Case Studies #3
Answers
Spring 2005

1. B.F. is a 5’ 4”, 72 kg, 30 year old female who suffered a severe burn that has since been infected by S. aureus. Her $C_p^{\text{crea}}$ is measured at 0.6 mg/dL. Design a dosing regimen of half-hour i.v. infusions of gentamicin that will give her a true $C_{\text{max}}$ of 7.5µg/ml and a true trough concentration of 0.5µg/ml.

First calculate $\tau$, but in order to calculate $\tau$ you will need $k_e$, and for $k_e$ you will need to know $\text{Cl}_{\text{crea}}$ and her ideal body weight.

IBW = 45.5 + 4*2.3 = 54.7kg

$\text{Cl}_{\text{crea}} = (140 - 30)*54.7 = 118\text{ml/min} \text{ or } 7.1 \text{ L/hr}$

$k_e = .00293 (118) + 0.014 = 0.36 \text{ h}^{-1}$ or $k_e = \text{Cl}/\text{V} = 7.1/15.4(\text{from below}) = .46 \text{ h}^{-1}$

$\tau = \ln \left( \frac{7.5}{0.5} \right) = 7.52 \text{ hr} \sim 8 \text{ hrs or } 5.88-6 \text{ hours if } .46 \text{ is used as } k_e$

In order to calculate the dose you will first need to estimate the $V_d$, for this you will need the dosing weight.

Dosing weight = 54.7kg + 0.4(72kg-54.7kg) = 61.6 kg

$V_d = 0.25 \ (61.6) = 15.4 \text{ L}$

$D = 7.5 * (0.36) * 15.4 * (0.5) * \left( \frac{1- e^{(-0.36*8)}}{1- e^{(-0.36*0.5)}} \right) = 119 \sim 120 \text{mg every 8 hours}$

or

$D = 7.5 * (0.46) * 15.4 * (0.5) * \left( \frac{1- e^{(-0.46*6)}}{1- e^{(-0.46*0.5)}} \right) = 121.1 \sim 120 \text{mg every 6 hours}$

2. B.F. is given the infusion you recommended at 8:00 am. At 9:00 am a plasma sample is taken and yields a $C_p^{\text{*max}}$ of 9.2 µg/ml. Another sample is taken one half hour before the next infusion to give a $C_p^{\text{*min}}$ of 2.4µg/ml. Calculate the actual $k_e$ and $V_d$ for B.F. and recommend a dosing change to give a true $C_{\text{max}}$ of 7.5µg/m. What is the new true $C_{\text{min}}$ expected with this dosing change.
First calculate the $ke$

$$ke = \ln \left( \frac{9.2}{2.4} \right) = \frac{1.34}{6.5 \text{hrs}} = 0.21 \text{ h}^{-1}$$

(15:30-9:00)

or

$$ke = \ln \left( \frac{9.2}{2.4} \right) = \frac{1.34}{4.5 \text{hrs}} = 0.30 \text{ h}^{-1}$$

(13:30-9:00)

Next in order to calculate the $Vd$ you must calculate the true $C_{\text{max}}$ and $C_{\text{min}}$

$$C_{\text{max}} = \frac{9.2}{e^{-0.21 \times 0.5}} = 10.2 \mu \text{g/ml for an 8h } \tau \text{ or with a 6h } \tau 10.7 \text{ mg/ml}$$

$$C_{\text{min}} = 2.4 \times e^{-0.21 \times 0.5} = 2.1 \mu \text{g/ml for an 8h } \tau \text{ or with a 6 hr } \tau 2.1 \text{ mg/ml}$$

Now you can calculate a $Vd$

$$Vd = \frac{120}{(0.21 \times 0.5)} \times \left( \frac{1 - e^{-0.21 \times 0.5}}{10.2 - 2.1 e^{-0.21 \times 0.5}} \right) = 13.7 \text{L}$$

or with a 6 h $\tau$

$$Vd = \frac{120}{(0.30 \times 0.5)} \times \left( \frac{1 - e^{-0.30 \times 0.5}}{10.7 - 2.1 e^{-0.30 \times 0.5}} \right) = 12.5 \text{L}$$

Now you can calculate the new dose.

$$D = 7.5 \times 0.21 \times 13.7 \times 0.5 \times \left( \frac{1 - e^{-0.21 \times 8}}{1 - e^{-0.21 \times 0.5}} \right) = 88 \text{ mg} \sim 90 \text{mg}$$

or with a 6 hr $\tau$

$$D = 7.5 \times 0.30 \times 12.5 \times 0.5 \times \left( \frac{1 - e^{-0.30 \times 6}}{1 - e^{-0.30 \times 0.5}} \right) = 84.3 \text{ mg} \sim 85 \text{mg}$$

