Acute Otitis Media in Children

Role of antibiotic therapy

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SUMMARY

In a review and critical appraisal of the literature on antibiotic therapy for acute otitis media in children between 1939 and 1991, poor evidence supported the routine use of antibiotic therapy. Good evidence supported initial symptomatic treatment and institution of antibiotic therapy only in cases of an irregular course (fever or pain for more than 48 to 72 hours) in children 2 years and older. This approach cannot be recommended for children 2 years and younger because this age group has been excluded from most studies.

RÉSUMÉ

Une revue et une évaluation critique de la littérature publiée entre 1939 et 1991 sur l'antibiothérapie prescrite dans les cas d'otite moyenne chez les enfants démontre la faible qualité des preuves à l'appui de recommander l'utilisation systématique de l'antibiothérapie. Par contre, il existe une bonne qualité des preuves à l'appui d'un traitement initial symptomatique et d'une antibiothérapie chez les enfants de plus de deux ans lorsque l'évolution est atypique (fièvre ou douleur qui persistent plus de 48 à 72 heures). On ne peut toutefois recommander cette approche chez les enfants de moins de deux ans parce que ces nourrissons ont été exclus de la plupart des études.

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UNTIL ABOUT 2 YEARS AGO, I considered the routine use of antibiotics for treating acute otitis media (AOM) in children as one of the few uncontroversial therapies in medicine. I had never met a physician who would not prescribe antibiotics for AOM or even the faintest suspicion of AOM in children.

I was quite surprised when I became aware of evidence that antibiotic treatment is indeed quite controversial and that prescribing habits of physicians in different countries vary greatly, from 31.2% of patients prescribed antibiotics in the Netherlands to 98.2% of patients in Australia and New Zealand.[1] In the United States, 97.9% of patients are prescribed antibiotics. There is no reason to believe that figures are different for Canada.

I then reviewed and critically appraised the literature to decide the question: Is there a benefit to the routine use of antibiotics for AOM in children or not?

Article selection methods

A computer MEDLINE search was done looking for articles dating back to 1985. Key words used were "otitis media" and "children/adolescence." One hundred nine articles were identified: 13 that dealt with the antibiotic and nonpharmacologic treatment of AOM and seven review articles. All retrieved articles were read and the reference sections checked for studies or articles pertinent to my research question.

These methods turned up seven randomized, controlled trials (RCTs) dating from June 1954 to September 1991,[2-8] seven descriptive studies dating from May 1939 to July 1991,[9-15] and 16 review articles dating from May 1980 to April 1992.[1,16-30]

After excluding unblinded RCTs and small descriptive studies, six papers remained to be evaluated. Five papers were double-blinded RCTs,[3,5-8] and one paper was a descriptive study[14] that was evaluated because of its design and large scale (4860 persons). For readers' information I also reference current recommendations by a panel of Canadian pediatric infectious disease specialists.[23]

Review criteria

The studies I reviewed were evaluated by the following criteria.

Random allocation. Did every patient who entered the study have the same probability (typically 50%) of receiving one or the other of the treatments prescribed? Was the method of randomization described?

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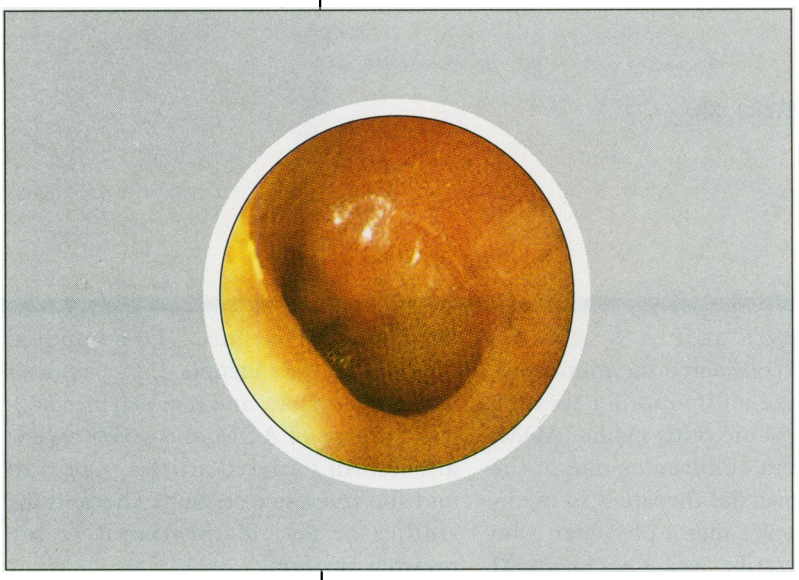
Blinding. Was the study blinded or double-blinded? What were the patient and the physician told?

