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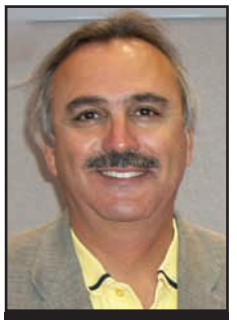
Observation Option for AOM: A Second Look

Two new, well-designed trials published in the New England Journal of Medicine have demonstrated that when acute otitis media is correctly diagnosed, treatment with effective antibiotics is of clear and substantial benefit. To me, this suggests that the confusion about whether antibiotics help children get better faster is about getting the diagnosis right, a challenging task for pediatricians and family physicians with squirming patients and ear canal wax occluding visualization of the eardrum.



MICHAEL E. PICHICHERO, M.D.

All along, I have believed that the American Academy of Pediatrics' 2004 "watchful waiting" option for treating acute otitis media (AOM) was well intentioned but not based on good evidence. In an effort to address the growing problem of antimicrobial resistance, the AAP recommended the "observation option" for otherwise healthy children aged 6 months to 2 years with nonsevere illness and an uncertain diagnosis, and for all children above the age of 2 years who were not systemically ill (Pediatrics 2004;113:1451-65).

Problem is, the studies cited by the AAP as evidence for this recommendation were nearly all seriously flawed, because they excluded children with the very criteria that signal a true AOM diagnosis: a full or bulging eardrum … and in some studies, because it was determined that they were too "unwell" and/or they "needed an antibiotic"! And, many of these trials excluded children younger than 2 years old and included many children who likely did not have AOM at all or had otitis media with effusion.

Dr. Janet R. Casey and I reviewed 25 of the studies in a paper published 3 years ago (Pediatr. Infect. Dis. J. 2008;27:958-62). We found so many serious flaws in the inclusion and exclusion criteria, and diagnostic and outcome criteria, that we were obliged to conclude that no evidence-based conclusion could be drawn.

The flaws we found in individual AOM trials call into question the validity of the conclusions of two major meta-analyses cited by the AAP, one involving 5,400 children from 33 randomized trials (J. Pediatr. 1994;124:355-67), the other of 6 studies of children aged 7 months to 15 years (BMJ 1997;314:1526-9), both of which found only modest benefit for the use of antimicrobials.

Now in the New England Journal of Medicine papers, we have two well-designed studies clearly demonstrating that treatment should not be withheld in children with proven AOM.

One of the studies, from the University of Pittsburgh, randomized 291 children aged 6-23 months to receive amoxicillin-clavulanate or placebo for 10 days. To be eligible, patients had to have AOM that was diagnosed on the basis of three criteria:

- onset of symptoms within 48 hours that parents rated with a score of at least 3 on the Acute Otitis Media Severity of Symptoms scale,
- presence of middle-ear effusion, and
- moderate or marked bulging of the tympanic membrane or slight bulging accompanied by either otalgia or marked erythema of the membrane.

Patients also had to have received at least two doses of pneumococcal conjugate vaccine.

Among the children who received amoxicillin-clavulanate, 35% had initial resolution of symptoms by day 2, 61% by day 4, and 80% by day 7, compared with 28%, 54%, and 74% among those who received placebo, respectively. For sustained resolution of symptoms, the corresponding values were 20%, 41%, and 67% with amoxicillin-clavulanate, vs. 14%, 36%, and 53% with placebo (N. Engl. J. Med. 2011;364:105-15).

The other trial, from Finland, used equally strict criteria for 319 children aged 6-35 months who were randomized to receive amoxicillin-clavulanate or placebo for 7 days. Treatment failure occurred in 18.6% of the children who received amoxicillin-clavulanate, compared with 44.9% of the children who received placebo, a highly statistically significant difference that was already apparent at the first scheduled visit on day 3 (13.7% vs. 25.3%). Overall, amoxicillin-clavulanate reduced the progression to treatment failure by 62% (N. Engl. J. Med. 2011;364:116-26).

As I see it, the problem really lies in our inability to adequately diagnose AOM. For one thing, it's essential to clean the wax out of the child's ear in order to visualize the eardrum, given that two-thirds of children diagnosed with AOM have partially or fully occluded ear canals blocking visualization of the eardrum. Yet, physicians often don't do that because it takes time and it's difficult to get the child to hold still. It's far simpler to simply take a quick look and say that the diagnosis is "uncertain," or to say that the eardrum is "red" in order to justify a diagnosis and antibiotic prescription.

