

Population pharmacokinetics models of vancomycin among critically ill obese patients: A systematic review Running head: Population Pharmacokinetic of vancomycin word count 5179

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Abstract

Background: Vancomycin is a glycopeptide antibiotic used for gram-positive infections. Several vancomycin population pharmacokinetic models have been introduced in the last decades. Thus, a systematic review was performed to compare published pharmacokinetics models and (ii) to summarise and explore identified covariates influencing the vancomycin pharmacokinetics models. **Methods:** A search of publications for population pharmacokinetic analyses of vancomycin in critically ill obese patients from inception to October 2022 was conducted in PubMed and SCOPUS databases. Reviews, methodology articles, in vitro and animal studies, and noncompartmental analyses were excluded. Data on study characteristics, patient demographics, clinical parameters, pharmacokinetic parameters, and outcomes were collected. **Results:** Six studies were included in this review. Vancomycin pharmacokinetics was described as one-compartment in most of the studies. Significant interindividual variations of vancomycin pharmacokinetic parameters were found in most of the included studies. Age, sex, body weight, fibrinogen, aspartate aminotransferase, blood urea nitrogen, cystatin, and concomitant nephrotoxic drugs were the most commonly identified covariates affecting these parameters. External validation was only performed in one study to determine the predictive performance of the models. **Conclusions.** Large pharmacokinetic variability remains despite the inclusion of several covariates. This can be improved by including other potential factors, such as metabolic factors and significant drug-drug interactions in a well-designed population pharmacokinetic model in the future, taking into account the incorporation of a larger sample size and a more stringent sampling strategy. External validation should also be performed to the previously published models to compare their predictive performances.

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