The objective of this study was to characterize vancomycin pharmacokinetics in obese patients with sepsis or septic shock, and to develop a novel pharmacokinetic dosing model based on pharmacokinetic-pharmacodynamic target requirements” Masich et al (2020).

Abstract:

STUDY OBJECTIVES: Obese patients with sepsis or septic shock may have altered vancomycin pharmacokinetics compared with the general population, which may result in improper dosing or inadequate drug concentrations. The objective of this study was to characterize vancomycin pharmacokinetics in obese patients with sepsis or septic shock, and to develop a novel pharmacokinetic dosing model based on pharmacokinetic-pharmacodynamic target requirements.

DESIGN: Prospective, observational pharmacokinetic study.

SETTING: Large quaternary academic medical center.

PATIENTS: Sixteen obese (body mass index ≥30 kg/m²) adults with sepsis and either a gram-positive bacteremia or requiring vasopressor support (septic shock), who were receiving vancomycin between November 2016 and June 2018, were included. Patients were excluded if they were receiving renal replacement therapy or extracorporeal membrane oxygenation, treatment for central nervous system infections, pregnant or receiving vancomycin for surgical prophylaxis.

INTERVENTION: Four blood samples per patient were collected following a single dose of vancomycin; one peak serum vancomycin level (within 1-2 hours of infusion completion), two random levels during the dosing interval, and one trough level (within 30-60 minutes of the next dose) were measured.

MEASUREMENTS AND MAIN RESULTS: A population pharmacokinetic model was developed to describe vancomycin concentrations over time. Simulations to determine optimal dosing were performed using the pharmacokinetic model with different ranges of creatinine
clearance (CrCl) and different vancomycin daily doses. Median age of the patients was 62 years; median body mass index was 36.1 kg/m², Acute Physiology and Chronic Health Evaluation (APACHE) II score was 26, and Sequential Organ Failure Assessment (SOFA) score was 11. Eleven patients (69%) had an acute kidney injury. Median initial vancomycin dose was 15 mg/kg; median vancomycin trough concentration was 17 mg/L. A one-compartment model best characterized the pharmacokinetics of vancomycin in obese patients with sepsis or septic shock. Volume of distribution was slightly increased in this population (0.8 L/kg) compared with the general population (0.7 L/kg). Only CrCl effect on drug clearance was found to be significant (decrease in the objective function value by 16.4 points), confirming that it is a strong predictor of vancomycin clearance.

CONCLUSION: To our knowledge, this study provides the first population-based pharmacokinetic model in obese patients with sepsis or septic shock. The nomograms generated from this pharmacokinetic model provides a simplified approach to vancomycin dosing in this patient population.

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Reference: