PHA 5128 dose Optimization II
Spring 2011

Case study 2

1. **Neonates VS Adults**

   True or false:

   A. The total body water (in % of body weight) in neonates is usually smaller than in adults (F)
   B. The extracellular water (in % of body weight) in neonates is usually smaller than in adults(F)
   C. The glomerular filtration rate (GFR) in neonates is usually smaller than in adults(T)
   D. The gastric emptying time of neonates is usually shorter than adults' (F)

2. **Body surface area and body weight**

   Patient A: male, 40- year-old, 170cm, 70kg

   Patient B: Female, 40-year-old, 158cm, 50kg
   Please calculate the body surface area, ideal body weight for them.
   Body surface area 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 patient A:
BSA= $(70/70)^{0.7}*1.73=1.73(m^2)$
Or
BSA=$70^{0.425}*170^{0.725}*0.007184=1.81(m^2)$

For patient B
BSA= $(50/70)^{0.7}*1.73=1.37(m^2)$
Or
BSA=$50^{0.425}*158^{0.725}*0.007184=1.49(m^2)$

Ideal body weight can be calculated by:
For male: IBW (kg) = 50 + 0.9*(height in cm - 150)
For female: IBW (kg) = 45.5 + 0.9*(height in cm - 150)

For patient A: IBW=50 + 0.9*(170 - 150) =68(kg)
For patient B: IBW= 45.5 + 0.9*(158 – 150) =52.7(kg)

3. Clearance of creatinine

For the patients in question 2, assume concentration of serum creatinine is 1.2 mg/dL, please calculate their Cl_{cr} based on the Cockcroft-Gault-Equation

TBW is smaller than 120% IBW (70<68* 120% and 50<52.7*120%) so we can use TBW to calculate their Cl_{cr} based on the Cockcroft-Gault-Equation.

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

Patient A: CL_{cr}= (140-40) *70/1.2/72=81.02 (ml/min)

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

Patient B: CL_{cr}= (140-40) *50/1.2/85=49.01 (ml/min)

4. A 45-year-old male patient (65kg, Cpcreat=1mg/dL, 170cm) is treated with 100mg Gentamicin i.v. short-term infusions (45min) TID. Assuming linear pharmacokinetics (Vd=0.25L/kg, Cl=Clcreat), please predict the measured peak concentration one hour after the infusion was started and the measured trough concentration 30min before the next infusion at steady state.

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

IBW= 50+0.9*(170-150) =68(kg)
TBW=65kg is smaller than IBW*120%, use TBW to calculate the Cl_{cr}

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

= (140-45) *65/1/72=85.76 (ml/min)≈5(L/h)

K=Cl/Vd=5/ (0.25*65) =0.31(/h)

$$C_{max}= \frac{100}{0.25*65*0.31*0.75*(\frac{1-e^{-0.31*8}}{1-e^{-0.31*0.75}})}$$

=5.99(mg/L)

$C_{max}'= C_{max}*e^{-0.31*0.25}$= 5.99*0.93=5.54(mg/L)

$C_{min}'= C_{max}*e^{-0.31*(8-0.75-0.5)}$=5.99*0.123=0.74(mg/L)

5. Determinate a regimen (dose and dosing interval) for Amikacin to treat a patient (CL=5L/h, Vd=0.25L/kg, 80 kg) that suffers from a pulmonary infection if the "true" peak and trough concentrations at steady state are supposed to be 30 mg/L and 5 mg/L, respectively? Assume a short-term infusion over 45 minutes.

First to calculate the dosing interval:

Vd= 0.25*80=20(L)

CL=5L/h

K=CL/Vd=5/20=0.25 (/h)

$$\tau = \frac{\ln\left(\frac{cmax}{cmin}\right)}{k} + T = \frac{\ln\left(\frac{30}{5}\right)}{0.25} + 0.75 = 7.92\ (h) \approx 8(h)$$

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

$$= 30*0.25*20*0.75*\frac{(1-e^{-0.25*8})}{(1-e^{-0.25*0.75})}$$

$$= 30*0.25*20*0.75*5.05 = 569.0(mg) \approx 570(mg)$$

So the regimen is 570mg, TID.