Spring 2004

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. C.S., a 10-year-old, 32 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.

Cl=(13mL/kg/hr)(32kg)=416mL/hr or 0.416L/hr

Cpss ave=(1)(1)(250mg/8hr)/(0.416L/hr)=75.1 mg/L

3. M.A., a 78 kg liver transplant patient, is receiving 400 mg of cyclosporine QD as an IV infusion. Currently, his hepatic function tests appear to be stable, and for the past three days he has been improving clinically with steady-state trough cyclosporine concentrations of approximately 220 µg/L. What would be an approriate oral cyclosporine dose for M.A.?

$$Dose_{new} = \frac{cp_{ssdesired}}{cp_{sscurrent}} \cdot \frac{F_{current}}{F_{new}} \cdot Dose_{current} = \frac{220\mu g / L}{220\mu g / L} \cdot \frac{1.0}{0.3} \cdot 400mg = 1333mg \cong 1200mg / day$$

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.

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

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

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).

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