Nonsevere acute otitis media: a clinical trial comparing outcomes of watchful waiting versus immediate antibiotic treatment

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The health technologies under evaluation were watchful waiting (WW; symptom medication only) versus immediate antibiotic treatment (ABX; amoxicillin plus symptom medication) for children with nonsevere acute otitis media (AOM).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised children 6 months to 12 years of age, with nonsevere AOM. To enrol, children were required to have symptoms of ear infection, otoscopic evidence of AOM including middle-ear effusion, and nonsevere AOM. Children were ineligible if they had a co-morbidity requiring ABX, an anatomic defect of the ear or nasopharynx, or an allergy to study medication. They were also ineligible if they had an immunologic deficiency, major medical condition, and/or indwelling tympanostomy tube or draining otitis in the affected ear(s).

Setting
The setting was a paediatric clinic (it was unclear if this was secondary or tertiary care). The economic study was carried out in Texas, USA.

Dates to which data relate
The effectiveness data and resource use data were gathered between 1 May 2000 and 30 March 2003. The price year was 2004.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was carried out prospectively on the same sample of patients as that used in the effectiveness analysis.

Study sample
Power calculations were carried out to determine the sample size. A total of 223 children were recruited. Seventy-three per cent were nonwhites, 57% were under 2 years old, 47% attended day care, 82% had experienced prior AOM, and
83% had not been fully immunised with heptavalent pneumococcal vaccine. A total of 112 were randomised to ABX and 111 to WW.

**Study design**
In design terms, the study was an investigator-blinded (but not parent-blinded), randomised controlled trial that was carried out in a single centre. Five of every 10 participants were assigned randomly to the immediate-ABX group and the other 5 to the WW group, to closely maintain the numbers of patients in the two groups within any given time period. The randomisation scheme was constructed using the random-number generator function in the SAS 8.2 software. The duration of follow-up was 12 days and 30 days. Ninety-four per cent of the participants were followed to the 30-day end point.

**Analysis of effectiveness**
The analysis of effectiveness was conducted on the basis of treatment completers only. The primary outcomes included parent satisfaction with AOM care, resolution of symptoms, AOM failure/recurrence, and nasopharyngeal carriage of Streptococcus (S.) pneumoniae strains resistant to ABX. The secondary outcomes included:

- medication-related adverse events;
- serious adverse events;
- unanticipated AOM-related office and emergency department visits and telephone calls;
- the child's absence from day care or school resulting from AOM; and the parent's absence from school or work because of their child's AOM.

The groups were shown to be comparable at the analysis.

**Effectiveness results**
Total parent satisfaction scores for the immediate-ABX group compared with the WW group were not different at day 12 (44.4 versus 44.0) or day 30 (44.6 versus 44.6). Compared with WW, symptom on days 1 to 10 resolved faster in children treated with immediate ABX. At day 12, 69% of tympanic membranes and 25% of tympanograms were normal among the immediate-ABX group, compared with 51% (tympanic membranes) and 10% (tympanograms) in the WW group. Parents of children in the ABX group gave their children fewer doses of pain medication than did parents of children in the WW group. Children in the ABX group experienced 16% fewer failures than children in the WW group. Of the children in the WW group, 66% completed the study without needing ABX.

Immediate ABX resulted in the eradication of S. pneumoniae carriage in the majority of children, but S pneumoniae strains cultured from children in the ABX group at day 12 were more likely to be multidrug-resistant than strains from children in the WW group (p<0.02). More ABX-related adverse events were noted in the ABX group than in the WW group (12% versus 5%). No serious AOM-related adverse events were observed in either group.

**Clinical conclusions**
Sixty-six per cent of children in the WW group completed the study without ABX. Parent satisfaction was the same between groups, regardless of treatment. Compared with WW, immediate ABX was associated with decreased numbers of treatment failures and improved symptom control. However, it increased ABX-related adverse events and there was a higher percentage carriage of multidrug-resistant S. pneumoniae strains in the nasopharynx at the day-12 visit.

