Case Study 6 2008

1. B.F. is 30 year old, 65 kg, 5'6" female patient to be started on gentamicin to treat a gram-negative infection. The target true maximum concentration is 8mg/L and the target true minimum concentration is 1mg/L. The clearance of the drug is equal to creatinine clearance and the Vd=0.25L/kg. This drug is typically given as a 30 minute IV infusion. Serum creatinine is 1.2mg/dL. This drug displays a two-compartment body model.

   A. Calculate the ke and half-life.

   B. Calculate the dosing interval. (Hint on your equation sheet tau (τ) is the dosing interval.)

   C. Calculate the dose (mg).

   D. Once steady state was reached, blood was drawn at 1 hr after the start of the infusion and 0.5 hr before the next infusion is started. The levels come back as 12mg/L and 4mg/L, respectively. Calculate the true Cmax and Cmin (these concentrations should be used to see if we are in the therapeutic window).

   E. If trough concentration is not below at least 2mg/L there is a chance of toxicity. Please recommend a new dose using the information obtained from the therapeutic monitoring (the blood draws) assuming that Vd is correct. (Meaning that the estimate of CL is incorrect).

2. The next table shows the resulting pharmacokinetic parameters in this Patient 1. Let's assume a second patient will receive the same dose of this drug given orally as well. Both patients differ in the tissue and plasma protein binding to this drug. 100% of the drug in plasma and tissue is free for Patient 1. Contrary to this, in Patient 2, 50% of the drug present in tissue is free (fuT = 0.5) and 50% of the drug in plasma is free (fu=0.5). Ka is equal in both patients.

In the following table indicate whether the PK parameter will be higher, lower, or the same in patient 2 compared to patient 1.

PK parameter	Patient 1	Patient 2
Vd (L)	40	
CL (L/hr)	80	
Peak (mg/L)	5	
F	0.001	

3. You wish to begin a patient on an oral formulation of Drug X and maintain an average plasma concentration of 15mg/L. You take the population average for Vd and Ke to be 10 L and $0.4 hr^{-1}$.

A. If the bioavailability is 70% and the normal dosing interval is 8 hours, what dose should we give?

B. After steady-state is reached the patient's blood is drawn and this patient has a supratherapeutic Cpaverage of 25mg/L. What is the patient's clearance?

C. At this concentration toxicity is a concern, calculate a new dose based on this clearance.