PHA 5128

Homework 3 (revised 2/28/06)

Spring 2006

1. B.W. is a 50-year-old, 5'2'', 55kg female with a serum creatinine of 2.2 mg/dL. She is given gentamicin for soft tissue infections. Calculate the gentamicin concentration 1 hour after initiating the one-half hour infusion of a 200 mg dose, using the short-term infusion model.(2pt)

$$\text{IBW} = 45.5 + 2.3 \cdot 2 = 50.1 \text{ kg}$$

$$\text{TBW} < 120\% \text{ IBW}$$

$$CL_{cr} = \frac{(140 - age) \cdot TBW}{Cpcr \cdot 85} = \frac{(140 - 50) \cdot 55}{2.2 \cdot 85} = 26.47 mL/\min = 1.59 L/hr$$

$$\text{Vd} = 25\% \cdot \text{TBW} = 0.25 \cdot 55 = 13.75 \text{ L}$$

$$k_e = \frac{CL}{V_d} = \frac{1.59 \text{ L/hr}}{13.75 \text{ L}} = 0.12 \text{hr}^{-1}$$

Short-term infusion (single dose):

$$C = \frac{D}{CL \cdot T}(1 - e^{-ke \cdot T}) \cdot e^{-ke \cdot t} = \frac{200}{1.59 \cdot 0.5}(1 - e^{-0.12 \cdot 0.5}) \cdot e^{-0.12 \cdot 0.5} = 13.8 mg/L \quad \text{(2pt)}$$

2. S.H. with a CL of 6.1 L/hr, Vd of 17.5 L was given tobramycin 7mg/kg QD in a 30-minute-infusion. Predict the steady-state peak concentration at the end of infusion and subsequent steady-state plasma concentration 12 hours after starting the infusion. Assume S.H. weighs 60 kg. (2pt)

$$k_e = \frac{CL}{V_d} = \frac{6.1 \text{ L/hr}}{17.5 \text{ L}} = 0.349 \text{hr}^{-1}$$

$$C_{ss\max} = \frac{D \cdot (1 - e^{-ke \cdot T})}{CL \cdot T \cdot (1 - e^{-ke \cdot \tau})} = \frac{7 \cdot 60 \cdot (1 - e^{-0.349 \cdot 0.5})}{6.1 \cdot 0.5 \cdot (1 - e^{-0.349 \cdot 24})} = 22.03 mg/L \quad \text{(1pt)}$$

$$C_{ss} = C_{ss\,max} \cdot e^{-ke \cdot t} = 22.03 \cdot e^{-0.349 \cdot 11.5} = 0.398 \text{ mg/L}$$ (1pt)

3. K. K., a 30-year-old, 65 kg, non-obese female patient with a gram-negative pneumonia, was being treated with gentamicin 100mg infused over 30 minutes every 8 hours at midnight, 8:00a.m., and 4:00 p.m. Blood samples were obtained just before the 8:00 a.m. and at 9:00 a.m to evaluate therapy and prevent toxicity. The gentamicin concentrations reported were 0.4 mg/L and 4.5 mg/L respectively. Assuming these concentrations represent steady-state levels, make a dosing adjustment to achieve a peak concentration of 8 mg/L. (2pt)

Calculateing k by transposing $C_{ss\,max}$ into the same interval as $C_{ss\,min}$, so 7 hour interval between these two concentration.

$$k = \frac{\ln \frac{4.5}{0.4}}{7} = 0.346 hr^{-1}$$ (1pt)

True peak concentration: $C_{max} = \frac{4.5}{e^{-0.346 \cdot 0.5}} = 5.35 mg/L$

True trough concentration: 0.4mg/L

$$Vd = \frac{100}{0.346 \cdot 0.5} \cdot \frac{\left(1 - e^{-0.346 \cdot 0.5}\right)}{\left(5.35 - 0.4 \cdot e^{-0.346 \cdot 0.5}\right)} = 18.33 L$$

$$D = 8 \cdot 0.346 \cdot 18.33 \cdot 0.5 \cdot \frac{\left(1 - e^{-0.346 \cdot 8}\right)}{\left(1 - e^{-0.346 \cdot 0.5}\right)} = 25.37 \cdot \frac{0.937}{0.159} = 149.5 mg$$ (1pt)

