## Lithium Cases

1. MJ is a 50-year old, 70 kg (5’10”) male with bipolar disease. He is not currently experiencing an episode of acute mania. His Scr = 0.9 mg/dL. Your medicine team has asked you for an oral lithium dose for this patient for maintenance therapy.

*Estimate Crcl:*  [140-age x (BW)]/(72 x Scr)

[(140-50y) x 70 kg/ (72 x 0.9)]

Crcl (est) = 97 ml/min

*Estimate lithium drug clearance* (L/day)*:* Cl = 0.288 x (Crcl)

Use drug clearance vs crcl relationship to estimate Li clearance for this patient

Cl = (0.288 x 97 ml/min) = 27.9 L/day

*Use average SS concentration equation to calculate Li maintenance dose*.

(desired conc for maintenance therapy = 0.6 mmol/L)

D/τ = (Css x Cl)/F

D/τ = (0.6 mmol/L x 27.9 L/d)/1 = 16.7 mmol/day

D/τ = 300 mg Li carb/8.12 mmol Li x 16.7 mmol/day = 617 mg/day

Rounded to 600 mg /day 🡪 300 mg lithium carbonate CR po every 12 hours

Monitoring: Measure serum concentrations every 2-3 days in patients predisposed to lithium toxicity. Once desired SS concentration achieved, recheck every 1-2 weeks for ~2 months or until concentrations have stabilized, then maintenance every 3-6 months. Monitor for development of common SE/toxicities.

1. Same patient as in #1, but his Scr = 3.5 mg/dL

*Estimate Crcl:*  [140-age x (BW)]/(72 x Scr)

Crclest = [(140-50 y) x 70 kg]/ (72 x 3.5 mg/dL) = 25 ml/min

*Estimate lithium drug clearance* (L/day)*:* Cl = 0.288 x (Crcl)

Cl = 0.288 x 25 ml/min = 7.2 L/day

*Use average SS concentration equation to calculate Li maintenance dose*

D/τ = (Css x Cl)/F

D/τ = (0.6 mmol/L x 7.2 L/day)/1 = 4.3 mmol/day

D/τ = 300 mg Li carb/8.12 mmol Li x 4.3 mmol/day = 159 mg/d

Rounded to 150 mg/day 🡪 150 mg lithium carbonate po daily

Monitoring: Measure serum concentrations every 2-3 days in patients predisposed to lithium toxicity. Once desired SS concentration achieved, recheck every 1-2 weeks for ~2 months or until concentrations have stabilized. Monitor for development of common SE/toxicities.

1. KR is a 21-year old, 70 kg (5’9”) female with bipolar disease. She needs lithium therapy and is currently experiencing an **acute manic phase**. Her Scr = 0.8 mg/dL. Suggest an initial lithium carbonate dosage regimen to achieve a SS lithium concentration of 0.8 mmol/L.

*Estimate Crcl:*  [140-age x (BW)]/(72 x Scr)

[(140-21) x 70]/(72 x 0.8) x 0.85

Crclest = 123 ml/min

*Estimate lithium drug clearance* (L/day)*:* **Cl = 0.432 x (Crcl)**

Use drug clearance vs. crcl relationship to estimate Li clearance for this patient

Cl = 0.432 x 123 ml/min = 53.1 L/day

*Use average SS concentration equation to calculate Li maintenance dose*.

(acute mania desired conc = 0.8-1)

D/τ = (Css x Cl)/F

D/τ = (0.8 mmol/L x 53.1 L/d)/1 = 42.5 mmol/day

D/τ = 300 mg Li carb/8.12 mmol Li x 42.5 mmol/day = 1570 mg/day

Round to 1500 mg/day 🡪 600 mg of lithium carbonate IR at 8 am and 8 pm and 300 mg at 2 pm

Upon initiation of therapy, measure Li concentration every 2-3 days for safety. Once SS achieved, measure every 1-2 weeks for ~ 2 months until stabilized. Reassess current dose once manic phase has subsided; Her dose may need to be adjusted because her lithium clearance will likely return to baseline values after the manic phase.

1. YC is a 37-year old, 55 kg (5’1”) female with bipolar disease. She is currently not experiencing an acute manic episode and requires treatment with lithium. Her Scr = 0.6 mg/dL. She is receiving 900 mg of lithium carbonate at 0800, 1400, and 2000 (8am, 2pm, 8pm), and her 12-hr postdose steady-state lithium serum concentration equals 1.1 mmol/L. Calculate her new lithium dose to achieve a SS concentration of 0.6 mmol/L.

### Calculate new dose to achieve desired serum concentration

Linear, dose-proportional PK – ss concentrations change in proportion to dose

Dnew/Css, new = Dold/Css, old

Dnew = (Css, new /Css, old ) x Dold

Dnew = (0.6 mmol/L/1.1 mmol/L) x 2700 mg/day = 1473 mg

Rounded to 1500 mg/day.

The patient would be administered 600 mg of lithium carbonate IR at 8am and 8pm, and 300 mg of lithium carbonate at 2 pm.

When lithium dosage changes are needed, serum concentrations should be measured within 3-5 days (~ 1 week) after the change. During lithium maintenance therapy, SS lithium concentrations should be repeated every 3-6 months. This time period can be every 6-12 months for patients with stable mood or every 1-2 months for patients with frequent mood alterations.

1. MC is a 55-year old woman receiving lithium carbonate 300 mg po bid. At 11:30 am her blood was drawn and the plasma lithium concentration was reported to be 2.7 mEq/L. List possible reasons why her lithium serum concentration may be elevated and discuss how MC should be managed.

* Level was obtained during the distribution phase (< 12 hrs from last dose)
* Drug hasn’t been on board for ~ 3-5 days, so this isn’t a SS concentration
* Over-compliance (confusion with regimen/administration of extra doses)
* Drug interactions (thiazides, NSAIDs, ACEIs)
* Renal insufficiency
* Dehydration state
* Sodium depletion

What questions would you ask?

Interpretation of this serum concentration is important as clinicians – First, you would want to confirm the timing of patient’s last dose and timing of the lab sample to ensure that complete distribution has occurred (12 hours have elapsed), as well as how long (how many days) the patient has been taking this regimen of 300 mg po BID (SS achieved?). A thorough review of pertinent laboratory data, current medications, adherence (timing of lithium), diet/exercise (sodium-related), presence of manic symptoms, etc. would be important also. If the level was drawn at the appropriate time, the next step would be to assess MC’s clinical presentation. You would expect to see signs of toxicity (coarse tremor, agitation, confusion, ataxia, GI effects). If there are no signs of toxicity, it is likely that the lithium sample was obtained during the distribution phase and therefore, cannot be correlated with efficacy or toxicity. The best approach would be to schedule another lab draw that is at least 12 hours after her next dose and reassess.