Spring 2005

PHA 5128

Homework 4

1. A 75 kg patient is to be treated p.o. with sodium phenytoin capsules. Assuming a phenytoin volume of distribution of 0.7 L/kg, Km of 4 mg/L and Vmax of 7 mg/kg/day, calculate the following:
   a. The loading dose to produce an initial concentration of 18 mg/L. How would you administer this dose? (1 pt)
   b. The daily maintenance dose to produce an average steady state concentration of 15 mg/L. (1 pt)

   a.

$$Vd = \boldsymbol{0.7}\,L/kg \cdot \boldsymbol{75}\,kg = \boldsymbol{52.5}\,L$$

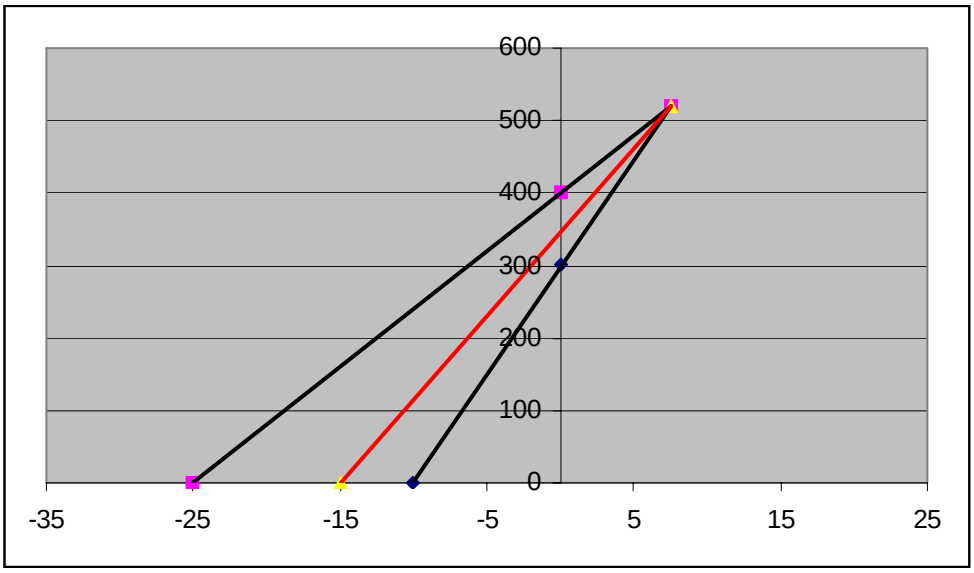
$$LD = \frac{Cp \cdot Vd}{S \cdot F} = \frac{\boldsymbol{18}\,mg/L \cdot \boldsymbol{52.5}\,L}{\boldsymbol{0.92} \cdot \boldsymbol{1}} = \boldsymbol{1027.17}\,mg \approx \boldsymbol{1000}\,mg$$

   The dose is given as a 400mg dose, followed by two 300mg doses at two-hour intervals to decrease the possibility of nausea and vomiting which may be associated with a single large dose. **(note: if student approximate salt factor to 1 is ok too, the answer would be slightly different)**

   b.

$$MD = \frac{Vm \cdot Cpss \cdot \tau}{(Km + Cpss) \cdot S \cdot F} = \frac{\boldsymbol{7}\,mg/kg/day \cdot \boldsymbol{75}\,kg \cdot \boldsymbol{15}\,mg/L \cdot \boldsymbol{1}\,day}{(\boldsymbol{4}\,mg/L + \boldsymbol{15}\,mg/L) \cdot \boldsymbol{0.92} \cdot \boldsymbol{1}} = \boldsymbol{450.51}\,mg \approx \boldsymbol{450}\,mg$$

2. A phenytoin patient has a plasma concentration of 10mg/L at 300mg/day and 25mg/L at 400mg/day. Using graph paper, determine the Km and Vmax as well as the dose needed to produce a concetration of 15mg/L. (2 pts)



Dose needed to produce a concentration of 15mg/L ⇒ 350mg/day

3. A patient (35 years old, 65 kg) is to be started on intravenous phenobarbital sodium. The therapeutic range is 10-30 mg/L. A loading dose is given so as to yield a Cp_0 of 30 mg/L. Calculate this loading dose and the daily maintenance dose to produce an average steady state concentration of 20 mg/L. (2 pts)

$$LD = \frac{Cp \cdot Vd}{S \cdot F} = \frac{30mg/L \cdot 0.7L/kg \cdot 65kg}{0.9 \cdot 1} = 1517mg \approx 1.5g$$

$$MD = \frac{Cp \cdot Cl \cdot \tau}{S \cdot F} = \frac{20mg/L \cdot 0.1L/kg/day \cdot 65kg \cdot 1day}{0.9 \cdot 1} = 144mg$$

(note: if student approximate salt factor to 1 is ok too, the answer would be slightly different)

4. C.S., a 10-year-old, 28 kg female, is receiving valproic acid sprinkles 250 mg (2x125mg) po Q 8 hr for her seizure disorder. Calculate her valprioc aicd level at steady state. (2 pts)

Cl = (13mL/kg/hr)(28kg) = 364mL/hr or 0.364L/hr

Cpss ave = (1)(1)(250mg/8hr)/(0.364L/hr) = 85.85 mg/L

5. M.W. is a 50-year-old, 70kg male with glomerular nephritis. His creatinine clearance is reasonably good, but he has a serum albumin concentration of 2.2g/dL. M.W. is receiving 350mg/day of phenytoin and has a steady-state

phenytoin concentration of 6mg/L. What would be his phenytoin concentration be if his serum albumin concentration were normal? (normal serum albumin=4.4g/dL). (2 pts)

$$Cp_{normal} = \frac{Cp'}{\left((\mathbf{1} - \alpha) \cdot \frac{Patient'sAlbumin}{NormalAlbumin} \right) + \mathbf{0.1}} = \frac{\mathbf{6}mg/L}{\left((\mathbf{1} - \mathbf{0.1}) \cdot \frac{\mathbf{2.2}g/dL}{\mathbf{4.4}g/dL} \right) + \mathbf{0.1}} = \mathbf{10.9}mg/L$$