PHA 5128

Spring 2006

Case Study 5

1 T.P., a 65-year-old, 72 kg male (SrCr1.5mg/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 third day, just before his morning dose (two doses of digoxin have been administered each day at 9.00am), a second digoxin sample was obtained. Using the expected pharmacokinetic parameters, calculate L.P.'s digoxin concentration on the morning of the third day. (2 pts.)

$Cl_{cr} = \frac{(140-65)\times 72}{72\times 1.5} = 50\text{mL/min}$

Cl = 0.33×72 + 0.9×50 = 68.76 mL/min = 99L/day

Vd = 3.8×72+3.1×50=428.6L

Ke=Cl/Vd=99/428.6 = 0.231day^{-1}

Cestimated = Cmeasured×e^{-ket} + [$e^{-ke\cdot t1}$+$e^{-ke\cdot t2}$]×F×D/Vd

= 1.1×$e^{-0.231\times 2days}$ + [$e^{-0.231\times 2days}$ + $e^{-0.231\times 1days}$]×0.7×250/428.6

=0.693 + [0.63+0.794] ×0.41

=1.28μg/L

2. CK is a 23 year old 48 Kg female admitted to the ER for the exacerbation of her asthma caused by excessive exercise. Estimate an IV loading dose and an IV infusion rate of aminophylline (80% theophylline) to achieve plasma levels of 15mg/L (assumingVd and Cl are normal)

Vd = 0.5×48 = 24L

LD = Cpss × Vd = 15×24=360mg theophylline = 450mg aminophylline

Cl = 0.04×48 = 1.92L/h

MD = D/τ = (Css×Cl)/(S×F) = (15×1.92)/(0.8) = 36 mg/h aminophylline

3. HG is a 64kg 53 year old male (CrCl is 3.4 mL/min) admitted to the hospital for digoxin toxicity. Regular at home dose was 0.25mg QD of Lanoxin (F = 0.7). At admission, his plasma digoxin concentration was 3.5μg/L

a. How long will it take for the digoxin concentration to fall from 3.5μg/L to 2.0μg/L?
b. Calculate a daily dose which will maintain HG's average digoxin concentration at 1.5μg/L

(assuming CHF)

a. $Cl = \frac{F \times D}{C \times \tau} = \frac{0.7 \times 0.25}{3.5 \times 2.4} = 2.1\text{L/h}$ or

$Cl_{cr} = \frac{(140-64) \times 53}{85 \times 3.4} = 13.9\text{mL/min} = 0.84\text{ L/h}$

Estimated Cl = 0.33×53+0.9×13.9 = 30mL/min = 1.8L/h

Vd = 3.8×53 +3.1×13.9 = 244.5L

K_e = Cl/Vd = $0.0086h^{-1}$ ($0.0073h^{-1}$)

T = $\frac{\ln(3.5/2)}{0.0086} = 65\text{h}$ (77h)

D/24 = $\frac{C \times Cl}{F} = \frac{1.5 \times 2.1}{0.7} = 4.5$

D=4.5×24 = 108 μg (93 μg)

4. HL is a 9 year old 35 kg child receiving a theophylline drip is started at a rate of 1 mg/kg/h. Drug levels obtained at 1 and 6 hours produce results of 15.7 mg/L and 11.3 mg/L, respectively. What would be your dosing recommendation to maintain a theophylline levelof 15 mg/L?

Cl = 2R0/(C1+c2) + 2Vd(C1-C2)/(C1+C2)(T2-T1)
= 2×1×35/27 +1.14
=3.74L/h

R0 = Cpss×Cl = 56mg/h

5. Ms D.H., a 53-year-old, 82-kilogram patient with congestive cardiac failure for the past three years, was admitted on April 16 to the hospital at 16:00 because of a worsening of her congestive cardiac failure symptoms. Her admission history indicated that she had taken her digoxin tablet (0.25 mg) that morning at the usual time (8:00-9:00), but had failed to take a tablet on Sunday (April 15). A plasma sample (blood withdrawn at 17:00) was obtained to see if the symptoms were consistent with noncompliance. A plasma digoxin concentration of 0.9 microgram/liter and a serum creatinine of 0.9 milligram/ deciliter were reported
From the information available, conclude if noncompliance is likely

Calculate the expected concentration

$$Cl_{cr} = 0.85 \times \frac{(140-53)\times 82}{72\times 0.9} = 93.6\text{mL/min}$$

Cl = 0.33×82 + 0.9×93.6 = 111.3mL/min = 6.7L/h

$$Cpss = \frac{F\cdot D}{Cl\cdot \tau} = \frac{0.7\times 0.25}{6.7\times 24} = 1.1\text{ng/mL}$$

Not likely