# Case Study 5 Answers
# PHA 5127
# Fall 2005

A. M. is a 60 year old, 70 kg female patient admitted to the emergency room with severe pneumonia. As treatment, her doctor orders that she be administered 200mg of bacqilmycin by I.V. bolus every 8 hours for one week. Baqilmycin is a novel aminoglycoside that is solely eliminated through by the kidneys. Its clearance can be estimated as being equal to creatinine clearance. The volume of distribution for Baqilmycin is 1.114L/kg. A. M.'s $Cp_{creat}$ is 0.588mg/dl.

1. What is the initial drug concentration after the first dose?

To calculate the initial drug concentration lets use this equation:

$$C_0 = \frac{D}{Vd}$$

We know the dose is 200mg and we are told that the Vd for Baqilmycin is 1.114 L/kg. To calculate the Vd for A.M. we just multiply her mass (70kg) by the 1.114 L/kg and obtain a Vd for A.M.:

$$Vd = 70kg \cdot 1.114L/kg = 78L$$

Now to calculate the initial concentration, divide the dose by A.M.'s volume of distribution:

$$C_0 = \frac{200mg}{78L} = 2.56mg/L$$

2. What would the drug concentration be 20 hours into the dosing regimen?

To determine what the concentration will be 20 hours into the dosing regimen lets first calculate the $k_e$.

$$k_e = \frac{Cl}{Vd}$$

We know the Vd is 78L, and the Cl should be equal to the creatinine clearance. We are given that A.M. is a 60 year old 70 kg female with a $Cp_{creat}$ is 0.588mg/dl. With this information we can calculate her creatinine clearance, which should be equal to her Cl.

$$CL_{creat}(female) = \frac{(140 - age) \cdot weight}{85 \cdot Cp_{creat}} = \frac{(140 - 60) \cdot 70}{85 \cdot 0.588} = 112ml/\min = CL_{baqilmicin}$$

Since the Vd is in L and our time unit is in hours lets convert the Cl to L/hr

$$\frac{112ml}{\min} \cdot \frac{60\min}{1hr} \cdot \frac{1L}{1000ml} = 6.72L/hr$$

Now we can calculate the $k_e$.

$$k_e = \frac{Cl}{Vd} = \frac{6.72L/hr}{78L} = 0.0862hr^{-}$$

Let's now calculate the half-life and determine if A.M. is at steady state conditions at 20 hours into the dosing regimen. (Remember it takes about 5 half-lives to reach steady state)

$$t_{1/2} = \frac{0.693}{k_e} = \frac{0.693}{0.0862hr^{-}} = 8.0hr$$

At 20 hours it has only been 2.5 half-lives, so we can not assume that steady state conditions have been reached. We can use the following equation to determine the concentration at 20 hours. Where n is the number of doses given, D is the dose given each time (200mg), Vd is the volume of distribution (78L), τ is the dosing interval (8hr), and t is the time since the last dose.

$$Cn(t) = \frac{D}{Vd} \cdot \frac{(1 - e^{-nk_e\tau})}{(1 - e^{-k_e\tau})} \cdot e^{-k_e t}$$

We need to calculate n and t.

$$n = 3\,(\text{at 20 h 3 doses have been given, one at time 0;}$$
$$\text{1 at time 8; and a 3rd at time 16 hrs)}$$
$$t = 20hr - (2\ doses\ given \cdot every\ 8\ hrs) = 4hrs\ \ past\ the\ last\ dose$$

So now we can solve for the concentration 20 hours into the dosing regimen.

$$C_{(20)} = \frac{200mg}{78L} \cdot \frac{(1 - e^{-3 \cdot 0.0862hr^{-} \cdot 8hr})}{(1 - e^{-0.0862hr^{-} \cdot 8hr})} \cdot e^{-0.0862hr^{-} \cdot 4hr} = 3.19mg / L$$

3. What are the peak and trough concentrations at steady state?

To calculate the peak steady state concentrations we can use the following equation

$$C_{\max ss} = \frac{D}{Vd} \cdot \frac{1}{(1-e^{-k_e \tau})} = \frac{200mg}{78L} \cdot \frac{1}{(1-e^{-0.0862hr^{-} \cdot 8hr})} = 5.15mg/L$$

For trough concentration we can do this

$$C_{\min ss} = \frac{D}{Vd} \cdot \frac{e^{-k_e \tau}}{(1-e^{-k_e \tau})} = \frac{200mg}{78L} \cdot \frac{e^{-0.0862hr^{-} \cdot 8hr}}{(1-e^{-0.0862hr^{-} \cdot 8hr})} = 2.58mg/L$$

4. Another doctor recommends giving a loading dose to A. M. Calculate a loading dose that will give A. M. the same average concentration at steady state as before.

A simple way to calculate the loading dose is to take the $C_{max\ ss}$ and multiply it by the Vd to give the loading dose.

$$Loading\ \ Dose = C_{\max\ ss} \cdot Vd = 5.15mg / L \cdot 78L \approx 400mg$$

5. What would be the AUC for one dosing interval at steady state?

The AUC for one dosing interval will be equal to the dose divided by the clearance.

$$AUC = \frac{Dose}{CL} = \frac{200mg}{6.72L/hr} = 29.8mg \cdot hr/L$$

6. At steady state, how much drug is eliminated during one dosing interval?

At steady state one dose is eliminated during one dosing interval, so 200mg is eliminated.

7. Are the following statements true or false regarding an i.v. bolus multiple dosing regimen.

| | | |
|---|---|---|
| T | **F** | The accumulation is increased in patients with increased clearance. |
| T | **F** | The larger the Vd the lower the average steady state concentration. |
| T | **F** | The longer the half-life the more pronounced the differences between peak and trough concentrations. |
| T | **F** | The time to reach steady state depends on the dosing interval. |