Antibiotic therapy to prevent the development of asymptomatic middle ear effusion in children with acute otitis media: a meta-analysis of individual patient data


CRD summary
This individual patient data review pooled five trials and concluded that antibiotic therapy had little or no effect in preventing development of middle ear effusion. Ambiguity surrounding statistical assumptions resulted in some uncertainty regarding the reliability of the results.

Authors' objectives
To identify predictors of middle ear effusion and assess the effect of antibiotic therapy in preventing the development of middle ear effusion in children with acute otitis media.

Searching
PubMed, EMBASE, The Cochrane Library and proceedings of symposia on otitis media were searched in December 2005. Search terms and language restrictions were unreported.

Study selection
Randomised trials that compared antibiotic therapy with placebo or no antibiotic treatment in children (aged up to 12 years) with acute otitis media were eligible for inclusion. Studies needed to measure middle ear effusion and have a follow-up of one month. Age, sex and recurrence of acute otitis media were among potential baseline predictors of middle ear effusion. Middle ear effusion was defined as Type B tympanogram. Antibiotic therapy was amoxicillin in four trials (1,207 children) and amoxicillin-clavulanate in one trial (121 children). Four comparisons were to placebo and one was to delayed treatment. Intervention duration was seven to 10 days.

The authors did not report how many reviewers performed study selection.

Assessment of study quality
Individual patient data were checked for consistency, plausibility and integrity of randomisation and follow-up. Discrepancies were resolved by the relevant trialist.

The authors did not report how many reviewers performed validity assessment.

Data extraction
Individual patient data on the number of children with middle ear effusion at one month was extracted. Also extracted was a range of baseline candidate predictors of middle ear effusion, such as age younger than two years, sex, season, pain, fever, crying, coughing, siblings, otorrhea, runny nose, recurrent acute otitis media, smoking, breastfeeding and tympanic membrane variables. Data were extracted on an intention-to-treat basis.

Methods of synthesis
A forward stepwise logistic regression procedure was used to identify predictors of middle ear effusion using control group participants only. Predictor variables identified in this analysis were then entered into a fixed-effect logistic regression model that provided an overall pooled effect of antibiotic therapy on middle ear effusion and effects for the subgroups of interest. Between-study heterogeneity was measured using $I^2$. Missing data were imputed using linear regression.

Results of the review
Six studies met the inclusion criteria. Individual patient data were available for five trials (1,328 children).

The relative risk of antibiotic therapy preventing development of middle ear effusion was 0.9 (95% CI 0.8 to 1.0,
Predictors of middle ear effusion were age younger than two years (odds ratio 2.2, 95% CI 1.6 to 3.0) and recurrent acute otitis media (odds ratio 1.5, 95% CI 1.1 to 2.1). Neither these variables nor their interactions had a detectable relationship with treatment effectiveness.

**Authors' conclusions**
Antibiotic therapy had little or no effect in preventing development of middle ear effusion. Predictors of middle ear effusion were age younger than two years and recurrent acute otitis media.

**CRD commentary**
This generally well-conducted review incorporated a search of multiple sources and obtained a high proportion of the available information in the form of individual patient data. Data were checked for consistency and intention-to-treat analyses were undertaken, which minimised potential quality biases.

Logistic regressions were performed to assess effectiveness and identify prognostic factors, but the assumptions made in the modelling were neither subject to sensitivity analyses nor fully described. Specifically, although common effects were assumed, the controls on the regression intercept and slopes were ambiguous and no information was provided on covariate interactions or linearity. Likewise the impact of imputation, and ancillary information from the unavailable aggregate data were not considered.

The impact of these potential sources of uncertainty on the reliability of the results and conclusions is unclear.

**Implications of the review for practice and research**

**Practice:** The authors stated that prescribing antibiotics to prevent middle ear effusion was not recommended.

**Research:** The authors stated that use of antimicrobial prophylaxis in high-risk subgroups (Down syndrome, cleft palate) merited future trials.

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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.