

The objectives of this study were to characterize the population pharmacokinetics of vancomycin in trauma patients and to propose dosing schemes to optimize therapy” Medellín-Garibay et al (2015).

Abstract:

OBJECTIVES: The objectives of this study were to characterize the population pharmacokinetics of vancomycin in trauma patients and to propose dosing schemes to optimize therapy.

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PATIENTS AND METHODS: Trauma patients from Hospital Universitario Severo Ochoa (Spain) receiving intravenous vancomycin and routine therapeutic drug monitoring were included. Concentrations and time data were retrospectively collected, and population modelling was performed with NONMEM 7.2; internal and external validations were performed to probe the final model. Finally, several simulations were executed to propose dosing guidelines to reach expected vancomycin concentrations.

RESULTS: A total of 118 trauma patients were included; the population was 45% males, with a mean age of 77 years (range 37-100 years) and a mean total body weight (TBW) of 72 kg (range 38-110 kg). The pharmacokinetics of vancomycin was best described by a two-compartment open model; creatinine clearance (CLCR) was related to vancomycin clearance (0.49 ± 0.04 L/h), being diminished by the presence of furosemide (0.34 ± 0.05 L/h). TBW influenced both the central volume of distribution ($V1 = 0.74 \pm 0.1$ L/kg) and peripheral volume of distribution ($V2 = 5.9 \pm 2$ L/kg), but patients with age >65 years showed a larger $V1$ (1.07 ± 0.1 L/kg). Bootstrapping was performed to internally validate the stability of the final model. External validation was developed using an alternate population of 40 patients with the same characteristics. The validated model was compared with population pharmacokinetic models previously published and showed better predictive performance for trauma patients than the current one. This final model allowed us to propose a new practical

dose guideline to reach higher trough concentrations (15-20 mg/L) and AUC₀₋₂₄/MIC ratios of more than 400 after 4 days of vancomycin treatment.

CONCLUSIONS: A new population model was described for trauma patients to optimize vancomycin therapy, showing precise predictive performance to be applied for therapeutic drug monitoring and providing a new practical dose guideline that considers CLCR and concomitant administration of furosemide for these patients.

Reference:

Medellín-Garibay, S.E., Ortiz-Martín, B., Rueda-Naharro, A., García, B., Romano-Moreno, S. and Barcia, E. (2015) Pharmacokinetics of vancomycin and dosing recommendations for trauma patients. *The Journal of Antimicrobial Chemotherapy*. November 14th. .

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