**Measure of benefits used in the economic analysis**
No summary measure of benefits was derived. The study was therefore categorised as a cost-consequences analysis.
Direct costs
The direct costs included the costs of medications only. The costs of ABX were calculated using Galveston community pharmacy retail charges (as of June 2004) and data on the numbers of initial prescriptions and failure or recurrence prescriptions for each intervention group. These calculations were simplified by assuming that all children were at the median age (1.6 years) and weight (11.5 kg) and were able to take oral ABX for all failure or recurrence episodes. Discounting was not necessary as the costs were incurred within a year. The price year was 2004.

Statistical analysis of costs
No statistical analysis of the costs was reported.

Indirect Costs
The indirect costs were not included because the number of visits and days of work lost by the parents were not significantly different between the groups.

Sensitivity analysis
No sensitivity analysis was reported.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
Children in the immediate-ABX group required 109 initial prescriptions for amoxicillin and 28 prescriptions of high-dose amoxicillin-clavulanate for failure or recurrence episodes (total $5,167.26; $47.41 per child).

Children in the WW group required 34 prescriptions for amoxicillin and 4 prescriptions for high-dose amoxicillin-clavulanate for failure or recurrence episodes (total $1,143.24; $11.43 per child).

Synthesis of costs and benefits
The costs and benefits were not combined.

Authors' conclusions
Sixty-six per cent of patients in the watchful waiting (WW) group completed the study without antibiotic treatment (ABX). Parent satisfaction was the same between groups, regardless of treatment. Compared with WW, immediate ABX was associated with a decreased number of treatment failures and improved symptom control. However, it increased ABX-related adverse events and there was a higher percentage carriage of multidrug-resistant Streptococcus (S.) pneumoniae strains in the nasopharynx at the day-12 visit.

CRD COMMENTARY - Selection of comparators
Although no explicit justification was given for the comparator used, immediate ABX would appear to represent current practice in the authors' setting. You should decide if it is a widely used health technology in your own area.

Validity of estimate of measure of effectiveness
The analysis was based on an investigator-blinded, randomised controlled trial, which was appropriate for the study question. The patient groups were shown to be comparable at analysis. However, as the authors acknowledged, since the study design was parent-unblinded, parent satisfaction might have been influenced by the parents' personal beliefs and preconceptions about the advantages or disadvantages of ABX.
Validity of estimate of measure of benefit
The authors did not derive a summary measure of health benefit. The study was therefore categorised as a cost-consequences analysis.

Validity of estimate of costs
The authors stated that the perspective of the patients’ parents was used. Since the number of visits and days of work lost by the parents were not significantly different between the groups, only the direct costs of medications were included. Resource use was reported separately based on observational data. The costs and the quantities were reported separately, which may aid the reproducibility of the results. The year to which the prices referred was reported.

Other issues
The authors made appropriate comparisons of their findings with those from other studies. They noted that the percentage difference in failures between ABX and WW for nonsevere AOM was larger than they had expected from their review of the literature, and their overall day-0 to day-12 failure rate and recurrence rate were lower than rates published in recent studies. The issue of generalisability to other settings was addressed. The authors reported several limitations of the study. For example, the parent-unblinded study design, the lack of data to answer some important safety questions, and the lack of sufficient power to document altered risk of AOM-related serious adverse events.

Implications of the study
The results suggested that some children with nonsevere AOM might be observed with WW as long as they maintain nonsevere status and are kept comfortable with appropriate symptom management. Under these conditions, WW seems to be an alternative that is acceptable to parents, reduces the number and cost of ABX prescriptions, and reduces the percentage of multidrug-resistant bacteria colonising the nasopharynx of children after an episode of AOM. The authors recommended that key factors in implementing a WW strategy are:

- a method of classifying AOM severity;
- parent education;
- management of AOM symptoms;
- access to follow-up care; and
- the use of an effective ABX regimen, when needed.

If these caveats are observed, WW may be an acceptable alternative to immediate ABX for some children with nonsevere AOM.

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