Spring 2003

PHA 5128

Homework 4

1. A 100 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?
   b. The daily maintenance dose to produce an average steady state concentration of 15 mg/L.

   a.

$$Vd = 0.7L/kg \cdot 100kg = 70L$$

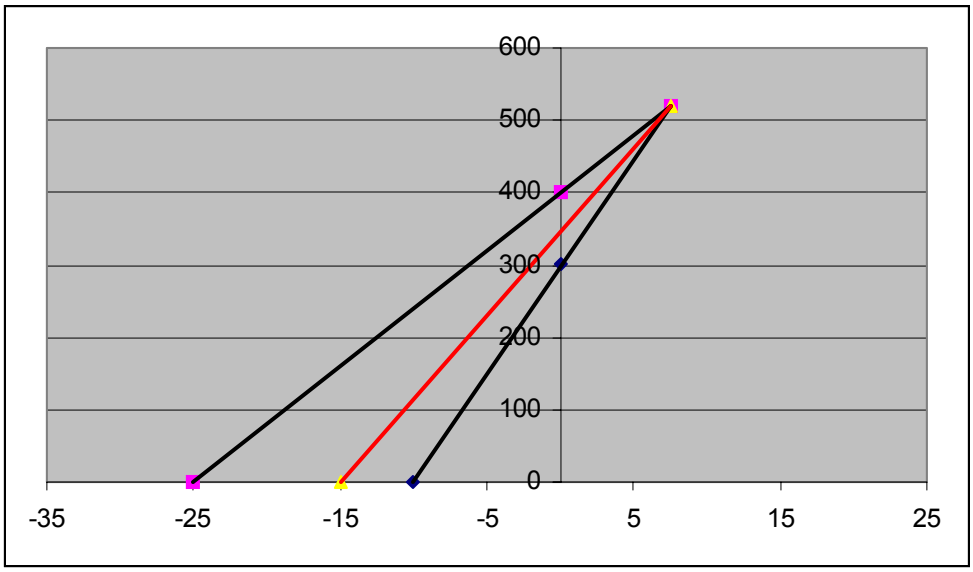
$$LD = \frac{Cp \cdot Vd}{S \cdot F} = \frac{18mg/L \cdot 70L}{0.92 \cdot 1} = 1369.57mg \approx 1300mg$$

The dose is given as a 400mg dose, followed by three 300mg doses at two-hour intervals to decrease the possibility of nausea and vomiting which may be associated with a single large dose.

b.

$$MD = \frac{Vm \cdot Cpss \cdot \tau}{(Km + Cpss) \cdot S \cdot F} = \frac{7mg/kg/day \cdot 100kg \cdot 15mg/L \cdot 1day}{(4mg/L + 15mg/L) \cdot 0.92 \cdot 1} = 600.69mg \approx 600mg$$

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.



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

3. W.R., a 39-year-old, 70kg male, developed generalized seizures several months after an automobile accident in which he sustained head injuries. Phenobarbital is to be initiated. Calculate a loading dose of Phenobarbital that will produce a plasma level of 20mg/L. Calculate an oral maintenance dose for W.R. which will maintain a Phenobarbital concentration of 20mg/L. How should the dose be administered? If W.R. does not receive a loading dose, how long will it take to achieve a minimum therapeutic level of 10mg/L following the initiation of the maintenance dose? How long will it take to achieve a steady-state level of 20mg/L?

$$LD = \frac{Cp \cdot Vd}{S \cdot F} = \frac{20mg/L \cdot 0.7L/kg \cdot 70kg}{1 \cdot 1} = 980mg \equiv 1g$$

$$MD = \frac{Cp \cdot Cl \cdot \tau}{S \cdot F} = \frac{20mg/L \cdot 0.1L/kg/day \cdot 70kg \cdot 1day}{1 \cdot 1} = 140mg$$

$$t_{1/2} = \frac{0.693 \cdot 49}{7} = 4.85days \approx 5days$$

dose is usually divided into 2 portions, but with a half-life of 5 days once daily should be fine

No LD, how long will it take to achieve a minimum therapeutic level of 10mg/L?

$$k_e = \frac{0.693}{5} = 0.139days^{-1}$$

$$t = \frac{\ln\left(\frac{C\max}{C\min}\right)}{k_e} = \frac{\ln\left(\frac{20}{10}\right)}{0.139} = 4.99days \approx 5days$$

steady-state after 3-5 half-lives $\Rightarrow$ $t_{1/2}$=5days
$\Rightarrow$ after 15-25 days $\Rightarrow$ Cpss=20mg/L

4. 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.

$$LD = \frac{Cp \cdot Vd}{S \cdot F} = \frac{30mg/L \cdot 0.7L/kg \cdot 65kg}{1 \cdot 1} = 1365mg \approx 1.3g$$

$$MD = \frac{Cp \cdot Cl \cdot \tau}{S \cdot F} = \frac{20mg/L \cdot 0.1L/kg/day \cdot 65kg \cdot 1day}{1 \cdot 1} = 130mg$$

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).

$$Cp_{normal} = \frac{Cp'}{\left((1-\alpha)\cdot\frac{Patient'sAlbu\min}{NormalAlbu\min}\right)+0.1} = \frac{6mg/L}{\left((1-0.1)\cdot\frac{2.2g/dL}{4.4g/dL}\right)+0.1} = 10.91mg/L$$