Case Study VI
Answers
Fall 2005

1. A 65-year-old, 75 kg, 5’8” tall male patient X with a serum creatinine of 1.3mg/dL, is about to receive drug X orally (assume: absorption is so fast that we can use IV bolus model). Design a dosing regimen (calculate dosing interval, dose, average concentration) that will produce a steady-state peak concentration of 15mg/L and a steady-state trough concentration of 9mg/L. How would you give the drug if only tablets of 200mg are available? Show all calculations. (Assume Vd=0.6L/kg, CL=CrCL)

First, let us calculate his IBW :

\[ \text{IBW} = 50 + 8 \times 2.3 = 68.4 \, \text{kg} \]

Then we can use this IBW to calculate his CL

\[ \text{CL} = \text{CrCL} = \frac{(140-\text{age}) \times \text{IBW}}{(72 \times \text{SeCr})} = \frac{75 \times 68.4}{(72 \times 1.3)} = \frac{5130}{93.6} = 54.8 \, \text{ml/min} = 3288 \, \text{ml/hr} = 3.3 \, \text{L/hr} \]

Then we can calculate his \( V_d \) by:

\[ \text{Vd} = 75 \times 0.6 \, \text{L/kg} = 45 \, \text{L} \]

So, the \( K_e = \frac{\text{CL}}{\text{Vd}} = 0.073 \, \text{hr} \)

\[ \tau \ (\text{dosing interval}) = \frac{\ln \left( \frac{C_{\text{max, desired}}}{C_{\text{min, desired}}} \right)}{K_e} \]

\[ = \frac{\ln \left( \frac{15}{9} \right)}{0.073} = 6.9 \, \text{hr} \approx 8 \, \text{hr} \]

Dose = Cave*CL*\( \tau \) = \( \frac{(15+9)}{2} \times 3.3 \times 8 = 316.8 \, \text{mg} \approx 300 \, \text{mg} \)

Therefore, 1.5 tablet every 8 hours.

2. Drug Y was given ORALLY to two patients, A and B, respectively. As reported from literature, drug X follows first order absorption and elimination. Please find out if the following statements are correct. (Assume the other pharmacokinetic parameters are the same)

1.) If the dose for patient A is 200 mg and the dose for patient B is 400 mg, then T max for A is larger than that for patient B. 

**False**: Since Tmax is depend on \( K_a \) and \( K_e \), however it has nothing to do with dose.

2.) Because patient A has chronic GI tract disease, \( K_a \) for patient A is 0.25 hr. \(^{-1}\), whereas the \( K_a \) value for patient B is 0.5 hr. \(^{-1}\), then the average steady state concentration for patient A is lower than that of patient B.

**False**: Since the average concentration at steady state for orally administration is independent of \( K_a \). Recall the formula: \( C_p = F \times \text{Dose/CL} \times \tau \), there is no \( K_a \) in the equation.

3. A 60-kg patient is begun on a continuous intravenous infusion of theophylline at 40 mg/hr (based on theophylline, not aminophylline). Forty-eight hours after beginning of the infusion, the plasma concentration is 15 mg/L.

a. If we assume that this concentration is at steady state, what is the theophylline clearance.

\[ \text{Css} = \frac{K_0}{\text{CL}} \]
b. If the volume of distribution is estimated to be 30 L, what is the half-life?
Ke=CL/Vd=2.7/30=0.09/hr
T_{1/2}=0.693/ke=0.693/0.09=7.7hr

c. What would the plasma concentration be 10 hr after beginning the infusion.
C_p=k_0/CL*(1-exp(-Ke*t))=40/2.7*(1-exp(-0.09*10))=40/2.7*0.59=8.74mg/L

d. If the infusion is continued for 3 days and then discontinued, what would the plasma concentration be 12 hours after the stop of the infusion.
C_p=C_{ss}*exp(-Ke*t)=15*exp(-0.09*12)=5.1mg/L

4. A 58 kg patient is started on 80 mg of gentamycin and is given as 1-hr infusion every 6 hr. If this patient is assumed to have an “average” volume of distribution (value of the population mean) of 0.25 L/kg and a normal half–life of 3 hr, what would be the peak plasma concentration at steady state (the true $C_{\text{max}}$ value)? Is the 6 hr dosing interval sufficient to achieve a fluctuation of not more than 6.

$V_d= 0.25*58=14.5 \, \text{L}$
$K_e=0.693/3=0.231/\text{hr}$
$C_{\text{max}} = \frac{\text{Dose} \times \left(1 - e^{-Ke\times T}\right)}{C_L \times T \times \left(1 - e^{-Ke\times T}\right)} = \frac{80 \times \left(1 - e^{-0.231\times6}\right)}{3.35 \times 1 \times \left(1 - e^{-0.231\times6}\right)} = \frac{80 \times (1 - 0.79)}{3.35 \times 1 \times (1 - 0.25)} = \frac{16.8}{2.5125} = 6.7 \, \text{mg}$

$F= e^{Ke\times T} = e^{0.231\times6} \approx 4$, therefore, 6 hr is enough to achieve a fluctuation of no more than 6.