2.7. Digoxin

Solutions

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

1. A. *Note*: F was assumed to be 0.6 for tablets by the authors who developed this predictor.

$$CL_{adults\text{-}CHFabsent} = 1.303 \times CrCl + 41 \text{ mL/min}$$
$$= (1.303 \times 54 \text{ mL/min}) + 41 \text{ mL/min}$$
$$= 111.362 \text{ mL/min}$$

$$CL = 111.362 \text{ mL/min} \times 0.06 = 6.682 \text{ L/hr}$$

Note: 1 L/1000 mL × 60 min/1 hr = 0.06

$$Css_{avg} = \frac{S \times F \times D}{\tau \times CL} = \frac{1 \times 0.6 \times 500 \text{ mcg}}{24 \text{ hr} \times 6.682 \text{ L/hr}} = \mathbf{1.87 \text{ mcg/L}}$$

B. $$CL_{adults\text{-}CHF} = 1.303 \times CrCl + 20 \text{ mL/min}$$
$$= (1.303 \times 54 \text{ mL/min}) + 20 \text{ mL/min}$$
$$= 90.362 \text{ mL/min}$$

$$CL = 90.362 \text{ mL/min} \times 0.06 = 5.422 \text{ L/hr}$$

$$Css_{avg} = \frac{S \times F \times D}{\tau \times CL} = \frac{1 \times 0.6 \times 500 \text{ mcg}}{24 \text{ hr} \times 5.422 \text{ L/hr}} = \mathbf{2.31 \text{ mcg/L}}$$

Note: DO NOT USE F = 0.75 from the bioavailability of dosage form table (Table 1.7-3).

2. A. Ideal body weight.

IBW_{males} = 50 kg + 2.3(69″–60″) kg

= **70.7 kg**

B. Why? Digoxin tends to accumulate in lean organ tissues (heart, muscle, kidneys, and liver) and ideal weight roughly approximates this (although other formulas are better at calculating lean weight).

3. To avoid overloading the patient. Distribution of digoxin to its sites of action takes several hours, so maximum pharmacological effect is not seen until then. Splitting the loading dose allows the opportunity to check heart rate before administering the second and third doses. If the heart rate is too low (e.g., < 60 bpm), the additional loading dose(s) may be held.

4. A. 0.25-mg tablets (F = 0.75)

$$Css_{new} = Css_{IV} \times \left(\frac{F_{po} \times D_{po}}{F_{IV} \times D_{IV}}\right)$$

$$= 1.3 \times \left(\frac{0.75 \times 0.25\ mg}{1 \times 0.25\ mg}\right)$$

= **0.975 mcg/L**

B. **0.2 mg** capsules (F = 0.95)

$$Css_{new} = Css_{IV} \times \left(\frac{F_{po} \times D_{po}}{F_{IV} \times D_{IV}}\right)$$

$$= 1.3 \times \left(\frac{0.95 \times 0.2\ mg}{1 \times 0.25\ mg}\right)$$

= **0.988 mcg/L**

C. 0.25 mg elixir (F = 0.80)

$$Css_{new} = Css_{IV} \times \left(\frac{F_{po} \times D_{po}}{F_{IV} \times D_{IV}}\right)$$

$$= 1.3 \times \left(\frac{0.8 \times 0.25\ mg}{1 \times 0.25\ mg}\right)$$

= **1.04 mcg/L**

Note: There would be slight differences than these exact values due to the relatively minor impact of absorption rate on the trough.

5. **Method 1**

$$V\ (L/1.73\ m^2) = V_{min} + \frac{V_n(CrCl)}{K_d + CrCl}$$

$$V\ (L/hr/1.73\ m^2) = 226\ L/1.73\ m^2 + \frac{298\ L/1.73\ m^2 (25\ mL/min/1.73\ m^2)}{29.1\ mL/min/1.73\ m^2 + 25\ mL/min/1.73\ m^2}$$

= 363.71 L/1.73 m^2

V = 363.71 L/1.73 m^2 × 2.11 m^2/1.73 m^2

= **443.6 L**

6. D. Presence of endogenous digoxin-like substances

Endogenous digoxin-like substances likely interfered with assays in earlier studies, giving false positive concentration to add to the actual concentration. Another possibility is that babies are just different (e.g., receptors and receptor responsiveness are decreased).

7. A. Neonates (~44 hr)

B. Infants (~18 hr)

C. Children (~36 hr)

D. Adults (~36 hr)

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

$$= \left(\frac{(1\ mcg/L \times (1.8\ L/hr/m^2 \times 0.22\ m^2) \times 24\ hr)}{1 \times 0.8}\right)$$

= **11.9 mcg every 24 hr** or 0.012 mg

9. B. **No earlier than 6 hours after a dose.**

Waiting 4–6 hours after a dose is important due to a slow distribution phase, where concentrations are NOT reflective of pharmacological response. Any time after this is acceptable, but it should probably be fairly consistent in subsequent measurements. The concentration variation over 18 hours for patients with a t½ of 36 hours is 31%, and it is 23% if a patient had a t½ of 48 hours.