A resident's guide to lithium

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Lithium has been used in psychiatry for more than half a century and is considered the gold standard for treating acute mania and maintenance treatment of bipolar disorder.[1] Evidence supports its use to reduce suicidal behavior and as an adjunctive treatment for major depressive disorder.[2] However, lithium has fallen out of favor because of its narrow therapeutic index as well as the introduction of newer psychotropic medications that have a quicker onset of action and do not require strict blood monitoring. For residents early in their training, keeping track of the laboratory monitoring and medical screening can be confusing. Different institutions and countries have specific guidelines and recommendations for monitoring patients receiving lithium, which adds to the confusion.

We completed a literature review to develop clear and concise recommendations for lithium monitoring for residents in our psychiatry residency program. These recommendations outline screening at baseline and after patients treated with lithium achieve stability. ***Table 1***[3-11] (***page e4***) outlines medical screening parameters, including bloodwork, that should be completed before initiating treatment, and how often such screening should be repeated. ***Table 2*** (***page e5***) incorporates these parameters into progress notes in the electronic medical record to keep track of the laboratory values and when they were last drawn. Our aim is to help residents stay organized and prevent missed screenings.

How often should lithium levels be monitored?

After starting a patient on lithium, check the level within 5 to 7 days, and 5 to 7 days after each dose change. Draw the lithium level 10 to 14 hours after the patient's last dose (12 hours is best).[1] Because of dosage changes, lithium levels usually are monitored more frequently during the first 3 months of treatment until therapeutic levels are reached or symptoms are controlled. It is recommended to monitor lithium levels every 3 months for the first year and every 6 months after the first year of treatment once the patient is stable and considering age, medical health, and how consistently a patient reports symptoms/adverse effects.[3,5] Continue monitoring levels every 3 months in older adults; in patients with renal dysfunction, thyroid dysfunction, hypercalcemia, or other significant medical comorbidities; and in those who are taking medications that affect lithium, such as pain medications (nonsteroidal anti-inflammatory drugs can raise lithium levels), certain antihypertensives (angiotensin-converting-enzyme inhibitors can raise lithium levels), and diuretics (thiazide diuretics can raise lithium levels; osmotic diuretics and carbonic anhydrase inhibitors can reduce lithium levels).[1,3,5]

continued

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Table 1

Medical screening and frequency for patients receiving lithium

	Baseline	Week 4	Week 12	6 months	12 months
Medical history	x				x
Height	x				x
Weight	x		x	x	x
BMI	x				x
Waist circumference	x				x
Blood pressure	x				x
Pulse	x				x
Pregnancy test[a]	x				
ECG[b]	x				x
Fasting glucose/ hemoglobin A1c[c]	x		x	x	x
Creatinine[d]	x		x	x	x
BUN[d]	x		x	x	x
eGFR[d]	x		x	x	x
Serum electrolytes[d]	x		x	x	x
TSH w/reflex to T4[e]	x		x	x	x
Lipid panel[c]	x				x
CBC with differential[f]	x		x	x	x
Lithium level	5 to 7 days after starting	5 to 7 days after each dose change			

[a]Repeat pregnancy testing in patients of childbearing potential when patient had unprotected intercourse or there is concern for pregnancy
[b]For patients with cardiac history, family cardiac history, age >40, or receiving other medications known to prolong QTc
[c]If there is concern for metabolic syndrome, or the patient is receiving an antipsychotic
[d]Included in a complete metabolic panel or basic metabolic panel. Order serum parathyroid level when there is elevated serum calcium
[e]In a patient with symptoms of thyroid dysfunction or a history of thyroid dysfunction, order a free T3 and anti-thyroid peroxidase antibodies (AbTPO)
[f]Lithium can cause leukocytosis

BMI: body mass index; BUN: blood urea nitrogen; CBC: complete blood count; ECG: electrocardiogram; eGFR: estimated glomerular filtration rate; TSH: thyroid-stimulating hormone

Source: References 3-11

Clinical Point

As lithium levels approach 1.5 mEq/L, patients are at increased risk for intolerable adverse effects

Lithium levels could vary by up to 0.5 mEq/L during transition between manic, euthymic, and depressive states.[12] On a consistent dosage, lithium levels decrease during mania because of hemodilution, and increase during depression secondary to physiological effects specific to these episodes.[13,14]

Recommendations for plasma lithium levels (trough levels)

Mania. Lithium levels of 0.8 to 1.2 mEq/L often are needed to achieve symptom control during manic episodes.[15] As levels approach 1.5 mEq/L, patients are at increased risk for intolerable adverse effects (eg, nausea and vomiting) and toxicity.[16,17] Adverse effects at higher levels may result in patients abruptly discontinuing lithium. Patients who experience mania before a depressive episode at illness onset tend to have a better treatment response with lithium.[18] Lithium monotherapy has been shown to be less effective for acute mania than antipsychotics or combination therapies.[19] Consider combining lithium with valproate or antipsychotics for patients who have tolerated lithium in the past and plan to use lithium for maintenance treatment.[20]

