Adenoidectomy with or without grommets for children with otitis media: an individual patient data meta-analysis

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Scientific summary

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Background

Otitis media (OM) continues to be one of the leading causes of medical consultations and the most frequent reason for antibiotic prescription and surgery in children in high-income countries. The surgical procedures offered to children with recurrent or persistent OM are (1) insertion of grommets (ventilation tubes), (2) adenoidectomy and (3) a combination of the two. Although clear National Institute for Health and Care Excellence (NICE) guidance is available for the use of grommets in subgroups of children with persistent OM with effusion (OME), similar guidance is not available for adenoidectomy, either in persistent OME or in recurrent acute otitis media (AOM). NICE recognises a need for further studies documenting the effect of adenoidectomy, either alone or as an adjuvant to grommet insertion, in the management of recurrent or persistent OM in children. In particular, it recognised a need for studies to identify any subgroups that might benefit more or less from surgical intervention than others. An individual patient data (IPD) meta-analysis, that is, a meta-analysis of the original individual data from previous trials, offers a unique opportunity to identify subgroups that may be more or less likely to benefit from adenoidectomy.

Objectives

In this IPD meta-analysis we therefore (1) developed a model to predict the risk of children referred for adenoidectomy having a prolonged duration of their otitis media. Then, (2a) having evaluated the overall effect of adenoidectomy, with or without grommets, on OM using these IPD, we (2b) identified those subgroups of children who benefit most, or who are most likely to benefit, from adenoidectomy with or without grommets.

Methods

The study was registered on 13 September 2011 in the PROSPERO register (CRD42011001549). We searched the following databases from their inception: the Cochrane Ear, Nose and Throat Disorders Group Trials Register, the Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library Issue 1, 2009, and Issue 5, 2012), PubMed, EMBASE, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Latin American and Caribbean Health Sciences Literature (LILACS), KoreaMed, IndMED, PakMediNet, CAB Abstracts, Web of Science, BIOSIS Previews, China National Knowledge Infrastructure (CNKI), the *meta*Register of Current Controlled Trials (*m*RCT), ClinicalTrials.gov, the International Clinical Trials Registry Platform (ICTRP), ClinicalStudyResults.org and Google. We used the following keywords with their synonyms: 'adenoidectomy' and 'otitis'. The first search was completed on 30 March 2009. Thereafter we received weekly updates from PubMed and performed a full updated search on 7 June 2012.

Studies were eligible for inclusion in this IPD meta-analysis if they were a randomised controlled trial in children up to 12 years of age diagnosed with OM (being recurrent AOM and/or persistent OME) in which adenoidectomy (with or without grommets) was compared with non-surgical treatment or grommets. Desirable time points for outcome assessment were 6, 12, 18 and 24 months.

For the quality assessment of the eligible studies we used The Cochrane Collaboration's quality assessment (risk of bias) tool. After checking the quality of the data sets and reproducing the findings of the individual studies, we developed one overall data set by recoding the variables from the individual data sets to the set of variables used for the IPD meta-analysis.

Our main comparison was adenoidectomy with or without grommets compared with non-surgical treatment or grommets only. This comparison was selected on the basis of prior knowledge of the available data sets included in our conventional meta-analysis, to maximise the statistical power to identify subgroups. Secondary comparisons studied were:

1. adenoidectomy with unilateral or bilateral grommets compared with non-surgical treatment
2. adenoidectomy with unilateral or bilateral grommets compared with unilateral or bilateral grommets
3. adenoidectomy without grommets compared with non-surgical treatment
4. adenoidectomy without grommets compared with unilateral or bilateral grommets.

We did not study the following comparisons as these analyses do not fulfil the criteria for inclusion in this IPD meta-analysis:

1. adenoidectomy with unilateral or bilateral grommets compared with adenoidectomy without grommets
2. unilateral or bilateral grommets compared with non-surgical treatment.

