

Update on acute otitis media in children younger than 2 years of age

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Abstract

Question As concern about antimicrobial resistance grows, I am aware of the need to reduce unnecessary antibiotic treatment; however, in my practice I see many children with acute otitis media (AOM) and this is the most common reason I prescribe antibiotics. Most of these children are young and otherwise healthy, and I am uncertain about when to prescribe antibiotics and when to endorse “watchful waiting.” Which children will benefit from antibiotic treatment?

Answer Current Canadian guidelines recommend all children younger than 2 years of age with otalgia due to AOM and fever greater than 39°C be considered for treatment with amoxicillin. Watchful waiting is indicated only for children older than 6 months with mild-to-moderate AOM. Recent evidence suggests young children with a definitive diagnosis of AOM will benefit from antibiotics and experience fewer treatment failures compared with placebo, regardless of the severity of otitis. These studies do not challenge watchful waiting directly, and determining which children will improve spontaneously remains an enigma.

Mise à jour sur l'otite moyenne chez les enfants de moins de 2 ans

Résumé

Question Étant donné les inquiétudes grandissantes concernant la résistance aux antimicrobiens, je suis conscient de la nécessité de ne pas recourir inutilement aux antibiothérapies; par ailleurs, dans ma pratique, je vois de nombreux enfants souffrant d'une otite moyenne aiguë (OMA) et c'est la raison la plus fréquente pour laquelle je prescris des antibiotiques. La plupart de ces enfants sont jeunes et autrement en santé, et je ne suis pas certain de savoir quand il faut prescrire des antibiotiques et quand adopter une approche d'attente vigilante. Quels sont les enfants qui vont bénéficier d'une antibiothérapie?

Réponse Les guides de pratique canadiens actuels recommandent d'envisager un traitement à l'amoxicilline pour tous les enfants de moins de 2 ans qui ont une otalgie en raison d'une OMA et une fièvre de plus de 39°C. L'attente vigilante n'est indiquée que pour les enfants de plus de 6 mois qui ont une OMA de légère à modérée. De récentes données probantes font valoir que les jeunes enfants qui ont un diagnostic défini d'OMA bénéficieront de l'antibiothérapie et que le traitement échouera moins souvent en comparaison d'un placebo, quelle que soit la gravité de l'otite. Ces études ne contestent pas directement l'attente vigilante, et la manière de déterminer chez quels enfants l'état s'améliorera spontanément demeure une énigme.

Acute otitis media (AOM) is a common pediatric condition that affects most children by their second birthday,¹ with peak incidence between 6 and 18 months of age.² Acute otitis media results in a visit to a physician in an estimated 1.8 million Canadian children younger than 5 years of age each year³ and it is the most common reason for prescribing antibiotics.⁴ Each episode of AOM is estimated to cost \$59 to the health system and as much as \$262 to families.⁵ Children younger than 2 years are physiologically predisposed to AOM because their eustachian tubes are shorter, of smaller calibre, and more horizontal compared with those of adults.⁶

Diagnostic certainty

A diagnosis of AOM requires 3 criteria to be met: acute onset of symptoms, signs of middle ear inflammation, and effusion.⁷ The symptoms of AOM include otalgia, ear-rubbing, fever, irritability, restless sleep, diminished appetite, and excessive crying⁸; however, none is sensitive or specific,⁹ and these symptoms are not helpful in distinguishing AOM from a respiratory tract infection.⁸ Even upon examination, AOM remains a difficult diagnosis, demonstrated by a 22% overdiagnosis rate in a recent study of French GPs.¹⁰ Examination of the tympanic membrane (TM) for colour, position, mobility, and translucency might be difficult owing to an uncooperative child or obstruction with cerumen.⁹

Reliance on a red TM alone should be avoided, as the mobility and position of the TM appear to be most important for diagnosis.⁹

Guidelines and treatment strategy

The Infectious Diseases and Immunization Committee of the Canadian Paediatric Society published guidelines in 2009 that outline the management of uncomplicated AOM.⁷ The guidelines recommend watchful waiting for 48 to 72 hours in children 6 months of age and older for whom otalgia appears to be mild and fever is less than 39°C.⁷ The guidelines recommend that these children receive analgesics, and if their condition does not improve, or reliable follow-up cannot be guaranteed during the observation period, antibiotics (first-line amoxicillin) should be administered.⁷ More definitively, all children younger than 6 months and children with severe otalgia or fever greater than 39°C should start taking amoxicillin therapy after first consultation.⁷ The recommended dose of amoxicillin is 75 to 90 mg/kg divided into 2 daily doses for 10 days in children younger than 2 years of age.⁷ Use of amoxicillin is supported by a systematic review that demonstrated there is no statistically significant benefit to treating with alternative antimicrobials.¹¹ With its low cost, favourable side-effect profile, and long-term safety record,¹² amoxicillin remains the treatment of choice in patients younger than 2 years with severe illness.⁷

The 2004 guidelines of the American Academy of Pediatrics and American Academy of Family Physicians incorporate the child's age, illness severity, and diagnostic certainty when considering the option of an observation period without antimicrobial therapy.¹³ Children younger than 6 months of age all should receive antibiotics and children older than 6 months but younger than 2 years with mild-to-moderate illness and an uncertain diagnosis might be deemed appropriate for observation.¹³

