

Altered aminoglycoside pharmacokinetics in critically ill patients with sepsis

Abstract:

The pharmacokinetic disposition of aminoglycosides in critically ill patients with sepsis was studied. In an open-label study of the disposition of gentamicin and tobramycin, individualized pharmacokinetic values of 100 critically ill patients in the surgical intensive-care unit were compared with those of a concurrently monitored group of 100 surgery patients who were not critically ill. The a priori computer-predicted dosage requirements of the critically ill patients were also compared with the dosages derived from their individualized pharmacokinetic values, and inpatient variation in the critically ill patients was studied. Serum concentration-time data were analyzed using a one-compartment model and the DataMed Clinical Support Services system to provide individualized dosage requirements. Initial dosing guidelines were also generated for the critically ill patients using the a priori model of the DataMed Clinical Support Services program and patient demographic information. The critically ill patients were significantly older, had higher serum creatinine concentrations (SCr), and had lower elimination rate constants (k) and total body clearances (CL) than the surgery patients who were not critically ill. The volume of distribution (V) was not significantly different. The a priori computer predictions for the critically ill patients were significantly lower than the individualized values for V , CL, dose, and amount of drug per 24 hours. The dosing regimen from the a priori model was the same as the individualized regimen in only 2/100 patients. In the 76 critically ill patients who had a second pharmacokinetic analysis performed, there was a significant decrease in k and CL from the first analysis.