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

\[
K = \frac{\ln \left( \frac{c_1}{c_2} \right)}{t_2 - t_1} = \frac{\ln \left( \frac{7.20}{1.40} \right)}{(8-0.5) - (0.5+0.5)} = \frac{1.64}{6.5} = 0.25 \text{ (/h)}
\]

\[
C_{\text{max}} = \frac{C_{\text{max}}}{e^{-k(T-T_1)}} = \frac{7.20}{e^{-0.25*(0.5+0.5-0.5)}} = \frac{7.20}{0.88} = 8.18 \text{ (mg/L)}
\]

\[
C_{\text{min}} = C_{\text{max}} * e^{-k t_2} = 8.18 * e^{-0.25*(8-0.5)} = 8.18 * 0.15 = 1.23 \text{ (mg/L)}
\]

\[
V_d = \frac{dose}{C_{\text{max}} K T (\frac{1-e^{-kT}}{1-e^{-kT}})} = \frac{100}{8.18*0.25*0.5*(\frac{1-e^{-0.25*8}}{1-e^{-0.25*0.5}})} = \frac{100}{8.18*0.25*0.5*(\frac{0.86}{0.12})}
\]

= 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 Clcr

\[
Cl_{cr} = \frac{(140-\text{age}) \cdot BW}{C_{pcreat} \cdot 85}.
\]

\[
Cl_{cr} = (140-40) \cdot 60 / 1.0 / 85 = 70.59 \text{ (ml/min)} \approx 4.24 \text{ (L/h)}.
\]

\[
Vd = 0.25 \cdot 60 = 15 \text{ (L)}.
\]

\[
K = Cl / Vd = 4.24 / 15 = 0.28 \text{ (/h)}.
\]

\[
C_{\text{max}} = \frac{\text{dose}}{Vd \cdot K \cdot T \cdot (\frac{1-e^{-k \cdot t}}{1-e^{-k \cdot T}})} = \frac{300}{15 \cdot 0.28 \cdot 0.5 \cdot (\frac{1-e^{-0.28 \cdot 12}}{1-e^{-0.28 \cdot 0.5}})} = 19.14 \text{ (mg/L)}.
\]

\[
C_1 = C_{\text{max}} \cdot e^{-k \cdot t_1} = 19.14 \cdot e^{-0.28 \cdot 0.5} = 19.14 \cdot 0.87 = 16.65 \text{ (mg/L)}.
\]

\[
C_2 = C_{\text{max}} \cdot e^{-k \cdot t_2} = 19.14 \cdot e^{-0.28 \cdot (12 - 0.5 - 0.5)} = 19.14 \cdot 0.046 = 0.88 \text{ (mg/L)}.
\]

Or
\[
C_2 = C_1 \cdot e^{-k \cdot (t_2 - t_1)} = 16.65 \cdot e^{-0.28 \cdot (12 - 0.5 - 0.5 - 0.5)} = 16.65 \cdot 0.053 = 0.88 \text{ (mg/L)}.
\]
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)**

\[
D_{\text{pat}} = D_{\text{norm}} \times [1 - f_{\text{ren}} \times (1 - RF)]
\]

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