Patient selection and comparability of study groups. What were the inclusion and exclusion criteria? What age groups were included or excluded? Was the age distribution described? From what population base did the patients come? Was the population group typical for the study of the disease?



Acute Otitis Media: *Reprinted with permission from Michael Hawke, MD.*

Placebo control. Did any group receive placebo? Was the placebo described?

Diagnosis and course of the disease. What criteria were used to diagnose the disease studied? How well were "improvement," "no improvement," "cure," "not healed," etc, and complications defined?

Follow up. What percentage of patients were seen at each follow-up assessment? Were all patients who entered the study accounted for at its conclusion? Who did the follow up?

Treatment. Were the different treatments well described? Who prescribed the treatments (general practitioner or specialist)?

Adequacy of sample size. Was the number of patients studied large enough to establish statistically significant differences in treatment outcome?

Compliance. Was patient and physician compliance with the treatment measured and described?

Statistical analysis. Was the method of statistical analysis adequate? What was the *P* value?

Generalizability. How closely does the population studied resemble patients I would see? Is the study relevant to patients in my practice?

Results

Halsted and colleagues. This study[3] was conducted by a group of specialists (pediatricians, internists, and microbiologists) at the University of Cleveland during 1965-1966. Eighty-nine children aged 2 months to 5 ½ years were investigated; 94% of the children were older than 3 years. The study was designed to investigate the relationship of bacteria, viruses, and *Mycoplasma* in otitis media.

Two types of antibiotic therapy were compared with placebo. Patients were randomly divided into three groups: 1) 30 patients received ampicillin; 2) 32 patients received phenethicillin and sulfisoxazole, and 3) 27 patients received placebo. Randomization was done according to a predetermined code unknown to the physicians. The study was double-blind. The method of statistical analysis was given (χ^2 test). Diagnosis of AOM was based on a bulging tympanic membrane, loss of light reflex and landmarks, or diffuse redness. Most patients had aspiration of the middle ear for culturing.

Follow up was at 24 to 72 hours and 14 to 18 days. Fifty-six percent of patients attended the initial follow-up appointment. Improvement was defined as decrease of symptoms at the early follow-up appointment and normal tympanic membrane findings at the late follow-up visit. The authors reported a slightly better outcome in the placebo group, but this improvement was not statistically significant. No cases of mastoiditis were reported in any of the groups.

Howie and Ploussard. Two pediatricians in Alabama conducted this study[5] in 1968 to 1970. Two hundred

eighty patients younger than 2 ½ years were seen. The study was designed to compare the effectiveness of four different antibiotics. A placebo group was included. A collaborating pharmacist assigned the patients randomly to one of the treatment groups without informing the physician to which group the patient was assigned. The groups were: 1) erythromycin for 25 patients, 2) erythromycin and a sulfonamide for 80 patients, 3) a sulfonamide for 23 patients, 4) ampicillin for 36 patients, and 5) placebo for 116 patients.

Compliance with treatment was measured. Criteria for diagnosis of AOM were not described. Most ears were aspirated and cultures were done at the initial visit and the follow-up visit 2 to 7 days later. All patients were seen at the follow-up visit. Dosing schedules for the antibiotics and components of the placebo were described. Subsidence of fever, pain, and aural discharge were recorded. Yates' correction of Fisher's exact test for small numbers was used for the χ^2 calculations.

The authors concluded that antibiotic therapy was superior to placebo, because most of the middle ear aspirates of the antibiotic groups were sterile by the 2- to 7-day follow-up visit. No significant difference in culture reports was noted in the placebo group. Otorrhea lasted significantly longer in the placebo group.

All patients in the placebo group became afebrile and had fewer symptoms in a 4-day period. There were no cases of mastoiditis in any of the groups. Ampicillin and the erythromycin-sulfonamide combination eradicated the most pathogenic organism.

Van Buchem et al (1979-1980). This trial[6] was conducted by 12 general practitioners and one otolaryngologist in Tilburg, Netherlands, during 1979 and 1980. Researchers examined 171 children between the ages of 2 and 12 years. Investigators randomly assigned patients to four treatment groups: 1) antibiotics only for 47 patients, 2) myringotomy only for 36 patients, 3) antibiotics and myringotomy for 48 patients, and 4) placebo for 40 patients.

