed treatment allocation; for the others, most (11) descriptions were "unclear." In 4 studies, antipyretic analgesics were forbidden, lessening the applicability of the findings.

Overall, antibiotics shortened the duration of symptoms by one day about halfway through the illness (the time of maximal effect) and by about 16 hours overall. For throat pain at 3 and 7 days, the numbers needed to treat were 5 (95% CI 5 to 6) and 9 (95% CI 7 to 13), respectively. Dividing patients into subgroups with positive and negative cultures for *Streptococcus* demonstrated antibiotics had a greater effect on throat pain at 3 days in the swab-positive group (number needed to treat 4, 95% CI 3 to 4, versus number needed to treat 6, 95% CI 4 to 11). For throat pain at 7 days, antibiotics benefited swab-positive (number needed to treat 7, 95% CI 7 to 9) but not swab-negative (OR 0.65, 95% CI 0.38 to 1.12) patients.

Antibiotics reduced the number of people with fever at 3 days by 29% (number needed to treat 15, 95% CI 10 to 39). Fever was reduced in adults (number needed to treat 8; 95% CI 6 to 12) but not children (OR 1.87, 95% CI 0.48 to 7.23) on

day 3 and in unblinded (number needed to treat 13, 95% CI 7 to 24) but not blinded (OR 0.79, 95% CI 0.49 to 1.26) studies. Antibiotics reduced the occurrence of rheumatic fever (number needed to treat 41, 95% CI 35 to 52), otitis media (number needed to treat 25, 95% CI 21 to 34), and peritonsillar abscess (number needed to treat 28, 95% CI 25 to 36), but not headache, glomerulonephritis, or sinusitis. For rheumatic fever, only studies reported before 1975 showed benefit; studies after 1975 did not because there were no cases of rheumatic fever in the placebo (95% CI 0.0% to 0.3%) or treated groups. No attempt was made to report adverse reactions to antibiotics, such as diarrhea, rash, and thrush, because of inconsistencies in recording these symptoms in the included studies.

CONCLUSIONS

Antibiotics have been shown to decrease symptoms of throat pain and fever in patients with sore throat, especially those with proven streptococcal infection. Antibiotics have been shown to decrease the development of some complications (otitis media, peritonsillar abscess, and rheumatic fever), but not of others (sinusitis, headache, and glomerulonephritis).

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COMMENTARY: CLINICAL IMPLICATIONS

In the United States, sore throat is a common emergency department (ED) and primary care presentation. Although pharyngitis is largely a self-limited disease, even without antibiotic treatment, complications do occur in cases where *Streptococcus pyogenes* are causative. Most important, rheumatic fever has an annual incidence of approximately 1 per 1,000,000 and a prevalence of 1.7 million, accounting for 3,582 deaths per year in the United States.[1] Decision rules for examination alone or in combination with rapid bedside testing are now available to help make the diagnosis of β-hemolytic group A streptococcal throat infection.[2,3] Bedside testing for *S pyogenes* has limitations of both sensitivity and specificity, the latter being a particular problem because the carrier rate in asymptomatic patients can be as high as 10%.[4]

In the ED, the decision to treat sore throat is a clinical one. Although antibiotic use reduces the duration of sore throat and fever, other medications that are not antibiotics may offer equal benefit.[5] Prophylaxis with antibiotics against the rare complications of pharyngitis (otitis media, peritonsillar abscess, and rheumatic fever) also has risks. The benefits must be weighed against the risks of allergic reactions, antibiotic-associated diarrhea, and proliferation of antibiotic-resistant organisms. The decision to prescribe antibiotics should take into account the local patient population and the clinical likelihood of streptococcal pharyngitis.[6] In addition, the clinician should keep informed about reports from local health departments because sporadic outbreaks of rheumatic fever have been reported.[7,8] Antibiotic treatment, although beneficial in preventing complications, should be weighed against the clinical likelihood of streptococcal pharyngitis and drug side effects.

Table. Risk versus odds.

