Category :**Renal: extracorporeal support**

A182 - ***Population pharmacokinetics of multiple dose fosfomycin in critically ill patients during continuous veno-venous hemodialysis***

K Götz [1] ; S Kreuer [1] ; T Hüppe [2] ; T Lehr [1]

[1]Saarmetrics GmbH, Saarbruecken, Germany, [2]Saarland University Medical Center and Saarland University Faculty of Medicine, Department of Anaesthesiology, Intensive Care and Pain Therapy, Homburg, Germany

Introduction:

To investigate the pharmacokinetics (PK) of intravenous fosfomycin in critically ill patients with and without continuous veno-venous hemodialysis (CVVHD), a population pharmacokinetic model was developed.

Methods:

Critically ill patients with acute renal failure and need of CVVHD were included. Patients received 5 g fosfomycin over 120 minutes every 6 hours intravenously. PK was measured two times for each patient, once with CVVHD and once without. Model development and simulation was performed using non-linear mixed effects modelling (NONMEM® V.7.4.3).

Results:

Two of 15 patients were female. Median (range) age was 57 (49 - 80) years. Six patients were anuric. Creatinine clearance (CRCL) ranged from 5.89 to 210 ml/min for patients retaining urine production. 300 blood samples were collected in total. A two-compartment model with zero-order input and inter-individual variability on intrinsic clearance (CL_{RENAL}) and volume of the central compartment (Vc) was used. An additional dialysis clearance (CL_{CVVHD}) was incorporated. CRCL accounted for the variability on CL_{RENAL}. V_C increased linearly with time after first dose. Population estimates were 0.34 l/h for CL_{RENAL}, 18.1 l for V_C at first dose, 4.89 l/h for intercompartmental clearance and 19.7 l for volume of the peripheral compartment. Simulations on basis of the model showed that approved daily doses of 12 to 24 g intravenous fosfomycin in two or three daily doses do not result in critical accumulations within five days after the first dose in anuric patients with and without CVVHD. For patients with CRCL > 50 ml/min and CVVHD, dosage should be increased to at least 15 g fosfomycin in three daily doses.

Conclusion:

Model based simulations reveal a safe and effective use of the approved fosfomycin dosing regimens against bacteria with minimum inhibitory concentrations up to 64 mg/l in critically ill patients with and without CVVHD.

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