Watchful waiting is often considered appropriate because AOM has a favourable natural history of spontaneous resolution. One meta-analysis demonstrated that otitis spontaneously resolved in 70% of children after 7 to 14 days.¹⁴ A Cochrane review that summarized randomized controlled trials (RCTs) comparing antimicrobial therapy with placebo or watchful waiting reported a marginal benefit in pain reduction in children at 2 to 7 days if they received antimicrobials (number needed to treat [NNT]=16).¹⁵ A 2006 meta-analysis identified benefit from treatment with antimicrobials for children younger than 2 years of age with bilateral AOM, or children with AOM and otorrhea (NNT of 4 and 3, respectively).¹⁶

Impact of pneumococcal conjugate vaccine

Introduction of the 7-valent pneumococcal conjugate vaccine (PCV-7) has reduced the impact of AOM, as shown in one study from Quebec,¹⁷ especially in children younger than 2 in whom *Streptococcus pneumoniae*

is the most common pathogen.^{17,18} Before routine vaccination, the 3 main species found in middle ear isolates were *S pneumoniae* (42%), *Haemophilus influenzae* (31%), and *Moraxella catarrhalis* (16%),¹⁹ with a recent shift toward lower *S pneumoniae* and higher *H influenzae* prevalence.¹¹ Despite this observation, a 2010 study of children 6 to 30 months of age showed that 6 to 8 years after the introduction of the PCV-7 vaccine, there has been a replacement with non-PCV *S pneumoniae* serotypes, along with a surge toward pre-vaccine levels.²⁰

Recent research

In 2005 Le Saux et al conducted a large RCT that included 512 Canadian children aged 6 months to 5 years. They compared the criterion standard of amoxicillin for 10 days with placebo and assessed clinical resolution of symptoms at 14 days.²¹ Almost all (93%) of the children using amoxicillin had resolution of symptoms compared with 84% of the children receiving placebo (NNT=11).²¹ In the 6-month to 23-month age group, clinical resolution of symptoms was documented in 85% of the children using amoxicillin compared with 79% using placebo.²¹ The smaller benefit in the younger age group was possibly due to a lack of certain diagnosis in these children (only 60% to 70% of patients had an accurate clinical diagnosis of AOM).²¹

Two recent RCTs of treatment with amoxicillin-clavulanate or placebo in children with AOM support the use of antibiotics for AOM in young children.^{22,23} Hoberman et al randomized 291 children, 6 to 23 months of age, to receive amoxicillin-clavulanate or placebo, irrespective of the severity of their otitis.²² The primary outcomes were the time to resolution of symptoms and the burden of symptoms over time.²² Initial resolution of symptoms by day 7 was 80% in the treatment group and 74% in the placebo group ($P=.14$).²² This was consistent with an earlier Cochrane review that showed only a marginal benefit with antibiotic treatment.¹⁵ However, the sustained resolution of symptoms at day 7 was 67% and 53% in the treatment and placebo groups, respectively ($P=.04$), supporting antimicrobial therapy for sustained response.²² Clinical failure at day 4 or 5 was 4% and 23% in the treatment and placebo groups, respectively; and at days 10 to 12, 16% and 51% experienced clinical failure in the treatment and placebo groups, respectively ($P<.001$, NNT=3).²² Interestingly, the authors of this study found that on analysis, there were substantial clinical improvements in the children who were severely affected and nonseverely affected.²²

Tähtinen et al from Finland randomized 319 children aged 6 to 36 months to receive amoxicillin-clavulanate or placebo.²³ At day 3, 14% of children treated with antibiotics and 25% taking placebo had treatment failure. At day 8, 19% and 45% were categorized as failing treatment, respectively, (NNT=4).²³

The most common adverse event in these 2 recent studies was the development of diarrhea in the children receiving amoxicillin-clavulanate. Hoberman's group found that 24% of patients using amoxicillin-clavulanate had diarrhea compared with 7% of those using placebo²²; while the group from Finland discovered that 48% of patients using amoxicillin-clavulanate had diarrhea versus 27% using placebo.²³ In the Canadian study, only 22.5% of children younger than age 2 developed diarrhea when using amoxicillin, compared with 18.5% using placebo ($P = .80$).²¹

An editorial in the *New England Journal of Medicine*²⁴ highlighted the fact that both the study by Hoberman et al and the study by Tähtinen et al were conducted on children with a certain diagnosis of AOM, which appears to be the key to optimal management. The authors also attribute the high rate of clinical failure in the placebo group to the certainty of the AOM diagnosis by eliminating the patients who spontaneously improve because they do not have AOM.^{22,23} The new research suggests that when there is a certain AOM diagnosis in children younger than 2 years old, there is a significant benefit for treatment with antimicrobial therapy.²⁴

Conclusion

These new studies demonstrate a real advantage for antibiotic therapy compared with placebo to avoid treatment failure—as long as the AOM diagnosis is certain in the office setting. Canadian guidelines support the use of amoxicillin (and not amoxicillin-clavulanate) for young children with severe AOM and for those with early signs of treatment failure.

Competing interests

None declared

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