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MEETING ABSTRACT

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Pharmacokinetics of anidulafungin in ascites and pleural effusion

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Background: Echinocandins are recommended for treatment of invasive candidiasis in critically ill patients. Anidulafungin displays particularly favourable pharmacokinetics, because its elimination is independent from hepatic and renal function. Data on anidulafungin target-site penetration and kinetics is sparse so far. Therefore, we determined anidulafungin pharmacokinetics in ascites and pleural effusion of critically ill patients. We addressed the question whether effective anidulafungin concentrations can be achieved by standard doses in these compartments.

Methods: Samples of ascites and of pleural effusion were taken during routine paracentesis or via ascites or pleural drain applied for therapeutic purpose. When sampling was performed via drainage seven samples were drawn within the dosage interval for assessment of anidulafungin kinetics. Anidulafungin was measured by high-performance liquid chromatography (HPLC) and UV detection after sample preparation by protein precipitation with acetonitrile. Gradient elution was done with ammonium acetate and acetonitrile at a flowrate of 1.0 ml/min. Anidulafungin was detected at 306 nm. Quantification was validated according to the European Medicine Agency (EMA) guidelines. The lower limit of quantification was 0.05 mg/l.

Results: Seven critically ill patients suffering from septic shock and multi-organ dysfunction syndrome were enrolled. Anidulafungin kinetics was determined in ascites of four patients and in pleural effusion of two patients. A single concentration was measured in one sample obtained from paracentesis. Ascites concentrations were lower than plasma levels (peak level [C_{max}] 0.34–0.98 *vs.* 3.82–7.70 mg/l) and displayed a slower rise and decline than in plasma (t_{max} [time to C_{max}] 4–12 h versus 1 h). The penetration ratio expressed by the ratio between the area under the concentration–time curve (AUC) in ascites and the AUC in plasma was 0.07–0.37. C_{max} values of anidulafungin in pleural effusion were 1.02 and 2.02 mg/l.

Discussion: Anidulafungin was detectable in all samples. Ascites and pleural effusion concentrations exceeded the minimal inhibitory concentrations (MICs) reported for numerous *Candida* strains. But less susceptible isolates have also been described. Antifungal activity of anidulafungin in ascites and pleural effusion has to be assessed by further studies.

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