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Good, Better, Best: Antibiotics for AOM

Upon returning from the annual Inter-science Conference on Antimicrobial Agents and Chemotherapy,

I wanted to share my view of what seemed to emerge as a theme from the many papers published on ear infection treatment.

First, consensus exists on the importance of a bulging tympanic membrane in the diagnosis of acute otitis media (AOM) and its differentiation from otitis media with effusion (OME). Most AOM experts appear to agree that antibiotic treatment is warranted and recommended for children with clear-cut AOM as distinguished by a bulging eardrum.

Watchful observation or placebo treatment should involve less ill, older children who are verbal enough to describe their pain accurately.

Second, in children with a bulging tympanic membrane, the chances for bacterial infection are high, probably around 90%-98%. These children are not the ones with an 80% or greater likelihood of "spontaneous resolution" of their ear infections at the same speed as those who receive antibiotics.

Third, the spontaneous resolution rate of bacterial otitis media depends on when you ask the question: 1-2 days into treatment, on days 3-5, on days 10-14, or on day 28.

Most of the symptomatic benefit of antibiotics occurs during the early days of treatment.

The rates of persistent effusion, measured later, will be lower if appropriate antibiotics are used.

Fourth, the effectiveness of antibiotic therapy should be gauged against the likelihood of resolution that would accom-

pany placebo treatment of otitis media.

Research in this area involves ethical, medicolegal, and practical concerns. The patient populations who enroll in trials in which children could be receiving antibiotic, placebo, or possibly one or two tympanocenteses (ear taps) are almost certainly different from each other and different from what we see in everyday practice.

The situation is dynamic in terms of study populations, investigative sites, causative bacteria, and antibiotic resistance.

Thus, comparisons across studies and across time should be made with extreme caution; frankly, I don't think they should be made at all.

Absent new data to the contrary—and I know of none—among children who have AOM of sufficient severity to receive an ear tap, bacterial eradication by

natural host defense occurs 3-5 days after the onset of symptoms in 20% of these patients with *Streptococcus pneumoniae*, in 50% of those with *Haemophilus influenzae*, and in 70% with *Moraxella catarrhalis*. These numbers have been confirmed in multiple studies.

The bacterial profile for AOM in the United States has changed significantly because of the conjugate pneumococcal vaccine (Prenvar).

In vaccinated children, the No. 1 bacterial species is now *H. influenzae*, and more than half of those organisms make β -lactamase, rendering them resistant to the current first-line antibiotic choice, amoxicillin.

In fact, it appears that about 60% of AOM in Prenvar-vaccinated children involve *H. influenzae*.

But we can't ignore *S. pneumoniae*, which makes up about 30% of the total bacterial burden.

Although most of those strains are now penicillin susceptible because of the vaccine, the resistant strains are still

around. The ratios may change with time, but *S. pneumoniae* is more worrisome because of its invasiveness and suppurative complications.

Finally, at least for the moment, we see a clearer distinction emerging among antibiotics as "good, better, and best" for anticipated effectiveness and for tolerability in the current U.S. pathogen mix. (See table below.)

Of course, there are caveats to these distinctions.

Measures of efficacy include bacterial cure (by double tympanocentesis study designs) and pharmacokinetic/pharmacodynamic antibiotic measurements of the key pathogens in middle-ear fluids.

Although I'm tempted to add "tolerability to the pocketbook (monetary cost)" and "annoyance cost of phone calls from the managed care policy police" as measures of tolerability and adherence to the prescribed regimen, the tolerability measurements in the table refer to taste, the number of doses per day, the duration of treatment, and the number of office visits involved.

Not included in the table are cefixime and cefibuten because these agents are

not satisfactorily effective against penicillin-nonsusceptible *S. pneumoniae*. (Combined with high-dose amoxicillin, however, such a combination would be expected to work very well.)

Also not listed are cefaclor and loracarbef because their efficacy, by current standards, has not been tested and they are anticipated not to be that good, although the tolerability is excellent.

Now the debate will continue around what to do in practice: Do we start with a good antibiotic, then go to a better one? Or start with a better one, and then jump to the best? Or start with the best and go to other "bests"—or to ear taps or tubes?

The best antibiotics in efficacy are not the same as the best in tolerability, so which one takes precedence? The most effective antibiotic won't work if it is not taken, and the most tolerable antibiotic won't work if it is not effective.

Stay tuned for the next chapter. ■

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Antibiotics for Acute Otitis Media

	Efficacy	Tolerability
BEST	Amoxicillin/clavulanate ES Ceftriaxone (three injections) Gatifloxacin* Levofloxacin*	Amoxicillin Azithromycin Cefdinir
BETTER	Cefdinir Cefpodoxime Cefprozil Cefuroxime	Cefzil Gatifloxacin* Levofloxacin*
GOOD	Amoxicillin Azithromycin	Amoxicillin/clavulanate ES Trimethoprim/sulfamethoxazole
MARGINAL	Trimethoprim/sulfamethoxazole	Cefpodoxime Ceftriaxone (three injections) Cefuroxime

*Not approved by the Food and Drug Administration or available for AOM treatment.

Notes: Efficacy is measured by double ear tap results and pharmacokinetic/pharmacodynamic parameters. Tolerability is measured by taste, dosing frequency, duration of treatment, and number of visits.

Source: Dr. Pichichero

Topical Ciprofloxacin/Dexamethasone Good for AOM With Otorrhea

BY ELAINE ZABLOCKI
Contributing Writer

LOS ANGELES — Topical ciprofloxacin/dexamethasone is effective in treating acute otitis media with otorrhea through tympanostomy tubes, Dr. Joseph E. Dohar wrote in a poster presentation at the annual meeting of the American Academy of Otolaryngology-Head and Neck Surgery Foundation.

Topical ciprofloxacin 0.3% and dexamethasone 0.1%, marketed as Ciprodex sterile otic suspension, produced more clinical cures, earlier cessation of otorrhea, and caused fewer side effects than oral amoxicillin/clavulanate potassium (Augmentin), wrote Dr. Dohar, an oto-

laryngologist at the Children's Hospital of Pittsburgh. Alcon Laboratories, maker of Ciprodex, sponsored the study.

Dr. Dohar is a clinical investigator, consultant, and speaker for the company.

"My personal experience has been extremely favorable when using topical ciprofloxacin/dexamethasone," Dr. Dohar said in an interview.

"The topical combination is superior to systemic antibiotics, due to better cure rates, more effective killing of bacteria,

less treatment-related resistance, and far fewer side effects."

In this observer-masked, prospective multicenter trial, 80 children aged 6 months to 8 years (mean 2 years) with acute otitis media and otorrhea were randomized to treatment with either topical ciprofloxacin/dexamethasone drops or a 5-mL oral suspension of 600 mg amoxicillin/42.9 mg clavulanate potassium.

The median time to cessation of otorrhea was 4 days in the ciprofloxacin/dex-

amethasone group and 7 days in the amoxicillin/clavulanic acid group.

Ciprofloxacin/dexamethasone also had fewer side effects.

Of the children receiving the drops, 5% complained of ear pain, compared with 20% of children taking the suspension had diarrhea.

The treatment failure rate was 17% for ciprofloxacin/dexamethasone and 41% for amoxicillin/clavulanic acid.

These results are impressive, Dr. Dohar said in an interview.

"The study design was meticulous, and a relatively small sample size resulted in such a positive outcome. It is rare in the modern era of anti-infectives to be able to demonstrate superiority." ■

The combination is superior to systemic antibiotics due to better cure rates, more effective killing of bacteria, and far fewer side effects.