Glycerol Effective for Children's Bacterial Meningitis

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WASHINGTON — Adjunctive treatment with oral glycerol was more effective than intravenous dexamethasone for preventing death and severe neurologic sequelae in children with bacterial meningitis in a controlled study with 640 patients.

"Because oral glycerol is safe, cheap, and easily available and does not have special storage requirements, it seems to be the best approach for improving the outcome of bacterial meningitis in children," Heikki Peltola, M.D., said at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy.

Although dexamethasone is often used as an adjunctive treatment for children with bacterial meningitis, its efficacy has never been proven. Several physicians have hypothesized that glycerol would be an effective adjunctive agent because of its activity as a free-radical scavenger.

To test both agents, a study was done in the pediatric departments of 10 university hospitals in South America and Helsinki, Finland.

The study was supported by a grant from GlaxoSmithKline, but the study's design, conduct, and analysis were independent of commercial influence, said Dr. Peltola, a professor of infectious diseases at the Hospital for Children and Adolescents at Helsinki University Central Hospital.

Children aged 2 months or older with bacterial meningitis were all treated with ceftriaxone. They were also randomized to one of four adjunctive treatment groups: dexamethasone only, glycerol only, both dexamethasone and glycerol, or placebo. About 160 patients were randomized to each treatment group.

Patients treated with glycerol received a dosage of 6.0 g/kg daily, given orally in four divided doses. Patients who received dexamethasone were given a dosage of

Most Don't Present With Meningitis Triad

WASHINGTON — Less than half of patients with bacterial meningitis have the classic symptom triad of fever, stiff neck, and a change in mental status, Diederick van de Beek, M.D., said while presenting a poster at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy.

Many patients present with just two classic symptoms, one of which may also be headache, said Dr. van de Beek, a neurologist at the Academic Medical Center in Amsterdam.

In a review of 696 patients with community-acquired, acute bacterial meningitis, the classic symptom triad occurred in only 44% of the patients, Dr. van de Beek reported in his poster. (The data have been published: N. Engl. J. Med. 2004;351:1849-59).

In contrast, 95% of patients had at least two classic symptoms. The most common classic symptom was headache in 87%, followed by neck stiffness in 83%, fever in 77%, and a change in mental status in 69% (defined as a Glasgow Coma Scale score of less than 14).

Of the 696 patients, 21% died and 13% had other unfavorable outcomes including a vegetative state or severe or moderate disability. The likelihood that a patient would have an unfavorable outcome was sixfold higher among patients who were infected with *Streptococcus pneumoniae* than among those infected with *Neisseria meningitides* when the incidence rates were adjusted for potential clinical confounders.

This study is the first report of a prospective, large-scale analysis of the clinical factors associated with bacterial meningitis and its outcomes, Dr. van de Beek said at the conference, sponsored by the American Society for Microbiology. The study data were drawn from information on all patients who were at least 16 years old and diagnosed with bacterial meningitis in the Netherlands Reference Laboratory database from October 1998 through April 2002.

Of 1,108 cases in the database, complete data were retrieved for 754 patients, of whom 58 were excluded either because their infection was nosocomial, they had had recent neurosurgery, or they had received a neurosurgical device.

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0.6 mg/kg daily, administered intravenously in four divided doses. All adjunctive treatments were administered for 2 days, and the children were followed until the end of their hospitalization. The primary end points of the study were death and severe neurologic sequelae, including blindness, profound hearing loss, quadriparesis or quadriplegia, hydrocephalus requiring placement of a shunt, and/or severe psychomotor retardation.

Patients treated with glycerol had a 42% reduced risk of death, compared with placebo, a statistically significant difference. Patients treated with dexamethasone had a 15% reduced risk of death, compared with placebo, a difference that was not statistically significant. Patients who received both treatments had a mortality reduction of 32%.

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In all groups, the benefit of adjunctive treatment was best in the subgroup of patients with the most severe disease at baseline, those with a Glasgow Coma Scale score of less than 13. In this subgroup, mortality was cut by 21% among patients treated with dexamethasone, and by 61% among those treated with glycerol, said Dr. Peltola at the conference, sponsored by the American Society for Microbiology.

Glycerol treatment led to better outcomes for all parameters analyzed. When death and severe neurologic sequelae were combined as an end point, patients with Glasgow Coma Scale scores of less than 13 who were treated with glycerol had 55% fewer events than those treated with placebo.

"The mechanisms of glycerol's effect are not fully understood, but improved cerebral circulation seems a likely explanation," Dr. Peltola said. It's also unclear why the combination of glycerol and dexamethasone was less effective than glycerol alone.

"I'm pleased to see these results. It's a superb idea because of the low cost and ready availability of glycerol," commented Neal A. Halsey, M.D., director of the Institute for Vaccine Safety at Johns Hopkins University in Baltimore. ■