
TWICE WEEKLY FLUCONAZOLE PROPHYLAXIS FOR PREVENTION OF INVASIVE FUNGAL INFECTION IN HIGH-RISK PRETERM INFANTS LESS THAN 1000 GRAMS.

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Background: We demonstrated a 100% decrease in fungemia with fluconazole prophylaxis in high-risk preterm infants (NEJM 2001;345:1660). One concern with this antifungal strategy is the emergence of azole resistance. In an attempt to further reduce the potential for the development of azole resistance, this study compares our previously studied prophylactic schedule to a less frequent dosing schedule of twice a week.

Design/Methods: We conducted a prospective randomized double-blind clinical trial over a 24-month period in 81 high-risk preterm infants with birth weight less than 1000 grams and the presence of an endotracheal tube or central venous catheter. Infants were randomized in the first 5 days of life to receive 1 of 2 dosing schedules of intravenous fluconazole (3 mg/kg) for up to 6 weeks. Schedule A dosing, from our previous study, (every 72h during weeks 1 and 2, then every 48h during weeks 3 and 4, and every 24h for weeks 5 and 6) was compared to schedule B (twice a week). We obtained weekly surveillance cultures and all fungal isolates were speciated and had sensitivities performed.

Results: The 41 infants randomized to schedule A and the 40 to schedule B dosing were similar in mean birth weight (691 vs. 704 grams), gestational age (24.9 vs. 25.8 weeks) and risk factors for fungal infection. Baseline fungal colonization was present in 2 patients in each group (P=1.00). During the 6-week prophylaxis period, fungal colonization was documented in 5 (12.2%) of schedule A and in 4 (10%) of schedule B patients (relative difference, -0.02; 95% CI, -0.18 to 0.14, P=0.83). Invasive fungal infection with fungal blood isolates developed in 2 (4.9%) of schedule A and 1 (2.6%) of schedule B patients (relative difference, -0.02; 95% CI, -0.14 to 0.10, P=0.68). All fungal isolates remained sensitive to fluconazole [MIC (mg/ml) of *C. albicans*: 0.125-0.5, *C. parapsilosis*: 0.5-4.0, *C. glabrata*: 1-16]. Fungal isolate sensitivities to fluconazole did not change during the study and no untoward drug side effects were documented.

Conclusions: Fluconazole prophylaxis twice a week during the first 6 weeks is comparable in efficacy to the prior dosing schedule in preventing fungal colonization and invasive infection in high-risk infants with birth weight less than 1000 grams. This antifungal prophylaxis strategy further limits dosing factors that may contribute to antibiotic resistance.