Glycerol Aids Outcomes in 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 often is 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.

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Infants and children aged 2 months or older with bacterial meningitis were all treated with ceftriaxone.

They also were 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 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 to 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%.

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. ■