Caspofungin in the management of invasive fungal infections
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Invasive fungal diseases remain difficult-to-treat infections, with significant morbidity and mortality. In particular, *Candida* is now common in Intensive Care Units and in Internal Medicine Departments, while *Aspergillus* is a typical pathogen for hematological patients, including recipients of HSCT. Echinocandins are the cornerstone of treatment for invasive candidiasis, with some space left to fluconazole in less critical patients. For aspergillosis, first line therapy includes voriconazole and the liposomal formulation of AmB, while the echinocandins are considered for combination therapy. Only caspofungin was tested in a prospective, controlled, although non comparative trial as monotherapy in first line therapy of invasive aspergillosis. At least in Europe, caspofungin is the only echinocandin approved for second line therapy of aspergillosis.

Caspofungin is a very easy to handle drug, not differently from the other echinocandins. Dosage should not be changed in renal insufficiency, hemodyalisis and continuous veno-venous hemofiltration and hemodyalisis. In moderate hepatic insufficiency, dosage should be reduced to 35 mg /daily, not because of toxicity but for PK considerations. Higher dosages have been used both in candidiasis and in aspergillosis, without appreciable toxicity, but also without any apparent clinical advantage. Caspofungin has not be tested in patients with severe hepatic toxicity. Patients weighting 80 kg or more should stay with the loading dose dosage. Clinically significant interactions with other drugs are rare. Tacrolimus blood concentrations should be monitored if case of co-administration. Increased hepatotoxicity with cyclosporine was initially reported, but then not confirmed. Caspofungin dosage should be increased to 70 mg/day in case of concomitant administration with a liver enzyme inducer.

In the first pivotal candidemia study, caspofungin was tested against deoxycholate AmB and showed to be non-inferior to AmB and much less toxic, as expected (Mora-Duarte J, et al, NEJM, 2002). In another study caspofungin was tested against 2 dosages of mikafungin and no difference was found (Pappas P, et al, CID, 2007). In a subsequent non comparative study in deep-seated candidemia, caspofungin obtained excellent results in very difficult cases, although the sample size was small (Cornely O et al, JAC, 2007).

For aspergillosis there are at least 3 studies. Maertens et al published a positive experience with caspofungin as salvage therapy in about 100 patients failing or intolerant to previous therapies (CID, 2004). The study led to the approval of caspofungin for this indication Subsequently, Viscoli et al (JAC 2009) and Herbrecht et al (BMT, 2010) published the results of a controlled, prospective, multicenter non-comparative study of caspofungin as first line therapy of invasive aspergillosis in patients with acute leukemia and undergoing HSCT, respectively, which confirmed that the drug is active in aspergillosis, although the response rate was lower than expected.

In conclusion, caspofungin is a safe and effective drug for the management on candida infections. In aspergillosis, caspofungin showed documented activity. For several reasons, it is unlikely that additional studies will be conducted with an echinocandin as first line monotherapy of invasive aspergillosis.