O606

Abstract (oral session)

Doripenem pharmacokinetics in critically-ill patients with acute kidney injury receiving continuous venovenous haemodiafiltration

J. Roberts*, A. Udy, P. Jarrett, T. Starr, M. Lassig-Smith, J. Stuart, R. Deans, N. Roberts, R. Dunlop, Y. Hayashi, J. Lipman (Brisbane, AU)

Objectives: Doripenem is a valuable broad spectrum antibiotic for severe infections in critically ill patients, although little data exists to guide dosing during continuous renal replacement therapy in critically ill patients. The aim of this study was to describe the pharmacokinetics of doripenem in critically ill patients with acute kidney injury receiving continuous veno-venous hemodiafiltration (CVVHDF). Methods: This was a prospective pharmacokinetic study in critically ill patients with acute kidney injury receiving CVVHDF. The blood, dialysate and replacement fluid rates were 200, 1000 and 1000ml/hr)). All patients were administered 500mg doripenem IV eight-hourly. Serial pre- and post filter blood and filtrate samples were collected on two days of therapy between day 1 and 5. Biological samples were measured with a validated liquid chromatography tandem mass spectrometry assay. Results: Five males and 7 females, median age of 61 (interquartile range 53-71) years and weight 77 (67-96) kg, were enrolled. The median SOFA and APACHE II scores on Day 1 were 10 (10-11) and 29 (19-32). RRT filter compliance was acceptable during the study period. The area under the concentration time curve from 0-8 hours (AUC0-8) on Day 2 was 73% greater than on Day 1. The following are the median (interquartile range) pharmacokinetic parameters of doripenem on the first occasion of sampling: plasma terminal elimination half-life 3.7 (3.2-5.7) h; terminal volume of distribution 0.51 (0.37-0.70) L/kg; observed peak and trough doripenem plasma concentrations were 13.0 (10.9-15.3) and 3.4 (2.9-4.7) mg/L respectively. Conclusions: Doripenem is effectively cleared by CVVHDF and with the settings used in our hospital, a dose of 500mg IV eight hourly is appropriate for targeting pathogens with a MIC of 4mg/L or less using a pharmacodynamic target of concentrations above the MIC for 40% of the dosing interval.