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Update on Acute Bacterial Rhinosinusitis

Summary

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Introduction

This is an update of the original evidence report, *Diagnosis and Treatment of Acute Bacterial Rhinosinusitis,* published in March 1999 by the Agency for Health Care Policy and Research.[1] Our objective is to summarize and analyze comparative studies on the antibiotic efficacies in the treatment of acute bacterial sinusitis. The research questions in this evidence report are:

1. Given a clinical diagnosis of acute bacterial rhinosinusitis, what are the comparative efficacies of the antibiotics in resolving symptoms and preventing complications or recurrence?
   - 1a. Is there evidence that duration of antibiotic treatment in acute bacterial rhinosinusitis affects efficacy?
2. What adverse effects are reported for antibiotics used for acute bacterial rhinosinusitis?
3. How does the introduction of the pneumococcal vaccine affect the resistance patterns of pneumococcus and the treatment decisions in acute bacterial rhinosinusitis?

Methods

Acute bacterial rhinosinusitis is defined by clinical signs and symptoms of inflammation of sinuses and nasal passages of less than 30 days. Cure, improvement, and treatment failure definitions are based on the original reports. Studies of subjects with either acute sinusitis or acute exacerbation of chronic sinusitis were included. Studies of sinusitis with complications, those that exclusively evaluated chronic sinusitis and studies of acute sinusitis along with other respiratory infections were excluded.

Inclusion Criteria

- Pertinent to the research questions.
- Included subjects with acute rhinosinusitis or acute exacerbation of chronic sinusitis.
- Any age group.
- Included at least 10 subjects in each arm.
- Comparative studies for the evaluation of antibiotic efficacy. (Non-comparative studies were included in the review of adverse events only.)
- Reported clinical and/or radiological and/or microbiological failures.

Exclusion criteria

- Studies that included only patients with chronic sinusitis.
- Studies that included other upper respiratory infections in addition to acute sinusitis.

Search Strategy and Retrievals

We searched MEDLINE® using a broad search strategy covering the period from 1997 to September 2004. The search terms were: "sinusitis," "rhinosinusitis," "anti-bacterial agents," "anti-infective agents" and other relevant terms. We limited the search results to human studies and English-language studies. We conducted a separate search using terms such as "vaccines" and "pneumococcal vaccine" to look for studies to address the question of pneumococcal vaccine and sinusitis. This separate search identified a total of 273 abstracts for screening. None of these qualified for inclusion in this update. We also sought additional articles by reviewing reference lists of selected review articles and meta-analyses and contacting members of the Technical Expert Panel. We did not seek unpublished studies.

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Evidence-Based Practice

Meta-analysis

We constructed an antibiotic comparative matrix to assess the feasibility of performing meta-analyses of clinical failure. We determined that it would be feasible to compare the efficacy of antibiotics with placebo, as well as four different antibiotic classes with each other. Comparisons were made between amoxicillin-clavulanate, cephalosporins, quinolones and the combined category of macrolides, azalides and ketolide. We calculated the risk ratios and risk differences for clinical failure. All meta-analyses were performed using a random effects model.

Adverse Events Data Extraction

Adverse event data were extracted from the antibiotic comparison studies that met the inclusion criteria. In addition, adverse event data were also taken from non-comparative antibiotic studies that reported this data. We abstracted for each study the percentage of subjects who experienced at least one adverse event, the percentage who withdrew from a study due to adverse events, the percentage with severe adverse events and the percentage who experienced gastrointestinal, central nervous system, skin/extremity and/or cardiovascular events.

Results

The MEDLINE® search identified 704 abstracts. After screening the abstracts, 87 articles were retrieved for further evaluation. A total of 39 studies ultimately qualified for inclusion in this update. These trials enrolled 15,739 subjects from 1997 to 2004 and studied antibiotic comparisons in treatment of acute bacterial rhinosinusitis. With the exception of five studies that did not provide the information, all the studies were either funded by pharmaceutical companies or had authors associated with the pharmaceutical industries. No study exclusively evaluated a pediatric population. The classes of antibiotics studied consist of penicillins, cephalosporins, macrolides, azalides, ketolides, quinolones, carbapenems and tetracyclines. There were 22 comparisons with amoxicillin/clavulanate and only five comparisons with amoxicillin.

