This prospective study quantifies vancomycin pharmacokinetics in morbidly obese and non-obese individuals, in order to guide vancomycin dosing in the obese” Smit et al (2019).

Abstract:

AIMS: For vancomycin treatment in obese patients, there is no consensus on the optimal dose that will lead to the pharmacodynamic target (AUC 400-700 mg*h L-1 ). This prospective study quantifies vancomycin pharmacokinetics in morbidly obese and non-obese individuals, in order to guide vancomycin dosing in the obese.

METHODS: Morbidly obese individuals (n=20) undergoing bariatric surgery and non-obese healthy volunteers (n=8) (total body weight (TBW) 60.0-234.6 kg) received a single vancomycin dose (obese: 12.5 mg kg-1, maximum 2500 mg; non-obese: 1000 mg) with plasma concentrations measured over 48 hours (11-13 samples per individual). Modelling, internal validation, external validation using previously published data and simulations (n=9950 individuals, TBW 60-230 kg) were performed using NONMEM.

RESULTS: In a three-compartment model, peripheral volume and clearance increased with TBW (both p<0.001), which was confirmed in the external validation. A dose of 35 mg kg-1 per day (maximum 5500 mg/day) resulted in a >90% target attainment (AUC>400 mg*h L-1 ) in individuals up to 200 kg, with corresponding trough concentrations of 5.7-14.6 mg L-1 (twice daily dosing). For continuous infusion, a loading dose of 1500 mg is required for steady
state on day 1.

CONCLUSIONS: In this prospective, rich sampling pharmacokinetic study, vancomycin clearance was well predicted using TBW. We recommend that in obese individuals without renal impairment, vancomycin should be dosed as 35 mg kg\(^{-1}\) per day (maximized at 5500 mg/day). When given over two daily doses, trough concentrations between 5.7-14.6 mg L\(^{-1}\) correspond to the target exposure in obese individuals.

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