Gatifloxacin Found Safe, Effective for Otitis Media

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Gatifloxacin appears to be both safe and highly effective in treating acute and recurrent otitis media in children, and is not associated with either acute or long-term joint disorders, Michael Pichichero, M.D., and his colleagues reported.

In the compilation of four clinical trials (two phase II and two phase III), they also concluded that the drug, a fluoroquinolone, was more effective in eradicating middle-ear pathogens than was amoxicillin/clavulanate.

The effect of a 10-day course of gatifloxacin (10 mg/kg per day) was evaluated in 867 children aged 6 months to 7 years. The phase III trials also included 309 children who received amoxicillin/clavulanate as a comparator.

All children had acute otitis media (OM), recurrent OM, or OM treatment failure (Clin. Infect. Dis. 2005;41:470-8).

In the phase II trials (414 children), the high rate of discontinuation (8%) was primarily due to vomiting because of the bitter taste of an early formulation of the drug, said Dr. Pichichero of the University of Rochester (N.Y.) and his coinvestigators. In the phase III studies, with a new formulation, the rate of discontinuation was similar in both groups (2%).

Transient arthralgia occurred in 12 (1.4%) of the 867 children. There were no abnormal imaging studies in any of the 7 who were examined by an orthopedist. One child discontinued therapy due to knee swelling and abnormal gait; no joint abnormalities were seen on imaging.

In the phase III studies, the rate of arthralgia was similar between the gatifloxacin and amoxicillin/clavulanate groups (1.5% and 1.3%).

One-year safety data were available for 671 gatifloxacin-treated children. There was no evidence of arthropathy in any. A 4-year-old girl treated with the study drug developed Achilles tendon pain, which resolved in 5 days with rest and ice.

Gatifloxacin was not associated with hepatotoxicity, clinically relevant hypoglycemia, phototoxicity, or central nervous system toxicity.

The study drug was especially effective in children younger than 2 years with severe acute otitis media; the cure rate was 90%, vs. 75% with amoxicillin.

The cure rate of the pooled phase II studies was 81%. In the first phase III study, the cure rate of gatifloxacin was 90%, compared with 84% for amoxicillin/clavulanate. The cure rate for gatifloxacin in the second phase II study was 85%, compared with 79% for amoxicillin/clavulanate.

The study drug was especially effective in children younger than 2 years with severe acute otitis media; the cure rate was 90%, compared with 75% for the amoxicillin regimen. Gatifloxacin eradicated both *Streptococcus pneumoniae* and *Haemophilus influenzae*. It achieved highly significant clinical cure rates for pathogens that were resistant to one or two other antibiotics.

Pediatric use of gatifloxacin remains controversial, not only because of concerns about arthropathy, but also because childhood resistance could impact the drug's usefulness in future adult populations, the authors noted.

However, in an accompanying editorial, Colin Marchant, M.D., said the drug deserves a chance.

Promising trial results, scheduled for discussion at a May 2004 meeting of the Food and Drug Administration's Anti-Infective Drugs Advisory Committee, were scrapped at the last minute when Bristol-Myers Squibb, the drug's manufacturer, abruptly withdrew its new drug application. The stated reason was that the drug company and the FDA could not agree on a risk-management program for the drug, said Dr. Marchant of the Boston Medical Center (Clin. Infect. Dis. 2005;41:479-80).

"The safety data on gatifloxacin use in children should be reviewed in a public forum [such as the committee]," he said. "If there are no data indicating increased risks of side effects with gatifloxacin … then recommendations for further safety studies should be put forward; and the nature and basis for a risk-management program should also be exposed to public scrutiny and discussion." ■