Overall, antibiotics were more effective than placebo, reducing the risk of clinical failure by about 25 to 30 percent within 7 to 14 days after treatment initiation ($p<0.01$). However, symptoms improved or were resolved in 65 percent of patients without any antibiotic treatment at all (95% CI, 40-91%). Amoxicillin-clavulanate, compared to antibiotics in the cephalosporin class, was 41 percent more effective in reducing clinical failure within 10 to 25 days after treatment initiation ($p=0.01$). In absolute terms, this means treating 100 patients with antibiotics in the cephalosporin class will lead to 3.5 more failures (95% CI, 0.86 to 6) as compared to amoxicillin-clavulanate. The results 24 to 45 days after treatment initiation, however, did not show significant difference ($p=0.5$). There was no consistent trend observed when comparing amoxicillin-clavulanate, cephalosporins and quinolones to the group encompassing macrolides, azalides and ketolides.

There are eight studies that reported data on comparison of treatment duration with outcome efficacy. One study showed that 10 days vs. 5 days of amoxicillin-clavulanate 500 mg three times a day showed a non-significant 28 percent reduction in clinical failure rate.[2] Two studies on 10 days vs. 5 days of telithromycin showed that the clinical failure rate between the two treatment durations was comparable.[3,4] The studies on gemifloxacin (5 days vs. 7 days),[5] azithromycin (3 days vs. 6 days),[6] and gatifloxacin (5 days vs. 10 days)[7] showed therapeutic equivalence of the two durations.

Thirty-four comparative trials and five non-comparative trials reported adverse events. Descriptions of adverse events were diverse among studies. It was not possible to make meaningful comparisons of adverse event rates across different antibiotic classes given the enormous variation in the reported rate of adverse events within the same antibiotic class. For example, the reported rate of diarrhea with amoxicillin-clavulanate across different studies ranged from under 2 percent to more than 30 percent. Overall, the most common adverse events involved the gastrointestinal and the central nervous system. Severe adverse events were rare, occurring in less than 10 percent of any given study population. We did not identify any article in our literature search that directly addressed the effect of pneumococcal vaccine in the treatment of acute bacterial sinusitis.

Discussion

- About two-thirds of the patients receiving placebos recovered without antibiotics.
- Antibiotic is more effective than placebo.
- Amoxicillin-clavulanate is more effective than cephalosporin in the short-term followup.
- There are no significant differences between other classes of antibiotics.
- There is a lack of studies that compare newer antibiotics with inexpensive ones like amoxicillin and trimethoprim/sulfamethoxazole.

Limitations

Heterogeneous study population and definitions of clinical success/failure across studies, studies powered primarily for non-inferiority rather than superiority, few studies within each comparison grouping, and the possibility of publication bias all

lend limitations to our meta-analyses. Sinus aspirations and cultures, the gold standard for diagnosing and assessing bacterial sinusitis were performed in a minority of trials. Almost all the studies that were sponsored by pharmaceutical companies concluded that the sponsored drug was either superior or therapeutically equivalent to the comparator. In actuality, virtually all the studies demonstrate non-inferiority only. It is possible that there may be unpublished trials with negative results. This could be a continual limitation if mandatory registration of drug trials is not implemented. A notable omission compared to our previous report is the lack of comparative studies between newer expensive antibiotics and older inexpensive ones (like amoxicillin and trimethoprim/sulfamethoxazole). This is an important issue to be addressed for health care cost containment.

Future Research

Future trials should incorporate bacteriologic data to help characterize the changing epidemiology of acute bacterial rhinosinusitis. In order to make meaningful comparisons across studies, there should be general agreement in defining inclusion/exclusion criteria, clinical success/failure, and the appropriate time of outcome assessment. To reduce the possibility of bias, the intent-to-treat population should be uniformly defined across studies and data should be collected and reported in addition to per-protocol results. Also, results from all drug trials should be duly reported. Prevalence of different pneumococcal serotypes and their resistance patterns will have to be continually monitored to help guide the optimal treatment of acute bacterial rhinosinusitis.

Availability of the Full Report

The full evidence report from which this summary was taken was prepared for the Agency for Healthcare Research and Quality (AHRQ) by the Tufts-New England Medical Center Evidence-based Practice Center under Contract No. 290-02-0022. It is expected to be available in summer 2005. At that time, printed copies may be obtained free of charge from the AHRQ Publications Clearinghouse by calling 800-358-9295. Requesters should ask for Evidence Report/Technology Assessment No. 124, *Update on Acute Bacterial Rhinosinusitis.* In addition, Internet users will be able to access the report and this summary online through AHRQ's Web site at www.ahrq.gov.

Suggested Citation

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