The primary outcome was failure at 12 months, which was defined as one or more of the following:

- four or more AOM episodes (including episodes of otorrhoea) per year
- presence of effusion for $\geq$ 50% of the time (i.e. effusion for > 6 months)
- need for additional surgery
- hearing* improved by < 10 dB.

*Hearing was expressed as a mean air conduction hearing level measured by age-appropriate audiometry (if possible averaged over 0.5, 1, 2 and 4 kHz). In all children the binaural average was taken. This includes trials that used unilateral grommets and randomised ears rather than children.

Secondary outcomes studied were:

1. all individual items of failure at 12 months
2. number of episodes of AOM (including episodes of otorrhoea) during follow-up
3. time with effusion during follow-up measured in number of weeks
4. additional surgery during follow-up
5. average hearing loss measured in dBHL (hearing level in decibels as assessed on an audiometer)
6. improvement in hearing level of < 10 dB
7. adverse effects and events (including morbidity of surgery).

Multivariate prognostic modelling was performed to develop a model predicting the risk of children referred for adenoidectomy but randomised to the non-surgical group having a prolonged duration of their OM. Absolute risks of failure at 12 months were calculated using the predictors identified in the multivariate analyses. To assess whether the effect of adenoidectomy was modified by age and indication for surgery, we performed an analysis using a binominal model with an identity link to calculate rate differences, a Poisson regression analysis with robust standard errors to calculate (adjusted) rate ratios (RRs) and an analysis using a linear regression model to calculate (adjusted) mean differences. In the Poisson and linear regression models, the independent variables were adenoidectomy, the potential effect modifier (age) and an interaction term (defined as adenoidectomy times potential effect modifier). We also used a categorical dummy variable to identify each study within the regression analysis. Dependent variables were the outcome measures mentioned above. Sensitivity analyses were performed to study the robustness of our findings. Although analyses of other types were carried out, all analyses reported in detail here were performed according to the intention-to-treat principle.

Results

In total, 15 trials were eligible for inclusion in this IPD meta-analysis of which 10, including 1761 participating children, were included. The 10 trials differed in a number of ways, with the most important being the indication for surgery, interventions studied and frequency of outcome assessment. Of the 10 included studies, eight were at a low risk of bias and two were at a moderate risk.

Of the 343 children who were referred for adenoidectomy but who were randomised to the non-surgical groups and included in the prognostic analyses, 193 (56%) failed to improve at 12 months. The independent predictor of failing to improve was indication. The absolute risk of failing to improve for children with an indication of persistent OME was 89% and that for children with an indication of recurrent AOM was 38%.

The proportion of children who failed at 12 months in the adenoidectomy group (adenoidectomy with or without grommets) was 32% whereas the proportion of children who failed at 12 months in the no adenoidectomy (non-surgical or grommets alone) group was 45%. The unadjusted for failure at 12 months was –13% [95% confidence interval (CI) –17% to –8%], resulting in a number needed to treat (NNT) of eight children to prevent one failure. The adjusted RR was 0.76 (95% CI 0.69 to 0.85), which was similar to the unadjusted RR (0.72, 95% CI 0.63 to 0.81). For all secondary outcomes, with the exception of presence of effusion for ≥ 50% of the time in the first 12 months, results for children in the adenoidectomy group were also statistically significantly better than results for those in the no adenoidectomy group.

The effects in the secondary comparisons also showed that children who have had their adenoid removed have a greater chance of clinical improvement. The size of that effect is, in general, small but persists for at least 2 years after surgery.

