2.10. Phenobarbital

Solutions

To view a video demonstrating solutions to phenobarbital problems, go to https://www.youtube.com/user/murphyassessment.

1. *Note*: All calculations below are for the exact dose. The dose would be rounded to a reasonable amount for delivery.

   S = 1 for oral doses, F = 0.9 for oral doses.

   $$LD = \frac{C_{\Delta} \times V}{S \times F} = \frac{25\ mg/L \times (0.63\ L/kg \times 25\ kg)}{1 \times 0.9} = \mathbf{437.5\ mg}$$

   $$MD = \frac{Css_{avg} \times CL \times \tau}{S \times F}$$

   $$= \frac{25\ mg/L \times (0.0082\ L/hr/kg \times 25\ kg) \times 24\ hr}{1 \times 0.9} = \mathbf{136.7\ mg}$$

2. A. IV bolus loading dose for an initial concentration of 35 mg/L.

   V = 0.96 L/kg × 2.4 kg = 2.304 L

   S = 0.9 for IV phenobarbital sodium, F = 1

   $$LD = \frac{C_{\Delta} \times V}{S \times F} = \frac{35\ mg/L \times (0.96\ L/kg \times 2.4\ kg)}{0.9 \times 1} = \mathbf{89.6\ mg}$$

   MD can be 136.7 mg every 24 hours or 68.3 mg every 12 hours.

   B. $$MD = \frac{Css_{avg} \times CL \times \tau}{S \times F}$$

   $$= \frac{35\ mg/L \times (0.0047\ L/hr/kg \times 2.4\ kg) \times 12\ hr}{0.9 \times 1}$$

   = 5.26 mg every 12 hours

3. A. *Note*: All calculations below are for the exact dose. The dose would be rounded to a reasonable amount for delivery. The patient's volume of distribution is larger than anticipated. A C_o of 35 mg/L was the target and the measured concentration turned out to be 30 mg/L. The easiest way to solve this problem is to remember that it is a simple ratio. 89.6 mg produced a C_Δ of 30 mg/L.

Another 10 mg/L is needed, so:

89.6 mg × 10/30 = **29.9 mg**.

Another way to look at it is that 89.6 mg produced a change of 30 mg/L. To get a change of 40 mg/L we would need:

89.6 mg × 40/30 = **119.5 mg**.

Then the 89.6 mg already given must be subtracted from the loading dose it would have taken to get to 40 mg/L:

119.5 mg – 89.6 mg = **29.9 mg**.

Finally, the patient's actual volume of distribution can be determined from the dose and concentration achieved. It can then be plugged into the formula to solve for the dose to change concentration an additional 10 mg/L.

$$V = \frac{S \times F \times D}{C_\Delta} = \frac{0.9 \times 1 \times 89.6\ \text{mg}}{30\ \text{mg/L}}$$

$$= \frac{2.688\ \text{L}}{2.4\ \text{kg}}$$

= 1.12 L/kg (compared to the population value of 0.96 L/kg)

$$\text{New LD} = \frac{C_\Delta \times V}{S \times F}$$

$$= \frac{(40 - 30)\ \text{mg/L} \times (2.688\ \text{L})}{0.9 \times 1}$$

= **29.9 mg**

B. Because the decision has been made to increase the concentration from the original desired Css_{avg} of 35 mg/L to 40 mg/L, the maintenance dose predicted to produce 35 mg/L as Css_{avg} should also be increased. Since the volume of distribution is different than predicted, it might also be considered that clearance is also different from the population value. Unfortunately, there is no way to be sure that k (elimination rate constant) did not also change. Thus, the dose can be changed and a steady state concentration measured sometime in the future to determine the baby's actual clearance.

The easiest way to determine the new dose is by ratio (assume the 5.26 mg every 12 hours was to be used):

5.26 mg × 40/35 = **6.01 mg every 12 hours**

The original equation can also be used by substituting 40 mg/L for 35 mg/L.

$$MD = \frac{Css_{avg} \times CL \times \tau}{S \times F}$$

$$= \frac{40\ \text{mg/L} \times (0.0047\ \text{L/hr/kg} \times 2.4\ \text{kg}) \times 12\ \text{hr}}{0.9 \times 1}$$

= **6.01 mg every 12 hours**

4. A. $$CL = \frac{S \times F \times D}{Css_{avg} \times \tau} = \frac{0.9 \times 1 \times 6.01\ \text{mg}}{31\ \text{mg/L} \times 12\ \text{hr}}$$

$$= \frac{0.0145\ \text{L/hr}}{2.9\ \text{kg}} = \mathbf{0.005\ L/hr/kg}$$

Thus, clearance per kg is not much different than originally predicted from population values (0.0047 L/hr/kg). The concentration is lower than hoped for and may have been due mostly to the decreasing mg/kg dose as the baby rapidly gains weight.

B. The new maintenance dose can be determined by ratio:

6.01 mg every 12 hours × $\frac{40}{31}$ = **7.75 mg every 12 hours**

Or, by plugging back into the maintenance dose equation with the new clearance and desired Css_{avg}:

$$MD = \frac{Css_{avg} \times CL \times \tau}{S \times F}$$

$$= \frac{40\ \text{mg/L} \times (0.005\ \text{L/hr/kg} \times 2.9\ \text{kg}) \times 12\ \text{hr}}{0.9 \times 1}$$

= **7.75 mg every 12 hours**