A review of antibiotics for the management of Acute Otitis Media in children

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INTRODUCTION AND AIMS

Acute Otitis Media (AOM) in children is a commonly seen medical problem in general practice and in the Ear, Nose and Throat (ENT) specialty. AOM is defined as the presence of middle-ear effusion with a rapid onset of symptoms of middle-ear inflammation, such as ear pain, otorrhoea or fever.¹ More than two thirds of children will experience one or more attacks of AOM by the age of 3, and 50% will experience more than 3 episodes before the age of 7.² In particular, AOM is a health care burden in the developing world, where the annual global incidence of AOM is around 10%.³ This burden of disease calls for effective management plans across the health care system. After a fall in antibiotic use in the late 1990s, antibiotic prescribing in the United Kingdom (UK) has now reached a plateau but the rate remains considerably higher compared with northern European countries.⁴ In the UK, the National Institute of Clinical Evidence (NICE) has published a Clinical Knowledge Summary (CKS)⁵ (last revised in July 2015) on the management of AOM in children. The recommendations regarding antibiotics in this CKS mostly stem from the NICE guideline "Prescribing of antibiotics for self-limiting respiratory tract infections in adults and children in primary care".⁴ In this review, I will be discussing the recommendations in the guideline using current evidence based literature. In particular I will be focusing on the use of antibiotics in AOM.

Current guideline:

As discussed, the current guideline related to antibiotic prescribing for AOM within the NICE CKS (2015) "Otitis Media – acute"⁵ is "Prescribing of antibiotics for self-limiting respiratory tract infections in adults and children in primary care".⁴ The following points have been attained from the NICE Clinical Knowledge Summary (2015) in relation to antibiotic prescribing.

Point 1.1.3 states:

a no antibiotic prescribing strategy or a delayed antibiotic prescribing strategy should be agreed for patients with AOM.

Point 1.1.4 states:

depending on clinical assessment of severity, patients in the following subgroups can also be considered for an immediate antibiotic prescribing strategy (in addition to a no antibiotic or a delayed antibiotic prescribing strategy):

bilateral acute otitis media in children younger than 2 years
acute otitis media in children with otorrhoea

Point 1.1.7 states:

an immediate antibiotic prescription should only be offered to patients in the following situations:

if the patient is systemically very unwell

if the patient has symptoms and signs suggestive of serious illness and/or complications, particularly mastoiditis

if the patient is at high risk of serious complications because of pre-existing comorbidity. This includes young children who were born prematurely

In summary, the current guideline suggests 3 approaches to the clinical management of AOM in children:

no antibiotic prescribing

delayed antibiotic prescribing- where an antibiotic prescription is written for use at a later date should symptoms worsen

immediate antibiotic prescribing

DISCUSSION

Antibiotics vs no antibiotics

In children presenting with uncomplicated AOM, treatment with Amoxicillin has shown to carry the risk of side-effects such as diarrhoea and/or rash. Marcy et al⁶ conducted a meta-analysis where it was shown that in a group of 100 average-risk children with AOM, 80 would improve within 10 days without treatment of antibiotics, and 92 if treated with antibiotics. In addition, 3 to 10 children would develop a rash or diarrhoea. This study also found that the group of children who would benefit most from antibiotics are children under 2 or those with otorrhoea (NNTB 3-4).

Venekamp et al⁷ conducted a similar meta-analysis, taking 5 RCTs (1149 children) to compare the outcomes between immediate antibiotic prescribing and expectant observation, concluding that antibiotics had little or no effect on pain experienced in AOM in children between days 3 to 7 or 11 to 14. Results indicated that immediate treatment with antibiotics led to an increased risk of children developing vomiting/diarrhoea/rash in comparison with the observation group (RR 1.71, 95% CI 1.24 to 2.36, NNTB 9). The results also demonstrated that antibiotics resulted in lower tympanic membrane perforations (NNTB 33) and reduced cases of contralateral AOM compared with placebo (NNTB 11).

The studies by Marcy et al⁶ and Venekamp et al⁷ show that whilst antibiotics do offer clinical improvement in a small population of children, they also increase the risk of potential side effects. Therefore, it is important for health care professionals to consider these benefits and risks when deciding to prescribe antibiotics to children with uncomplicated AOM.

Furthermore, it has been suggested that the use of antibiotics for AOM can increase the risk of recurrent AOM due to changes in the microbial flora.⁸ In 2009 a double-blinded placebo-controlled randomised trial

by Bezáková et al⁹ found an increased risk of AOM recurrences up to 3.5 years after randomisation in children treated with antibiotics. It found that AOM recurred in 63% (47/75) of children treated with Amoxicillin and in 43% (37/86) of the placebo group (risk difference 20%, 95% confidence interval 5% to 35%).⁹ This is a statistically significant difference and supports the clinical guideline under discussion; and the careful use of antibiotics in children with AOM. Te Molder et al,¹⁰ in a more recent study of 848 children, investigated the effect of antibiotic treatment for a first AOM episode occurring during infancy on AOM recurrences later in life. The study concluded that antibiotic treatment of the first AOM episode during infancy did not affect the number of AOM recurrences, therefore providing conflicting evidence with the earlier Bezáková study.⁹ It is however important to consider that parents consult their family doctor with their child in case of AOM symptoms in only approximately 50% of cases. Therefore, the reported incidence of AOM is likely to be higher than the numbers found in the study by Te Molder.¹⁰