Pediatricians and family physicians should all have a good, high-grade otoscope with a fresh battery and bulb, along with the training and ability to use the pneumatic attachment in order to distinguish between a bulging and retracted eardrum, which often look alike with just the otoscope.

Frankly, I find it embarrassing that with a condition as common as AOM, pediatricians and family physicians receive so little training in diagnosing it and, therefore, just don't do a good job. In otitis media workshops that include testing for competency in diagnosis (Outcomes Management Educational Workshops, West Palm Beach, Fla.), I found that physicians got the diagnosis of AOM wrong at least 50% of the time on video presentation testing. And that was without wax, under ideal classroom conditions.

Diagnosing otitis media needs to become a critical part of medical education, and physicians in practice should be retrained via CME courses. Pharmaceutical companies no longer sponsor those, so now the professional societies such as the American Academy of Pediatrics, the American Academy of Family Physicians, and the nursing organizations need to step up.

With the new evidence from the two well-controlled trials, I don't see how any clinician can withhold antibiotic treatment in good conscience. AOM is a painful condition that infants and toddlers are too young to explain to us. Can you imagine asking an adult to agree to withholding effective treatment when they are in pain and propose they take acetaminophen instead? Or can you imagine telling an adult who seeks care for an earache that the diagnosis is uncertain after examination, so the recommendation is to "observe"?

As advocates for our pediatric patients, how in the world can we allow a child to remain in severe pain for 24-48 hours longer than is necessary and keep parents up all night and away from work for 2-3 extra days?

Once everyone learns how to better diagnose AOM, we will stop overprescribing antibiotics for those children who don't have the condition. For the rest, I contend that treatment is a moral imperative. ■

DR. PICHICHERO, *a specialist in pediatric infectious diseases, is director of the Rochester (N.Y.) General Research Institute. Dr. Pichichero disclosed that he is the medical director of Outcome Management Educational Workshops that train providers to improve diagnosis but has no disclosures related to antibiotic use in AOM. E-mail him at pdnews@elsevier.com.*

Immunoglobulin Doesn't Boost HBV Vaccine Prophylaxis

BY DIANA MAHONEY

FROM THE ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

BOSTON – The recombinant hepatitis B vaccine confers as much protection when given alone as it does when given together with hepatitis B immunoglobulin to newborns of chronically infected mothers, but neither regimen is optimally effective, a study has shown.

The randomized controlled trial assessed the hepatitis B virus (HBV) status of 222 infants born to mothers who tested positive for hepatitis B surface antigen (HBsAg). The rate of protection observed in infants who received only the vaccine was statistically similar to that of infants who received the vaccine plus hepatitis B immune globulin (HBIG).

A total of 39% of the vaccine-only group and 41% of the combination group remained infection free at a minimum of 18 weeks after birth, Dr. Shiv K. Sarin reported, noting that nearly half of the babies in both groups developed occult HBV infections.

The current standard of care for preventing HBV infection in babies born to mothers who are HBsAg positive is the recombinant hepatitis B virus vaccine plus HBIG, however previous studies have suggested the possibility that the vaccine alone may be as effective as the combination therapy, said Dr. Sarin of the Institute of Liver and Biliary Sciences in New Delhi.

To test this hypothesis, Dr. Sarin, along with lead investigator Dr. Chandana Pande, a research associate at G.B. Pant Hospital in New Delhi, and colleagues randomized the newborns of 222 women who screened positive for HBsAg during their prenatal care to receive the 0.5-mL recombinant HBV vaccine at birth, 6 weeks, 10 weeks, and 14 weeks, either alone (116 infants) or with 0.5 mL intramuscular HBIG (106 infants).

All of the babies were assessed at a minimum of 18 weeks for HBsAg, HBV-DNA, and antibodies to HBsAg (anti-HBs). The study's primary end point was freedom from overt or occult HBV infection with adequate immune response, defined as anti-HBs titers of at least 10 IU/mL, Dr. Sarin said in a poster presentation.

At 18 weeks after birth, 43 babies in the combination group and 45 in the vaccine-only group remained free of overt or occult HBV infection with adequate immune response, an insignificant difference. Of the babies not meeting the primary end point, 9 had overt HBV infection, including 2 in the combination group and 7 in the vaccine-only group, and 106 developed occult HBV infection, including 52 in the combination group and 54 in the vaccine-only group. Neither of these differences attained statistical significance.The large number of babies in both groups who developed occult HBV infection "may be due to intrauterine transmission of the infection," Dr. Sarin suggested.

Dr. Sarin and Dr. Pande said they had no relevant financial disclosures. ■