2.9. Lithium

Solutions

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

1. Converting mL/min to L/hr:

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

   A. The therapeutic range in acute mania = 0.5 to 1.2 mEq/L. In the elderly it is often recommended that the initial target be lower, 0.5 to 0.8.

   Begin by solving for clearance with each method.

   Pepin method:

   $CL_{Lithium}$ = 0.235 × CrCl = 0.235 × 80 mL/min = 18.8 mL/min × 0.06

   = **1.128 L/hr**

   Jermain method: Begin by solving for lean body weight (LBW):

   LBW_{male} = (1.1 × ABW) – {120 × (ABW/Ht)^2}

   where ABW is in kg and Ht is in cm.

   $$70\text{ in} \times \frac{2.54\text{ cm}}{\text{in}} = 177.8\text{ cm}$$

   LBW_{male} = (1.1 × 92 kg) – {120 × (92/177.8)^2} = 69.07 kg

   $CL_{Lithium}$ = [0.0093 (L/hr/kg) × LBW] + (0.0885 × CrCl)

   $CL_{Lithium}$ = [0.0093 (L/hr/kg) × 69.07 kg] + [0.0885 × (80 mL/min × 0.06)]

   = **1.067 L/hr**

1. (continued)

Next, solve for dose using the clearances determined. Use 1 mEq/L for dose determination.

Pepin dose:

$$D\ (mEq/L) = \frac{CL \times Css_{avg} \times \tau}{S \times F}$$

$$= \frac{1.128\ L/hr \times 1\ mEq/L \times 12\ hr}{1 \times 1}$$

$$D\ (mEq/L) = 13.54\ mEq/day \times \frac{300\ mg}{8.12\ mEq}$$

= 500.1 mg per day

Jermain dose:

$$D\ (mEq/L) = \frac{CL \times Css_{avg} \times \tau}{S \times F}$$

$$= \frac{1.067\ L/hr \times 1\ mEq/L \times 12\ hr}{1 \times 1}$$

$$D\ (mEq/L) = 12.80\ mEq/day \times \frac{300\ mg}{8.12\ mEq}$$

= 473.1 mg per day

For both methods the nearest dose is **450 mg twice daily (every 12 hours)**. Each would yield a slightly different Css_{avg} due to the difference in predicted clearance. If 450 mg twice daily is used, the Css_{avg} would be expected to be different than 1 mEq/L. The differences could be determined by ratio:

Pepin:

$$1\ mEq/L \times \frac{450\ mg/12\ hr}{500.1\ mg/12\ hr} = \mathbf{0.90\ mEq/L}$$

Jermain:

$$1\ mEq/L \times \frac{450\ mg/12\ hr}{473.1\ mg/12\ hr} = \mathbf{0.95\ mEq/L}$$

Css_{avg} can also be determined by plugging the new dose into **Equation 5**.*

B. Variation would occur if an extended-release product is used vs. standard release, with lower peaks and higher troughs, assuming the dose delivered was equivalent. Because the extended-release product has reduced bioavailability, the dose would need to be higher to have the same Css_{avg}. If the extended-release product were used (F = 0.8), the predicted concentrations drop by 20% in both cases. For both, the dose would need to increase to 600 mg every 12 hours to be closer to the 1 mEq/L mark.

Pepin:

$$1\ mEq/L \times \frac{0.8 \times 600\ mg/12\ hr}{500.1\ mg/12\ hr} = \mathbf{0.96\ mEq/L}$$

Jermain:

$$1\ mEq/L \times \frac{0.8 \times 600\ mg/12\ hr}{473.1\ mg/12\ hr} = \mathbf{1.01\ mEq/L}$$

C. Thiazide diuretics reportedly decrease lithium clearance to between 32% and 74% of normal. If the patient's Css_{avg} is 1 mEq/L, the range of alteration in Css_{avg} based on the range of alteration of clearance is:

$$\frac{1\ mEq/L}{0.74} = \mathbf{1.35\ mEq/L}$$

$$\frac{1\ mEq/L}{0.32} = \mathbf{3.13\ mEq/L}$$

It would be reasonable to decrease the dose empirically to 300 mg every 12 hours. Concentrations should be measured before and after initiation (e.g., at ~1 week) because the diuretic may be given long term.

2. One approach that may be used is to solve for clearance assuming that the 12-hour concentration is equivalent to Css_{avg}.

450 mg = 12.18 mEq

Use F = 1 for tablets and capsules (range 95% to 104%).

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

$$CL = \frac{S \times F \times D}{Css_{avg} \times \tau} = \frac{1 \times 1 \times 12.18\ mEq}{1.2\ mEq/L \times 12\ hr}$$

= 0.846 L/hr

* Equation 5 and other numbered equations used in this chapter can be found in ***Select Pharmacokinetic Equations***, p xix.