The method of randomization was not described. The study was double-blind. Seventy-two percent of the children were 36 months and older. Diagnosis was based on "history, clinical picture, diffuse redness and/or bulging of the eardrum." Amoxicillin was the antibiotic used. The method of statistical analysis was not described. Follow up was at days 2 and 7, at 1 month, at 2 months, and at 1 or 2 years. Otoscopy findings, otorrhea, and audiograms were recorded. "Score cards" were kept for episodes of pain and fever. The percentage of patients attending follow-up appointments was not given.

The authors reported no statistically significant difference in outcome among the four treatment groups with regards to pain, fever, duration of otorrhea, otoscopy findings, audiography, and recurrence rate. No cases of mastoiditis or other septic complications were reported during the 2-year study period.

Mygind and colleagues. This study[7] was done by a general practitioner and four otolaryngologists in Copenhagen during 1977 and 1978. Examiners saw 149 children between the ages of 1 and 10 years. The study was designed to compare the outcome of AOM between a penicillin-treated group of 72 patients and a placebo group of 77 patients. The study was randomized and double-blind. Pretreatment characteristics of the two groups were compared. The diagnosis was based on "an earache for 1-24 hours and redness and inflammation of the tympanic membrane."

Follow up was at 2 or 3 days, 7 days, 1 month, and 3 months. The percentages of children seen at the follow-up visits were not given. Patients were given a score card to chart pain, fever, common cold symptoms, secretion from the ear, number of acetylsalicylic acid tablets consumed, and satisfaction with treatment (to be charted by parents) at each follow-up visit. The method of statistical analysis was the χ^2 test and Mann-Whitney test.

The investigators found no statistically significant difference in the two groups for duration of fever and otorrhea, but pain was significantly reduced on the second day of treatment in the penicillin group. There were no differences in otoscopy findings and tympanometry at 1 week, 1 month, and 3 months. One child in the penicillin group developed mastoiditis.

Burke et al. Forty-eight general practitioners in Southampton, Bristol, and Portsmouth, Engl, conducted this double-blind study[8] between October 1986 and April 1989. For 7 days 232 children aged 3 to 10 years received either amoxicillin (114 patients) or placebo (118 patients). Randomization was done with computer-generated random numbers. The randomization code was kept sealed and was unknown to any participants in the study. Statistical analyses were done by χ^2 and Mann-Whitney *U* tests. Diagnosis of AOM was based on acute earache and tympanic membrane finding (colour, contour, light, reflex, bulging, fluid levels, perforation, etc). Short-term (1 to 8 days) medium-term (1 to 3 months) and long-term (1 year) outcome was measured.

The researchers found differences between the treatment and placebo groups in the short-term outcome. Children in the placebo group showed significantly higher incidence of fever, mean analgesic consumption, mean duration of crying, mean absence from school, and treatment failure (lack of resolution or recurrence of symptoms). Differences in pain recorded were not significant.

There was no statistically significant difference in the prevalence of middle ear effusions between the two groups at 1 month and 3 months (medium-term). There was also no difference in the number of referrals to an otolaryngologist or number of episodes of otitis media in the subsequent year (long-term).

No cases of mastoiditis or meningitis were recorded in either group. The authors conclude that short-term outcome is improved by antibiotic treatment but medium- and long-term outcome is unaffected.

Van Buchem and colleagues (1981-1982). Sixty general practitioners and three otolaryngologists were involved in this large study[14] carried out in the Tilburg area, Netherlands, between March 1981 and August 1982. An estimated 4860 children were seen. The design was to withhold routine antibiotic therapy and to refer all patients in whom the condition took an "unsatisfactory course" to one of the specialists.

One hundred patients were referred and randomly divided into three treatment groups: 1) myringotomy alone for 34 patients, 2) antibiotics alone for 30 patients, and 3) myringotomy and antibiotics combined for 35 patients. Diagnosis was based on "history, clinical findings and diffuse redness and/or bulging of the tympanic membrane." The age of the patients seen was 2 to 12 years. Patients younger than 2 years were excluded. Eighty-four percent of the patients were 3 years and older.

"Unsatisfactory course" was defined as "appreciable illness after 3-4 days with persistent high temperature or severe pain, or both, and discharge from the ear persistent for more than 14 days." Of all the patients initially seen by the general practitioners, 4.6% fulfilled these criteria and were referred. Of the patients referred by the general practitioners, 4.5% had received antibiotics for a concurrent infection before referral.

The referred patients were then entered into the clinical trial. Randomization was done from a computer list. The study was double-blind. The authors found that antibiotics either alone or in combination with myringotomy were more effective than myringotomy alone.

