Medication does not lower risk of fungal infection, death among ELBW infants

May 3 2014

Use of the antifungal medication fluconazole for six weeks for extremely low birth-weight infants did not significantly reduce the risk of death or invasive candidiasis, a serious infection that occurs when candida (a type of fungus) enters the bloodstream and spreads through the body, according to a study in the May 7 issue of *JAMA*, a theme issue on child health. This issue is being released early to coincide with the Pediatric Academic Societies Annual Meeting.

Invasive candidiasis is an important cause of infection in premature infants; despite treatment with antifungal therapy, invasive candidiasis has serious effects on premature infants, including severe neurodevelopmental impairment and death. Current recommendations include the use of fluconazole for prevention of this infection for infants with a birth weight of less than 1,000 grams (2.2 lbs.) who receive care in neonatal intensive care units (NICUs). However, most NICUs in the United States and the European Union have not uniformly adopted preventive use of fluconazole, based on controversies regarding high-risk patients, resistance, and safety, according to background information in the article.

Daniel K. Benjamin Jr., M.D., Ph.D., of Duke University, Durham, N.C., and colleagues evaluated the efficacy and safety of fluconazole in preventing death or invasive candidiasis in extremely low birth-weight infants (weighing less than 750 grams [1.7 lbs.] at birth). The study included 361 infants from 32 NICUs in the United States who were randomly assigned to receive either fluconazole (6mg/kg of body

weight) or placebo twice weekly for 42 days.

The primary composite end point of death or invasive candidiasis by study day 49 was not statistically different between the 2 groups (fluconazole, 16 percent vs placebo, 21 percent). The percentage of infants who died prior to study day 49 was not different between the groups (14 percent vs 14 percent). Fewer infants developed definite or probable invasive candidiasis in the fluconazole (3 percent) vs in the placebo group (9 percent).

"Fluconazole prophylaxis compared with placebo was not associated with a statistically significant difference in the composite primary end point—death or definite or probable invasive candidiasis— although it was associated with a statistically significant reduction in the incidence of definite or probable candidiasis alone. This study adds new evidence regarding the efficacy of fluconazole prophylaxis, but raises the question of whether prevention of invasive candidiasis translates into substantial improvements in the outcomes of prematurity."

"Based on both the results of our study in NICUs with a low incidence of invasive candidiasis, and previous prophylaxis trials in high-incidence NICUs, the routine use of fluconazole prophylaxis should be limited to units with moderate-to-high incidence of invasive candidiasis. However, additional research is needed to precisely define the incidence at which the benefits of fluconazole prophylaxis outweigh the risks," the authors write.

More information: DOI: 10.1001/jama.2014.2624