

# Effectiveness of normal saline diuresis in treating lithium overdose

David D. Boltan, MD, and Andrew Z. Fenves, MD

Lithium carbonate is a common treatment for mood disorders, but it has a very narrow therapeutic index and can be toxic to multiple organ systems. Unfortunately, many patients suffer toxic effects through the course of their therapy. We describe a patient with toxic effects from a high dose of lithium who was successfully treated with normal saline diuresis. We discuss the properties that make lithium susceptible to normal saline diuresis and explore alternative options for treatment of lithium toxicity.

Lithium carbonate is a common treatment for affective disorders. Unfortunately, lithium has a narrow therapeutic index and at toxic doses can cause multisystem dysfunction and even death. Many Americans suffer lithium toxicity through the course of their maintenance therapy. The treatment of lithium overdose depends on the severity of signs and symptoms in the individual patient and is also influenced by the degree of renal insufficiency. We present a patient with severe lithium toxicity who was treated successfully with saline diuresis.

## CASE REPORT

A 47-year-old white woman, a resident at a halfway house, was transferred to Baylor University Medical Center's emergency department due to altered mental status, nausea, and vomiting. The patient had a long history of schizophrenia and bipolar disorder. Her psychiatric medications included lithium 300 mg twice a day, trazodone 50 mg at night, fluoxetine 120 mg once a day, and doxepin hydrochloride 50 mg at night. She was also taking propranolol 10 mg twice a day and amlodipine 5 mg once a day for hypertension; pancrelipase 1 tablet with meals for pancreatic insufficiency; phenytoin 300 mg once a day for seizure history; metoclopramide 10 mg four times a day for gastroparesis; tizanidine 4 mg at night; carisoprodol 350 mg three times a day and hydrocodone 10/325 mg as needed for chronic back pain; and levothyroxine 75 mcg daily as thyroid replacement therapy.

The patient's blood pressure on admission was 106/69 mm Hg with a pulse of 59. Her respiratory rate was 16 breaths per minute, and she was afebrile and had normal oxygen saturation on 2 L of oxygen via nasal cannula. She looked disheveled and

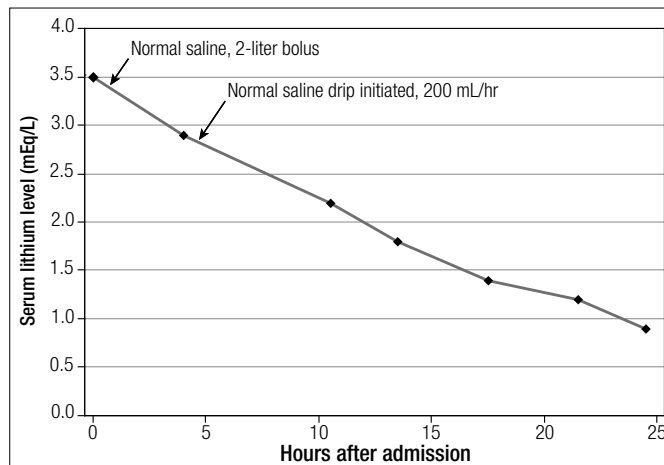


Figure 1. Patient's serum lithium level over the course of normal saline diuresis.

was somnolent. Her pupils were of equal size and reactive to light. Her pulmonary, cardiovascular, and abdominal examination was unremarkable. She had multiple cuts on her knees. Neurologic assessment was limited by the patient's mental status but did not show any focal deficits.

Laboratory values for arterial blood gases and blood chemistries were within normal limits, including a serum creatinine level of 0.7 mg/dL. The peripheral blood smear was unremarkable. Blood alcohol, acetaminophen, and salicylate levels were undetectable. The urine drug screen was positive for benzodiazepines, methadone, and opiates. The lithium level was 3.5 mEq/L (therapeutic range, 0.6–1.2 mEq/L).

The patient received 2 L of normal saline in the emergency department, and nephrology was consulted for possible initiation of dialysis. Since the patient had normal renal function and no evidence of pulmonary edema or heart failure, normal saline diuresis was initiated. After the 2-L bolus, she received a 200-mL/h drip of normal saline. The patient's symptoms and lithium level were carefully monitored (Figure 1).

From the Department of Internal Medicine (Boltan) and the Division of Nephrology, Department of Internal Medicine (Fenves), Baylor University Medical Center, Dallas, Texas.

**Corresponding author:** Andrew Z. Fenves, MD, Division of Nephrology, Department of Internal Medicine, Baylor University Medical Center, 3500 Gaston Avenue, Dallas, Texas 75246 (e-mail: fenvesa@dneph.com).

The following morning the patient returned to her baseline mental status, and intravenous fluids were discontinued. She was transferred to the psychiatric unit. Forty-eight hours after admission her lithium level was 0.3 mEq/L, at which point lithium was restarted.

## DISCUSSION

Lithium salts were first introduced in the 19th century as a treatment for gout and to alleviate sadness. It was observed that in normal individuals lithium did not appear to have any noticeable effects at therapeutic levels. This false sense of safety led to lithium chloride being substituted for table salt in cardiac patients in the late 1940s, resulting in overdoses, deleterious neurological side effects, and even death (1). It wasn't until 1948 when John Cade gave lithium carbonate to manic psychiatric patients that lithium's specific effects in mania were appreciated (2). Today the Food and Drug Administration approves lithium for both treatment of acute mania and prevention of recurrences of mania in otherwise healthy adults. Still, the primary indication for lithium use is long-term prevention of both mania and depression in primary affective disorders such as bipolar disorder. It is also commonly used as an adjunct therapy in refractory major depressive disorders.

