

Is early surgical referral for children with persistent otitis media with effusion (OME) appropriate?

Trial: Paradise JL, Feldman HM, Campbell TF, et al. Effect of early or delayed insertion of tympanostomy tubes for persistent otitis media on developmental outcomes at the age of three years. *N Engl J Med* 2001; 344: 1179-1187.

Question

Is early surgical referral for children with persistent otitis media with effusion (OME) appropriate?

Trial details

Design: Randomised, assessor-blinded, controlled trial.

Setting: Two hospitals and six private paediatric group practices from the Pittsburgh region in the United States.

Participants: 429 children aged less than 3 years who had otitis media with effusion (OME) that had persisted despite treatment with antimicrobial drugs for the equivalent of: 90 days in the case of bilateral effusion; or 135 days in the case of unilateral effusion.

Interventions: Children assigned to the early treatment group were scheduled to have ventilation tubes (grommets) inserted as soon as possible. Children assigned to the late treatment group were scheduled to undergo the operation 6 months later if bilateral effusion persisted (or 9 months later if unilateral effusion persisted). Children in the late treatment group could receive grommets earlier if their parents requested the operation.

Main outcome measures: Standardised assessment of cognitive ability, receptive language ability, expressive language ability, parenting stress, and child behaviour at 3 years of age.

Main results: 169 children in the early treatment group (82%) and 66 children in the late treatment group (34%) had had ventilation tubes (grommets) inserted by 3 years of age. There were no significant differences (mean \pm standard deviation) for early treatment versus late treatment in the General Cognitive Index of McCarthy's Scales of Children's Abilities (99 ± 14 v 101 ± 13); Peabody Picture Vocabulary Test-Revised (92 ± 13 v 92 ± 14); Number of Different Words Test (124 ± 32 v 126 ± 30); Percentage of Consonants Correct-Revised Test (85 ± 7 v 86 ± 7); Total Parenting Stress Index, Short-form-Total Stress (66 ± 18 v 68 ± 21); and Child Behaviour Checklist-Total Problems (50 ± 10 v 49 ± 10).

Conclusion: In young children with persistent OME, prompt insertion of ventilation tubes (grommets) does not measurably improve developmental outcomes by 3 years of age.

Commentary

Rationale for the trial

Otitis media with effusion (OME) is the most prevalent form of middle ear disease in young children. It is defined as the presence of fluid behind the tympanic membrane without the symptoms or signs of acute otitis media (AOM).¹ It is usually associated with some hearing loss. OME with persistent hearing loss may contribute to delays in speech and language development.² Recommended interventions include the use of antibiotics and the insertion of ventilation tubes (grommets).²⁻⁴

There have been concerns about the overuse of grommet surgery. Substantial variation in rates of this procedure have been documented.^{5,6} Clinical practice guidelines have recommended that grommets are an option for children who have bilateral OME associated with a hearing loss of > 20 decibels for at least 3 months.²⁻⁴ The intervention is most likely to benefit younger children (during the most critical phase of language development) and those with most hearing loss.

Trial methods

This trial was part of the largest otitis media cohort study ever conducted.⁷ The study was generally well designed and well reported.^{8,9} A total of 6350 healthy infants were enrolled in their first 2 months of life and were evaluated monthly for otitis media; 588 of these children had persistent or very frequent OME. They were regarded as typical of children who might receive surgery in the United States. The aim of the study was to determine the benefits of early referral for surgery compared with delayed referral (where "watchful waiting" continued for an additional 6 months).

Random assignment was made by designated non-clinical staff using separate, computer-generated lists of random numbers. Children were stratified according to site, age (in 6-month categories), and whether the eligibility criteria were met on the basis of bilateral or unilateral effusion. Assignment within each of the predetermined strata occurred in permuted blocks of four. This ensured that the allocation was balanced after every four new children (in a stratum) were randomly allocated.

Children underwent developmental assessment as soon as possible after their third birthday (and always within 2 months). Standardised assessment tools were used. Assessors were unaware of the child's medical history, health insurance status, and mother's level of education. The investigators proposed that a difference of 0.33 standard deviations between groups on any outcome measure could be clinically important. Follow-up of participants over a prolonged period was reasonably good (95% and 92% of the early- and late-treatment groups, respectively). All analyses were based on the intention-to-treat principle (although children who were not assessed could not be included in the analysis).

Any weaknesses in the methods and the quality of reporting were relatively minor. Ideally, the authors should have also described (i) how random allocation was concealed from the investigators, (ii) how block size was concealed from investigators (so they couldn't guess which intervention would be allocated next), (iii) the adequacy of blinding,

(iv) the primary outcome for the study, and (v) an assessment of adverse outcomes. The choice of a 0.33-standard-deviation difference between the groups in any of the assessments as the minimal clinically important difference was controversial. While this approach should be able to identify reasonably small statistical differences attributable to the intervention, the clinical importance of such a difference is not easily understood. In the end, because there were no statistically significant differences in any of the outcome measures, this issue did not arise.

