

Reevaluating the Use of Antibiotics in Acute Otitis Media in Children

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Summary

Increasing concern about the antibiotic resistance in acute otitis media (AOM) has led to debate over use of antibiotic in AOM and duration of therapy. Many studies have proved that watchful waiting should be used more often for acute otitis media. In children over two years, the most appropriate treatment was found to be initial observation followed by 5 days of an antibiotic if the child failed to improve spontaneously. In children less than 2 years or one with severe symptoms antibiotic can be started after 24 hours if there is no improvement with symptomatic treatment. Physician should be more selective in the prescription of antibiotics early in AOM.

Key Words: Acute otitis media, Antibiotics, Drug resistance

Introduction

Acute otitis media is one of the most commonly diagnosed conditions, affecting up to 83% of children by the age of 3 years¹. It is estimated that in USA, over \$5 billion is spent annually on the management of AOM, with 40 million prescriptions written for oral antibiotics^{2,3}. *Streptococcus pneumoniae* (25 to 40%), *Haemophilus influenzae* (10-30%) and *Moraxella catarrhalis* (5-15%) are the three most common organisms isolated in children with acute otitis media⁴. It has been reported that AOM resolves spontaneously in up to 80% of cases⁵. Increasing concern in the recent years about antibiotic resistance to *streptococcus pneumoniae* has led physician to rethink about the use of antibiotics in AOM⁶.

Impact of antibiotic treatment in acute otitis media

The impact of antibiotic therapy in terms of increasing resistance is of great concern. Studies has shown that antibiotic use increases the carriage rate of penicillin non susceptible pneumococci (PNSP)^{7,8}. One study suggested that low dosage of β -lactams and lengthy treatment duration are risk factors for carriage of PNSP⁹. The effect of antibiotic treatment differs according to the drug prescribed and the bacterial species, being more marked with *Branhamella catarrhalis* and *Streptococcus pneumoniae* than with *Hemophilus influenzae*^{10,11}. The drugs with most potency in vitro against wild type strains of *Streptococcus pneumoniae* (e.g. amoxicillin) induced a drastic fall in the carriage of penicillin- susceptible pneumococci, thereby increasing the proportion of PNSP carried after treatment¹¹.

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Management of AOM has become more challenging since the worldwide emergence of antibiotic resistance among otitic pathogens. An increasing proportion of resistant pneumococci isolated from cases of AOM has been reported from the United States¹². The increasing prevalence of β -lactamase producing *Haemophilus influenzae* and *Moraxella catarrhalis*, coupled with pneumococcal resistance, further complicates the choice of appropriate antibiotic therapy for AOM, particularly for those patients who have failure of an initial course of amoxicillin therapy. In a study in US¹³, 41% of the *Haemophilus influenzae* were β -lactamase producers.

Justification for using antibiotics in AOM

The rationale for using antibiotics in AOM has been that they treat the active infection, thereby minimizing morbidity and preventing complications. There has been dramatic fall in the complications of AOM in the developed world since the introduction of antibiotics in the 1940s¹⁴. Bluestone¹⁵ has justified using antibiotics in AOM based on the reduction in morbidity and mortality. In his view, with the introduction of antibiotics in US there is more rapid resolution of the disease and reduction in the rate of rare but potentially serious complications of AOM. Another study showed a higher incidence of perforation, deafness at 3 months secondary to OME and contra lateral AOM in patients who did not receive antibiotics early¹⁶.

Reasons against using antibiotics in AOM

About 50% of cases of AOM are viral in origin¹⁷ although it is difficult to distinguish clinically from bacterial AOM. A recent study showed that both bacteria and viruses were isolated in the middle ear fluid of 65% of children with otitis media. Thirty five percent had viruses isolated as the sole middle ear pathogen¹⁸. Studies have shown that antibiotics confer, at best, only modest benefit^{19, 20, 21}. In particular antibiotics did not appear to influence the resolution of pain within 24 hours of presentation.

Spontaneous resolution

Spontaneous resolution occurs in two thirds of children with AOM within 24 hours of presentation and in 80% of children in 2-7 days²². Hence only about 20% of the patients might benefit from antibiotic treatment.

Over diagnosis

There is high incidence of over diagnosis of AOM. This may be a contributory factor in the development of antibiotic resistance and the apparently high spontaneous remission rate of AOM. It is important to distinguish acute otitis media from otitis media with effusion (OME) because antibiotics are seldom indicated for the latter condition. Improving the medical diagnostic skills will reduce the incidence of over diagnosis of AOM. Accurate diagnosis of AOM is the key element in reducing unnecessary antibacterial usage.

Should watchful waiting be used more often for AOM

In Netherlands, a policy of initial non-antibiotic treatment and close observation has been recommended by the Dutch College of Practitioners. The Dutch group recommends that in children over 2 years, symptomatic treatment for the first 3 days then reevaluate and if necessary prescribe antibiotics for 7 days²³. For children between 6 months and 2 years, the treatment protocol is similar but mandatory contact is required between the doctor and the parent after 24 hours. A Dutch study compared the efficacy of antibiotics alone, myringotomy alone, a combination of two, and no treatment and concluded that children who did not receive any form of treatment had equivalent rates of pain⁵.

