PHA 5128

Case Study III (Answers)

1. TL is a 25 year old male who was admitted for a soft tissue infection in his abdomen. He is 5'10", 175 Ibs, WBC = 19, and BUN/SCr = 12/1.1. Wound cultures are positive for Klebsiella pneumoniae. You are asked to review is medication records and initiate gentamicin therapy. Complete and initial workup and evaluation (prospective series) on this patient and counsel tile patient on his antibiotic therapy and write and order for the pharmacy to fill.

    1. Recommend a desirable regimen for this patient
    2. List three important physical characteristics you should assess when counseling the patient.
    3. How would you write (wording) the order to for this drug therapy?

    After two days, you review his chart and find that the levels that you requested have been completed and reported as follows:

gentamicin (peak)	6.9 mcg/ml
gentamicin (trough)	0.9 mcg/ml

    Please evaluate (calculate) what his true serum concentrations were using these reported values. Assume that the infusion was 30 minutes, the peak was drawn 30 after the end of the infusion, and that the trough was drawn 30 minutes prior to the next dose (under ideal conditions)

    Would you recommend any changes in the regimen based on these recent laboratory data?

Dosing regimen design:
Age=25 yr; BW=79.5 kg; SCr=1.1 mg/dl; T=30min; C_{peak}(desired)=8 ug/mL, C_{trough}(desired)=1 ug/mL

First, CrCL:

IBW=50+2.3*10=73 kg

$$CL_{cr} = \frac{(140-25)\cdot 73}{72\cdot 1.1} = 106mL/\min = 6.36L/h$$

Then V_d and find k:

V_d=0.25*BW = 0.25*79.5 = 19.9 L

k= CL/V_d=6.36/19.9 = 0.320 h^{-1}

Find Dosing Interval and needed dose:

$$\tau = \frac{\ln(8/1)}{0.320} + 0.5 = 7h \rightarrow 8h$$

$$D = 8 \cdot 0.320 \cdot 19.9 \cdot 0.5 \cdot \frac{(1 - e^{-0.320 \cdot 8})}{(1 - e^{-0.320 \cdot 0.5})} = 25.4 \cdot \frac{0.923}{0.148} = 160mg$$

So the dosing regimen: 160 mg q8h

Patient characteristics:

1) Edema
2) Weight
3) Renal function
4) Age
5) Other meds (penicillin)

Lab data after 2 d therapy: C_{peak} = 6.9 mcg/mL, C_{trough}=0.9 mcg/mL

True C_{peak} and C_{trough}:

$$C_{\max} = \frac{C^*_{\max}}{e^{-k \cdot t^*}} = \frac{6.9}{e^{-0.320 \cdot 0.5}} = 8.1 mcg/ml$$

$$C_{\min} = C^*_{\min} \cdot e^{-k \cdot t^*} = 0.9 \cdot e^{-0.320 \cdot 0.5} = 0.77 mcg/ml$$

From the suggested dosing regimen, true steady-state peak and troughs should be

$$C_{\max} = \frac{160}{0.320 \cdot 19.9 \cdot 0.5} \cdot \frac{(1 - e^{-0.320 \cdot 0.5})}{(1 - e^{-0.320 \cdot 8})} = 50.3 \cdot \frac{0.148}{0.923} = 8.1 mcg/ml$$

$$C_{\min} = 8.1 \cdot e^{-0.320 \cdot 7.5} = 0.74 mcg/mL$$

$t_{1/2}$ based of 2 d data = 2h, $t_{1/2}$ based on CrCL = 2.2 h
little difference in predicted and actual blood values…no need to adjust

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 true 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 mL/min

True Peak = 10 *mg/L*

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

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

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

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 drug 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)?

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

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

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

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

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

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