Now for your new $C_{\text{min}}$

$$C_{\text{min}} = 7.5 \times e^{-0.21 \times (8 - 0.5)} = 1.6 \mu \text{g/ml}$$

or with a 6 hr $\tau$

$$C_{\text{min}} = 7.5 \times e^{-0.3 \times (6 - 0.5)} = 1.4 \mu \text{g/ml}$$
3. I.P. is admitted to the hospital after a major auto accident. At admission he weighed 71kg, and is 5’9”. The day following surgery I.P. weighs 76kg and is suffering from an infection. At 10:00 am he is given a half an hour infusion of 350mg of amikacin.
   a. Predict his volume of distribution.
   b. What will his plasma concentration be at 3:00pm if his creatinine clearance is 7.2 L/hr or 120ml/min?

   a. First calculate his ideal body weight.

   \[
   \text{IBW} = 50 + 2.3 \times 9 = 70.7 \text{ kg} \approx 71 \text{ kg}
   \]

   \[
   \text{ESF} = 76 - 71 = 5 \text{ L}
   \]

   Now for Vd

   \[
   Vd = 0.25 (71) + 5 = 22.8 \text{ L}
   \]

   b. Now for \( C_{\text{min}} \) @ 3:00 you must first calculate \( C_{\text{max}} \). But first You need the \( k_e \).

   \[
   k_e = \frac{7.2}{22.8} = 0.32 \text{ hr}^{-1} \quad \text{or} \quad k_e = 0.00293 (120) + 0.014 = 0.37
   \]

   \[
   C_{\text{max}} = \frac{350}{7.2 \times 0.5} \times (1 - e^{-0.32 \times 0.5}) = 14.4 \text{ mg/L} \quad \text{or} \quad \text{if } k_e = 0.37 \quad C_{\text{max}} = 16.4 \text{ mg/ml}
   \]

   For \( C_{\text{min}} \),

   \[
   C_{\text{min}} = 14.4 \times e^{-0.32 \times 4.5} = 2.9 \text{ mg/L} \quad \text{or} \quad \text{if } k_e = 0.37 \quad C_{\text{min}} = 2.6 \text{ mg/L}
   \]
4. G.W., a 30 year old, 50kg man, is receiving 70 mg of tobramycin infused IV over a 30 minute period every 8 hours. His serum creatinine has increased from 1mg/dl to 2mg/dl over the past 24 hours. Because his renal function appears to be decreasing, three plasma samples were obtained to monitor serum gentamicin concentrations as follows: just before a dose, 1 hour after the end of the infusion, and at the end of the dosing interval (two troughs and one peak level. The serum gentamicin concentrations at these times were 4mg/L, 8mg/L, and 5mg/L. Calculate the volume of distribution, elimination rate constant and clearance of tobramycin for G.W.

First calculate the ke from the 2 concentrations during the elimination phase,

\[ ke = \frac{\ln(8/5) }{6.5} = 0.072 \]  this corresponds to a half life of 9.63 hours suggesting that little drug is lost during the infusion, so we can treat as a bolus dose.

To calculate the Vd we first need the Cmax.

\[ C_{\text{max}} = \frac{8}{e^{-0.072*1}} = 7.44 \text{ mg/L} \]

Now for the Vd, use the trough value that is measured just before the peak.

\[ Vd = \frac{70}{8.6-4} = 15.2 \text{ L} \quad \text{or} \quad Vd = \frac{70}{0.072*0.5} \left(1 - e^{-0.072*0.5}\right) = 14.5 \text{ L} \]

The Vd and ke can now be used to calculate the Cl,

\[ Cl = 0.072 \times 15.2 = 1.09 \text{ L/h} \quad \text{or} \quad 0.072 \times 14.6 = 1.04 \text{ L/h} \]

5. H.K., 55 year old, 55kg woman with a serum creatinine of 1.0mg/dl, has been empirically started on 500mg of vancomycin every 8 hours for treatment of a staphylococcal infection. What are the expected peak and trough vancomycin concentrations for H.K.

First, the Vd, Cl and ke must be calculated.

For the Vd,

\[ Vd = 0.17(55 \text{ years}) + 0.22 (55 \text{ kg}) + 15 = 36.5 \text{ L} \]

Creatinine clearance can be used to estimate her Cl

\[ Cl_{\text{creat}} = \frac{(140-55)*55}{55} = 55.0 \text{ ml/min} = 3.3 \text{ L/h} \sim Cl \]
Now $k_e$ can be determined

$$K_e = \frac{3.31}{36.5} = 0.091 \text{ h}^{-1}$$

Now you can determine peak and trough concentrations

$$C_{ss \ max} = \frac{500/36.5}{1 - e^{-0.091 \times 8}} = 26.5 \text{ mg/L}$$

$$C_{ss \ min} = 26.5e^{-0.091 \times 8} = 12.8 \text{ mg/L}$$