Acute Otitis Media Treatment Duration: Is There a Reason We Have Ten Fingers?
by Dr Bud Wiedermann MD, MA, Evidence eMended Editor, Grand Rounds

This study, comparing 10 days versus 5 days of antibiotic treatment for acute otitis media (AOM), resulted in some surprising conclusions and a host of study design topics for discussion. Read on.


Normally I try to keep my blog commentaries concise, primarily by trying to control my desire to describe everything I think is interesting about a given article. I'll keep to that goal here, but still hope to mention 3 key features, plus a very important caveat.

The study was 1 of the few studies in pediatric infectious disease that tries to answer more precisely the optimal duration of antibiotic treatment. Most studies just compare 1 antibiotic to another; it's tough to get funding for studies aiming to refine treatment duration. Here, though, a group of investigators simply set out to compare treating AOM with 5 days of antibiotics, compared to 10. Of course, experienced pediatricians know there is nothing simple about ear infections in children, and the study design is very key to reaching a credible conclusion. The study concluded that, for children 6 - 23 months of age with AOM, the 5-day amoxicillin/clavulanate therapy group had a demonstrably inferior outcome compared to those receiving 10 days of amoxicillin/clavulanate.

Let's examine some key features more closely.

1. Defining the study population
One of the most difficult problems in otitis media research is actually making sure all the enrollees truly have AOM. The best ear infection studies train all the study clinicians to uniformly score their otoscopic findings, and this study did just that. A supplement to the article has some examples. In fact, the University of Pittsburgh, where this study originated, has some nice training modules you might want to check out.

2. Block randomization
This study randomized participants to 10 days of amoxicillin/clavulanate versus 5 days of antibiotic plus 5 days of placebo, in blocks of 4. This is a very important feature when studying any condition for which the risk or type of infection might vary during the study period. In this case, for example, a viral respiratory peak during the study
enrollment could result in a string of patients with RSV otitis media being enrolled. If, by chance, the randomization string contained a concentrated assignment of patients to the 10-day arm, it might alter the study conclusions, since the duration of antibiotic treatment should have little effect on treatment failure for viral otitis media. Randomization in blocks of 4, where the randomization is redone for every 4 patients, prevents such long strings from occurring.

3. Noninferiority trial

We've talked about this before in these pages. It allows investigators to limit the cost of studies by enrolling fewer patients, but is a trade-off since the sample size may not be large enough to demonstrate true inferiority of 1 treatment versus another. For this AOM study, the investigators decided that they would allow up to a 10% poorer response rate (using the extreme of the 95% confidence interval) in the 5-day treatment group and still say it was non-inferior, meaning OK to use (in the opinion of the investigators). Given that treatment failure in AOM in this age group is about 15%, they were saying they would accept up to a 25% failure rate. What they found, however, was that the 5-day group was significantly worse: a 34% failure rate, versus a 16% failure rate in the 10-day group. So, even though this was a noninferiority trial design, the study found a statistically significant degree of inferiority, i.e. the 5-day regimen is worse than 10 days, for the outcome of interest.

Caveat:

An issue with this study, and many others as well, is how the outcome is defined. The primary outcome of this study was clinical failure, defined as "...worsening of symptoms or of otoscopic signs of infection (primarily tympanic-membrane bulging) or if they did not have complete or nearly complete resolution of symptoms and signs attributable to acute otitis media by the end of treatment." It took me a while to unravel this and think about what it meant. Clearly a child could be labelled as a clinical failure even if they felt completely well; they might just have some otoscopic findings that weren't entirely resolved. All of the failures were retreated, so this was a major clinical decision. In trying to dissect this further, I came across a comment from 1 of the pioneers of evidence-based medicine, Paul Glasziou. Please look at the link. After a great amount of scrutiny of tables of data from the article, he was able to construct a graph showing that, for the component of clinical failure related to a validated scoring system of how the child actually felt, the difference wasn't impressive. Seen in this light, the study conclusions are less clear-cut. I'll still stick with recommending the standard 10 days of therapy for younger children with AOM, but I'm less likely to condemn anyone who prefers 5 days, especially if the child's symptoms are resolved at that time.

I second Dr. Glasziou's recommendation that journal "editors should insist on clear, simple presentations of the main results - preferably in graphical formats. Without that, authors and editors will continue to contribute to the considerable waste in research and gaps between research and practice."