Most of the adverse effects of lithium are manageable—and a little knowledge goes a long way here.
I have an unhealthy fear of certain medications, specifically tricyclics, MAOIs, and lithium. It’s not their efficacy that scares me, but their reputation for side effects. In spite of this, I’m constantly surprised by how well-tolerated they are in practice. In the case of lithium, that surprise has been confirmed in both medical research and patient surveys. When it comes to the side effects that matter most to patients—sedation,[1] weight gain,[1] and cognition[2,3]—lithium’s tolerability ranks right behind lamotrigine. That tolerability may partly explain why these 2 medications were also the top-rated mood stabilizers in an online survey where patients rated the interventions they found most helpful for bipolar disorder (n = 3330 and counting).
Strategies for managing lithium’s adverse effects

Most of the side effects that occur with lithium are manageable, and a little knowledge goes a long way here. To begin with, titrate slowly (eg, raise the dose by 300 mg every 5-7 days) and use slow-release versions (these cut the rate of most side effects in half).[4] Dose reduction improves most adverse reactions, and though serum levels of 0.8 to 1.2 mEq/L may be necessary for acute mania, the optimal level for acute depression and long-term prevention in bipolar disorder is lower (0.4-0.8; optimal is 0.6 mEq/L).[5] In the elderly, even lower levels are often necessary for tolerability, and—due to their unique blood-brain distribution—the level can usually be reduced in this population without losing its effectiveness.[6]
I. Tremor

As a first step, reduce caffeine and other tremor-promoting drugs. Beta-blockers tend to be effective, and though propranolol (average dose, 120 mg/d) is the most commonly used, there are papers that support other options (atenolol, metoprolol, nadolol).[7] Beta-blockers have a minor interaction with lithium, raising its levels by up to 20%. The calcium-channel blocker nimodipine (120 mg/d) has good research for essential tremor and potential benefits in mania and rapid cycling.[7] High-dose vitamin B6 (900-1200 mg/d) has 2 studies for lithium-induced tremor and may improve akathisia and tardive dyskinesia from antipsychotics as well.[7]
Mild gastrointestinal symptoms tend to start early and disappear after the first week on lithium. Nausea is the most common, and this improves by taking it with food or switching to an extended-release form. Diarrhea, on the other hand, tends to improve with the immediate-release version of lithium.[8] Common remedies for nausea (eg, ondansetron, promethazine, ginger capsules) or diarrhea (eg, loperamide, milk of magnesia) can be used.
Weight gain is relatively mild with lithium. About 30% of patients gain 4 to 10 lb on lithium, and most of that weight gain occurs in the first few years of treatment.[9] Strategies include avoiding caloric beverages, optimizing thyroid function, and any reasonable approaches for weight loss (eg, diet, topiramate)
4. Erectile dysfunction

Sexual side effects are understudied in lithium, but aspirin improved erectile dysfunction in a randomized, double-blind trial of men on lithium (dosage, 240 mg/d).[10] PDE5 inhibitors (sildenafil, tadalafil, vardenafil) can also be used.[10]
Lithium’s most serious risk is renal insufficiency, and there are at least 3 ways to protect against this adverse effect. Single-day dosing (usually at night) improves renal function and polyuria.[4,8] Lower serum levels are less nephrotoxic, so reduce the dose if renal function starts to slow and consult a nephrologist if creatinine rises to 1.5 mg/dL.[8] Nephrogenic diabetes insipidus is both a side effect of lithium and a risk factor for renal insufficiency. Treating this syndrome with amiloride appears to reduce fibrotic changes in the kidneys.[11]
6. Thyroid disorders

Thyroid problems on lithium are usually treatable, and even subclinical hypothyroidism may warrant intervention. A controlled study found that patients were less likely to relapse into depression on lithium if their thyroid-stimulating hormone level was close to 2.4 microIU/mL.[12]
7. Dermatologic disorders

Any standard treatment for acne can be used with lithium,[10] but attention should be given to minocycline as this neuroprotective agent has positive studies for bipolar and unipolar depression (the dose for depression is 200 mg/d[13]; lower doses are used for acne, eg, 1 mg/kg/d).[14] Probiotics should be taken along with oral antibiotics. Psoriasis is a relative contraindication with lithium, but studies suggest it may be manageable with 2 therapies that also treat bipolar depression: inositol (6 g/d)[8] and high-dose omega-3 fatty acids (4-6 g/d).[15]
Lithium is among the top-ranked, but least utilized, therapies for bipolar disorder,[16] treatment-resistant depression,[17] and suicidality.[18] Patients with those problems deserve a trial of it, and it’s our job to make those trials as tolerable as possible. I hope these strategies help, and that you’ll post some of your own below.
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References

For references, see: 7 Ways to Improve Lithium’s Tolerability