There was one case of mastoiditis at the time of referral and one case of mastoiditis in the treatment group with myringotomy alone. Both patients recovered fully with amoxicillin. Overall the authors concluded that more than 90% of patients with AOM recover spontaneously and do not need antibiotic treatment. If after the first 3 or 4 days the children do not improve, they can then be treated with antibiotics without any serious complications.

Gold et al. A consensus statement[23] on the treatment of AOM by a group of eight Canadian pediatric infectious disease specialists in 1989 acknowledged that up to 60% of all episodes of AOM can resolve spontaneously, but recommended the routine use of antibiotics in all cases of AOM, mainly because of the rarity of complications, eg, mastoiditis, since the introduction of antibiotics in the late 1940s. Amoxicillin remains the antibiotic of first choice.

Discussion

The five double-blind RCTs[3,5-8] showed different results. Three concluded that there was no benefit to routine use of antibiotic therapy for AOM,[3,6,7] and two studies showed some benefit in the short-term outcome, but no difference in medium- and long-term outcome.[5,8] One large-scale descriptive study (4860 patients) used a "step approach" to managing AOM (antibiotic therapy only in cases of an irregular course) and reported extremely low complication rates.[14]

Three of the studies excluded patients younger than 2 years.[6,8,14] One study excluded patients younger than 1 year,[7] and in one other study 94% of the children were 3 years and older.[3] Only one trial looked exclusively at children younger than 2 ½ years.[5] In this study the authors reported a faster clearing of middle ear aspirates in the antibiotic group at days 2 through 7. There was no follow up after day 7.

The two main findings from my research are the lack of complications, such as mastoiditis and meningitis, in all studies regardless of their conclusions, and the lack of good, large-scale, well-designed studies supporting the routine use of antibiotics for all children.

Why prescribe antibiotics?

Through the literature I found three main reasons for prescribing antibiotics: preventing septic complications, preventing opportunistic bacterial infections, and expecting better outcome.

Preventing septic complications. The first and most often cited argument is the marked overall decline of septic complications, mainly mastoiditis and meningitis, since the introduction of antibiotics in the late 1940s.

In my literature review I also looked at some studies from the preantibiotics era.[9,10] These studies described complications of AOM. All these early studies were done by otolaryngologists on hospitalized patients with complications of AOM, such as prolonged septic discharge and mastoiditis. Of course, the outcome of these patients was greatly improved with the introduction of antibiotics. These patients needed antibiotics desperately. But does this mean that every "red ear" or "bulging eardrum" needs antibiotics? Unfortunately there are no studies from general practice in this era, where most patients with AOM would have been seen.

Preventing opportunistic bacterial infections. The second reason often cited for prescribing antibiotics is the presence of bacterial pathogens in the middle ear in a certain percentage of AOM cases. But is the mere presence of bacteria in the middle ear a good reason to treat? In every upper respiratory tract infection, bacterial pathogens temporarily colonize the respiratory tract and then clear spontaneously in most cases if left alone. One study[5] suggested a faster rate of clearing of bacteria from the middle ear with antibiotics but no difference in clinical outcome. One study[7] reported more pain on the second day in the placebo group. But do we treat pain with antibiotics?

Expecting better outcome. The third reason often cited for treatment with antibiotics is that a number of large-scale studies showed superior outcome with antibiotics. This is simply not fact. In my literature review I found no such studies.

Conclusion

Based on the findings of my review of the literature, I believe that there is a definite role and need for antibiotics in certain cases (5% to 10%) of AOM, especially cases that take an irregular course. To define subgroups of children who should be given antibiotics initially is impossible from this review.

On the other hand, we are certainly overtreating AOM. A more symptomatic and expectant approach during the first 48 to 72 hours with close follow up, especially for older patients (2 years and older), poses no risk of increased complications.

The following practice-oriented recommendations summarize my findings.

Age 2 years and older. Good evidence supports initial symptomatic treatment and institution of antibiotic therapy only in cases of an irregular course (fever or pain for more than 48 to 72 hours or aural discharge for more than 14 days). Close follow up during the first 48 to 72 hours is essential.

Age 2 years and younger. Symptomatic treatment only cannot be recommended, because of the exclusion of this age group from most studies.

