PHA 5128 dose Optimization II
Spring 2012

Case study 2

1. **True or False**

   A. It is reasonable to assume that liver function is proportional to BSA. (T)
   B. Weakly or moderately lipophilic drugs are poorly distributed in obese patients(T)
   C. Total body water (% of body weight) in neonates is usually smaller than in adults(F)
   D. Generally, the gastric emptying time of neonates is shorter than adults' (F)

2. The recommended regimen for a new drug X is 400 mg / m^2 (BSA) or 10 mg / kg (IBW) once a day. What is the dosage for a patient (male, 35 years-old, 165 cm, and 60 kg) based on BSA and IBW?

   BSA can be calculated by:

$$BSA[m^2] = \left(\frac{TBW[kg]}{70[kg]}\right)^{0.7} \cdot 1.73[m^2]$$

   Or

$$BSA[m^2] = TBW[kg]^{0.425} \cdot H[cm]^{0.725} \cdot 0.007184$$

   For this patient:

   BSA= $(60/70)^{0.7}$*1.73=1.55(m^2)

   Or

   BSA=$60^{0.425}$*$165^{0.725}$*0.007184=1.66(m^2)

   Ideal body weight can be calculated by:

   For male: IBW (kg) = 50 + 0.9*(height in cm - 150)

   For this patient: IBW=50 + 0.9*(165 - 150) =63.5 (kg)

   Dosage based on BSA can be calculated by:

   Dosage (mg) =400 (mg / m^2)*BSA =400 (mg / m^2)* 1.55 (m^2) =620 (mg) or
   = 400 (mg / m^2)*1.66 (m^2) = 664(mg)

   Dosage based on IBW can be calculated by:

   Dosage (mg) =10 (mg / kg)*IBW=10 (mg / kg)*63.5 (kg) =635 (mg)

3. A female patient (42 years-old, 155 cm, and 58 kg) has a concentration of serum creatinine of 1.1 mg/dL. Please calculate her Cl_{cr} based on the Cockcroft-Gault-Equation.

   For female, IBW can be calculated by:

   IBW (kg) = 45.5 + 0.9*(height in cm - 150)

   For this patient: IBW (kg) =45.5 + 0.9*(155 - 150) =50 (kg)

   TBW is smaller than 120% IBW (58<50* 120%), so use TBW to calculate her Cl_{cr} based on the Cockcroft-Gault-Equation.

For female $$CL_{Cr} = \frac{(140 - age) \cdot BW}{Cp_{Cr} \cdot 85}$$

This patient: CL_{cr}= (140-42) *58/1.1/85=60.79 (ml/min)

4. A 50-year-old male patient (60 kg, 160 cm, Cpcreat=1.2 mg/dL,) is treated with 100mg gentamicin i.v. short-term infusions (30 min) Q8h. Assuming linear pharmacokinetics (Vd=0.25L/kg, Cl=Clcreat), please predict the measured peak concentration 1 hour after the infusion was started and the measured trough concentration 30 min before the next infusion at steady state.

For male: IBW=50 + 0.9*(height in cm - 150) = 50+0.9*(160-150) =59(kg)

TBW=60 (kg) is smaller than IBW*120%, use TBW to calculate the Cl_{cr}

For male: $$CL_{Cr} = \frac{(140 - age) \cdot BW}{Cp_{Cr} \cdot 72}$$

= (140-50) *60/1.2/72=62.5 (ml /min) =3.75 (L)

K=Cl/Vd=3.75/ (0.25*60) =0.25(/h)

T= 0.5 h t= 0.5 h τ = 8 h

$$C_{max} = \frac{dose}{Vd*K*T*(\frac{1-e^{-k*\tau}}{1-e^{-k*T}})}$$

$$C_{max} = \frac{100}{0.25*60*0.25*0.5*(\frac{1-e^{-0.25*8}}{1-e^{-0.25*0.5}})}$$

=7.44 (mg/L)

$C_{max'} = C_{max} * e^{-kt} = 7.44 * e^{-0.25*0.5}$ =6.55 (mg/L)

$C_{min'} = C_{max} * e^{-k*(\tau - T - 0.5)} = 7.44 * e^{-0.25*(8-0.5-0.5)} = 7.44*0.17 = 1.26$ (mg/L)

5. Determinate a regimen (dose and dosing interval) to treat a patient (CL=5 L/h, Vd=0.25 L/kg, 90 kg) that suffers from a pulmonary infection if the "true" peak and trough concentrations at steady state are supposed to be 25 mg/L and 5 mg/L, respectively. Assume a short-term infusion over 30 minutes.

   First to calculate the dosing interval:

   Vd= 0.25*90= 22.5(L)
   CL=5L/h
   K=CL/Vd=5/22.5= 0.22 (/h)

   $\tau = \frac{\ln\left(\frac{cmax}{cmin}\right)}{k} + T = \frac{\ln\left(\frac{25}{5}\right)}{0.22} + 0.5 = \frac{1.61}{0.22} + 0.5$=7.32+0.5 (h) ≈8(h)

   $D = C_{max(desired)} * k * Vd * T * \frac{(1-e^{-k*\tau})}{(1-e^{-k*T})}$

   $= 25*0.22*22.5*0.5*\frac{(1-e^{-0.22*8})}{(1-e^{-0.22*0.5})}$

   =25*0.22*22.5*0.5*(0.83/0.10) = 513.6(mg)≈500(mg)

   So the regimen will be 500 mg, Q8h.