

Case Study 3
2/16/2007

1. JM is a 50-year-old male with gram-negative infection. He is started on 180 mg gentamicin every 8 hours. At steady state his measured peak and trough concentrations are 9.4 µg/ml and 1.2 µg/ml respectively. Calculate his true peak and trough concentrations assuming that the measured peak concentration is taken 30 minutes after the end of a 30 minute i.v. infusion and the measured trough concentration is taken 30 minutes before the start of the next dose.

$$k_e = \ln(C_1/C_2)/(\Delta t) = \ln(9.4/1.2)/(8-1-0.5) = 0.317 \text{ hour}^{-1}$$

$$C = C_0 * e^{-k_e * t} \quad C_{\max \text{ True}} = C_{\max} / e^{-k_e * t} \quad C_{\max \text{ True}} = 9.4 / e^{-0.317 * 0.5} = 11.01 \mu\text{g/ml}$$

$$C_{\min \text{ True}} = C_{\min} * e^{-k_e * t} \quad C_{\min \text{ True}} = 1.2 * e^{-0.317 * 0.5} = 1.02 \mu\text{g/ml}$$

2. Why is it necessary to take the peak concentration of gentamicin 1 hour after the start of infusion? What is the impact on the elimination rate constant and half-life? How can this effect the safety for the drug?

Gentamicin, along with the other aminoglycosides, undergoes a distribution phase after administration. This means that it takes time for the drug to distribute to the tissues. If the peak concentration were taken immediately after the infusion the elimination rate constant calculated would be too high and the half-life would be shorter than it actually is. This can lead to an erroneous interpretation and underestimate the risk or potential toxicity.

3. Why can we use the i.v. bolus equation to calculate the true C_{\max} and C_{\min} .

Once the drug reaches the elimination phase (the beta phase) the elimination rate is constant. The clinical C_{\max} and C_{\min} obtained will be on a straight line when plotting the natural log concentration vs. time profile. This is similar to what occurs in a one compartment body model with i.v. bolus injection.

4. TL is a 55 year old male who was admitted for a soft tissue infection in his abdomen. He is 5'7", 210 lbs with a serum creatinine of 0.9 mg/dL . Wound cultures are positive for Klebsiella pneumoniae. Design a dosing regimen if the target peak and trough concentrations are 7µg/ml and 1µg/ml and Gentamicin is to be given as a 0.5 hr infusion.

$$\text{Ideal Body Weight (IBW)} = 50\text{kg} + 2.3 * 7 = 66.1\text{kg}$$

$$\text{Total body weight (TBW)} = 210\text{lbs} / (2.2\text{lbs/kg}) = 95.45 \text{ kg}$$

$$95.45 \text{ (TBW)} > (66.1 * 0.2 + 66.1)$$

$$\text{Need to use Adjusted Body Weight (ABW)} = 66.1 \text{ kg} + 0.4(95.45 - 66.1) = 77.84 \text{ kg}$$

$$Cl_{cr} = (140 - \text{age}) * \text{weight} / (72 * C_{p \text{ creat}}) = (140 - 55) * 77.84\text{kg} / (72 * 0.9) = 102.11 \text{ ml/min}$$

Two ways to find k_e :

$$k_e = 0.00293 * 102.11 + 0.014 = 0.313 \text{ hr}^{-1}$$

$$k_e = Cl/Vd = 102.11 \text{ ml/min} * 60(\text{min/hr}) / 1000(\text{ml/L}) / (0.25 * 77.84 \text{ kg}) = 0.315 \text{ hr}^{-1}$$

$$\tau = \ln(C_{\text{maxtrue}}/C_{\text{mintrue}}) / k_e + T = \ln(7/1) / 0.313 + 0.5 = 6.716 \sim 6 \text{ hours}$$

$$\text{or } \tau = \ln(7/1) / 0.315 + 0.5 = 6.677 \sim 6 \text{ hours}$$

$$\text{Dose} = C_{\text{maxtrue}} * k_e * Vd * T * ((1 - e^{-k_e \tau}) / (1 - e^{-k_e T})) = 7 * 0.313 * 19.46 * 0.5 * (1 - e^{-0.313 * 6}) / (1 - e^{-0.313 * 0.5}) = 124.66 \sim 125 \text{ mg}$$

$$\text{Or Dose} = 7 * 0.315 * 19.46 * 0.5 * (1 - e^{-0.315 * 6}) / (1 - e^{-0.315 * 0.5}) = 124.99 \sim 125 \text{ mg}$$

Dose 125 mg every 6 hours of gentamicin as a 0.5 hour i.v. infusion

5. FW is a 60 year old male admitted to the Shands hospital with a probable urosepsis in need of parenteral tobramycin. A dose of 450 mg q36h is administered as a one-hour infusion (from 8-9am). Following the third dose of this regimen the tobramycin concentrations were determined as 16 µg/mL (11am) and 6 µg/mL (11pm).

What would the concentration be before the next dose if it were taken 0.5 hr before the start of the next infusion?

$$k_e = \ln(C_1/C_2) / \Delta t = \ln(16/6) / 12 = 0.082 \text{ hr}^{-1}$$

$$C = C_0 * e^{-k_e * t} = 6.0 * e^{-0.082 * 20.5} = 1.12 \text{ µg/mL}$$

Where did 20.5 hours come from? If the first dose is given at 8 AM on day 1. The second dose is given at 8 PM on day 2 and the third dose is given at 8 AM on day 4. So at 11 pm following the third dose at 8 AM we have 21 hours till the next dose. We want to sample 0.5 hour before the next dose is given. Therefore we can use 6 µg/mL as the starting concentration and 20.5 as the time the drug is being eliminated (t).