The Centers for Disease Control and Prevention and the American Academy of Pediatrics, in response to increasing concerns about antimicrobial resistance and the overuse of antibiotics, published the Principles of judicious use of antimicrobial agents for pediatric upper

respiratory infections in 1998²⁴. Since that time there has been considerable debate over whether antibiotics are indicated at all for the initial treatment of suspected AOM^{25,26,27,28,29}. Reduction in the excessive use of antibiotics for otitis media may be one effective way of controlling the spread of antimicrobial resistance.

A study done in UK³⁰, to find out the predictors of poor outcome and benefits from antibiotics in children with AOM, showed that children without systemic features (higher temperature, vomiting) are unlikely to have poor short-term outcome. Immediate use of antibiotics is unlikely to make a difference to outcomes in such children. Using a clinical decision analysis model for the treatment of AOM in a child over 2 years of age, the most appropriate treatment was found to be initial observation followed by 5 days of an antibiotic if the child failed to improve spontaneously³¹.

The report, by the Southern California Evidence-Based Practice Center (SC-EPC), is the most recent of 15 literature syntheses published by the Agency for Healthcare Research and Quality (AHRQ)³². Children receiving placebo or no antimicrobial had a pooled clinical success rate of 81% at 1 to 7 days, with no increase in suppurative complications when followed closely. Amoxicillin or ampicillin increased the absolute success rate by 12.3% in 5 studies pooled using random effects meta-analysis.

Treatment with antibiotics

Once a decision has been made to start on antibiotics there is not much controversy. Amoxicillin will be the first line antibiotic. It is effective, reasonably well tolerated and inexpensive. There has been some doubt about the duration of therapy. A recent meta analysis suggests that a 5-day course is effective for uncomplicated AOM³³. Cefixime has been shown to be as effective as amoxicillin and can be given to patients allergic to penicillin. Erythromycin is also a suitable first line antibiotic in those who are penicillin sensitive but has limited activity against

some strains of *Hemophilus influenzae* and is therefore combined with sulphisoxazole.

If there is no improvement in symptoms within 48-72 hours then a second line antibiotic (amoxicillin - clavulanate, cefixime, cefuroxime, cefaclor, erythromycin - sulphisoxazole) is prescribed. The common causes of treatment failures are either poor patient compliance or an inappropriate initial antibiotic prescription and not necessarily the result of beta lactamase producing organisms³⁴. If the infection still persists, then the child should be admitted for myringotomy and intra venous antibiotics should be considered.

Conclusion

AOM has enormous social and economic implications because of its high incidence and expense. The natural course of AOM is quite favorable and if left untreated 80% will recover spontaneously within 2 weeks. The addition of antibiotics provides at best a modest reduction in symptoms, while adding cost, adverse drug reaction and drug resistance. Minimizing the use of antibiotics in patients with AOM does not increase the risk of perforation, deafness or recurrent AOM significantly. Many physicians in Europe have adopted a policy of non-antibiotic prescription early in the treatment of AOM. Many studies have proved that watchful waiting should be used more often for acute otitis media. In children over two years, the most appropriate treatment was found to be initial observation followed by 5 days of an antibiotic if the child failed to improve spontaneously. In children less than 2 years or one with severe symptoms antibiotic can be started after 24 hours if there is no improvement with symptomatic treatment. Physician should be more selective in the prescription of antibiotics early in AOM. This is a difficult policy for primary care physicians to adopt, due to parental pressure for prescription. Thinking in terms of a balance of harms and benefits would result in a decreased proportion of children prescribed antibiotics for acute otitis media.

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MCQ's on the Role of Antibiotics in Acute Otitis Media in Children:

1. Which of the following statements regarding acute otitis media (AOM) is not true:
 - A. Is viral in origin in only about 10% of cases.
 - B. Affects about 20% of children by the age of 3 years.
 - C. The commonest bacteria is *Streptococcus pneumoniae*.
 - D. *Hemophilus influenzae* rarely causes AOM.
 - E. Amoxicillin is the drug of choice in AOM.

2. Regarding carriage rate of penicillin non-susceptible pneumococci (PNSP).
 - A. Antibiotic use increases the carriage rate.
 - B. Low dose of β -lactams is a risk.
 - C. Lengthy treatment with β -lactams is a risk factor.
 - D. Amoxicillin causes increasing proportion on PNSP carried after treatment.
 - E. PNSP is not found in USA.

3. Regarding the role of antibiotics in acute otitis media (AOM)
 - A. Minimises the complication.
 - B. Minimises morbidity.
 - C. Not justified in all cases because about 50% of cases are viral in origin.
 - D. Antibiotic offer only modest benefit.
 - E. Antibiotic markedly influence the resolution of pain within 24 hours.

4. Regarding acute otitis media:
 - A. Spontaneous resolution occurs in 20% of cases.
 - B. 80% of patients benefit from antibiotic treatment.
 - C. AOM and otitis media with effusion (OME) are the same.
 - D. Otitis media is one of the leading indication for antibiotic use in children.
 - E. Reduction in the use of antibiotic will control the spread of antimicrobial resistance.

5. Regarding the management of acute otitis media:
 - A. 5- day course of antibiotics is not very effective in uncomplicated AOM.
 - B. Immediate use of antibiotic in a child with fever and vomiting will improve the outcome.
 - C. Erythromycin is used in penicillin sensitive patients as first line antibiotic.
 - D. Erythromycin is very effective against all strains of *Hemophilus influenzae*.
 - E. In children under 2 years wait and watch policy suggests that antibiotic should not be started for 72 hours.