4. H.W., a 65-year-old, 5'4'', 60kg woman with a serum creatinine of 1mg/dL, has been started on 1g of vancomycin over 1 hour infusion q12h for the treatment of staphylococcal. Calculate initial peak and trough vancomycin concentration and steady-state peak and trough vancomycin concentration. (2pt)

$$V_d = 0.178 \cdot age + 0.22 \cdot TBW + 15$$

$$= 0.178 \cdot 65 + 0.22 \cdot 60 + 15$$

$$= 39.77 \text{ L}$$

$$(\text{or } 0.7\text{L/kg} \cdot 60 = 42 \text{ L})$$

$$\text{IBW} = 45 + 2.3(\text{height in inches-60}) \text{ kg}$$

$$= 45 + 2.3 \cdot 4$$

$$= 54.2\text{kg}$$

$$\text{TBW} < 1.2 * \text{IBW using TBW}$$

$$CL_{cr} = \frac{(140 - age) \cdot TBW}{Cpcr \cdot 85} = \frac{(140 - 65) \cdot 60}{1 \cdot 85} = 52.94 mL/\min = 3.18 L/hr$$

$$k_e = \frac{CL}{V_d} = \frac{3.18 \text{ L/hr}}{39.77\text{L}} = 0.08\text{hr}^{-1}$$

Two acceptable models: i.v. bolus and short-term infusion

1) i.v. bolus model

Initial peak and trough

$$C_{\max} = \frac{D}{Vd} = \frac{1000}{39.77} = 25.14 mg/L \quad (0.5\text{pt})$$

$$C_{min} = C_{\max} \cdot e^{-ket} = 25.14 \cdot e^{-0.08 \cdot 12} = 9.63 \text{ mg/L} \quad (0.5\text{pt})$$

Steady state peak and trough

$$C_{ss\max} = \frac{D}{Vd \cdot (1 - e^{-ke \cdot \tau})} = \frac{1000}{39.77 \cdot (1 - e^{-0.08 \cdot 12})} = 40.75 mg/L$$ (0.5pt)

$$C_{ss\,min} = C_{ss\,max} \cdot e^{-ke\tau} = 40.75 \cdot e^{-0.08 \cdot 12} = 15.6 mg/L$$ (0.5pt)

2) short-term infusion

Initial peak and trough

$$C_{\max} = \frac{D}{CL \cdot T}(1 - e^{-ke \cdot T}) = \frac{1000}{3.18 \cdot 1}(1 - e^{-0.08 \cdot 1}) = 24.18 mg/L$$

$$C_{min} = C_{max} \cdot e^{-ke(\tau - T)} = 24.18 \cdot e^{-0.08 \cdot 11} = 10.03 \text{ mg/L}$$

Steady state peak and trough

$$C_{ss\max} = \frac{D \cdot (1 - e^{-ke \cdot T})}{CL \cdot T \cdot (1 - e^{-ke \cdot \tau})} = \frac{1000 \cdot (1 - e^{-0.08 \cdot 1})}{3.18 \cdot 1 \cdot (1 - e^{-0.08 \cdot 12})} = 39.19 mg/L$$

$$C_{ssmin} = C_{ss\,max} \cdot e^{-ke(\tau - T)} = 39.19 \cdot e^{-0.08 \cdot 11} = 16.26 \text{ mg/L}$$

5. K.T. is a 65-year-old, 5'7'', 105kg man with a serum creatinine concentration of 2.2mg/dL. He is going to receive vancomycin for a nafcillin-resistant S.aureus (NSRA) infection. Design a dosing regimen (dose and dosage schedule) that will produce peak concentration of 30mg/L and trough concentration of 10mg/L. (2 pt)

$$Vd = 0.178 \cdot age + 0.22 \cdot TBW + 15$$
$$= 0.178 \cdot 65 + 0.22 \cdot 105 + 15$$
$$= 49.67 \text{ L}$$

$$IBW = 50 + 2.3(\text{height in inches} - 60) \text{ kg}$$
$$= 50 + 2.3 \cdot 7$$
$$= 66.1 \text{kg}$$

TBW > 1.2* IBW using ABW

$$ABW = IBW + 0.4(TBW - IBW) = 66.1 + 0.4 \cdot (105 - 66.1) = 81.66kg$$

$$CL_{cr} = \frac{(140 - age) \cdot ABW}{Cpcr \cdot 72} = \frac{(140 - 65) \cdot 81.66}{2.2 \cdot 72} = 38.66mL/\min = 2.32L/hr$$

$$k_e = \frac{CL}{V_d} = \frac{2.32\,L/hr}{49.67\,L} = 0.047hr^{-1}$$

$$\tau = \frac{\ln\left(\frac{C_{max}}{C_{min}}\right)}{k} = \frac{\ln\left(\frac{30}{10}\right)}{0.047} = 23.4hr \approx 24hr \text{ (1pt)}$$

$$Dose = V_d \cdot C_{max} \cdot (1 - e^{-ke \cdot \tau}) = 49.67 \cdot 30 \cdot (1 - e^{-0.047 \cdot 24}) = 1g \text{ (1pt)}$$

1g q24h