Education needed. I realize that this approach to treatment of AOM in children will require parent education. The family doctor is in a unique position to provide the essential close follow-up surveillance and information that is needed to make this new approach work. ■

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References

1. Froom J, Culpepper L, Grob P, Bartelds A, Bowers P, Bridges-Webb C, et al. Diagnosis and antibiotic treatment of acute otitis media: report from International Primary Care Network. *BMJ* 1990;300:582-6.
2. Rudberg RD. Acute otitis media. *Acta Otolaryngol Suppl (Stockh)* 1954;(Suppl 113):1-69.
3. Halsted C, Lepow ML, Balassanian N, Emmerich J, Wolinsky E. Acute otitis media: clinical observations, microbiology and evaluation of therapy. *Am J Dis Child* 1968;115:542-51.
4. Laxdal OE, Merida J, Trefor-Jones RH. Treatment of acute otitis media: a controlled study of 142 children. *Can Med Assoc J* 1970; 102:263-8.
5. Howie VH, Ploussard JH. Efficacy of fixed combination antibiotics versus separate components in otitis media: effectiveness of erythromycin estolate, triple sulfonamide, ampicillin, erythromycin estolate–triple sulfonamide and placebo in 280 patients with acute otitis media under two and one-half years of age. *Clin Pediatr* (Phila) 1972;11:205-14.
6. Van Buchem FL, Dunk JHM, van't Hof MA. Therapy of acute otitis media: myringotomy, antibiotics, or neither? *Lancet* 1981;2:883-7.
7. Mygind N, Meistrup-Larsen KI, Thompson J, Thompson VF, Josefsson K, Sorensen H. Penicillin in acute otitis media: a double-blind, placebo-controlled trial. *Clin Otolaryngol* 1981; 6:5-13.
8. Burke P, Bain J, Robinson D, Dunleavey J. Acute red ear in children: controlled trial of non-antibiotic treatment in general practice. *BMJ* 1991;303:558-62.
9. Bakwin H, Jacobziner H. Prevention of purulent otitis media in infants. *J Pediatr* 1939; 14:730-6.
10. Heller G, Engelwood NJ. A statistical study of otitis media in children. *J Pediatr* 1940;17:322-30.
11. Fry J. Antibiotics in acute tonsillitis and acute otitis media. *BMJ* 1958;2:883-6.
12. Lowe JF, Bamforth JS, Pracy R. Acute otitis media. One year in general practice. *Lancet* 1963; 2:1129-32.
13. Townsend EH. Otitis media in clinical practice. *N Y J Med* 1964;64:1591-7.
14. Van Buchem FL, Peeters MF, van't Hof MA. Acute otitis media: a new treatment strategy. *BMJ* 1985;290:1033-7.
15. Bollag U, Bollag-Albrecht E. Recommendations derived from practice audit for the treatment of acute otitis media. *Lancet* 1991;338:96-9.
16. Paradise JL. Otitis media in infants and children. *Pediatrics* 1980;65:917-42.
17. Bluestone CD. Otitis media in children: to treat or not to treat? *N Engl J Med* 1982;306:1399-404.
18. Bluestone CD. Otitis media and sinusitis: management and when to refer to the otolaryngologist. *Pediatr Infect Dis J* 1987;6(1): 100-6.
19. De Melker RA, Burke PD. Epidemiology of otitis media and the role of the general practitioner in management. *Fam Pract* 1988;5:307-13.
20. Giebink GS, Canafax DM. Controversies in the management of acute otitis media. *Adv Pediatr Infect Dis* 1988;3:47-63.
21. Giebink GS. The microbiology of otitis media. *Pediatr Infect Dis J* 1989;8(Suppl):S18-S20.
22. Leung AK, Robson WL. Otitis media in infants and children. *Drug Protocol* 1990;5:29-35.
23. Gold R, Delage G, Dery P, Jadavji T, Law B, Marchessault V, et al. Consensus recommendations for the management of otitis media. *Can J Diag* 1989;6:67-76.
24. Stool SE. Otitis media: update on a common, frustrating problem. *Postgrad Med* 1989;85:40-53.
25. Bluestone CD. Modern management of otitis media. *Pediatr Clin North Am* 1989;36(6):1371-87.
26. Dixon T. International approaches to otitis media. *Can Fam Physician* 1990;36:1451-2 (Engl), 1454-5 (Fr).
27. Wilson I. Acute otitis media: issues and options. *Can J CME* 1991;1:27-38.
28. Jordan MJ. Clinical approach to treatment of otitis media. *Otolaryngol Clin North Am* 1991;24(4):901-4.
29. Giebink GS, Canafax DM, Vempthorne J. Antimicrobial treatment of acute otitis media. *J Pediatr* 1991;119:495-500.
30. Burke P. Otitis media – antibiotics or not? *Practitioner* 1992;2236(1513):425-9.

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