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 Cp_{creat} 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_{max} of 7.5μg/ml and a true trough concentration of 0.5μg/ml.

First calculate τ, but in order to calculate τ you will need k_e, and for k_e you will need to know Cl_{creat} and her ideal body weight.

IBW = 45.5 + 4*2.3 = 54.7kg

$$Cl_{creat} = \frac{(140 - 30)*54.7}{85*0.6} = 118 \text{ml/min or } 7.1 \text{ L/hr}$$

ke = .00293 (118) + 0.014 = 0.36 h^{-} or ke =Cl/ V = 7.1/15.4(from below) = .46 h^{-}

$$\tau = \frac{\ln(7.5/0.5)}{0.36} = 7.52 \text{ hr} \sim 8 \text{ hrs or } 5.88 \sim 6 \text{ hours if .46 is used as ke}$$

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

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

Vd = 0.25 (61.6) = 15.4 L

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

or

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

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 Cp^*_{max} of 9.2 μg/ml. Another sample is taken one half hour before the next infusion to give a Cp^*_{min} of 2.4μg/ml. Calculate the actual ke and Vd for B.F. and recommend a dosing change to give a true C_{max} of 7.5μg/m. What is the new true C_{min} expected with this dosing change.

First calculate the ke

$$ke = \frac{\ln(9.2/2.4)}{(15{:}30 - 9{:}00)} = 1.34/6.5\text{hrs} = 0.21\ h^{-}$$

$$\text{or } ke = \frac{\ln(9.2/2.4)}{(13{:}30 - 9{:}00)} = 1.34/4.5\text{hrs} = 0.30\ h^{-}$$

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

$C_{max} = 9.2/e^{-0.21*0.5} = 10.2$ μg/ml for an 8h τ or with a 6h τ 10.7 mg/ml
$C_{min} = 2.4 * e^{-0.21*0.5} = 2.1$ μg/ml for an 8h τ or with a 6 hr τ 2.1 mg/ml

Now you can calculate a Vd

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

or with a 6 h τ

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

Now you can calculate the new dose.

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

or wih a 6 hr τ

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

Now for your new Cmin

$C_{min} = 7.5 * e^{-0.21*(8 - 0.5)} = 1.6$ μg/ml

or wih a 6 hr τ

$C_{min} = 7.5 * e^{-0.3*(6- 0.5)} = 1.4$ μg/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.

IBW = 50 + 2.3 * 9 = 70.7 kg ~71 kg

ESF = 76 – 71 = 5 L

Now for Vd

Vd = 0.25 (71) + 5 = 22.8 L

b. Now for C_{min} @ 3:00 you must first calculate C_{max}. But first You need the ke.

ke = 7.2/22.8 = 0.32 hr^{-} or ke = 0.00293(120) + 0.014 = 0.37

$$Cmax = \frac{350}{7.2*0.5} * (1 - e^{-0.32*0.5}) = 14.4 \text{ mg/L}$$ or if ke = 0.37 Cmax = 16.4mg/ml

For Cmin,

Cmin = 14.4 $e^{-0.32*4.5}$ = 2.9 mg/L or if ke = 0.37 Cmin = 2.6 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,

$ke = (\ln(8/5))/6.5 = 0.072$ 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.

$Cmax = 8/(e^{-.072*1}) = 7.44$ mg/L

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

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

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

Cl = 0.072 * 15.2 = 1.09 L/h or .072* 14.6 = 1.04 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 years) + 0.22 (55 kg) + 15 = 36.5 L

Creatinine clearance can be used to estimate her Cl

Clcreat = $\underline{(140-55)*55}$ = 55.0 ml/min = 3.3 L/h ~Cl

85*1.0

Now ke can be determined

Ke = 3.31/36.5 = 0.091 h^{-}

Now you can determine peak and trough concentrations

$$Css\ max = \frac{(500/36.5)}{(1 - e^{-0.091*8})} = 26.5 mg/L$$

Css min = 26.5e $^{-0.091*8}$ = 12.8 mg/L