Critical Appraisal Topic

Antibiotic Duration in Acute Otitis Media in Children

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Clinical Scenario:
A 2 year old female who presents with bilateral otalgia, decreased appetite, and irritability for three days. A fever of 101°F was recorded. Physical examination reveals bulging, erythematous TMs with decreased mobility. She has no prior history of ear infections.

Clinical Question:
In children with acute otitis media (AOM), are short courses of antibiotic therapy as effective as long courses in achieving clinical resolution?

Articles:


Critical Review of Study:
Gulani, Sachdev, & Qazi (2010) performed a systemic review of randomized controlled trials (RTCs) providing Grade A, lb level of evidence (CEBM, 2011). 35 trials were reviewed which compared the empiric treatment of acute otitis media of antibiotics regimens of <4 days versus >4 days in children between four weeks to eighteen years of age with a clinical diagnosis of acute otitis media and no history of immediate antibiotic use, immune deficiency, chronic disease or head and neck abnormalities. The trials were grouped by pharmacokinetic behavior of short-course antibiotics into short-acting antibiotics, parenteral ceftriaxone, and long-acting azithromycin. The outcomes were measured at 10-14 days and again at 1-3 months.

Kozyrskyj, Klassen, Moffatt, & Harvey (2010) completed a meta-analysis of randomized controlled trials (RCTs) providing Grade A, level la evidence (CEBM, 2011). 49 trials including 12,045 participants were reviewed which explored the empiric treatment of AOM, comparing two antibiotic regimens of different durations, a short course (less than seven days) and a long course (seven days or greater). Participants included children ages one month to 18 years with a clinical diagnosis of AOM and no history of immediate antibiotic use, immune deficiency, chronic disease or head and neck abnormalities. Clinical resolution indicated that the presenting signs or symptoms of AOM had improved or resolved. The primary outcome of treatment failure was defined as the absence of clinical resolution, relapse or recurrence of AOM during one month following initiation of therapy. Treatment outcomes were extracted from individual studies and combined in the form of a summary odds ratio (OR). A summary OR of 1.0 indicates that the treatment failure rate following less than seven days of antibiotic treatment was similar to the failure rate following seven days or more of treatment.

Results:

The review by Gulani, Sachdev, & Qazi (2010) indicates there was no evidence of an increased risk of treatment failure until one month with a short-course of antibiotics (RR=1.06, 95% CI 0.95 to 1.17, P=0.298). Use of short-acting oral antibiotic in short course was associated with a significantly increased risk of treatment failure (RR=2.27, 95% CI: 1.04 to 4.99). There was a slightly increased risk of treatment failure with parenteral ceftriaxone (RR=1.13, 95% CI 0.99 to 1.30). The risk of adverse effects was significantly lower with short-course regimens (RR=0.58, 95% CI: 0.48 to 0.70). There is no evidence of an increased risk of treatment failure with short course of antibiotics for acute otitis media. Among the short-course regimens, azithromycin use was associated with a lower risk of treatment failure while short-acting oral antibiotics and parenteral ceftriaxone may be associated with a higher risk of treatment failure.

Strengths of the review include that this is an updated systematic review, which also incorporates relevant sensitivity, subgroup and meta-regression analyses. There was no evidence of publication bias. The main conclusion regarding the primary outcome remained stable over a large spectrum of stratified analyses. Influence analysis did not reveal an overwhelming effect of any single trial. Limitations of the review include 1) a head to head comparison of different
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durations of the same antibiotic was done in only four trials; 2) interpretation is confounded by the wide variation in diagnostic and outcome criteria, where a lack of stringent diagnostic criteria could have resulted in treatment of children without acute otitis media; and 3) information on high-risk groups was limited and a majority of the trials were conducted in developed countries.

The review by Kozyrskyj et al. (2010) indicates that a reduction in the treatment of AOM from 10 to five days of short-acting antibiotics may slightly increase the risk of a child experiencing signs and symptoms, relapse or re-infection at eight to 19 days (OR 1.37, 95% CI 1.15 to 1.64). By 30 days following initiation of therapy, a longer course of short-acting antibiotics is comparable to a five-day course in terms of these outcomes (OR 1.17, 95% CI 0.95 to 1.43). When studies comparing the same antibiotics in both arms were analyzed the results favored the use of longer regimens of therapy (OR 1.65, 95% CI 1.35 to 2.01). Studies that had low risk of bias for the component of blinding had significantly higher risks of treatment failure (OR 2.03, 95% CI 1.48 to 2.77) compared to those with high risk of bias for blinding (OR 1.19, 95% CI 1.01 to 1.41). The long-term comparability between a short and long course of antibiotics is biologically credible, on the basis of: spontaneous resolution of untreated AOM; early eradication of pathogens after three to five days of treatment; poorer penetration of the antibiotic into the ear with continued administration as inflammation decreases; and treatment of children without AOM because of diagnostic uncertainty.

Potential weaknesses of meta-analysis techniques are that they incorporate existing biases and introduce new biases, some of which have predicted discordance of results between meta-analyses and single large RCTs. To minimize bias during study selection, pre-determined inclusion criteria was used, and most trials were assessed in a blinded fashion. Publication bias was not evident. The issue of trial heterogeneity was addressed in the grouping of antibiotics according to pharmacokinetic profile. This review combines both long-course arms in a single comparison against the short-course arm.

Clinical Bottom Line:

Expert opinion recommends a reduction in antimicrobial use from 10 to 5 days for uncomplicated otitis media over the age of six years. In comparison to a longer course (≥4 days) of any antibiotic treatment for otitis media, a short course (<4 days) of long acting azithromycin was associated with a lower risk of treatment failure while a short-course of short-acting oral antibiotics and possibly parenteral ceftriaxone were associated with a higher risk of treatment failure (Gulani, Sachdex, & Qazi, 2010).

A shortened course of antibiotics may protect the child from developing resistant microorganisms, although many clinical practice guidelines are proposing no antibiotic treatment or 'watchful waiting' as a first-line approach to treating AOM. The American Academy of Pediatrics recommends reserving antibiotic therapy for children that are less than or equal to two years with severe disease. More recently the Canadian Pediatric Society recommended a 'wait
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and watch' approach for children over six months with uncomplicated, non-severe disease. If antibiotics are used, results indicate that a long course of treatment can minimize the risks of treatment failure or recurrence post-treatment, but may not make a difference in the long term. Clinicians need to evaluate whether the minimal short-term benefit from longer treatment of antibiotics is worth exposing children to a longer course of antibiotics (Kozyrskyj et al., 2010).

Implications for Practice:

There is concern regarding resistant bacteria from the overuse of antibiotics and poor compliance is increasing, as is the cost of health care. By decreasing the duration of treatment for common infections there are many advantages such as better patient compliance, less adverse effects (particularly gastrointestinal disturbances), and lower financial burden both on a patient and society. In addition less pressure for selection for resistant bacterial strains is also a potential benefit, although this outcome is not always examined in RCTs. Therefore, it is desirable to determine the shortest duration of antibiotic treatment that would result in favorable outcomes.

References