Two subgroups of children are most likely to benefit from adenoidectomy. These are (1) children with recurrent AOM aged < 2 years and (2) children aged ≥ 4 years with persistent OME. The proportion of children aged **< 2 years with recurrent AOM** who failed at 12 months was 16% (44/281) in the adenoidectomy group and 27% (120/438) in the group who did not have adenoidectomy (RD 12%, 95% CI 6% to 18%; NNT = 8; adjusted RR 0.63, 95% CI 0.47 to 0.85). In contrast, in children aged **≥ 2 years with recurrent AOM**, no benefit of adenoidectomy was seen; 18% (8/44) of the children in the adenoidectomy group failed at 12 months and 3% (1/40) of the group who did not have adenoidectomy failed (RD 16%, 95% CI 3% to 28%, in favour of no adenoidectomy; adjusted RR 4.96, 95% CI 0.69 to 35.5). The proportion of children aged ≥ **4 years with persistent OME** who failed at 12 months was 51% (163/322) in the adenoidectomy group and 70% (289/415) in the group who did not have adenoidectomy (RD 19%, 95% CI 12% to 26%; NNT = 6; adjusted RR 0.77, 95% CI 0.68 to 0.86). In contrast, in children aged **< 4 years with persistent OME**, no significant benefit of adenoidectomy was seen; 23% (30/128) of the children in the adenoidectomy group failed at 12 months and 30% (33/111) of the group who did not have adenoidectomy failed (RD 7%, 95% CI –5% to 18%; adjusted RR 0.98, 95% CI 0.69 to 1.38). The secondary comparisons and outcomes produced results that were in the same direction but were less pronounced because of smaller numbers.

A series of sensitivity analyses using alternative definitions of 'failure at 12 months' showed similar results.

Discussion

Potential limitations of this IPD meta-analysis relate to the selection of studies, the number of subgroup analyses performed, the variety of interventions and the lack of uniformity of outcomes in the original studies, necessitating these being aggregated in a composite primary outcome measure – failure at 12 months. However, a set of sensitivity analyses based on alternative definitions of 'failure' did not result in a different set of results.

Our findings confirm the clinical reality of two related but distinguishable entities within the spectrum of OM across the age range birth to 12 years: recurrent AOM in younger children (aged < 2 years) and persistent OME in older children (aged ≥ 4 years). It may not be age per se that is relevant but rather the presence of differing pathophysiological mechanisms in different age groups that serve as the modifier, with age simply being a proxy for those. The mechanisms may include a relatively immature immune response, in particular in children aged < 2 years. As the immune response improves with age, problems with infection may recede and those associated with middle ear effusion, for example hearing loss, become relatively more apparent. This coincides with a period of social and behavioural change in the child's life. Starting school and becoming part of a peer group may be the factors that initiate concerns about performance and increase awareness of the child's hearing. More insight into the pathophysiology of OM is needed to understand better the causal mechanism of the subgroup effects.

Conclusion

Children with OM who have their adenoid removed have a greater chance of clinical improvement: eight children need to receive adenoidectomy to prevent one failure. Adenoidectomy is most beneficial in children aged ≥ 4 years with persistent OME (six children needing adenoidectomy to prevent one failure). A smaller beneficial effect was found in children with recurrent AOM aged < 2 years (nine children needing adenoidectomy to prevent one failure). No beneficial effect was seen in children aged < 4 years with persistent OME or in those aged ≥ 2 years with recurrent AOM.

The need to use a composite end point and the limited number of subgroup variables that could be studied are factors that reduce the robustness of these results but these do not, we believe, reduce the validity of the conclusions.

As with all interventions (and in particular in the case of surgical procedures), consideration must be given to the balance between benefits and harms. Clinicians can discuss these issues with the parents of children with OM to allow them to make an informed treatment decision.

Future research is required in a number of key areas, including defining the best methods of selecting, developing and administering patient-reported outcome measures to assess the value of treatments for children with persistent OME and recurrent AOM and upper respiratory infections; investigating the clinical effectiveness and cost-effectiveness of hearing aids and the use of interventions to improve classroom acoustics for children with different degrees of persistence and severity of hearing loss associated with OME; and investigating why professionals' and parents'/carers' treatment preferences vary so much both nationally and internationally. We do not understand why adenoidectomy works in different subgroups at different ages, nor its effects in special populations, such as children with Down syndrome. We also need further research on the impact and optimal management of otitis media in these special situations and others, such as in children with a cleft palate or developmental problems.

Study registration

This study is registered at PROSPERO as CRD42011001549.

Funding

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