PHA 5128

Case Study III
Spring 2006

1. A 3 month old infant, born at full- term gestational age, is admitted to Shands Hospital for possible pneumonia. The infant weighs 3.5 kg. Ampicillin 175 mg iv q6h and tobramycin 5 mg iv q8h (30 min infusion) is started and administered at 6 am, 2 pm and 10 pm. On day 3 of therapy, tobramycin serum concentrations are drawn as listed below:

   Tobramycin peak serum conc. 7.3 μg/ml drawn at 7 am on 4/23.
   Tobramycin trough serum conc. 2.1 μg/ml drawn at 1:30 on 4/23.

   Determine the estimated k_e, $t_{1/2}$, C_{max}, C_{min} and Vd of tobramycin in this patient.

$$k = \frac{\ln \frac{7.3}{2.1}}{6.5} = 0.192h^{-1}$$

$$t_{1/2} = \frac{0.693}{k} = 3.6h$$

$$C_{\max} = \frac{7.3}{e^{-0.192 \cdot 0.5}} = 8.04 \mu g / mL$$

$$C_{\min} = 2.1 \cdot e^{-0.192 \cdot 0.5} = 1.91\ \mu g / mL$$

$$Vd = \frac{5}{0.192 \cdot 0.5} \cdot \frac{\left(1 - e^{-0.192 \cdot 0.5}\right)}{\left(8.04 - 1.91 \cdot e^{-0.192 \cdot 0.5}\right)} = 52.08 \cdot \frac{0.092}{6.3} = 0.76L$$

2. Based on the data from #1, calculate the dose and dosage schedule necessary to achieve a peak serum tobramycin concentration of at least 10 μg/ml.

$$\tau = \frac{\ln\left(\frac{10}{1}\right)}{0.192} + 0.5 = 11.99h\ (12h)$$

$$D = 10 \cdot 0.192 \cdot 0.76 \cdot 0.5 \cdot \frac{\left(1 - e^{-0.192 \cdot 12}\right)}{\left(1 - e^{-0.192 \cdot 0.5}\right)} = 0.73 \cdot \frac{0.9}{0.092} = 7.14mg \Rightarrow 7mg\ q12h$$

3. C. Y. is a 69 year old male who is being treated for a post surgical wound infection (gram negative) with gentamicin for a 21 day course of antibiotics. He is currently on day seven of gentamicin. He is 5’4”tall and weighs 172 lbs and has been experiencing a decline in his urine output for the last 24 hours. His SCr prior to antibiotic therapy was 0.9 mg/dL. But currently, his SCr increased to 1.3 mg/dL. You suspect that his renal function may be declining due to this aminoglycosides. It is known that gentamicin is eliminated almost entirely by the renal route, so creatinine clearance can be used as an estimate for gentamicin clearance. Calculate the new clearance.

   Your patient weight is given in pounds, so you must convert to kilograms: 172/2.2=78

   Now we must determine if the patient is within 20% of his IBW:

   IBW=50 + 2.3(height in inches > 60 in)=50 + 2.3(4)=59.2

   Since the patient is obese, we use the ABW for the CL calculation:

   ABW=IBW + 0.4(TBW-IBW)=59.2 + 0.4(18.8)=66.72

   $\rightarrow$ 1.3 mg/dL $\rightarrow$ $CL_{cr} = \frac{(140-69)\cdot 66.72}{72\cdot 1.3} = 50.61 mL/\min$

4. A 5’ 6”, 40 year-old female patient (55 kg, SeCr 0.8 mg/dL) is treated with 100 mg gentamicin TID infused over 30 minutes. Assuming normal pharmacokinetics (Vd = 0.25 L/kg, CL=CLcr), predict the measured peak concentration one hour after the infusion was started and the measured trough concentration one half-hour before the next infusion at steady state.

   IBW for this patient is 45 + 2.3·6 = 58.8, so the patient is within normal limits of IBW. Therefore, we can use TBW in the CLcr calculation.

$$CL_{Cr} = .85\frac{(140-40)\cdot 55}{72\cdot 0.8} = 81.2mL/\min = 4.9L/h$$

$$k = \frac{CL}{V_d} = \frac{4.9}{13.75} = 0.36h^{-1}$$

$$C_{\max} = \frac{100}{4.9\cdot 0.5}\cdot\frac{\left(1-e^{-0.36\cdot 0.5}\right)}{(1-e^{-0.36\cdot 8})} = \frac{16.47}{2.31} = 7.12\mu g/mL$$

$$C_{\min} = 7.12\cdot e^{-0.36\cdot 7.5} = 0.48\mu g/mL$$

$$C^*_{\max} = C_{\max}\cdot e^{-0.36\cdot 0.5} = 7.12\cdot e^{-0.36\cdot 0.5} = 5.95\mu g/mL$$

$$C^*_{\min} = C_{\max}\cdot e^{-0.36\cdot 7} = 0.57\mu g/mL$$

5. K. T., a 62-year old, 60-kg, non-obese woman with a serum creatinine of 1.2 mg/dL, has been started on 500 mg of vancomycin every 12 hours for the treatment of staphylococcal infection. What are the expected peak and trough vancomycin concentrations for her at steady state?

Vd = 0.17(62)+0.22(60)+15=10.54+13.2+15=38.74 L

CL ≅ Cl_{cr} ≅ $0.85 \cdot \frac{(140-62)(60)}{72 \cdot 1.2}$ = 46.04 mL/min =2.76 L/h

Ke = CL/Vd =2.76/38.74=0.071 h^{-1}

$$C_{ss\,\max} = \frac{\frac{S \cdot F \cdot Dose}{Vd}}{1-e^{-k \cdot \tau}} = \frac{\frac{(1)(1)(500)}{(38.74)}}{1-e^{-0.071 \cdot 12}} = 22.5 mg/L$$

$$C_{ss\,\min} = Css\max \cdot e^{-k \cdot \tau} = 29.78 \cdot e^{-0.071 \cdot 12} = 9.6 mg/L$$