Clinical efficacy of antimicrobial drugs for acute otitis media: metaanalysis of 5400 children from thirty-three randomized trials

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Authors' objectives
To review the clinical effectiveness of antimicrobial drugs for acute otitis media (glue ear) in children.

Searching
MEDLINE was searched from 1966 to June 1992 using the MeSH (explode) 'otitis media' or (explode) 'drug therapy', and limiting the search by: (1) use of MeSH 'prospective studies', 'placebos', 'random allocation', 'double-blind method' or (explode) 'clinical trials'; (2) check tag comparative study; or (3) publication-type clinical trial. Current Contents (1992;35(13-26)), and references from textbook bibliographies, review articles, retrieved articles and symposium publications, were also searched.

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

Specific interventions included in the review
Antimicrobial drugs administered for initial empiric treatment of simple acute otitis media.

Participants included in the review
Children aged 4 weeks to 18 years old with acute otitis media and with no underlying disorders (e.g. Down's syndrome, cleft palate, concurrent illnesses), which might influence susceptibility to infection.

Outcomes assessed in the review
Primary end points were the absence (or otherwise) of all presenting signs and symptoms of acute otitis media at the evaluation point closest to 7 to 14 days after therapy was started, and improvement in the appearance of the tympanic membrane. The secondary end point was the presence or absence of middle ear effusion in both ears at the evaluation point closest to 30 days after therapy was started.

How were decisions on the relevance of primary studies made?
Two reviewers independently assessed blinded manuscripts using a checklist of eligibility criteria.

Assessment of study quality
RCTs in which at least one group was given 1 of 14 antimicrobial drugs to treat simple acute otitis media. Studies were excluded if they were of specific bacterial pathogens, if they included myringotomy as part of the treatment, and if they did not describe the type of otitis media. Included studies were evaluated independently by two reviewers using a checklist of methodological quality, and an overall quality score from 0 to 1 was calculated for each study based on its performance on 11 quality items.

Data extraction
Two reviewers independently extracted data, using patients (not ears) as the unit of analysis.

Methods of synthesis
How were the studies combined?
Studies were combined: (1) assuming a fixed-effect model, the exact maximum likelihood estimate of the common
odds ratio was calculated with 95% confidence intervals (CIs); (2) using a random-effects model, the pooled rate difference was calculated. If the pooled rate difference was statistically-significant, the numbers-needed-to-treat (NNT) was calculated.

How were differences between studies investigated?
Sensitivity analysis was used to assess the impact of diagnostic specificity, and of the methodological quality scores of the primary studies, on results. Pooled effect sizes were compared by type of antimicrobial drug.

Results of the review
Thirty-three RCTs, of which 47% were not double-blind, were included.

The spontaneous rate of primary control without treatment was 81% (95% CI: 69, 94). Compared with placebos or no drug, the rate difference for primary control for penicillin was 15.7% (95% CI: 4.7, 26.7), for aminopenicillin 12.9% (95% CI: 6.8, 19.0), and for any antibiotic 13.7% (95% CI: 8.2, 19.2). Six of every 7 children with acute otitis media either do not need antibiotics for primary control, or will not respond to antibiotic therapy (NNT = 7). Results from the fixed-effect and random-effects analyses were consistent. No significant differences were found between various antimicrobial agents. The sensitivity analysis showed that these results were robust to quality and diagnostic screening.

Authors' conclusions
Antimicrobial drugs have a modest but significant impact on the primary control of acute otitis media. Treatment with extended spectrum antibiotics does not increase resolution of acute symptoms or middle ear effusion; initial therapy should be guided by considerations of safety, tolerability, and affordability, and not by the theoretical advantage of an extended antibacterial spectrum.

CRD commentary
This review was rigorous in its methodology and the results appear robust. It is unclear that all the children included in the primary studies had bacteria in their middle ears, so the efficacy of antibiotics could be greater than reported in this review if they were given in a more targeted way. However, the review used diagnostic criteria which are likely to be reflected in practice.

Implications of the review for practice and research
Antibiotics are of some benefit in the management of acute otitis media in children if a bacterial cause is suspected. Cheaper standard-spectrum antibiotics are as effective as those with a broad spectrum.

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Other publications of related interest
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