

Pharmacodynamic Analysis of Vancomycin Based on Patient-Specific Protein Binding

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Staphylococcus aureus is a common pathogen in hospital setting resulting in a wide variety of infections; methicillin resistance among this organism (MRSA) has steadily increased further complicating its management. Vancomycin is the drug of choice for the treatment of MRSA infections and is subsequently a commonly used antimicrobial agent within the hospital setting. Despite its extensive use history, one important concept relating to its efficacy has been left relatively undescribed, namely vancomycin protein binding. It has been illustrated for a multitude of antimicrobials that only the unbound fraction of the exposure profile is responsible for antimicrobial activity. Unfortunately, clinical studies evaluating the protein binding of vancomycin have reported ranges of 7.1 to 96.3%, clearly complicating the ability of clinicians to evaluate free drug exposures and thus best adjust dosing. In a select group of antimicrobials, the relation between protein and antibiotic is dependent on the total drug concentration. It is quite possible that the variability noted in vancomycin protein binding may be due to this phenomenon. This variability in protein binding may also help explain clinical failures in patients infected with organisms well within the susceptibility range. The purpose of this study is to evaluate vancomycin protein binding in patients treated for presumed or documented *S. aureus* infections and assess the potential for concentration dependency in its binding. Further, using a published pharmacokinetic model and observed protein binding values, patient specific free drug profiles will be evaluated and compared to pharmacodynamic targets identified from animal models of infection. To do so, excess serum collected for vancomycin therapeutic drug monitoring as part of daily clinical practice will be analyzed for protein binding using the ultrafiltration method. Graphical analysis of protein binding and vancomycin concentration as a whole and within given patients from whom multiple samples are taken will be analyzed to assess concentration dependency. Much as is done for phenytoin, perhaps vancomycin free drug concentrations are preferable to total drug concentrations in guiding dosing recommendations.