



BY MICHAEL E. PICHICHERO, M.D.

ID CONSULT

Use Fluoroquinolones Judiciously

The American Academy of Pediatrics' new policy statement on fluoroquinolone use in children is a thoughtful,

measured step in the right direction. As we await the availability of new agents in this class, as well as new pediatric indications for those already licensed, it's very helpful to have a document that will help guide our judicious use of these potent antimicrobials.

I agree with the statement's overall message, that in order to minimize the chance of antimicrobial resistance, use of fluoroquinolones should be restricted to situations in which infection is caused by multidrug-resistant pathogens for which no other effective oral agent is available, or when parenteral therapy is not feasible and no other effective oral agent is available (Pediatrics 2006;118:1287-92).

The statement provides a list of specific clinical scenarios that qualify, including urinary tract infections caused by *Pseudomonas aeruginosa* or other multidrug-resistant gram-negative bacteria, chronic suppurative otitis media or malignant otitis externa caused by *P. aeruginosa*, chronic or acute osteomyelitis or osteochondritis caused by *P. aeruginosa* (often associated with foot puncture), and for exacerbation of pulmonary disease in patients with cystic fibrosis who are colonized with *P. aeruginosa*.

Unfortunately, though, the document is already somewhat out of date. Most of the data cited in it were published prior to 2004.

One important change that has occurred since then is the resurgence of difficult-to-treat ear infections in children due to multidrug-resistant *Streptococcus pneumoniae*.

We've had 4 or 5 years following the introduction of Prevnar when the rate of those infections were plummeting. Now, however, we're increasingly seeing cases of otitis media caused by the nonvaccine serotype 19A, a particularly nasty clonal strain that is resistant to amoxicillin, amoxicillin-clavulanate, and all the cephalosporins including intramuscular ceftriaxone.

In our practice, these children are relapsing even after tympanocentesis and following tube placement. The ear just keeps draining.

I suggest that this is an appropriate indication for a quinolone.

Such a scenario isn't spelled out in the AAP statement, but recurrent otitis media due to pneumococcal serotype 19A certainly does qualify under the general heading of a "multidrug-resistant pathogen for which there is no safe and effective alternative."

I think we can lay to rest the safety concerns regarding several of the fluoroquinolones in children.

In 2005, my colleagues and I published an article in which we summarized the available data on the use of gatifloxacin in children with recurrent ear infections and

ear infection treatment failure (CID 2005;41:470-8).

The database wasn't huge—a total of 867 children aged younger than 2 years from four clinical trials—but it was very reassuring in that during a full year of follow-up, we found no evidence of arthrogenotoxicity, hepatotoxicity, or central nervous system toxicity, nor were there the alterations in glucose homeostasis that had occurred in adults.

Earlier this year, gatifloxacin was pulled from the market worldwide because of glucose homeostasis concerns in adults. Prior to that, Bristol-Myers Squibb had withdrawn its application for a pediatric indication for the agent because it couldn't come to an agreement with the Food and Drug Administration about how to limit overprescribing (CID 2005;41:1824-5).

I think we can extrapolate the safety data on gatifloxacin to other fluoroquinolones, with some caution.

I believe we have enough data on ciprofloxacin and levofloxacin to support their use in children.

The only other major systemic fluoroquinolone, moxifloxacin, is probably okay, but I'd hesitate to endorse its use in children because there are no data—and it doesn't come in a liquid formulation, so it's very difficult to give to a young child.

Of course, resistance remains a major concern.

We must continue to be vigilant in reaching for the more narrow-spectrum drugs first, and only advance to more potent agents as the clinical situation demands.

However, even if we restrict our use of fluoroquinolones to the most difficult-to-treat ear infections, that could still mean several hundred thousand prescriptions nationwide.

If these bugs develop resistance to them, we're in trouble.

