Abstract

Pharmacokinetics of meropenem in patients with septic shock

PURPOSE

Optimised antibiotic dosing is associated with improved survival of critically ill patients, yet robust dosing regimens based on large patient cohorts is lacking. The purpose of this study was to use a population pharmacokinetic approach to define maximally effective meropenem dosing recommendations for treatment of *Acinetobacter baumannii* and *Pseudomonas aeruginosa* in patients with septic shock.

METHODS

This was a single centre observational pharmacokinetic study including adult patients with septic shock treated with meropenem. Seven blood samples were collected during one dosing interval and meropenem concentrations were measured by a validated HPLC-MS/MS method. Monte-Carlo simulations were employed to define dosing regimens that maximise success of treatment for empirical or targeted therapy of *Acinetobacter baumannii* and *Pseudomonas aeruginosa.*

RESULTS

Fifty patients were included. Mortality was 34%. A two-compartment linear model including creatinine clearance (CrCL) as a covariate, best described meropenem pharmacokinetics. For empirical treatment of *A. baumannii*, 2000 mg 6-hourly was required by intermittent (30-min) or prolonged (3-hour) infusion, whereas 6000 mg/day was required with continuous infusion. For *P. aeruginosa*, 2000 mg 8-hourly or 1000 mg 6-hourly was required. In patients with CrCL of ≤ 100 ml/min, successful concentration targets could be reached with intermittent dosing of 1000 mg 8-hourly.

CONCLUSIONS

In patients with septic shock and possible augmented renal clearance, doses should be increased and/or administration should be performed by prolonged or continuous infusion to increase the likelihood of achieving therapeutic drug concentrations. In patients with normal renal function however, standard dosing seems to be sufficient.