PHA 5128
Answers Case study 5
Spring 2010

1. A 32 year old 70 kg male received a kidney transplant, and is treated with cyclosporine 250 mg BID. His trough level is measured and comes back 80ng/mL. Design a new dosing regimen based on this information with a Cmax of 400ng/mL and a Cmin of 150ng/mL. (Cyclosporine is rapidly absorbed).

$$Vd = 4.5 * 70 = 315(L)$$

$$C\max = \frac{F * D}{Vd} + C\min = \frac{0.3 * 250}{315} * 1000 + 80 = 318(ng/ml)$$

K e= (ln318-ln80)/12=0.115(h^{-1})

Tau= (ln400-ln150)/0.115=8.52(h)=8(h)

$$Dose = \frac{C\max*[1 - e\text{^}(-ke * Tau)] * Vd}{F * S} = \frac{400 * [1 - e\text{^}(-0.115 * 8)] * 315 * 1000}{0.3 * 1} = 252 * 10\text{^}6(ng)$$

$$= 250(mg)$$

Dose regimen is 250mg tid.

2. A 57-year-old, 50kg woman with congestive heart failure, was admitted to the hospital for possible digoxin toxicity. Her serum creatinine was 2.8mg/dL, and her dosing regimen at home had been 0.25mg digoxin (tablets) daily for a year. Her digoxin plasma concentration on admission was 3.8µg/L. How long will it take for the digoxin concentration to fall from 3.8 to 2µg/L if no further doses are given?

Clcr(female)= $\frac{(140 - 57) * 50kg}{85 * 2.8mg/ml} = 17.44(ml/\min)$

$$Cl = \frac{S * F * Dose}{\tau * Css} = \frac{1 * 0.7 * 0.25 * 1000ug}{1day * 3.8ug/l} = 46.05(L/day)$$

Vd = 3.8L/day*IBW+3.1*Clcr=3.8*50+3.1*17.44=244(L)

Ke= Cl/Vd=46.05/244=0.189 (/day)

T=(lnC1-lnC2)/ke= (ln3.8-ln2)/0.189=3.4(day)

3. An 82 kg male became nauseated after receiving i.v. aminophylline 90mg/h for several days. A plasma sample for theophylline was obtained and the infusion was discontinued. Ten hours later a second plasma sample was obtained. The reported plasma theophylline concentrations were 40μg/mL and 20μg/mL, respectively. Estimate the hourly dose of aminophylline required to maintain the plasma theophylline concentration at 15mg/L. (Use aminophylline S = 0.85, V_d = 0.5L/kg)

   Ke=(lnC1-lnC2)/(t2-t1)=(ln40-ln20)/10=0.639/10=0.0693(h^{-1})

   Vd=0.5L/kg*82kg=41(L)

   Cl=Ke*Vd= 0.0693*41=2.84(L/h)

   MD=$\frac{Cl*Css}{F*S}=\frac{2.84*15}{1*0.85}=50.11(mg/h)$

4. A 34 year old female patient (54 kg, SeCr 1.1 mg/dl) received a 30 mg methotrexate loading dose I.V. followed by a 30 mg/h infusion over 36 hours. Her levels at 24h and 48h were 12.2 μM and 0.76 μM, respectively. Calculate the anticipated methotrexate level at 60 hours.

   $K_1=\frac{\ln(C1/C2)}{t}=\frac{\ln(12.2/0.76)}{12}=0.231(h^{-1})$

   $t_{1/2\ 1}$ = 0.693/0.231=3 (h)

   t at 0.5 μM

   t=$\frac{\ln(C1/C2')}{K1}=\frac{\ln(12.2/0.5)}{0.231}$=13.8 (h)

   $t_{1/2\ 1}$ = 3h $t_{1/2\ 2}$= 10h

   K_2 =0.693/10= 0.0693(h^{-1})

$T = 60-13.8-36=10.2(h)$

$Cp_{60h}=0.5*e^{-0.0693*10.2}=0.25(\mu M)$