

Pharmacokinetic of Caspofungin in Patients with Invasive Candidiasis

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INTRODUCTION

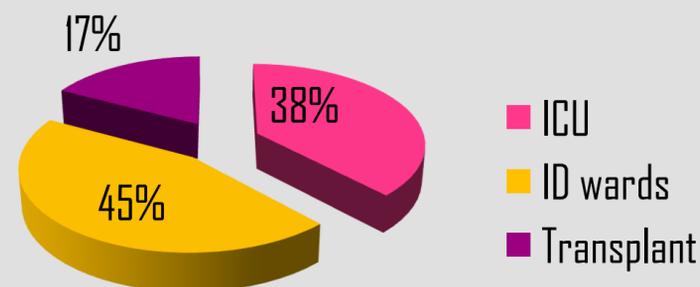
Caspofungin is approved as first line treatment in invasive candidiasis and as salvage therapy in invasive aspergillosis. Caspofungin is fungicidal against *Candida* spp. and has a concentration-dependent activity.

Pharmacokinetic data described a linear pharmacokinetic (PK), with an area under the concentration-time curve (AUC) and a steady-state plasma maximum concentration (C_{max}) of 87.9- 114.8 mg/L*h e 7.64 mg/L, respectively. According to literature the AUC/MIC parameter should be probably predictive of clinical efficacy, although specific breakpoints for caspofungin have not been clearly defined.

Aim of this study was to describe the PK of caspofungin in a group of patients treated with standard dosage for candidemia or invasive candidiasis and to correlate the PK parameters with clinical outcome. Blood samples were collected at 0,1,5, 12±4 hours after administration, at the steady state. Caspofungin plasma levels were determined by an UPLC/PDA method. PK parameters (AUC_{0-24} , C_{max} , C_{trough} , $t_{1/2}$, V, CL). Spearman Rank Correlation was used to assess the relationship among PK parameters and individual variables. A P value<0.05 was considered statistically significant.

RESULTS

23 patients were enrolled in the study: 11 admitted to intensive care unit (ICU), 13 in infectious diseases ward, 5 in transplant unit (Graphic 1). The majority of patients were male (15; 65%) with a median age of 54 years-old (DS ± 16), a median BMI of 25 (DS ± 6) and a median APACHE II score of 13 (DS ± 6). Mean C_{max} , C_{min} , AUC_{0-24} , Clearance, Volume of distribution (Vd) and half life were reported in Table 1.



| | |
|---------------------------|-----------------------------|
| C_{max} | 8.73 mg/L [4.69-17.32] |
| C_{min} | 2.15 mg/L [0.38-7.87]; |
| AUC_{0-24} | 99.13 mg/L*h [40.46-219.1], |
| Clearance | 0.58 L/h [0.22-0.79], |
| Vd | 12.31 L [6.82-15.71] |
| Half life | 17.36 h [9.76-83.58], |
| AUC/MIC (MIC =0.06) | 1652.19 |
| C_{max}/MIC MIC=0.06 | 145.55 |

Moreover, statistical analysis showed that in patients with APACHE III score ≥ 10 a higher AUC was associated with a lower mortality (105.9 Vs. 69.6 mg/L*h in survivors Vs. non survivors respectively; p=0.04).

CONCLUSIONS

In conclusion, our data showed that caspofungin AUC is similar to those reported in healthy volunteers, whilst C_{max} value were slightly higher. Moreover, in patients with APACHE score ≥ 10 a higher AUC was associated with a better outcome.

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