

Antibiotic therapy for children with acute otitis media

Teeranai Sakulchit MD Ran D. Goldman MD FRCPC

Abstract

Question Acute otitis media is one of the most common infections in childhood. Routine prescription of antibiotics has led to adverse events and bacterial resistance to antibiotics. I have heard that “watchful waiting” is a good strategy to reduce this potential problem in children older than 6 months of age. Should I apply this strategy in my clinical practice?

Answer Watchful waiting can be applied in selected children with nonsevere acute otitis media by withholding antibiotics and observing the child for clinical improvement. Antibiotics should be promptly provided if the child’s infection worsens or fails to improve within 24 to 48 hours. Guidelines and most ongoing studies support these recommendations. Correct choice of regimen, dose, frequency, and length of treatment are all important.

Acute otitis media (AOM) is an acute inflammation of the middle ear caused by viral (such as respiratory syncytial virus, rhinovirus, influenza viruses, and adenoviruses) or bacterial (such as *Streptococcus pneumoniae*, nontypeable *Haemophilus influenzae*, and *Moraxella catarrhalis*) infections.^{1,2} Preceding viral upper respiratory tract infection leads to eustachian tube obstruction; fluid stasis and colonization of pathogens then occurs within the middle ear. Young children are susceptible to AOM owing to their shorter and more horizontal eustachian tubes, through which pathogens ascend from the nasopharynx to the middle ear.^{3,4}

The estimated incidence of AOM worldwide is 11% (709 million cases each year), and half of cases occur in children younger than 5 years of age.⁵ After introduction of the heptavalent pneumococcal conjugate vaccine in the United States in 2000, the national prevalence rates of hospital admission for those younger than 21 years of age with AOM and its complications decreased from 3.9 to 2.6 per 100 000 persons ($P < .0001$), especially in children younger than 2 years of age (from 13.6 to 5.5 per 100 000 persons between 2000 and 2012, respectively; $P < .0001$).⁶

Signs and symptoms of AOM include otalgia as well as tugging, rubbing, or holding of the ear. Fever, irritability, and symptoms of upper respiratory tract infection such as cough or rhinorrhea might also be observed.^{1,4} According to the 2016 Canadian Paediatric Society and

2013 American Academy of Pediatrics guidelines, AOM can be diagnosed if there is middle ear effusion with signs of middle ear inflammation on otoscopic examination, such as moderate to severe tympanic membrane (TM) bulging, new onset of otorrhea not caused by otitis externa, or mild bulging of the TM associated with recent onset of otalgia (less than 48 hours) or erythema.^{7,8} Treatment of AOM includes administration of antipyretics and analgesics.^{7,8} Antimicrobial therapy should be considered in selected patients.^{7,8}

Role of antibiotics

The 2016 Canadian Paediatric Society guidelines suggest that for children older than 6 months of age (who are immunocompetent and without craniofacial abnormalities, tympanostomy tubes, or recurrent AOM), antibiotic administration is recommended for those with perforated tympanic membrane with purulent drainage and those with middle-ear effusion and a bulging TM who are moderately or severely ill (ie, with high fever $\geq 39^\circ\text{C}$), those with moderate to severe systemic illness or severe otalgia, or those who have already been severely ill for 48 hours). For children who are mildly ill, alert, with low grade fever ($< 39^\circ\text{C}$) responding to antipyretics and mild otalgia and mild or moderate bulging of the TM, watchful waiting can be advised. Antibiotics or a prescription to be filled if symptoms worsen or do not improve in 24 to 48 hours can be provided.⁷

Amoxicillin is the drug of choice if antibiotics are required, given as 45 to 60 mg/kg per day in 3 divided doses; if a twice-daily dosing regimen is used, higher total daily doses of 75 to 90 mg/kg per day are required. Amoxicillin-clavulanate should be considered if there is concurrent purulent conjunctivitis, a history of amoxicillin



This article is eligible for Mainpro+ certified Self-Learning credits. To earn credits, go to www.cfp.ca and click on the Mainpro+ link.

Cet article se trouve aussi en français à la page 688.

treatment within the previous 30 days, relapse of a recent infection, or nonresponse to amoxicillin. Consider a second-generation (cefprozil or cefuroxime) or third-generation cephalosporin if the child has a nonsevere allergic reaction to amoxicillin or penicillin. Other regimens such as macrolides or clindamycin can be used but have limited efficacy. If oral medication is not tolerated, intramuscular or intravenous ceftriaxone might be appropriate. Consider 10 days' duration of antibiotics in children younger than 2 years of age and those with recurrent AOM or AOM with perforated TMs; 5 days of antibiotics might be appropriate for children 2 years of age or older with uncomplicated disease.

