PHA 5128

Homework V (Answers)

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

Vmax = 515 mg/day

Km = 7.1 μg/mL

Dose = $\frac{V\max \cdot C}{Km + C} = \frac{515 \cdot 15}{7.1 \cdot 15} = \underline{350 mg}$

2. W.R., a 39-year-old, 70 kg 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 20 mg/L. Calculate an oral maintenance dose for W.R. which will maintain a phenobarbital concentration of 20 mg/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 10 mg/L following the initiation of the maintenance dose? How long will it take to achieve a steady-state level of 20 mg/L?

LD = 70 · 0.7 · 20 = 980 mg

MD = 0.1 · 70 · 20 = 140 mg/day once a day

$t_{1/2}$ = 5 days → 20 - 25 days to achieve steady state

time to reach 10 = $t_{1/2}$ or 5 days

3. What would be the expected serum digoxin concentration in an 85 year old lady with an ideal body weight of 55 kg while receiving 0.25 mg Lanoxin tablets (F=0.7) QD over the past 2 months? Her digoxin half-life is 62 hours and Vd is 6 L/kg.

$$k = \frac{0.693}{62} = 0.011 h^{-1}$$

CL = 0.011 · 6 · 55 = 3.63 L/h

$$C = \frac{0.7 \cdot 0.25}{3.63 \cdot 24} = 2 ng / mL$$

4. Doug Durango is 37 year old male executive with uncontrolled hyperthyroidism with PAT. He as no history of previous illnesses and is not currently receiving any medications. He is 6'3 and weighs 198 Ibs. Lab: serum potassium = 4.8 mEq/L, serum creatinine = 0.7 mg%. Design a loading and maintenance dosage regimen for IV or PO as you are not sure what the physician will prescribe. Three days after the patient receives your recommended regimen IV, the physician requests a serum digoxin conc. It is reported by the lab to be 0.9 ng/ml (1 hour before the next dose). The physician asks 3 questions: 1. What should be the dose IV if I want the trough to be 1.4 ng/ml at steady-state? 2. What should be the dose if we later switch to PO and keep 1.4 as the target trough for Lanoxicaps or Lanoxin tabs? 3. He plans to have surgery next week to control his hyperthyroidism. Will there need to be a change in his digoxin dosage at that time? If so what should be the recommended dosage regimen and a follow-up TDM plan?

$$CL_{cr} = \frac{(140-37)\cdot 90}{72\cdot 0.7} = 184 mL/\min$$

CL = 0.8·90 + 184 = 256 mL/min = 15.4 L/h

Hyperthyroid: 1.3 · 256 = 333 mL/min

Vd = 3.8 · 90 + 3.1 · 184 = 912 L Hyperthyroid: Vd = 1.3 · 912 = 1186 L

LD = 1.5 · 1186 = 1.8 mg IV or 1.8/0.7 = 2.6 mg PO

MD = 1.5 · 15.4 · 24 = 554 μg/day IV or 792 μg/day PO

1) dose proportional: $\frac{554\cdot 1.4}{0.9} = 862 mg/day\ IV$

2) oral dose; $\frac{862}{0.7} = 1231 mg/day$

3) decrease dose; $\frac{1231}{1.3} = 947 mg$

5. P.M., a 55 year-old, 70 kg males, was admitted to the coronary care unit with a diagnosis of heart failure, probable myocardial infarction (MI), and premature ventricular contractions (PVCs). Calculate a bolus dose of lidocaine that should achieve an immediate response for P.M. At what rate should this dose be administration.
Calculate a maintenance infusion rate that will achieve a steady-state plasma lidocaine concentration of 2 mg/L for P.M.

P.M.'s PVCs were controlled by the 70 mg bolus dose of lidocaine and an infusion of 1 mg/min was begun. Fifteen minutes later, PVCs were again noted. What might account for the reappearance of PVCs? What is an appropriate course of action at this point.

$$LD = \frac{3 \cdot 0.3 \cdot 70}{0.87} = 72mg$$ Slow i.v. push (25-50 mg/min)

$$MD = \frac{0.42 \cdot 2}{0.87} = 0.97mg/\min$$

distribution; give second and third loading dose (35 mg each)