Spring 2005

Answer
PHA 5128

Homework 5

1. T.M.., a 66-year-old, 72 kg male (SrCr 1.6mg/dL), has been taking 0.25mg of digoxin tablets orally for his CHF, and at 9.00am on the day of admission, a digoxin plasma concentration of 1.1µg/L was measured. He was continued on his outpatient maintenance dose. On the fifth day, just before his morning dose (four doses of digoxin have been administered each day at 9.00am), a second digoxin sample was obtained. Calculate L.P.'s digoxin concentration on the morning of the fifth day. (F = 0.7) (2 points)

$$CL_{Cr} = \frac{(140-66)\cdot 72}{72\cdot 1.6} = 46.25 mL/\min$$

$$CL = 0.33\cdot 72 + 0.9\cdot 46.25 = 65.39 mL/\min \approx 3.9 L/h \approx 93.6 L/day$$

$$Vd = 3.8\cdot 72 + 3.1\cdot 46.25 = 416.98 L \approx 417 L$$

$$k_e = \frac{CL}{Vd} = \frac{93.6}{417} = 0.22 days^{-1}$$

$$C_{\min(sum)} = C_{measured}\cdot e^{-k_e\cdot t_1} + \frac{F\cdot D}{Vd}\cdot\left[e^{-k_e\cdot t_1} + e^{-k_e\cdot t_2} + e^{-k_e\cdot t_3} + e^{-k_e\cdot t_4}\right]$$

$$= 1.1\cdot e^{-0.22\cdot 4 days} + \frac{0.7\cdot 250}{417}\cdot\left[e^{-0.22\cdot 4 days} + e^{-0.22\cdot 3 days} + e^{-0.22\cdot 2 days} + e^{-0.22\cdot 1 day}\right]$$

$$= 0.456 + 0.42\cdot[0.41 + 0.52 + 0.64 + 0.8]$$

= 1.45 µg/L

The students may have used an alternative, but correct, approach to solve this question. If they get $C_{min(sum)}$ = 1.55 µg/L, this is correct as well.

2. P.T, is a 62 year old, 50 kg woman, who has been admitted to the hospital for possible digoxin toxicity. Her serum creatinine level was 3 mg/dL and her dosing regimen at home had been 0.25 mg of digoxin daily for many months. The digoxin plasma concentration on admission was 4 µg/L. How long will it take for the digoxin concentration to fall from 4 µg/L to 2 µg/L? (1 point) Calculate a daily dose that will maintain here digoxin concentration at 2 µg/L. (1 point)

$$Cl_{CR}\ for\ \ females = (0.85)\frac{(140-age)(weight)}{72*SCr} = (0.85)\frac{(140-62)(50)}{72*3} = 15.3ml/\min$$

$$Total\ Cl_{digoxin}(ml/\min)\ for\ \ patients\ with\ CHF = (0.33mg/kg/\min)(weight) + (0.9)*(Cl_{Cr})$$

$$= (0.33)(50) + (0.9)(15.3) = 30.3\ ml/\min = 43.6\ L/day$$

or you can use a more patient-specific approach:

$$Cl = \frac{(S)(F)(Dose/tau)}{Css(ave)} = \frac{(1)(0.7)(250\mu g/day)}{Css(ave)} = 43.75\ L/day$$

$$V_{digoxin}(L) = (3.8L/kg)(weight) + (3.1)(Cl_{Cr}) = (3.8)(50) + (3.1)(15.3) = 237\ L$$

k = Cl/V = (43.75 L/day)/(237 L) = 0.184 day^{-1}

$$t = \frac{\ln(\frac{C_1}{C_2})}{ke} = \frac{\ln(\frac{4}{2})}{0.184\ day^{-1}} = \textbf{3.8 days}$$

$$Ma\text{int}.Dose = \frac{(Cl)(Cssave)(Tau)}{S*F} = \frac{(43.75)(2)(1)}{1*0.7}$$

= **125 µg daily**

Since the question did not specify whether or not the patient has CHF, the student may have used the equation for CL that does not take this into account. If he/she did this, the answers would be:

t = 49.5 hours or 2.08 days
Maint. Dose = 227 µg/day

Please give full credit if they did this.

3. G.H is a 65 y.o. man weighing 76 kg with CHF was admitted on March 25 to the hospital at 15:00 because his condition was worsening. His admission history indicates that he had taken his digoxin tablet (0.25 mg) that morning at the usual time (8:00-9:00), but he forgot to take a tablet on March 24. A plasma sample taken at 17:00 was obtained to see if the symptoms were consistent with non-compliance. A plasma digoxin concentration of 0.8 µg/L and a serum creatinine of 0.7 mg/dL were reported. Based on the population parameters, what concentration would you expect? (2 points)

$$CL_{CR} = \frac{(140-65)*76}{72*0.7} = 113.1\ ml/\min$$

$$CL = 0.33*76 + 0.9*113.1 = 126.87\ ml/\min = 182.7\ L/day$$

$$V_d = 3.8*76 + 3.1*113.1 = 639.4\ L$$

$C_{ave} \approx C_{min}$

$$C_{ave} = \frac{F*D}{Cl*tau} = \frac{0.7*0.25}{182.7*1} = 0.000958\ mg/L$$

= 0.96 µg/L

4. T.P. is a 75 kg, 45 year old man with asthma. Estimate a loading dose of aminophylline that will produce a plasma theophylline concentration of 15 mg/L. (1 point) What aminophylline infusion rate will maintain an average steady state level of 15 mg/L? (1 point)

$$L.D. = \frac{V * Conc}{S * F} = \frac{0.5\ L/kg * 75\ kg * 15\ mg/L}{0.8 * 1}$$ **= 703 mg = approx 700 mg**

CL = 0.04 L/kg/hr * 75 kg = 3 L/hr

$$\text{M.D.} = \frac{Cl * Css(ave) * Tau}{S * F} = \frac{(3L/hr)(15mg/L)(1hr)}{0.8 * 1}$$ = **56.25 mg per hour**

Please note: the answer above is correct if the student used F = 0.8

If the student used F = 0.85, the answer would be:

L.D. = 660 mg

M.D. = 53 mg per hour

5. 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 does it take for the serum level to drop to the upper limit of the therapeutic range (20 µg/ml)? (2 points)

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

$$C = C_0 e^{-k*t}$$

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

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

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

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

t = 9.3 h