Caspofungin for the treatment of fungal infections: a systematic review of randomized controlled trials
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CRD summary
This review evaluated the effectiveness and safety of caspofungin in the treatment of patients with fungal, mainly Candida, infections. The authors concluded that caspofungin is associated with a higher cure rate and fewer adverse effects in comparison with amphotericin B. These conclusions have to be viewed with caution since they are based on few studies with few participants.

Authors' objectives
To evaluate the efficacy and safety of caspofungin in patients with fungal, mainly Candida, infections.

Searching
PubMed was searched; the search terms were reported. Bibliographies of relevant articles and reviews were checked for additional studies. No language restrictions were applied. Two reviewers independently performed the literature search.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion.

Specific interventions included in the review
Studies comparing caspofungin with other antifungal agents for the treatment of patients with fungal infections were eligible for inclusion. The dose and regimen of caspofungin varied across the studies. Patients with oesophageal and/or oropharyngeal candidiasis were treated for 7 to 21 days, whereas those with invasive candidiasis were treated until 14 days after the last positive Candida culture. A longer treatment was provided to neutropenic patients. The control treatments were amphotericin B deoxycholate, liposomal amphotericin B, or fluconazole.

Participants included in the review
Studies of patients with fungal infections were eligible for inclusion. The patients had oesophageal, oropharyngeal, or invasive infections sustained by albicans or non-albicans Candida species. In one study, patients with Aspergillus species infections were also included. Most of the participants had a state of immunosuppression caused by neutropenia or human immunodeficiency virus infection.

Outcomes assessed in the review
The primary outcomes evaluated were cure of infection, mortality and toxicity.

How were decisions on the relevance of primary studies made?
Two reviewers independently selected studies for the review.

Assessment of study quality
Study quality was assessed using the Jadad scale. Each study was allocated a score ranging from 0 (lowest) to 5 (highest). Trials were considered of good quality if they had a quality score above 1. The authors did not state how many reviewers performed the validity assessment.

Data extraction
Two reviewers independently extracted the data. Data on numbers of events in the caspofungin and comparator groups
were extracted, and odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for outcomes related to toxicity.

**Methods of synthesis**

How were the studies combined?

A meta-analysis was performed to compare toxicity between caspofungin and amphotericin B. The Mantel-Haenszel fixed-effect model was used to pool data in the case of no statistical heterogeneity between the studies; otherwise, the DerSimonian and Laird random-effects model was used. Other outcomes were discussed in the text. The use of a funnel plot and Egger's test to assess publication bias was planned, but no results were reported.

How were differences between studies investigated?

Statistical heterogeneity was assessed using the chi-squared test (p<0.10 indicated statistical heterogeneity).

**Results of the review**

Six RCTs (n=1,974) were included in the review.

Three studies were assigned a score of 3 on the Jadad scale, 2 trials were given 5 points, and the remaining trial 2 points.

Treatment with caspofungin was associated with an infection cure rate of 52.6%, compared with 44.7% among amphotericin B-treated patients. Compared with amphotericin B, caspofungin was less frequently discontinued because of drug toxicity (OR 0.25, 95% CI: 0.07, 0.85) and it was associated with a lower incidence of nephrotoxicity (OR 0.23, 95% CI: 0.14, 0.36), hypokalaemia (OR 0.3, 95% CI: 0.12, 0.76) and fever (OR 0.26, 95% CI: 0.08, 0.79). Total mortality was 13.8% among caspofungin-treated patients and 16.9% in the amphotericin B group (4 studies).

**Authors' conclusions**

Treatment with caspofungin led to a higher cure rate with lower toxicity than amphotericin B in patients with fungal infections.

**CRD commentary**

This review addressed a well-defined question in terms of the participants, interventions, outcomes and study design. One relevant database was searched and attempts were made to identify additional articles. However, it is possible that relevant studies not included in PubMed could have been missed. The precise timeframe of the search strategy was not reported. The authors stated that the potential influence of publication bias was considered in the review, but no information about publication bias was reported in the text. No language restrictions were applied, thus reducing the possibility of language bias. The authors attempted to minimise bias and errors during the review process by carrying out the study selection and data extraction in duplicate. It was unclear if study quality was also assessed in duplicate, therefore reviewer error and bias might have been introduced at this stage.

The authors stated that statistical heterogeneity was assessed, but no information about it was reported in the text. The included studies were heterogeneous in terms of drug doses and duration of treatment, suggesting that the authors' decision not to pool the effectiveness data was appropriate. The statistical methods used in the meta-analysis of toxicity outcomes were appropriate. The authors' conclusions reflect the data presented and appear appropriate.

**Implications of the review for practice and research**

Practice: The authors stated that caspofungin can be considered as an alternative antifungal agent for patients with invasive or oesophageal candidiasis.

Research: The authors stated that further studies are needed to confirm the role of caspofungin in the treatment of fungal infections.
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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.