Management of Childhood Acute Otitis Media With or Without Oral Antibiotics: A Systematic Review and Meta-analysis

EPH211

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INTRODUCTION

- Acute otitis media (AOM) is one of the most common childhood infections, with an estimated 709 million cases annually, over half occurring in children under five.[1]
- Antibiotics are commonly used to treat AOM; however, rising antimicrobial resistance (AMR) has led recent guidelines to recommend delaying treatment in healthy children with mild symptoms.[2]
- The benefits of antibiotic use must be weighed against the risks of side effects and resistance, highlighting the need to evaluate the available evidence.

OBJECTIVE

The objective of this systematic literature review (SLR) was to investigate the use of oral antibiotics in children with AOM compared to treatment without the use of antibiotics to answer the following question: Should children (ages 0–19 years) with AOM receive treatment with oral antibiotics or no antibiotics?

METHODS

- This SLR was conducted following WHO guidelines,[3] reported per PRISMA 2020 statement;[4] registered in PROSPERO (CRD42023474006).
- RCT evidence was sourced from a Cochrane review (Venekamp *et al.*, 2015)[5] and updated; a separate search identified non-randomized studies (NRS, inception–July 2023)
- Embase, MEDLINE (including In-Process), and Cochrane (CENTRAL, CDSR) were searched for RCTs published since the search cutoff of Venekamp *et al.* (2015)[5] (Apr. 2015-Aug. 2023); clinical trial registries and conference proceedings were also searched.
- Included studies evaluated oral antibiotics vs. placebo/no treatment for AOM in children (≤19 years), reporting clinical outcomes, with no language restrictions.
- Outcomes included pain, abnormal tympanometry, TM perforation, contralateral otitis, late AOM recurrence, mastoiditis risk, symptom resolution, TM score normalization, fever, and adverse events (vomiting, diarrhea, rash).
- Two reviewers independently screened publications; disagreements were resolved by a third reviewer. Risk of bias was assessed using RoB 2[6] for RCTs and ROBINS-I[7] for NRS.
- Meta-analyses of binary outcomes used random-effects (DerSimonian–Laird) models, with fixed-effect (Mantel–Haenszel) models applied when <3 studies were available; analyses were conducted using the metabin function (meta v6.2-1) in R v4.2.3.
- Relative risks (RRs) with 95% CIs were calculated; a continuity correction (0.5) was applied for zero events. Studies with zero events in both groups were excluded from meta-analysis and summarized narratively.
- Certainty of evidence (CoE) for pooled estimates was determined using Grading of Recommendations Assessment, Development and Evaluation (GRADE).[8]

RESULTS

- Seventeen studies (13 RCTs, 4 NRS) from 22 publications were included (**Figure 1**). Across the RCTs, 3,401 children were recruited; ages ranged from 2 months–15 years. All RCTs compared oral antibiotics against placebo. Three of four NRS included 1,035 children with AOM; one reported 1,182,272 otitis media episodes in 462,904 children.

RCT Evidence (13 RCTs)

- Statistically significant reductions in pain were observed with antibiotics vs placebo at 2-3 days (RR: 0.71 [95% CI: 0.58, 0.88]; GRADE: High CoE) and 10-12 days (RR: 0.33 [95% CI: 0.17, 0.66]; GRADE: Low CoE). However, no significant effect was observed at 24 hours or 4-7 days (**Table 1**).
- Antibiotics significantly reduced the risk of TM perforation (RR: 0.43; GRADE: High CoE), contralateral otitis (RR: 0.49; GRADE: High CoE), and abnormal tympanometry at 2-4 weeks (RR: 0.83; GRADE: Moderate CoE). No significant difference was observed for late AOM recurrence (GRADE: Low CoE, **Table 1**).
- Patients treated with antibiotics had significantly higher rates of vomiting, diarrhea, or rash compared with placebo (RR: 1.38 [95% CI: 1.16, 1.63]; GRADE: High CoE, **Table 1**).

NRS Evidence (4 NRS)

- Antibiotics showed a non-significant trend toward lower pain at days 3–7 (RR 0.33 [95% CI: 0.08, 1.33]; very low CoE) and no difference in recurrent AOM rates vs. no antibiotics (RR 0.97 [0.87, 1.08]; very low CoE).
- Antibiotics halved the risk of post-OM mastoiditis (OR 0.56 [95% CI: 0.44, 0.71]; GRADE: Very Low CoE) and markedly improved TM normalization by day 8 (RR 61.00 [3.77, 985.83]; very low CoE)