Treatment with lithium is often fraught with adverse events similar to those in the prior century, most of these stemming from lithium's pharmacological properties and very narrow therapeutic index. Lithium's therapeutic range is 0.6 to 1.2 mEq/L, with mild to moderate toxic effects seen at levels as low as 1.5 mEq/L.

Chronic use of lithium has been associated with various ailments, including multiple renal effects such as transient natriuresis, nephrogenic diabetes insipidus, and partial distal renal tubular acidosis. Lithium intoxication is associated with renal insufficiency, which may progress to acute renal failure (3). Arrhythmias and electrocardiographic changes, including depression of the T wave, have been described. Other rare side effects include hypothyroidism, worsening myasthenia gravis, teratogenicity if used during pregnancy, and worsening acne vulgaris and alopecia. Effects of acute intoxication range from mild nausea, vomiting, and fine tremor to convulsions, hyperreflexia, focal neurological signs, coma, and death. Our patient presented with vomiting and altered mental status.

Lithium is not metabolized and is eliminated primarily through the kidneys. The plasma elimination half-life of a single dose ranges from 18 to 20 hours in young adults to approximately 36 hours in elderly patients. The half-life increases with duration of therapy. For patients without prior lithium therapy, those with 1 year of lithium use, and those with more than 1 year of use, the half-life is 29, 40, and 58 hours, respectively. Lithium is freely filtered through the glomerulus and reabsorbed by the proximal tubule in the same proportion

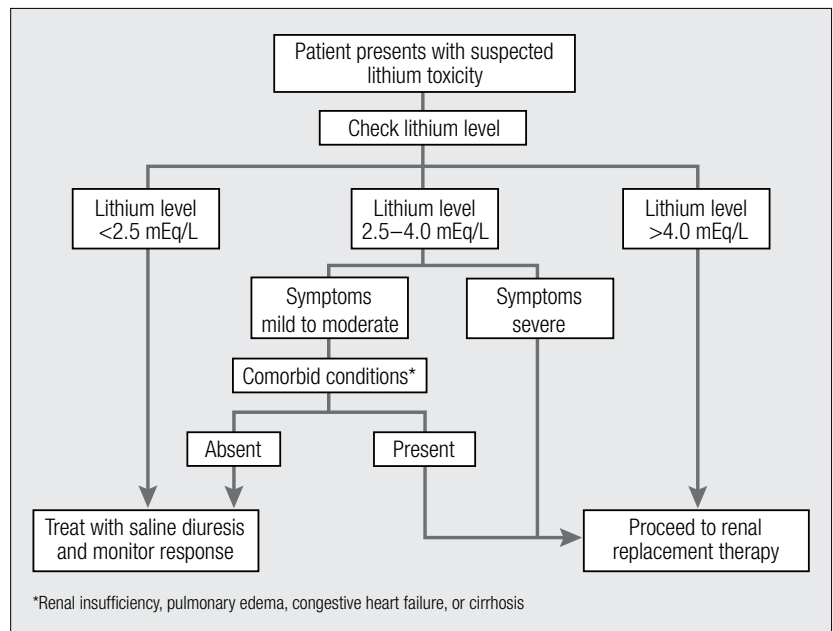


Figure 2. Indications for diuresis vs hemodialysis in cases of lithium overdose.

as sodium (60%–65%); another 15% to 20% is reabsorbed beyond the proximal tubule, and 20% is excreted in the urine. Since lithium is reabsorbed mostly by the proximal tubule in tandem with sodium, lithium clearance is decreased when the filtered load of sodium is decreased (e.g., in sodium depletion) (4).

The treatment for lithium intoxication can vary. Because there is no antidote, the goal is to provide supportive measures and treatments focused on removing the toxin from the body. Lithium is a small ion with low lipid affinity. It is not protein bound and distributes freely in total body water. However, lithium concentrations in red blood cells and cerebrospinal fluid are lower than those in plasma, while concentrations in saliva, brain, thyroid gland, and bone are higher. After equilibration, the apparent volume of distribution of lithium is 0.7 to 1.0 L/kg (4). These properties make it both easily dialyzable and readily extractable by the kidneys.

Indications for dialysis depend on the lithium level, the severity of symptoms, and comorbid conditions (Figure 2). Most experts agree that a lithium level >4.0 mEq/L indicates that the patient requires dialysis regardless of the clinical status; conversely, hemodialysis is rarely indicated for patients with a lithium level of <2.5 mEq/L. Hemodialysis is indicated for patients with severe symptoms or comorbid conditions such as renal insufficiency, pulmonary edema, congestive heart failure, or cirrhosis. For patients with mild to moderate symptoms and lithium levels between 2.0 and 4.0 mEq/L, the elimination rate of the drug can be determined by plotting the log of the serum levels obtained every 3 hours versus time and calculating the time required to reach a level of 0.6 mEq/L. If the estimated time exceeds 36 hours, dialysis is recommended (4).

Intermittent hemodialysis can effectively reduce plasma levels of lithium, but a rebound of lithium levels often occurs between dialysis sessions. Therefore, continuous forms of hemodialysis have also been used with much success (5).

Lithium clearances with continuous arteriovenous or venovenous hemodialysis are equivalent to 60 to 85 L/d compared with 30 to 40 L cleared during a conventional 4- to 6-hour hemodialysis session (5).

Despite the effectiveness and relative safety of these dialysis methods, they are invasive and carry a risk of serious complications. This case report shows that conservative therapy can be used safely and effectively in a relatively stable patient without renal, pulmonary, or cardiovascular disease. As shown in Figure 1, no rebound of the lithium level occurs with intravenous fluid administration. Treating appropriate patients with intravenous fluids while monitoring lithium levels and the progression of symptoms can reduce lithium levels safely and effectively.

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