Case Study 3
PHA 5127 2007

1. A drug is given as an iv bolus dose of 420 mg. The concentration two hours after administration is 23mg/L and the concentration 4 hours after administration is 15 mg/L.

a. Calculate the k_e and half-life of the drug.

$-k_e=Ln(C_2/C_1)/(t_2-t_1)$ $-k_e=Ln(15mg/L/23mg/L)/2hr$ $-k_e=-0.214hr^{-1}$
$k_e=0.214hr^{-1}$
$t_{1/2}=0.693/ke$ $t_{1/2}=0.693/0.214hr^{-1}=3.24hr$

b. How long does it take for the concentration to drop below 8mg/L, the lower limit of the therapeutic window?

$C=C_o*e^{-ke*t}$ $LnC=LnC_o-k_e*t$ $Ln(C/C_o)/-k_e=t$ $Ln(8mg/L/15mg/L)/-0.2hr^{-1}=3.14hr+4hr$(time since infusion)=7.14 hours since the time of infusion
or
$C=C_o*e^{-ke*t}$ $LnC=LnC_o-k_e*t$ $Ln(C/C_o)/-k_e=t$ $Ln(8mg/L/23mg/L)/-0.2hr^{-1}=5.28hr+2hr$ (time since infusion)=7.28hr hours since the time of infusion

c. Calculate the volume of distribution.

$Co=C/e^{-ke*t}$ $Co=23mg/L/e^{-0.214*2}$ $Co=35.3mg/L$ $Vd=Dose/Co$
$Vd=420mg/35.3mg/L=11.9L$

d. If this is a lipophilic drug that is 80% bound in plasma what is the fraction bound in tissue?

$Vd=VP+Vt*(f_u/f_{ut})$ $(Vd-Vp)/Vt=f_u/f_{ut}$ $f_{ut}=f_u*Vt/(Vd-Vp)$ $f_{ut}=0.2*38L/(11.9L-3L)=0.85$
Fraction bound in tissue is 0.15

2. Patient AM and patient CS are both given the same dose of a drug. The resulting starting concentration for patient AM is lower that that of patient CS. For this question you may want to look at the course website under simulations. Use the one-compartment model for a single IV bolus dose.

a. What pharmacokinetic parameter is different between the two patients?

Looking at the equation Co=D/Vd, if the dose between the two patients is the same but the Co for AM is lower than the Vd for AM must be bigger.

b. Please give three reasons for the difference in Vd between patients.

Looking at the equation $Vd=Vp+Vt*(f_u/f_{ut})$ we can say that AM may have an increased unbound fraction on plasma, a lower fraction unbound in tissue, or a higher volume of tissue for example like that of an obese patient.

c. Patient AM and patient CS are given the same dose of a different drug. They have the same starting concentration. However, the AUC of AM is less than the AUC of CS. What does this tell us about the elimination rate and the half life of the drug between the two patients.

This tells us that the elimination rate for AM is greater than the elimination rate for CS. Also the half-life for AM is less than the half-life for CS.