Nonetheless, the Bezáková trial⁹ assessed a shorter term impact (3.5 years) of antibiotic treatment compared with Te Molder¹⁰ (4 years), making it less significant. In addition, the response rate in the Bezáková study⁹ was only 70%. Other randomised controlled trials (RCTs) have compared antibiotics with placebo or watchful waiting in children with AOM, and have not found any differences in AOM recurrences at short term follow-up of up to 12 months.^{7, 11}

Whilst antibiotics were shown by Venekamp et al⁷ to have little effect on pain as a symptom of AOM, they have a direct effect on middle ear effusions (MEE) and associated hearing loss.¹² Tapiainen et al¹² conducted a RCT to determine if antibiotic treatment in AOM was linked to a reduced duration of MEE. The study looked at 85 children with AOM between the ages of 6 months to 15 years. The children were randomly assigned to take either a 40mg/kg dose of amoxicillin-clavulanate or a placebo for 7 days. The study showed that MEE disappeared 2 weeks earlier in the antibiotic group compared with the placebo group.¹² Also, normal otoscopy findings were observed 1.4 weeks earlier in the antibiotic group than in the placebo group. Therefore, this study shows that antibiotic treatment reduces the duration of MEE in children with AOM, and possible hearing loss too although further studies are needed before a definitive conclusion can be brought.

Duration of antibiotic prescribing

Recommendations for the duration of antibiotic therapy for AOM vary from 5 to 10 days in different guidelines globally.¹³ The NICE guideline states that the duration of antibiotics prescribing should be 5 days.¹⁴ Shorter duration of antibiotic treatment is desirable as it reduces antibiotic resistance, reduces the risk of adverse events, improves adherence, and lessens expense. However, a shorter duration has also shown to have its disadvantages. This was recently shown in a large prospective, double-blind study by Hoberman et al,¹⁵ where 520 children aged 6-23 months with a diagnosis of AOM received either a 5 day or 10 day treatment of Amoxicillin-clavulanate. The study

established that children treated for 5 days were at a higher risk of having clinical failure (34% vs. 16%). In addition, on their AOM-Severity of Symptoms scale (scores ranged from 0 to 14, with higher numbers indicating more severe symptoms) between day 6 to 14, the 5-day group had lower scores than the 10-day group, again signifying benefits from a longer duration of treatment. Although this study shows some promising results, it is important to recognise that the study does not address clinical outcomes in children over 23 months of age. A child's ENT anatomy and physiology changes in the first few years of life, and hence it is important to consider whether the same results would be depicted in an older age group. Furthermore, the study uses Amoxicillin-clavulanate, and whilst this is the most effective oral antibiotic for AOM, the results of the study cannot be applied to children with a penicillin allergy, for whom a macrolide for example, would be an alternative option.

Which antibiotics?

The NICE guideline does not mention which antibiotics should be prescribed for children with AOM.¹⁴ Instead it directs health care professionals to the British National Formulary for drug names and doses. However, it is regarded common practice to prescribe a course of Amoxicillin, or Erythromycin or Clarithromycin in penicillin allergic children amongst health care professionals globally. The 3 most commonly recovered bacteria associated with acute otitis media are *Streptococcus Pneumoniae*, *Haemophilus Influenzae* and *Moraxella Catarrhalis*, hence the use of beta-lactamase antibiotic is favoured.¹⁶ However, since the introduction of the pneumococcal vaccine the most common pathogen may be changing from *Streptococcus Pneumoniae* to *Haemophilus Influenzae*. Overall, as these organisms are still the commonest causes of bacterial AOM, the NICE guideline should include this in their recommendation, as it avoids health care professionals seeking help from other sources.

CONCLUSION

After undertaking this review, it is clear that the majority of the recommendations regarding antibiotics for AOM made by the NICE guideline are mostly consistent with recent literature. The review shows that antibiotics have little to no effect on pain in the first few days of children diagnosed with AOM. Tapiainen et al¹² demonstrated that antibiotics can reduce MEE children with AOM, however more clinical trials are needed to definitively attribute antibiotic use as a treatment which can be directly associated with hearing improvement in children with AOM and MEE, as in the Tapiainen et al study they associate MEE with reduced hearing as opposed to measuring it as a separate variable.

Furthermore, antibiotics are more useful for children under 2 years with bilateral AOM or children with otorrhoea. In mild AOM a watchful waiting or delayed antibiotics is justified.

It is important to note that this NICE guideline does not address babies under 3 months old, and hence this gap should be further researched with RCTs.

The Hoberman et al¹⁵ study has shown promising

clinical results regarding the length of antibiotics prescribing; further studies are needed to ensure result replication and if future results concur with the initial study, inclusion in an updated NICE clinical guideline would be justified to ensure evolving clinical practice in the management of childhood AOM.

In conclusion, there should be a clinical guideline solely dedicated to the diagnosis and management of AOM in children in the UK. Thus ensuring avoidance of uncertainty and empowering health care professionals to use a single guideline as opposed to evidence from different sources when diagnosing and managing children with AOM. Nonetheless, a guideline is merely an aid in deciding the management plan for a patient, and it should be emphasised that a health care professional's clinical judgement should be used adjunctively.

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