Combo Beats Azithromycin for Resistant AOM

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An amoxicillin/clavulanate combination was significantly more effective than azithromycin in eliminating bacterial acute otitis media, including penicillin-resistant strains, reported Alejandro Hoberman, M.D., of the Children's Hospital of Pittsburgh, and his colleagues.

In a randomized, investigator-blinded study sponsored in part by GlaxoSmithKline, 730 children aged 6-30 months were randomized to receive either a 90-mg amoxicillin and a 6.4-mg clavulanate/kg combination daily in 2 divided doses for 10 days, or a 10-mg/kg dose of azithromycin once daily for 1 day, followed by 5 mg/kg once daily for 4 days.

The study was conducted at 34 centers worldwide, including Bulgaria, Chile, the Dominican Republic, Guatemala, Israel, Peru, Romania, Latvia, Mexico, and the United States from April 2001 to November 2002.

The increasing evolution of antimicrobial resistance among the pathogens that cause acute otitis media (AOM) and the approval of a large-dose pediatric formulation of amoxicillin/clavulanate prompted the study.

At baseline, 494 (67.7%) of the children had at least one protocol-defined pathogen; 249 in the amoxicillin/clavulanate group and 245 in the azithromycin group. Of these, 19 (7.6%) children in the amoxicillin/clavulanate group and 38 (15.5%) in the azithromycin group had more than one pathogen at baseline (Pediatr. Infect. Dis. J. 2005:24:525-32). The children without discernible pathogens at baseline (118 in each group) were included in the safety analysis.

In addition, of the 229 total *Streptococcus pneumoniae* isolates (111 children in the amoxicillin/clavulanate group and 118 children in the azithromycin group), 48.5%, 11.4%, and 20.5% were not susceptible to penicillin, amoxicillin, and azithromycin, respectively.

Overall, clinical success rates among children with baseline AOM pathogens were significantly greater in the amoxicillin/clavulanate group (90.5%), compared with the azithromycin group (80.9%).

Clinical success was defined as the lessening or complete resolution of acute ear infection and inflammation, with or without middle-ear effusion, to the extent that no additional antibiotics were needed. Clinical response at 12-14 days after the start of therapy served as the primary end point of the study.

Amoxicillin/clavulanate was significantly more effective than azithromycin against both *S. pneumoniae*, and *H. influenzae*.

Bacteriologic success was defined as the eradication of the initial AOM pathogen with or without a new pathogen, based on a lack of middle-ear fluid.

Bacteriologic success at an "on-therapy" visit 4-6 days after the start of treatment was associated with clinical success at the end of therapy in 96 of 105 children (91.4%) in the amoxicillin/clavulanate group and 80 of 89 (89.9%) in the azithromycin group.

Amoxicillin/clavulanate was significantly more effective than azithromycin against both *S. pneumoniae*, (96.0% vs. 80.4%) and *Haemophilus influenzae*, (96.7% vs. 52.9%). The distribution of pathogens was similar between the two groups. *H. influenzae* was the more common, found in 48.6% of the amoxicillin/clavulanate group and 50.6% of the azithromycin group.

In the subset of 101 amoxicillin/clavulanate patients and 82 azithromycin patients who demonstrated bacteriologic responses after 4-6 days, amoxicillin/clavulanate was significantly more effective than azithromycin against penicillin-resistant *S. pneumoniae*, with eradication in 23 of 25 cases (92.0%) vs. 12 of 22 cases (54.5%), respectively.

Although significantly more children in the amoxicillin/clavulanate group withdrew from the study due to an adverse event, compared with the azithromycin group (21 vs. 7), the total number of adverse events was not significantly different between the two groups (139 vs. 128). ■