Antibiotics vs placebo or watchful waiting

Two recent meta-analyses reported similar results in relation to the limited role of antibiotics.^{9,10} Venekamp et al⁹ included 13 randomized controlled trials from high-income countries with approximately 3400 children receiving either antibiotics (ampicillin, amoxicillin, amoxicillin-clavulanate, and others) or placebo. Most (60%) children reported less pain with either antibiotics or placebo. Antibiotics did not reduce pain in the first 24 hours (risk ratio [RR]=0.89, 95% CI 0.78 to 1.01); they had only a slight effect on pain in the following days compared with placebo (at 2 to 3 days, RR=0.7, 95% CI 0.57 to 0.86, number needed to treat for an additional beneficial outcome [NNT]=20; at 4 to 7 days, RR=0.76, 95% CI 0.63 to 0.91, NNT=16; and at 10 to 12 days, RR=0.33, 95% CI 0.17 to 0.66, NNT=7). Antibiotics were associated with fewer abnormal tympanometry findings at 2 to 4 weeks (RR=0.82, 95% CI 0.74 to 0.90, NNT=11) and at 6 to 8 weeks (RR=0.88, 95% CI 0.78 to 1.00, NNT=16). At 3 months, however, no difference in the number of children with abnormal tympanometry findings was noted (RR=0.97, 95% CI 0.76 to 1.24).

Severe complications such as mastoiditis and meningitis were rare and not different between groups. Adverse events related to antibiotics (such as vomiting, diarrhea, and rash) occurred, as expected, more in the antibiotic group (RR=1.38, 95% CI 1.19 to 1.59, number needed to treat for an additional harmful outcome of 14).

When comparing antibiotics given immediately with waiting with "expectant observation," 5 trials with 1150 children suggested no difference in pain at 3 to 7 days of illness (RR=0.75, 95% CI 0.50 to 1.12).⁹ Further, no differences were found between groups in the number of children with abnormal tympanometry findings at 4 weeks (RR=1.03, 95% CI 0.78 to 1.35) or AOM recurrence (RR=1.41, 95% CI 0.74 to 2.69). Neither TM perforation nor serious complications occurred in either group. Immediate antibiotics were associated with more adverse events compared with "expectant observation" (RR=1.71, 95% CI 1.24 to 2.36; number needed to harm of 9).

Results from a meta-analysis of individual patient data that included 1643 children suggested antibiotics

were beneficial in children younger than 2 years of age with bilateral AOM or AOM with otorrhea.⁹

In a prospective study including Finnish children 6 to 35 months of age with AOM, 53 children received placebo but were changed to antibiotics after a watchful waiting period if no improvement was noted during follow-up, and 161 children received amoxicillin-clavulanate at diagnosis for 7 days.¹¹ Improvement was observed in 91% and 96% of children, respectively ($P=.15$). Children in the delayed antibiotics group had a longer time to normalization of symptoms and otoscopic findings (while on watchful waiting). Adverse events were similar in both groups. Other effects to consider in the watchful waiting period are the increased time with pain and delay in returning to regular activities.

Overall, delayed administration of antibiotics in children with AOM might not affect their clinical condition with the exception of social and economic effects for the family.

Type, frequency, and duration of antibiotics

A US-based study reported amoxicillin-clavulanate (80 mg/kg per day for 10 days) to be more effective than cefdinir (14 mg/kg per day for 5 days) in treating 330 children 6 to 24 months of age with AOM. The amoxicillin-clavulanate group had an 86.5% cure rate (resolution of signs and symptoms of AOM), which was significantly better than the 71% cure rate in the cefdinir group ($P=.001$).¹² Further, a logistic regression model suggested that the odds of cure with cefdinir significantly declined with age ($P=.01$).

Thanaviratnanich et al¹³ included 5 trials in a meta-analysis evaluating the frequency of antibiotics prescribed to 1600 children younger than 12 years of age and concluded that the efficacy of 1 to 2 daily doses of amoxicillin (with or without clavulanate) was comparable to that of 3 daily doses. Clinical cure at the end of 7 to 15 days of therapy (RR=1.03, 95% CI 0.99 to 1.07), during therapy (RR=1.06, 95% CI 0.85 to 1.33), and at follow-up at 1 to 3 months after treatment (RR=1.02, 95% CI 0.95 to 1.09); recurrent AOM (RR=1.21, 95% CI 0.52 to 2.81); the compliance rate (RR=1.04, 95% CI 0.98 to 1.10); and overall adverse events (RR=0.92, 95% CI 0.52 to 1.63) were not significantly different between the group receiving 1 or 2 daily doses and the group receiving 3 daily doses.


An American study reported that reduction in duration of amoxicillin-clavulanate from 10 to 5 days followed by placebo for 5 days resulted in less favourable outcomes among 520 children 6 to 23 months of age with AOM.¹⁴ Clinical failure (34% vs 16%; 95% CI 9% to 25%) and mean symptom scores (higher scores indicated more severe symptoms) at day 6 to 14 (1.61 vs 1.34; $P=.07$) and at day 12 to 14 (1.89 vs 1.20; $P=.001$) were significantly different in the 5-day group compared with that in 10-day group. There were fewer children whose symptom scores decreased more than 50% from baseline to the end

treatment in the 5-day compared with the 10-day group (80% vs 91%, respectively; $P=.003$). There were no significant differences in the rate of recurrence, adverse events, or nasopharyngeal colonization after treatment between groups. A 10-day course is preferable to a 5-day course.

