2.5. Aminoglycoside Antibiotics

Solutions

Videos that might be helpful in reviewing concepts can be found at https://www.youtube.com/user/murphyassessment.

1. To use the following equations, the concentrations must be assumed to be at steady state, so that the trough 0.5 hours before the 10 a.m. dose could be expected to be the same as the trough at 9:30 p.m.

   Determine k and half-life.

$$k = \frac{\ln\left(\frac{C_i}{C}\right)}{t_\Delta} = \frac{\ln\left(\frac{6.1\,mg/L}{1.1\,mg/L}\right)}{10.5\,h} = 0.163\ hours^{-1}$$

$$t½ = \frac{0.693}{k} = \frac{0.693}{0.163\,h^{-1}} = \mathbf{4.2\ hours}$$

   Determine V.

$$C = \left(\frac{S \times D}{k \times V \times t'}\right)\left(\frac{(1-e^{-kt'})}{(1-e^{-k\tau})}\right)\left(e^{-kT}\right)$$

   So,

$$V = \left(\frac{S \times D}{k \times C \times t'}\right)\left(\frac{(1-e^{-kt'})}{(1-e^{-k\tau})}\right)\left(e^{-kT}\right)$$

$$V = \left(\frac{1 \times 140\ mg}{0.163\,hr^{-1} \times 6.1\,mg/L \times 0.5\,hr}\right)\left(\frac{(1-e^{-(0.163\,hr^{-1})(0.5\,hr)})}{(1-e^{-(0.163\,hr^{-1})(12\,hr)})}\right)\left(e^{-(0.163\,hr^{-1})(0.5\,hr)}\right)$$

$$= 23.7\ L$$

1. (continued)

$$V = \frac{23.7\ L}{85\ kg}$$

$$= \mathbf{0.28\ L/kg}$$

2. Determine volume of distribution.

As the patient is < 20% above IBW, ABW is used. Volume of distribution is then determined by multiplying the weight-related volume of distribution (0.3 L/kg) times the ABW:

$$V\ (L) = 0.3\ L/kg \times 75\ kg = 22.5\ L$$

Determine the elimination rate constant (k) and half-life.

The estimated creatinine clearance for this 50-year-old female patient was reported to be 60 mL/min.

Estimating k by Estimating Aminoglycoside Clearance (CL_{ag}) from Creatinine Clearance

CL_{ag} = CrCl = 60 mL/min

Since CL = k × V

$$k = \frac{CL}{V}$$

Thus,

$$k\ (hr^{-1}) = \frac{[(60\ mL/min) \times (60\ min/hr \times 1\ L/1000\ mL)]}{22.5\ L}$$

$$= 0.160\ hours^{-1}$$

and

$$t½ = \frac{0.693}{0.16\ hr^{-1}} = 4.3\ hours$$

Estimating the Peak and Trough Concentrations Using the Population Estimates

Use **Equation 10*** and remember that peaks are drawn 0.5 hours after a 0.5-hour infusion and troughs 0.5 hours before a dose.

$$C = \left(\frac{S \times D}{k \times V \times t'}\right)\left(\frac{(1-e^{-kt'})}{(1-e^{-k\tau})}\right)\left(e^{-kT}\right)$$

$$\text{Peak} = \left(\frac{1 \times 160\ mg}{0.16\ hr^{-1} \times 22.5\ L \times 0.5\ hr}\right)\left(\frac{(1-e^{-(0.16\ hr^{-1})(0.5\ hr)})}{(1-e^{-(0.16\ hr^{-1})(12\ hr)})}\right)\left(e^{-(0.16\ hr^{-1})(0.5\ hr)}\right)$$

$$= \mathbf{7.39\ mg/L}$$

$$\text{Trough} = \left(\frac{1 \times 160\ mg}{0.16\ hr^{-1} \times 22.5\ L \times 0.5\ hr}\right)\left(\frac{(1-e^{-(0.16\ hr^{-1})(0.5\ hr)})}{(1-e^{-(0.16\ hr^{-1})(12\ hr)})}\right)\left(e^{-(0.16\ hr^{-1})(11\ hr)}\right)$$

$$= \mathbf{1.37\ mg/L}$$

Note: Rather than solving for trough as above, equation $C = C_i \times e^{-kt}$ may be used with C_i = predicted peak and t = 10.5 hr.

* Equation 10 and other numbered equations in this chapter can be found in ***Select Pharmacokinetic Equations***, p xix.