Figure 1. Study selection flowchart

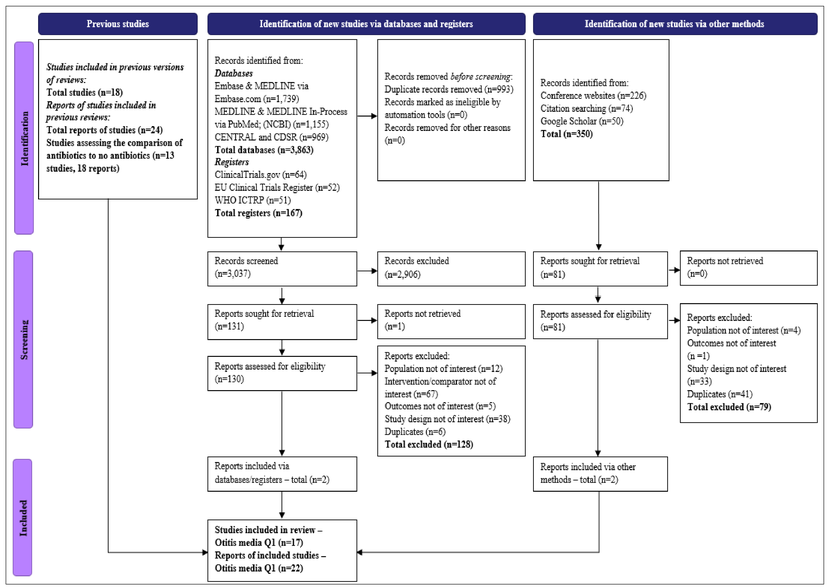

Table 1. GRADE evidence profile of antibiotics compared with no antibiotics (RCTs)

Outcome	Study Design (No. Studies)	Antibiotics n/N (%)	No Antibiotics n/N (%)	RR / OR (95% CI)	Absolute Effect (per 1,000)	GRADE CoE
Pain at 24 hours	RCTs (5)	267/709 (37.7%)	292/685 (42.6%)	RR 0.89 (0.78–1.01)	47 fewer (94 fewer to 4 more)	⊕⊕⊕◯ Moderate
Pain at 2–3 days	RCTs (7)	138/1186 (11.6%)	180/1134 (15.9%)	RR 0.71 (0.58–0.88)	46 fewer (67 fewer to 19 fewer)	⊕⊕⊕⊕ High
Pain at 4–7 days	RCTs (7)	119/680 (17.5%)	161/667 (24.1%)	RR 0.76 (0.53–1.10)	58 fewer (113 fewer to 24 more)	⊕⊕⊕◯ Moderate
Pain at 10–12 days	RCTs (1)	10/139 (7.2%)	30/139 (21.6%)	RR 0.33 (0.17–0.66)	145 fewer (179 fewer to 73 fewer)	⊕⊕◯◯ Low
Abnormal tympanometry (2–4 wks)	RCTs (7)	419/1070 (39.2%)	514/1068 (48.1%)	RR 0.83 (0.72–0.96)	82 fewer (135 fewer to 19 fewer)	⊕⊕⊕◯ Moderate
TM perforation	RCTs (5)	9/533 (1.7%)	26/542 (4.8%)	RR 0.43 (0.21–0.89)	27 fewer (38 fewer to 5 fewer)	⊕⊕⊕⊕ High
Contralateral otitis	RCTs (4)	48/453 (10.6%)	85/453 (18.8%)	RR 0.49 (0.25–0.95)	96 fewer (141 fewer to 9 fewer)	⊕⊕⊕⊕ High
Late AOM recurrence	RCTs (6)	208/1138 (18.3%)	213/1062 (20.1%)	RR 0.94 (0.79–1.11)	12 fewer (42 fewer to 22 more)	⊕⊕◯◯ Low
Vomiting, diarrhea, or rash	RCTs (8)	283/1044 (27.1%)	208/1063 (19.6%)	RR 1.38 (1.16–1.63)	74 more (31 more to 123 more)	⊕⊕⊕⊕ High

Abbreviations: AOM, acute otitis media; CI, confidence interval; CoE, certainty of evidence; GRADE, Grading of Recommendations Assessment, Development and Evaluation; OR, odds ratio; RCT, randomized controlled trial; RR, relative risk; TM, tympanic membrane;

DISCUSSION & CONCLUSIONS

- Antibiotic treatment demonstrated benefits including reduced pain at 2-3 and 10-12 days, lower rates of TM perforation, contralateral otitis, and abnormal tympanometry, as well as a decreased risk of mastoiditis. However, these benefits were accompanied by significantly higher rates of adverse events (vomiting, diarrhea, and rash).
- Evidence gap: All studies from high-income countries, most pre-2010. Research needed in resource-limited settings, where disease burden is higher and antibiotics may affect AOM outcomes differently.
- Benefits of antibiotic use must be weighed against the risks, in addition to the increased risk of AMR associated with antibiotic use.

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DISCLOSURES

Authors have no conflicts of interest to declare

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