Maintenance. In adults, the lithium level should be 0.60 to 80mEq/L, but consider levels of 0.40 to 0.60 mEq/L in patients who have a good response to lithium but develop adverse effects at higher levels.[21] For patients who do not respond to treatment, such as those with severe mania, maintenance levels can be increased to 0.76 to 0.90 mEq/L.[22] These same recommendations for maintenance levels can be used for children and adolescents. In older adults, aim for maintenance levels of 0.4 to 0.6 mEq/L. For patients age 65 to 79, the maximum level is 0.7 to 0.8 mEq/L, and should not exceed 0.7 mEq/L in patients age >80. Lithium levels <0.4 mEq/L do not appear to be effective.[21]

Depression. Aim for a lithium level of 0.6 to 1.0 mEq/L for patients with depression.[11]

Renal function monitoring frequency

Obtain a basic metabolic panel or comprehensive metabolic panel to establish baseline levels of creatinine, blood urea nitrogen (BUN), and estimated glomerular filtration rate (eGFR). Repeat testing at Week 12 and at 6 months to detect any changes. Renal function can be monitored every 6 to 12 months in stable patients, but should be closely watched when a patient's clinical status changes.[3] A new lower eGFR value after starting lithium therapy should be investigated with a repeat test in 2 weeks.[23] Mild elevations in creatinine should be monitored, and further medical workup with a nephrologist is recommended for patients with a creatinine level ≥1.6 mg/dL.[24] It is important to note that creatinine might remain within normal limits if there is considerable reduction in glomerular function. Creatinine levels could vary because of body mass and diet. Creatinine levels can be low in nonmuscular patients and elevated in patients who consume large amounts of protein.[23,25]

Table 2

Keeping track of monitoring: A table for the electronic medical record

Parameter	Date/value	
Height		
Weight		
BMI		
Waist circumference		
Blood pressure		
Heart rate		
TSH w/reflex to T4		
Creatinine		
BUN		
eGFR		
Serum electrolytes	Na	
	K	
	Ca	
Fasting glucose/or hemoglobin A1c (if risk factors present)		
Lipid panel (if risk factors are present)	LDL	
	HDL	
	CHOL	
	TG	
ECG (if there is personal or family cardiac history or other medications that prolong QTc)		
Pregnancy test for patients of childbearing potential		
Lithium level		

BMI: body mass index; BUN: blood urea nitrogen; CHOL: total cholesterol; ECG: electrocardiogram; eGFR: estimated glomerular filtration rate; HDL: high-density lipoprotein; LDL: low-density lipoprotein; TG: triglycerides; TSH: thyroid-stimulating hormone

Ordering a basic metabolic panel also allows electrolyte monitoring. Hyponatremia and dehydration can lead to elevated lithium levels and result in toxicity; hypokalemia might increase the risk of lithium-induced cardiac toxicity. Monitor calcium (corrected serum calcium) because hypercalcemia has been seen in patients treated with lithium.

continued

Clinical Point

Renal function can be monitored every 6 to 12 months in stable patients but more closely when a patient's clinical status changes

Thyroid function monitoring frequency

Obtain levels of thyroid-stimulating hormone with reflex to free T4 at baseline, 12 weeks, and 6 months. Monitor thyroid function every 6 to 12 months in stable patients and when a patient's clinical status changes, such as with new reports of medical or psychiatric symptoms and when there is concern for thyroid dysfunction.[3]

Clinical Point

Monitor thyroid function every 6 to 12 months in stable patients and when a patient's clinical status changes

Lithium and neurotoxicity

Lithium is known to have neurotoxic effects, such as effects on fast-acting neurons leading to dyscoordination or tremor, even at therapeutic levels.[26] This is especially the case when lithium is combined with an antipsychotic,[26,27] a combination that is used to treat bipolar I disorder with psychotic features. Older adults are at greater risk for neurotoxicity because of physiological changes associated with increasing age.[28]

Educate patients about adherence, diet, and exercise

Patients might stop taking their psychotropic medications when they start feeling better. Instruct patients to discuss discontinuation with the prescribing clinician before they stop any medication. Educate patients that rapidly discontinuing lithium therapy puts them at high risk of relapse[29] and increases the risk of developing treatment-refractory symptoms.[23,30] Emphasize the importance of staying hydrated and maintaining adequate sodium in their diet.[17,31] Consuming excessive sodium can reduce lithium levels.[17,32] Lithium levels could increase when patients experience excessive sweating, such as during exercise or being outside on warm days, because of sodium and volume loss.[17,33]

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Clinical Point

Educate patients that rapidly discontinuing lithium puts them at high risk of relapse