(Key to Case Study1)

Case study 1.

(PHA5127)

Fall 2003

Question 1.

A 80 year old, 70-Kg patient with pneumonia, was being treated by an iv. bolus of gentamicin (0.5 mg / kg). Serum samples were taken at 0.5 and 6 hours post injection, and the lab reported drug concentrations of 3.41μg/ml, and 0.83 μg/ml, respectively. Assume gentamicin follows one compartment, first-order elimination.

1.) Calculate the half-life of gentamicin in this patient.

$$Ke = \frac{\ln(C_2 / C_1)}{t_1 - t_2} = -\frac{\ln(0.83/3.41)}{0.5-6} = 0.26(hr^{-1})$$

$$t_{1/2} = \frac{0.693}{0.26} = 2.66(hr.)$$

2.) Calculate the volume of distribution of gentamicin in this patient.

Dose = 0.5 × 70 = 35 (mg)

Recall: $C_t = C_0 \cdot e^{-K_e t}$ then $C_0 = C_t \cdot e^{k_e t} = 3.41 \cdot e^{0.26 \cdot 0.5} = 3.88(\mu g / ml)$

Then: $Vd = \frac{Dose}{C_0} = \frac{35}{3.88} = 9.0(l)$

3.) Can you predict what is the drug concentration two half-lives after iv. bolus injection.

$t = 2 \cdot 2.66 = 5.32(hr.)$

$C_t = C_0 \cdot e^{-K_e t} = 3.88 \cdot e^{-0.26 \cdot 5.32} = 0.97(\mu g / ml)$

Or :

Recall the definition of half-life. In one half-life, $C_{t_{1/2}} = 0.5 * C_t$. Then two half-lives,

$C_{2t_{1/2}} = 0.5 \cdot C_{t_{1/2}} = 0.5 \cdot 0.5 \cdot C_t = 0.25 \cdot 3.88 = 0.97(\mu g / ml)$

Question 2.

A 25-year-old, 60-kg female patient was given an iv. bolus of a aminophyllline, (200 mg). Theophylline concentration-time profiles after the first dose was given as following (table). Given the fact that 1mg of aminophylline is equivalent to 0.8mg theophylline and elimination occurs by first-order kinetics, please answer the following questions.

Table1. Theophylline concentration-time profiles after iv. bolus of aminophylline.

t(hr)	Con (ug/ml)	AUC(t1-t2)
0	***9.64***	
1	7.89	***8.76***
3	5.29	***13.18***
5	3.55	***8.84***
7	2.38	***5.92***
12	0.87	***8.13***
AUC 0-12		***44.83***

1.) Calculate the $AUC_{0\text{-}12}$ of theophylline by using trapezoidal rule.

$$K_e = \frac{\ln(C_2 / C_1)}{(t_1 - t_2)} = \frac{\ln(0.87/7.89)}{(1-12)} = 0.2(hr^{-1})$$

Again: $C_t = C_0 \cdot e^{-K_e \cdot t}$ Then, $C_0 = C_t \cdot e^{K_e \cdot t} = 0.87 \cdot e^{0.2 \cdot 12} = 9.64(\mu g / ml)$

Then, using trapezoidal rule: $AUC_{1-2} = \frac{(C_1 + C_2)}{2} \cdot (t_2 - t_1)$

The final answer is: 44.83 mg*h/L.

2.) Calculate the AUC0-∞.

$$AUC_{12-\infty} = \frac{C_t}{K_e} = \frac{0.87}{0.2} = 4.35(mg \cdot hr / L)$$

Then, $AUC_{0-\infty} = AUC_{0-12} + AUC_{12-\infty} = 44.83 + 4.35 = 49.18(mg \cdot hr / L)$