Risk	Odds
0.80	4
0.60	1.5
0.50	1
0.40	0.66
0.20	0.25
0.10	0.11
0.05	0.052

The findings in this Cochrane Review suggest that antibiotics decrease symptoms of throat pain and fever in patients with sore throat, especially those with proven streptococcal infection; however, this benefit is remarkably modest. Although antibiotics do decrease the development of common complications such as abscess and otitis media, their effectiveness in preventing others (eg, sinusitis) is unproven. Examination of the references from this Cochrane Review indicate the studies were performed in patients from Western Europe or the United States. Many of the US studies involved Air Force servicemen in the 1950s to 1960s. In addition, as of 1996, there have been no reliable statistics involving nonwhite patients with rheumatic fever, as reported in the National Center for Health Statistics division of the Centers for Disease Control and Prevention.[1,9] Thus, the applicability of this Cochrane Review may be limited by the relatively narrow patient populations studied.

Finally, the size of the benefit of treating a disease to prevent an adverse event depends on the estimation of the baseline risk of that event in the population being considered. For acute rheumatic fever (number needed to treat 41) in the included studies, the baseline risk was 0.036, or approximately 1 in 28. Restricting analysis to data from only the 6 studies since 1975, the maximum risk is not more than 0.3%, or approximately 1 in 345. The actual incidence of rheumatic fever in the United States today may be as low as 1 in 1,000,000. The number needed to treat for treating rheumatic fever is 41 (95% CI 35 to 52) using the systematic review data. If, however, one uses a baseline risk of 1 in 345 (post-1975 results), the number needed to treat would be 494 (95% CI 432 to 628); if one assumes the risk were 1 in 1,000,000 (population data), the number needed to treat would be 1,430,000 (95% CI 1,250,000 to 1,820,000).

TAKE HOME MESSAGE

Benefits of treating sore throats with antibiotics are initially modest and rapidly decrease within a short time period. Thus, the primary reason for treating sore throats with antibiotics is preventing rheumatic fever. Because this disease is very rare in the United States, there is probably very little need to prescribe

antibiotics for prophylaxis against it. Rather than providing universal antibiotic treatment for all patients with sore throat, emergency physicians should use clinical rules and/or testing to select those who are most likely to benefit from treatment (*S pyogenes*–positive cases, particularly when the risk of developing rheumatic fever is significant).

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EVIDENCE-BASED MEDICINE TEACHING POINT

Numbers needed to treat from systematic reviews. Meta-analyses combine data from multiple studies, thereby increasing the accuracy and reliability of the results. However, one difficulty with meta-analyses is that you usually cannot derive a number needed to treat because the results are given as ORs and not as risk reduction. However, for rare diseases, the risk very closely matches the OR, allowing the physician to derive the number needed to treat from the OR. The formula to derive odds from risk is:

$$\text{Odds} = \text{risk}/(1 - \text{risk})$$

A more illustrative way to describe this is shown in the Table. Therefore, as the risk (or incidence) of disease decreases, it closely approximates the odds of having the disease. Hence, with a rare disease like rheumatic fever, the ORs from the Cochrane Review can be used to calculate the number needed to treat. (Incidentally, an alternative method for estimating this is to use the OR and control event rate in the online calculator at http://www.nntonline.net mentioned above.)

One other observation about the number needed to treat worth noting relates to baseline risk. The results from a systematic review may overestimate the baseline risks of a condition because only randomized controlled trials are included. In general, readers should remember to assess the baseline risks in the populations they serve and correct the numbers needed to treat accordingly. Overall, when the incidence of an event is high (eg, otitis media after sore throats), the numbers needed to treat are generally smaller for an effective treatment. Correspondingly, when the incidence of outcome is low (eg, rheumatic fever after sore throat), the numbers needed to treat are much higher for an effective treatment.

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CORRECTIONS

In the December 2004 issue, in the article by Schull et al ("Emergency Department Crowding and Thrombolysis Delays in Acute Myocardial Infarction"; pages 577-585), the authors inadvertently failed to acknowledge the important contribution of Ms. Shelly Moneta, program director of CritiCall Ontario, in the completion of the study.

In the November 2004 issue, in the article by Abisaab et al ("Emergency Department Presentation of Bilateral Carotid Artery Dissections in a Postpartum Patient"; pages 484-489), Figure 1 was erroneously labelled "Computed tomographic image" instead of "Magnetic resonance imaging."

In addition, there was an error in this sentence: "Recorded blood pressures throughout labor and the puerperium were 100 to 110 mm Hg diastolic and 50 to 60 mm Hg systolic, and protein was absent from her urine." The sentence should have read "...100 to 110 mm Hg systolic and 50 to 60 mm Hg diastolic..." We regret these errors.