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Abstract - Master Thesis Project, the Pharmacy Programme

Vancomycin and bromide pharmacokinetics in critically ill patients

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Introduction: Treating sepsis remains a significant challenge and antibiotics are central in therapy. Alterations in body fluid spaces occur during sepsis and these may affect antibiotics pharmacokinetics, particularly those distributed in the extracellular water (ECW) such as vancomycin. The purpose of this clinical study was to evaluate intravenous bromide dilution as a measure of ECW and relate this to the pharmacokinetics of vancomycin in intensive care patients with sepsis.

Methods: Intravenous doses of vancomycin and sodium bromide (5% w/v) were given to Intensive Care patients with sepsis. Serial blood samples were analysed by immunoassay (vancomycin) or HPLC (bromide) to determine plasma concentrations. Compartmental pharmacokinetic modeling was performed and compared to an estimation of ECW determined from the 4 hour post dose bromide level.

Results: The mean (\pm SD) bromide distribution space determined by compartmental analysis in 15 patients was 0.323 (\pm 0.193) L/kg and the values calculated by each method correlated well ($p < 0.0001$). No correlation was found between vancomycin volume of distribution (32 patients) and bromide space determined by 4 hour post dose estimation. A significant correlation was found between vancomycin clearance and creatinine clearance ($p < 0.005$).

Discussion: A 4 hour post dose level can be used for estimation of volume of distribution of bromide in critically ill patients with sepsis. Vancomycin distribution does not parallel this distribution even though it is thought to distribute in the extracellular water. The correlation between creatinine clearance and vancomycin clearance confirms renal function as a major determinant of vancomycin clearance in critically ill patients.