Liposomal amphotericin B as initial therapy for invasive mold infection: a randomized trial comparing a high-loading dose regimen with standard dosing (AmBiLoad trial).


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BACKGROUND: Treatment of invasive mold infection in immunocompromised patients remains challenging. Voriconazole has been shown to have efficacy and survival benefits over amphotericin B deoxycholate, but its utility is limited by drug interactions. Liposomal amphotericin B achieves maximum plasma levels at a dosage of 10 mg/kg per day, but clinical efficacy data for higher doses are lacking. METHODS: In a double-blind trial, patients with proven or probable invasive mold infection were randomized to receive liposomal amphotericin B at either 3 or 10 mg/kg per day for 14 days, followed by 3 mg/kg per day. The primary end point was favorable (i.e., complete or partial) response at the end of study drug treatment. Survival and safety outcomes were also evaluated. RESULTS: Of 201 patients with confirmed invasive mold infection, 107 received the 3-mg/kg daily dose, and 94 received the 10-mg/kg daily dose. Invasive aspergillosis accounted for 97% of cases. Hematological malignancies were present in 93% of patients, and 73% of patients were neutropenic at baseline. A favorable response was achieved in 50% and 46% of patients in the 3- and 10-mg/kg groups, respectively (difference, 4%; 95% confidence interval, -10% to 18%; P>.05); the respective survival rates at 12 weeks were 72% and 59% (difference, 13%; 95% confidence interval, -0.2% to 26%; P>.05). Significantly higher rates of nephrotoxicity and hypokalemia were seen in the high-dose group. CONCLUSIONS: In highly immunocompromised patients, the effectiveness of 3 mg/kg of liposomal amphotericin B per day as first-line therapy for invasive aspergillosis is demonstrated, with a response rate of 50% and a 12-week survival rate of 72%. The regimen of 10 mg/kg per day demonstrated no additional benefit and higher rates of nephrotoxicity.

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