

Caspofungin was as effective as amphotericin B for invasive candidiasis

Mora-Duarte J, Betts R, Rotstein C, et al. Comparison of caspofungin and amphotericin B for invasive candidiasis. *N Engl J Med.* 2002;347:2020-9.

QUESTION

In patients with invasive candidiasis, is caspofungin as effective as amphotericin B?

DESIGN

Randomized (allocation concealed*), blinded (clinicians, patients, and monitoring committee),* controlled trial with 6- to 8-week follow-up.

SETTING

56 centers in 20 countries.

PATIENTS

239 patients > 18 years of age who had ≥ 1 positive candida culture from blood or another sterile site in the past 4 days, and ≥ 1 clinical sign of infection in the past 2 days (fever, hypothermia, or hypotension) or signs of inflammation at a candida-infected site. Exclusion criteria included suspected endocarditis, osteomyelitis, or meningitis; and receipt of antifungal therapy > 2 days. 224 patients (94%) (median age 55 y, 56% men) were included in the modified intention-to-treat analysis (documented diagnosis of invasive candidiasis and receipt of study treatment ≥ 1 d). All patients were included in the safety analysis.

INTERVENTION

Patients were stratified by presence or absence of neutropenia and score ≤ 20 or > 20 on the

Acute Physiology and Chronic Health Evaluation (APACHE) II and were allocated to intravenous (IV) caspofungin, 70 mg loading dose followed by 50 mg/d ($n = 109$), or IV amphotericin B, 0.6 to 0.7 mg/kg of body weight per day (0.7 to 1.0 mg in patients with neutropenia) ($n = 115$), for 14 days.

MAIN OUTCOME MEASURES

Treatment response. A favorable response was defined as resolution of all symptoms and signs of candida infection and culture-confirmed eradication. Adverse events and withdrawals were also assessed.

MAIN RESULTS

Analysis was by intention to treat. At the end of IV therapy, the rate of favorable response was similar between the caspofungin and

amphotericin B groups (Table). The lack of difference was not affected after adjustment for neutropenic status and APACHE II score ($P = 0.09$). Caspofungin and amphotericin B groups did not differ for mortality (34% vs 30%, $P = 0.53$). Fewer adverse events occurred with caspofungin than with amphotericin B (Table).

CONCLUSION

In patients with invasive candidiasis, caspofungin was as effective as amphotericin B for resolving signs and symptoms of candida infection and was associated with fewer adverse events.

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*See Glossary.

Caspofungin vs amphotericin B for invasive candidiasis at 10 to 14 days†

Outcomes	Caspofungin	Amphotericin B	RBI (95% CI)	NNT (CI)
Favorable response	73%	62%	119% (99 to 144)	Not significant
RRR (CI)				
Any adverse event	42%	75%	44% (30 to 56)	4 (3 to 5)
Withdrawal because of adverse event	2.6%	23%	89% (66 to 96)	5 (4 to 8)

†A favorable response was the resolution of candida signs and symptoms. Abbreviations defined in Glossary; RBI, RRR, NNT, and CI calculated from data in article.

COMMENTARY

Amphotericin B, lipid formulations of amphotericin, and fluconazole are used to treat acute hematogenous candidiasis. Fluconazole or amphotericin B is currently used to treat candidemia in immunocompetent patients. Amphotericin B is the first-line agent in patients who are neutropenic, have received fluconazole prophylaxis, are hemodynamically unstable, or have suspected *Candida glabrata* or *C. krusei*. Lipid formulations of amphotericin are used when amphotericin B fails or is unacceptably toxic.

Mora-Duarte and colleagues show caspofungin to be as effective as amphotericin B in the treatment of invasive candidiasis.

Caspofungin is approved for the treatment of invasive aspergillus infections not responsive to other agents. This echinocandin inhibits synthesis of β -(1,3)D-glucan, an integral component of fungal—but not mammalian—cell walls. Cyclosporine increases caspofungin levels, and caspofungin may decrease tacrolimus levels.

In this study, caspofungin was compared with amphotericin B in predominantly immunocompetent patients. More non-albicans candidal infections occurred in the caspofungin group (64%) than in the amphotericin B group (46%). In these patients, the efficacy of caspo-

fungin was similar to that of amphotericin B. Caspofungin and fluconazole were not compared in this study, but the 2 drugs were shown to be equally efficacious and well tolerated in a study of patients with candida esophagitis (1).

The activity of caspofungin against non-albicans candida isolates that are less sensitive to fluconazole and its safety profile and efficacy in systemic candidiasis make it an exciting addition to the drugs used to treat systemic candida infections. Its therapeutic niche may be in patients with previous fluconazole treatment who develop candidemia and in those intolerant of amphotericin B. Efficacy of caspofungin in the neutropenic patient awaits further study.

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Reference

1. Villanueva A, Gotuzzo E, Arathoon EG, et al. A randomized double-blind study of caspofungin versus fluconazole for the treatment of esophageal candidiasis. *Am J Med.* 2002;113:294-9.