Complications of AOM

Acute mastoiditis as a complication of AOM was not more common in children who received delayed antibiotics when compared with those who received immediate antibiotics. A prospective observational study from Israel reviewed the medical records of children younger than 14 years of age with acute mastoiditis admitted to 8 hospitals.¹⁵ In 512 children, 216 (42%) had previous AOM; 73% received immediate antibiotics (amoxicillin) and 27% had delayed antibiotics. The rate of recurrent AOM was much higher in those treated immediately (29% vs 8.7%, respectively; $P=.0021$). Admission rates were similar (37% vs 29%; $P=.28$). Adjusted logistic regression suggested a higher risk of mastoiditis surgery in those treated immediately (RR=3.2, 95% CI 1.4 to 7.0). However, this is likely owing to illness severity.

Conclusion

Watchful waiting can be used in children with mild or moderate disease and it might not increase the risk of subsequent acute mastoiditis. High-dose amoxicillin is the drug of choice in Canada as first-line therapy. Ten days' duration of antibiotics is more effective than a 5-day course for children 6 to 23 months of age. 

Competing interests

None declared

Correspondence

Dr Ran D. Goldman; e-mail rgoldman@cw.bc.ca

References

1. Minovi A, Dazert S. Diseases of the middle ear in childhood. *GMS Curr Top Otorhinolaryngol Head Neck Surg* 2014;13:Doc11.
2. Ngo CC, Massa HM, Thornton RB, Cripps AW. Predominant bacteria detected from the middle ear fluid of children experiencing otitis media: a systematic review. *PLoS One* 2016;11(3):e0150949.

3. McWilliams CJ, Goldman RD. Update on acute otitis media in children younger than 2 years of age. *Can Fam Physician* 2011;57:1283-5.
4. Coticchia JM, Chen M, Sachdeva L, Mutchnick S. New paradigms in the pathogenesis of otitis media in children. *Front Pediatr* 2013;1:52.
5. Monasta L, Ronfani L, Marchetti F, Montico M, Vecchi Brumatti L, Bavcar A, et al. Burden of disease caused by otitis media: systematic review and global estimates. *PLoS One* 2012;7(4):e36226.
6. Tawfik KO, Ishman SL, Altaye M, Meinzen-Derr J, Choo DI. Pediatric acute otitis media in the era of pneumococcal vaccination. *Otolaryngol Head Neck Surg* 2017;156(5):938-45. Epub 2017 Mar 28.
7. Le Saux N, Robinson JL; Canadian Paediatric Society, Infectious Diseases and Immunization Committee. Management of acute otitis media in children six months of age and older. *Paediatr Child Health* 2016;21(1):39-50.
8. Lieberthal AS, Carroll AE, Chonmaitree T, Ganiats TG, Hoberman A, Jackson MA, et al. The diagnosis and management of acute otitis media. *Pediatrics* 2013;131(3):e964-99. Epub 2013 Feb 25. Erratum in: *Pediatrics* 2014;133(2):346.
9. Venekamp RP, Sanders SL, Glasziou PP, Del Mar CB, Rovers MM. Antibiotics for acute otitis media in children. *Cochrane Database Syst Rev* 2015;(6):CD000219.
10. Nitsche MP, Carreño M. Antibiotics for acute otitis media in children. *Medwave* 2015;15(Suppl 2):e6295.
11. Tähtinen PA, Laine MK, Ruuskanen O, Ruohola A. Delayed versus immediate antimicrobial treatment for acute otitis media. *Pediatr Infect Dis J* 2012;31(12):1227-32.
12. Casey JR, Block SL, Hedrick J, Almudevar A, Pichichero ME. Comparison of amoxicillin/clavulanic acid high dose with cefdinir in the treatment of acute otitis media. *Drugs* 2012;72(15):1991-7.
13. Thanaviratnanich S, Laopaiboon M, Vatanasapt P. Once or twice daily versus three times daily amoxicillin with or without clavulanate for the treatment of acute otitis media. *Cochrane Database Syst Rev* 2008;(4):CD004975.
14. Hoberman A, Paradise JL, Rockette HE, Kearney DH, Bhatnagar S, Shope TR, et al. Shortened antimicrobial treatment for acute otitis media in young children. *N Engl J Med* 2016;375(25):2446-56.
15. Grossman Z, Zehavi Y, Leibovitz E, Grisaru-Soen G, Shachor Meyouhas Y, Kassis I, et al. Severe acute mastoiditis admission is not related to delayed antibiotic treatment for antecedent acute otitis media. *Pediatr Infect Dis J* 2016;35(2):162-5.



Child Health Update is produced by the Pediatric Research in Emergency Therapeutics (PRETx) program (www.pretx.org) at the BC Children's Hospital in Vancouver, BC.

Dr Sakulchit is a member and Dr Goldman is Director of the PRETx program. The mission of the PRETx program is to promote child health through evidence-based research in therapeutics in pediatric emergency medicine.

Do you have questions about the effects of drugs, chemicals, radiation, or infections in children? We invite you to submit them to the PRETx program by fax at 604 875-2414; they will be addressed in future Child Health Updates. Published Child Health Updates are available on the *Canadian Family Physician* website (www.cfp.ca).
