Fluconazole Reduces Candidiasis in VLBW Infants

BY JANE SALODOF MACNEIL
Southwest Bureau

SAN FRANCISCO — Fluconazole prophylaxis reduced fungal infections and mortality in very low-birth-weight infants at two neonatal intensive care units in retrospective studies that were presented during the annual meeting of the Pediatric Academic Societies.

Incidence of invasive candidiasis in very low-birth-weight (VLBW) infants went from 6.7% to zero at Cooper University Hospital in Camden, N.J., Dr. Zubair H. Aghai reported. However, the intensive regimen used in the neonatal intensive care unit (NICU) led to a significant increase, from 16% to 45%, in conjugated hyperbilirubinemia.

At Brookdale University Hospital and Medical Center in Brooklyn, N.Y., a regimen given only to neonates colonized with *Candida* reduced candidal sepsis from 12.1% to 8.2% in VLBW infants.

Although the data reported by Dr. M. Roger Kim and colleagues at Brookdale was not statistically significant, associated mortality also declined from 16% to 9%. Dr. Vaishali Jha, the lead author, said in an interview that the Brookdale neonatologists did not see an increase in jaundice or any other adverse effects with their regimen.

Investigators from both groups said they introduced fluconazole prophylaxis because of the increased risk and incidence of invasive fungal infections with the growing number of VLBW infants in NICUs.

Dr. Manjula Mudduluru, the lead author of the poster on the Cooper hospital experience, cited a candidal sepsis rate of 5.5%-10% in neonates who weigh 1,000 g or less at birth. Fungal sepsis is associated with a mortality of 31.8% in premature neonates, according to Dr. Mudduluru, Dr. Aghai, and their colleagues from the hospital.

The Cooper hospital group compared 140 VLBW infants born from March 2002 to September 2005 with 137 historical controls born between January 1998 and February 2002, which was prior to the introduction of the fluconazole regimen. The only significant differences at baseline were that more infants on prophylaxis also received surfactant and prenatal steroids. The regimen delivered 3 mg/kg of fluconazole intravenously every 72 hours for 2 weeks, every 48 hours for 2 weeks, and daily for 3 weeks.

Fungal sepsis is associated with a mortality of 31.8% in premature neonates.

DR. MUDDULURU

Nine infants developed invasive candidiasis and six of them died during the 2 years prior to introduction of the prophylaxis. Overall mortality fell from 39.4% to 25.7% after the prophylaxis was introduced and invasive candidiasis eliminated.

The investigators estimated that treating 15 VLBW infants with the prophylaxis would prevent one invasive candidiasis infection in their NICU—and that they would need to treat 69 neonates to prevent one death.

Dr. Mudduluru said the clinicians are experimenting with a less frequent dosing schedule to see whether they can reduce the rate of conjugated hyperbilirubinemia.

The investigators at Brookdale hospital considered infants who weighed up to 1,500 g at birth in their review. They compared 141 neonates born from January 2002 to May 2004 with 85 neonates born from July 2004 through June 2005.

During the latter period, weekly surveillance cultures were performed for neonates weighing less than 1,500 g. Infants colonized by *Candida* species received 3 mg/kg of fluconazole every 48 hours for 6 weeks or until their weight reached 1,500 g. The number of cases of invasive candidiasis per 1,000 patient-days fell from 2.1 to 1.6 during this period.

Dr. Jha said the investigators believe the improved outcomes would reach statistical significance with a larger patient sample. They are planning a randomized, multicenter trial, she said at the meeting, which was sponsored by the American Pediatric Society, the Society for Pediatric Research, the Ambulatory Pediatric Association, and the American Academy of Pediatrics. ■

Pages 16a—16b