New information

This is the largest randomised trial to evaluate ventilation tubes in children with persistent OME. Previous studies had shown that surgery improved hearing by around 12 dB at 6 months and 6 dB at 12 months.⁵ Most of these studies involved older children and did not include an assessment of speech and language (which is generally regarded as the most important outcome).

The results of this study are consistent with those of previous studies in demonstrating that grommet surgery will substantially reduce the amount of time that a child has OME, and modestly improve hearing. However, by 3 years of age, early referral for surgery had no beneficial effect on development or behaviour. The consistent lack of effect for a range of outcome measurements was striking. These findings were not changed by the subsequent subgroup analyses.¹⁰ The results of this study are unlikely to be explained by a biased estimate of effect or by chance. Similar results have also been documented in other recent well designed studies in different populations.¹¹⁻¹³



Implications for clinical practice

Identifying young children with persistent OME is a common problem for general practitioners in Australia. For children who are otherwise well, this study shows that early referral for surgery does not improve developmental outcomes at 3 years of age. For individual families affected by long waiting times or preferring to avoid an operation, parents can be reassured that the child will not be disadvantaged by delaying the decision about surgery. The duration of "watchful waiting" can be extended to 9–12 months without serious consequences. Although hearing loss will persist longer, many episodes of persistent OME will resolve and potential complications of surgery (otorrhoea, chronic perforation) will be avoided.

It is still possible that the insertion of ventilation tubes will improve developmental outcomes in some children. The results of this study are not applicable to:

- children with established speech and language delay (or conditions known to be associated with speech and language delay);

- children with bilateral OME that persists longer than 9–12 months; and
- children with more substantial conductive hearing loss.

Parents of these more severely affected children can be advised that this simple and safe operation will improve their child's hearing. However, whether it will improve their speech and language development is still uncertain. Further trials targeting these specific subgroups should be supported.

Peter S Morris

Head

Amanda J Leach

Senior Research Fellow
Ear Health and Education Unit
Menzies School of Health Research, Darwin NT
peterm@menzies.edu.au

Competing interests

None identified.

References

1. Bluestone CD, Klein JO. Otitis media in infants and children. 2nd ed. Philadelphia: WB Saunders, 1995.
2. Rosenfeld RM, Bluestone CD. Evidence-based otitis media. Hamilton: BC Decker Inc, 1999.
3. Stool SE, Berg AO, Berman S, et al. Otitis media with effusion in young children. Clinical Practice Guideline No. 12. AHCPR Publication No. 94-0622. Rockville, Md: Agency for Health Care Policy and Research, Public Health Service, US Department of Health and Human Services, 1994.
4. Morris P, Ballinger D, Leach A, et al. Recommendations for clinical care guidelines on the management of otitis media in Aboriginal and Torres Strait Islander populations. Canberra: Office of Aboriginal and Torres Strait Islander Health, 2001.
5. Freemantle N, Sheldon TA, Song F, Long A. The treatment of persistent glue ear in children. Effective Health Care Bulletin No. 4. York: University of York, NHS Centre for Reviews and Dissemination, 1992.
6. Close GR, Rushworth RL, Rob MI, Rubin GL. Variation in selected childhood surgical procedures: the case of tonsillectomy and management of middle ear disease. *J Paediatr Child Health* 1993; 29: 429-433.
7. Paradise JL, Dollaghan CA, Campbell TF, et al. Language, speech sound production, and cognition in three-year-old children in relation to otitis media in their first three years of life. *Pediatrics* 2000; 105: 1119-1130.
8. Gebski VJ, Beller EM, Keech AC. Randomised controlled trials: elements of a good study. *Med J Aust* 2001; 175: 272-274.
9. Altman DG, Schulz KF, Moher D, et al. The revised CONSORT statement for reporting randomized trials: explanation and elaboration. *Ann Intern Med* 2001; 134: 663-694.
10. Paradise JL, Feldman HM, Campbell TF, et al. Early versus delayed insertion of tympanostomy tubes for persistent otitis media: developmental outcomes at the age of three years in relation to prerandomization illness patterns and hearing levels. *Pediatr Infect Dis J* 2003; 22: 309-314.
11. Maw R, Wilks J, Harvey I, et al. Early surgery compared with watchful waiting for glue ear and effect on language development in preschool children: a randomised trial [published erratum appears in *Lancet* 1999; 354: 1392]. *Lancet* 1999; 353: 960-963.
12. MRC Multicentre Otitis Media Study Group. Surgery for persistent otitis media with effusion: generalizability of results from the UK trial (TARGET). Trial of Alternative Regimens in Glue Ear Treatment. *Clin Otolaryngol* 2001; 26: 417-424.
13. Rovers MM, Straatman H, Ingels K, et al. The effect of ventilation tubes on language development in infants with otitis media with effusion: a randomized trial. *Pediatrics* 2000; 106: E42.

(Received 25 Jul 2003, accepted 9 Sep 2003)

□