There is one promising agent in the pipeline called faropenem. It's the first of a new class of beta-lactam antibiotics called the penems, which are essentially structural hybrids between the penicillins and cephalosporins. Faropenem appears to be far less vulnerable to beta-lactamase, compared with other cephalosporins and imipenem, giving it a lower propensity for resistance. It also has very potent activity against gram-positive bacteria, particularly multiresistant *S. pneumoniae*.

A new drug application for faropenem medoxomil was filed with the FDA in December 2005, with approval and launch expected in late 2006, according to Replidyne, which licensed the agent from Daiichi Suntory Pharmaceuticals in March 2004. Trials in children are set to begin this winter. ■

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Antibiotic Prescribing Patterns in U.S. Vary by Specialty

BY PATRICE WENDLING
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NICE, FRANCE — Family physicians prescribe penicillins most often, whereas surgeons prescribe fluoroquinolones more frequently than any other specialty.

These are some of the findings from a 3-year study examining prescribing patterns of oral antibiotics by physician specialty in the United States. This is the first study to offer a national perspective on outpatient antimicrobial prescribing by physician specialty, Katie J. Suda, Pharm.D., and her associates reported at

the 16th European Congress of Clinical Microbiology and Infectious Diseases.

"Over the 3 years, prescribing patterns did vary significantly by physician specialty," she said.

Investigators evaluated outpatient antibiotic prescriptions dispensed in 2001-2003 from nine managed health care plans. Medications were stratified into classes and formulations as defined by the American Hospital Formulary Service. Diagnostic codes were defined according to Medicode (now Ingenix).

A total of 7,613 physicians wrote 48,182 antibiotic prescriptions for 26,875 patients. The average patient age was 34 years.

The majority of patients were diagnosed with upper respiratory tract infection followed by sinusitis and genitourinary infections.

Physician specialties included family practice (42%), internal medicine (14%), pediatrics (21%), emergency medicine (5%), specialists (5%), dermatologists (4%), obstetricians/gynecologists (3%), surgeons (3%), and others such as pathologists and psychiatrists (3%).

Overall, penicillins were dispensed most frequently, followed by macrolides, cephalosporins, and fluoroquinolones, said Dr. Suda, of the University of Tennessee Health Science Center in Memphis.

Dermatologists most often prescribed tetracyclines (75%); emergency medicine physicians, macrolides (42%); ob.gyns, nitrofurans (27%); pediatricians, penicillins (38%); and surgeons, fluoroquinolones (25%). Family physicians prescribed penicillins most often, while internists prescribed fluoroquinolones.

All physician groups prescribed β -lactamase inhibitors more frequently than any other agent for the treatment of skin and skin structure infections.

Internists prescribed broader-spectrum agents for the treatment of urinary tract infections, whereas ob.gyns. prescribed narrower-spectrum agents, even though not all of their patients may be pregnant or lactating, she said.

Fluoroquinolones were used most often for UTIs by family physicians, internists, and emergency physicians, and nitrofurans by ob.gyns. and surgeons.

Beta-lactamase inhibitors were the treatment of choice for upper respiratory tract infections for family practitioners and specialists.

But internists and emergency physicians were more likely to prescribe macrolides, which may be because these physicians see more patients with complicated conditions, she said.

Pediatricians used penicillins most often, followed by macrolides and beta-lactamase inhibitors.

Overall, lower respiratory tract infections were treated most often with macrolides, followed by fluoroquinolones.

Audience members questioned whether the findings were representative

of family care in the United States, particularly in light of the high fluoroquinolone use that was reported.

Dr. Suda said she believed the findings were representative of a managed care population under the age of 65 years, but added that she was unable to validate the findings against data from other plans because most organizations won't release the information.

The most commonly prescribed fluoroquinolones were levofloxacin (more than 50%), followed by ciprofloxacin, moxifloxacin, and gatifloxacin, she said. ■

VERBATIM

'My usual health care delivery style is the ... [microwave] version. I contend that in a blindfolded taste test the consumer couldn't tell the difference between mine and the baked-from-scratch version.'

Dr. William G. Wilkoff, p. 36