Spring 2003

PHA 5128

Case Study III (Answers)

1. S.T., a 32-year-old, 64 kg female with a serum creatinine of 0.9 mg/dL is to be given tobramycin. Calculate a maintenance dose which will produce a "peak" concentration of 7 mg/L one hour after the half-hour infusion has been started, and a trough concentration of 1 mg/L. Assume that the tobramycin will be administered as a one-`half hour infusion. If S.T. was to be given tobramycin 5 mg/kg QD, what would be the calculated steady-state peak concentration one hour after starting the half-hour infusion? Also predict subsequent steady-state plasma concentration 12 hours after starting the infusion and at the trough.

$$CL_{CR} = \frac{(140-32)\cdot 64}{85\cdot 0.9} = 90mL/\min = 5.42L/h$$

$V_d = 0.25\cdot 64 = 16$ L

$k = 0.339\ h^{-1}$

$$C_{\max} = \frac{7}{e^{-0.339\cdot 0.5}} = 8.3\mu g/mL$$

$$\tau = \frac{\ln 8.3}{0.339} + 0.5 = 6.7h \rightarrow 8h$$

$$D = 8.3\cdot 0.339\cdot 16\cdot 0.5\cdot \frac{(1-e^{-0.339\cdot 8})}{(1-e^{-0.339\cdot 0.5})} = 22.5\cdot \frac{0.9336}{0.1559} = 135mg$$

<u>5mg/kg QD</u>

$$C_{\max} = \frac{320}{5.42\cdot 0.5}\cdot \frac{(1-e^{-0.339\cdot 0.5})}{(1-e^{-0.339\cdot 24})} = 118.1\cdot \frac{0.1559}{0.9997} = 18.4$$

measured peak:

$$C^*_{\max} = 18.4\cdot e^{-0.339\cdot 0.5} = 15.5\mu g/mL$$

$C_{12h} = 18.4\cdot e^{-0.339\cdot 11.5} = 0.37$ μg/mL

$C_{24h} = 18.4\cdot e^{-0.339\cdot 23.5} = 0.006$ μg/mL (undetectable)

2. L.F., a 28-year-old, 75 kg male, is receiving 100 mg of tobramycin infused IV over 30 minute period q8h. His serum creatinine has increased from 1 mg/dL to 1.8 mg/dL over the past 24 hours. Since his renal function appears to be decreasing, three plasma samples were obtained to monitor serum gentamicin concentrations as follows: just before a dose; one hour after that same dose; and eight hours after that dose (two troughs and one peak level). The serum tobramycin concentrations at these times were 4 mg/L, 8 mg/L, and 5 mg/L, respectively. Calculate the volume of distribution, elimination rate constant, and clearance of tobramycin for L.F. Also, using the pharmacokinetic parameters calculated for L.F. above, develop a dosing regimen that will produce reasonable peak (10 mg/L) and trough (1 mg/L)concentrations of tobramycin.

$$k = \frac{\ln\left(\frac{8}{5}\right)}{7} = 0.067h^{-1} \qquad C_{\max} = \frac{8}{e^{-0.067\cdot 0.5}} = 8.3\ mg/L$$

$$t_{1/2} = \frac{0.693}{0.067} = 10.3h$$

$$V_d = \frac{100}{0.067\cdot 0.5}\cdot\frac{\left(1-e^{-0.067\cdot 0.5}\right)}{\left(8.3-4\cdot e^{-0.067\cdot 0.5}\right)} = 2985\cdot\frac{0.033}{4.43} = 22.2L$$

↑pre-dose level

$$Cl = k\cdot V_d = 0.067\cdot 22.2 = 1.49L/h$$
$$= 25\text{ mL/min}$$

True Peak = 10 *mg/L*

$$\tau = \frac{\ln\frac{10}{1}}{0.067} + 0.5 = 34.8 \rightarrow 36h$$

$$D = 10\cdot 0.067\cdot 22.2\cdot 0.5\cdot\frac{\left(1-e^{-0.067\cdot 36}\right)}{\left(1-e^{-0.067\cdot 0.5}\right)}$$

$$= 7.44\cdot\frac{0.91}{0.033} = 205mg \Rightarrow 200\text{mg q36h}$$

Measured Peak = 10 *mg/L*

$$\tau = \frac{\ln\frac{10}{1}}{0.067} + 1.5 = 35.8 \rightarrow 36h$$

$$C_{\max} = \frac{10}{e^{-0.067\cdot 0.5}} = 10.3mg/L$$

No difference

3. A patient was given 80 mg gentamicin over 30 minutes (i.v.) from 9:30 to 10:00 am. The following two serum levels were measured: 6.5 µg/ml at 10:30 am and 1.2 µg/ml at 5:00 pm. Calculate:

a. the elimination rate constant k

$$k = \frac{\ln \frac{6.5}{1.2}}{6.5} = 0.26h^{-1}$$

b. the elimination half-life

$$t_{1/2} = \frac{0.693}{0.26} = 2.7h$$

c. the peak concentration at 10:00 am

$$C_{\max} = \frac{65.}{e^{-0.26 \cdot 0.5}} = 7.4\mu g / mL$$

d. the trough concentration at 5:30 pm

$$C_{\min} = 1.2 \cdot e^{-0.26 \cdot 0.5} = 1.1\mu g / mL$$

e. the volume of distribution

$$V_d = \frac{80}{0.26 \cdot 0.5} \cdot \frac{(1 - e^{-0.26 \cdot 0.5})}{(7.4 - 1.1 \cdot e^{-0.26 \cdot 0.5})} = 615.4 \cdot \frac{0.122}{6.434} = 11.7L$$

f. the clearance

$$CL = 0.26 \cdot 11.7 = 3.0L / h \; or \; 51\, mL / \min$$

4. A patient is admitted with an acute theophylline overdose. A serum level is measured at 45 µg/ml. Assuming an 8 hour half-life and no further drug absorption, how long dose it take for the serum level to drop to the upper limit of the therapeutic range (20 µg/ml)?

$$k = \frac{0.693}{8} = 0.087h^{-1}$$

$$20 = 45 \cdot e^{-0.087 \cdot t}$$

$$\frac{20}{45} = e^{-0.087 \cdot t}$$

$$\ln(0.44) = -0.087 \cdot t$$

$$-0.811 = -0.087 \cdot t$$

$$\text{t} = 9.3 \text{ h}$$