LITHIUM: Using the comeback drug

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Lithium is making a comeback for good reason. Aside from its tried and true efficacy for bipolar disorder, lithium has neuroprotective effects and antisuicide properties.[1,2]

Psychiatry residents who were taught to use divalproex and atypical antipsychotics to treat bipolar disorder are discovering lithium's benefits. However, all psychiatrists might need a refresher—outlined by the mnemonic LITHIUM—on the fundamentals of this "old school" medication.

Levels between 0.6 and 1.0 mEq/L are sufficient to maintain most bipolar patients, although acute manic patients might require higher levels.[2,3] Some patients who cannot tolerate lithium's side effects might benefit from lower levels near 0.4 to 0.5 mEq/L. Remember, lithium levels are standardized in 12-hour trough plasma concentrations.

Interactions. Nonsteroidal anti-inflammatory drugs (except aspirin and sulindac), angiotensin-converting enzyme inhibitors, thiazide and loop diuretics, verapamil, and diltiazem can increase lithium concentration.[4] Caffeine, theophylline, sodium bicarbonate, and dialysis could decrease lithium levels. Be careful when adding lithium to anticonvulsants or antipsychotics because of increased neurotoxicity risk.

Toxicity can lead to coma, seizures, cardiovascular collapse, and death, especially when serum concentrations exceed 3.5 mEq/L.[2,4,5] Be alert to early toxicity symptoms such as drowsiness, confusion, coarse hand tremor, worsening gastrointestinal complaints, dysarthria, impaired consciousness, cogwheel rigidity, and ataxia.

Table

Renal metabolism of lithium

Renal function	Half-life (hours)[4]	Steady state (days)*
Normal	20 to 27	2.5 to 5.6
Renally impaired or elderly patients	36 to 50	4.5 to 10.4

* Steady state is reached after 3 to 5 half-lives

Lithium's narrow therapeutic index requires prudent monitoring. Some patients could experience toxicity at low plasma concentrations, such as 1.0 to 1.5 mEq/L.

Half-life varies depending on the patient's renal function. Steady state is usually reached within 5 days[2] but can take up to 10 days because of prolonged half-life in elderly and renally impaired patients (***Table***). Drawing lithium levels too early could lead to lithium toxicity in these patients, who require modified dosing regimens and monitoring.

Indications. Lithium is FDA-approved for acute mania and bipolar maintenance, but it also has been used for bipolar depression, antidepressant augmentation, schizoaffective disorder, and mixed manic states.[3] Consider combining lithium with an atypical antipsychotic for inpatients with severe bipolar mania with psychotic features. Also consider lithium therapy for patients with recurrent unipolar depression who have been successfully treated with antidepressants but then relapse.

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continued

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Urinary excretion. Order creatinine measurements every 2 to 3 months for the first 6 months of therapy, then every 6 to 12 months. Although lithium is not a first-line mood-stabilizing drug for patients with renal impairment, it can be used safely in patients with hepatic dysfunction.[2,4] Dehydration and a low-sodium diet can cause lithium accumulation, so evaluate patients' sodium and water balance at the beginning of and throughout lithium therapy. Encourage patients to keep their sodium and water intake as consistent as possible to avoid fluctuations in lithium levels.

Managing side effects is essential to maximize lithium's effectiveness. Consider switching to a slow-release preparation if your patient cannot tolerate various side effects of regular lithium. If the patient continues to have side effects, consider lowering the dose in 300-mg increments or as clinically indicated. Closely monitor the patient for improved side effects while aiming to maintain an appropriate therapeutic level. Also, moving the entire lithium dose to bedtime could minimize side effects. If these strategies are not adequate, consider adding:

- thyroid replacement to manage elevated thyroid stimulating hormone or frank hypothyroidism
- propranolol, 40 to 100 mg/d in divided doses, for tremor
- amiloride, 5 to 10 mg/d, for polyuria
- loperamide as needed for diarrhea.[2,5]

Educate your patients on potential side effects, and encourage them to report any unwanted effects. Developing a good patient-provider relationship is essential to maximizing treatment adherence.

References

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