PHA 5128 dose Optimization II
Spring 2012

Homework 2

1. True or False **(0.5 points each, total 2 points)**
   A. Individual CL_{Cr} or GFR estimates can be used to evaluate renal function and dose adjustments. **(T)**
   B. Drugs with a high octanol/water lipid partition coefficient (LPD) will often exhibit a **smaller** volume of distribution in obese patients **(F)**
   C. Ideal body weight should always be used when determining the regimen for patients. **(F)**
   D. The gastric emptying time of neonates is usually **longer** than adults' **(T)**

2. A 50-year- old male patient is treated with 100 mg gentamicin i.v. short-term infusions (30 min) Q8h. The steady-state clinical pharmacokinetic data is shown below:
   A) 30 mins after the infusion was ended, the gentamicin concentration is 7.20 mg/L
   B) 30 mins before the next infusion, the gentamicin concentration is 1.40 mg/L

   Predict Vd, "true" peak and trough concentration based on the given information **(3 points)**

   T=0.5 h t_1= (0.5+0.5) h t_2= (8-0.5) h

   $$K=\frac{\ln(\frac{c1}{c2})}{t2-t1}=\frac{\ln(\frac{cmax'}{cmin'})}{t2-t1}=\frac{\ln(\frac{7.20}{1.40})}{(8-0.5)-(0.5+0.5)}=\frac{1.64}{6.5}=0.25\ (/h)$$

   $$C_{max}=\frac{Cmax'}{e^{-k*(t1-T)}}=\frac{7.20}{e^{-0.25*(0.5+0.5-0.5)}}=\frac{7.20}{0.88}=8.18\ (mg/L)$$

   $$C_{min}=C_{max}*e^{-k*t2}=8.18*e^{-0.25*(8-0.5)}=8.18*0.15=1.23\ (mg/L)$$

   $$Vd=\frac{dose}{Cmax*K*T*(\frac{1-e^{-k*\tau}}{1-e^{-k*T}})}=\frac{100}{8.18*0.25*0.5*(\frac{1-e^{-0.25*8}}{1-e^{-0.25*0.5}})}=\frac{100}{8.18*0.25*0.5*(\frac{0.86}{0.12})}$$

   =13.64 (L)

3. A female patient (40-year-old, 60 kg, Cpcreat=1.0mg/dL, 160cm) is treated with 300mg amikacin i.v. short-term infusions (30mins) every 12hrs. Assuming linear pharmacokinetics (Vd=0.25L/kg, Cl=Clcreat).
   Predict
   A. The concentration measured 30 mins after the infusion is ended
   B. The concentration measured 30 mins before the next infusion
   (3 points)

For female: IBW (kg) = 45.5 + 0.9*(height in cm - 150) =45.5+0.9*(160-150) =54.5(kg)

TBW is smaller than 120% IBW (60 <54.5* 120%) so we can use TBW to calculate her Cl_{cr}

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

CL_{cr}= (140-40) * 60 / 1.0/ 85=70.59 (ml/min) ≈ 4.24 (L/h)

Vd=0.25 * 60=15(L)

K= Cl/Vd=4.24/15=0.28 (/h)

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

$$C_{max} = \frac{300}{15*0.28*0.5*(\frac{1-e^{-0.28*12}}{1-e^{-0.28*0.5}})} = \frac{300}{15*0.28*0.5*(\frac{0.97}{0.13})} = 19.14 \text{ (mg/L)}$$

$C_1 = C_{max} * e^{-k*t1} = 19.14 * e^{-0.28*0.5} = 19.14 * 0.87 = 16.65$ (mg/L)

$C_2 = C_{max} * e^{-k*t2} = 19.14 * e^{-0.28*(12-0.5-0.5)} = 19.14 * 0.046 = 0.88$ (mg/L)

Or

$C_2 = C_1 * e^{-k*(t2-t1)} = 16.65 * e^{-0.28*(12-0.5-0.5-0.5)} = 16.65 * 0.053 = 0.88$ (mg/L)

4. A male patient (65-years-old, 70 kg, 173 cm) is currently taking 800 mg of a drug X that is to 80% excreted into the urine. Suddenly his creatinine clearance drops from 100 ml/min to 25 ml/min.
   Determine the new dose of his Drug X. **(2 points)**

$$D_{pat} = D_{norm} * [1 - f_{ren} * (1 - RF)]$$

$$\text{Dose}_{new} = 800 * [1 – 0.8 * (1 – 25/100)] = 800 * 0.4 = 320 \text{ (mg)}$$