AAP: Use Fluoroquinolones Sparingly in Children

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Fluoroquinolone use in children should be restricted to situations in which there is no safe and effective alternative either for treating an infection caused by multidrug resistant bacteria or in which parenteral therapy is not feasible.

The recommendations, released in a new policy statement from the American Academy of Pediatrics' Committee on Infectious Disease (COID), are in response both to concerns about increasing rates of bacterial resistance and to the potential association of fluoroquinolones with adverse musculoskeletal events (Pediatrics;doi:10.1542/peds.2006-1772).

"The COID felt that the use of fluoroquinolones in children was not necessary in most situations, and we wanted to be very specific about how they should be used," lead author and former COID chair Dr. Keith R. Powell said in an interview.

The use of a fluoroquinolone may be justified in special circumstances, after careful assessment of the risks and benefits for the individual patient.

The committee advises that appropriate use be limited to the following specific scenarios:

► Exposure to aerosolized *Bacillus anthracis* to decrease the incidence or progression of disease (Food and Drug Administration licensed use).

► Urinary tract infections caused by *Pseudomonas aeruginosa* or other multidrug-resistant, gram-negative bacteria (FDA licensed for complicated *Escherichia coli* urinary tract infections and pyelonephritis attributable to *E. coli* in patients 1-17 years of age).

► Chronic suppurative otitis media or malignant otitis externa caused by *P. aeruginosa*.

► Chronic or acute osteomyelitis or osteochondritis caused by *P. aeruginosa* (not for prophylaxis for nail puncture wounds to the foot).

► Exacerbation of pulmonary disease in patients with cystic fibrosis who have colonization with *P. aeruginosa* and who can be treated in an ambulatory setting.

► Mycobacterial infections caused by isolates known to be susceptible to fluoroquinolones.

► Gram-negative bacterial infections in immunocompromised hosts in whom oral therapy is desired or resistance to alternative agents is present.

► Gastrointestinal tract infection caused by multidrug-resistant *Shigella* species, *Salmonella* species, *Vibrio cholerae*, or *Campylobacter jejuni*.

► Documented bacterial septicemia or meningitis attributable to organisms with in vitro resistance to approved agents or in immunocompromised infants and children who have failed to respond to parenteral therapy with other appropriate antimicrobial agents.

► Serious infections attributable to fluoroquinolone-susceptible pathogen(s) in children with life-threatening allergy to alternative agents.

For many years, fluoroquinolones had been contraindicated in children because animal data suggested that the antimicrobials may cause joint toxicity.

Prior to 2004, ciprofloxacin was the only fluoroquinolone licensed for use in children less than 18 years of age, and only for inhalational anthrax. That year, the FDA approved ciprofloxacin for treating complicated urinary tract infections and pyelonephritis caused by *E. coli* in patients aged 1-17 years.

But despite the fact that inhalational anthrax was the only approved use of fluoroquinolones in children prior to 2004, U.S. pharmacy sales and distribution data from 2002 indicate that there were approximately 520,000 fluoroquinolone prescriptions written for children and adolescents younger than 18 years. Approximately 13,800 of those prescriptions were written for children aged 2-6 years, and 2,750 were written for infants younger than 2 years of age.

There has been no decrease in prescribing for children since 2002, COID member Dr. John S. Bradley said.

The increased use of fluoroquinolones in all age groups has resulted in a corresponding increase in bacterial resistance to these agents. One study in adults with cystic fibrosis demonstrated that the proportion of susceptible *P. aeruginosa* isolates de-

creased from 100% to 45% after 14 days of treatment (Am. J. Med. 1987;82:189-95).

Fluoroquinolone resistance in *Streptococcus pneumoniae* also has been increasing. Susceptibility testing of 5,640 *S. pneumoniae* strains isolated during the 1997-1998 respiratory illness season from 377 hospitals in the United States showed only 0.3% of isolates to be resistant to ciprofloxacin. In contrast, among isolates obtained from January 1999 through August 2000, 3% were resistant to ciprofloxacin, 0.5% to levofloxacin, and 0.4% to gatifloxacin (Diagn. Microbiol. Infect. Dis. 2002;43:207-17).

Concurrent with the overprescribing and increasing resistance are data showing that fluoroquinolones have been associated with arthropathy in children. Ciprofloxacin labeling by the FDA includes data regarding musculoskeletal adverse events in children aged 1-17 years who received the drug to treat complicated *E. coli* urinary tract infections and pyelonephritis attributable to *E. coli*. Compared with a rate of 6.0% (21/349) at 6 weeks among controls, musculoskeletal adverse events occurred in 9.3% (31/335) of children within 6 weeks of receiving ciprofloxacin. Most of these events associated with fluoroquinolones were transient and of moderate intensity.

None of the published studies reviewed for the AAP document showed a statistically significant increase in arthropathies, although there is a trend for mild to moderate events, noted Dr. Bradley, director of the division of infectious diseases at Children's Hospital and Health Center, San Diego.

The COID concluded that the use of a fluoroquinolone in a child or adolescent may be justified in special circumstances, after careful assessment of the risks and benefits for the individual patient. Although there is no compelling evidence linking fluoroquinolones with sustained injury to developing joints in humans, the possibility that this may occur infrequently has not been excluded, Dr. Powell and his associates said. ■

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'[FDA] management and [drug and device manufacturing] companies have found ways to manipulate this process in favor of approval.'

An anonymous respondent to the survey by the Union of Concerned Scientists, page 62