

Evaluation of exposure to vancomycin in neonates with current dosing approaches

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Abstract

Background: There is no single consensus regarding optimal dosing of vancomycin in term or preterm neonates. Various available dosing recommendations are based on age, kidney function and/or body weight to define a starting dose. Our objectives were (i) to develop a comprehensive population PK model of vancomycin in a large cohort of neonates and (ii) to evaluate and compare the performances of current dosing approaches with respect to target attainment, using simulations based on our model.

Methods: A total 405 neonates provided 1848 vancomycin concentrations during routine TDM. A one-compartment model with linear elimination incorporating covariates such as age, kidney function and body weight was developed (NONMEM[®]). The final model was applied to simulate in our population vancomycin exposure resulting from 20 dosing guidelines identified in the literature. Proportions of patients within and above target exposure were used as a performance measure. Target attainment meant AUC₂₄/MIC ratio of 400-700 h and trough concentration of 10-20 mg/L, both on days 1 and 7.

Findings: Median proportions of neonates within and above target exposure were 44% (IQR 27–64%) and 1% (IQR 0–4%) on day 1, and 47% (IQR: 43–54%) and 16% (IQR: 7–19%) on day 7, respectively. Only 2 out of 20 current recommendations (Neonatal Formulary 7 and Neofax[®] meningitis regimens) ensured target attainment in about 60% of neonates on both days 1 and 7.

Interpretation: Most current vancomycin dosing regimens fail to ensure target attainment in a majority of neonates. Insufficiently dosed regimens should be avoided, especially in centers with widespread coagulase negative Staphylococci. Adding a loading dose to simple regimens is best recommended to increase the proportion of early target attainment. Complex regimens seem to marginally improve exposure. Further efforts are warranted to optimize efficacy while minimizing toxicity of vancomycin in neonates.

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