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P0122 Comparative pharmacokinetics of the three echinocandins in intensive care units patients

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Background: Echinocandins are currently recommended as initial therapy for invasive candidiasis. Suboptimal exposures may be associated with treatment failure and emergence of resistance. We therefore assess the pharmacokinetics of the three echinocandins anidulafungin, micafungin and caspofungin in critically ill patients.

Materials/methods: Thirty for ICU patients [20Males/14Females, median (range) Age 63.50(31-83)y, BMI 25.1(18.3-62.3) kg/m2, APACHE II 25.5(11-46), SOFAadmission 9(3-17)] received the standard dose of one of the three echinocandins (13 were treated with anidulafungin, 14 with micafungin and 7 with caspofungin) as standard care of clinical practice. Serum samples were collected on day 7 (before and 0, 2, 3, 4, 8, 12 and 24h after infusion) and analyzed separately by a validated HPLC method with fluorescence detection (anidulafungin and micafungin) or HPLC-MS (caspofungin) that was developed and fully validated according to EMA and FDA regulations. Non-compartmental analysis was used to calculate the area under the curve (AUC0-24). Demographic (gender, age, height, BMI, BSA) and laboratory (creatinine, albumin, ALP, γ-GT, AST, ALT) data as well as APACHE II and SOFA scores were recorded and were correlated with Spearman correlation analysis with AUC0-24.

Results: The median (range) AUC0–24 was 74.21 (16.68-194.45) mg*h/L for anidulafungin, 78.60 (35.47-147.35) mg*h/L for micafungin and 52.36 (30.28-68.83) mg*h/L for caspofungin. The interindividual variability (CV) of anidulafungin, micafungin and caspofungin AUC0-24 was 60.2%, 40.8% and 17.5% with 3/13 (23%), 2/14 (14%) and 2/7 (29%) patients achieving a low exposure (<50 mg·h/l), respectively. Total exposure to anidulafungin was positively correlated with serum AST (rs 0.795, p=0.001) and ALT (rs 0.702, p=0.008). The exposure to micafungin correlated with the APACHE II score upon admission to the ICU, while the exposure to caspofungin positively, though weakly, correlated with the albumin concentration (rs=0.757, p=0.049).

Conclusions: Echinocandins exposure in ICU patients was (33-46)% lower than drug exposure in healthy volunteers. Considerable interindividual variability (60%) was observed for anidulafungin whereas 14-29% of patients had low exposures particularly among those treated with caspofungin. Therapeutic drug monitoring could help to adjust the dose in order to increase drug exposure and minimize the risk of treatment failure.