Pharmacokinetics of ceftriaxone administered as continuous or intermittent infusion | 1

Abstract:

OBJECTIVES: To describe the population pharmacokinetics and protein-binding characteristics of unbound ceftriaxone administered as continuous or intermittent infusion. Additionally, to determine the optimal dosing regimen in critically ill patients.

METHODS: A pharmacokinetic study was performed in the ICU of a tertiary teaching hospital. Patients were treated with ceftriaxone as continuous or intermittent infusion. A population pharmacokinetic model was developed with non-linear mixed-effects analysis. Subsequently, the PTA of a 100% T>MIC was assessed for influential patient characteristics using Monte Carlo simulation.

RESULTS: Fifty-five patients were included. The pharmacokinetics of ceftriaxone was best described by a one-compartment model with non-linear saturable protein binding including the following covariates: body weight, estimated CLCR, serum albumin concentration and mode of administration. For pathogens with an MIC of 1 mg/L, the simulation demonstrated that intermittent infusion of 2 g/24 h only resulted in a ≥90% PTA in patients with a reduced CLCR (0-60 mL/min). Intermittent infusion of 2 g/12 h led to sufficient exposure if CLCR was 0-90 mL/min and continuous infusion of 2 g/24 h led to a ≥90% PTA in all simulations (CLCR 0-180 mL/min).

CONCLUSIONS: In the critically ill, the clearance of unbound ceftriaxone is closely related to CLCR. Furthermore, ceftriaxone protein binding is saturable, variable and dependent on serum albumin concentration. Intermittent dosing of 2 g/24 h ceftriaxone leads to subtherapeutic exposure in patients with a normal or increased CLCR. Treating these patients with continuous infusion of 2 g/24 h is more effective than an intermittent dosing regimen of 2 g/12 h.

Reference: