Lithium toxicity: a case report

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Abstract

Lithium is a commonly used drug for bipolar disorders and requires therapeutic dose monitoring due to its narrow therapeutic index. Acute lithium toxicity frequently occurs due to intentional intake of an excessive amount or due to its interaction with various medicines and medical conditions which alter its absorption or excretion. It may present primarily with neurological and gastrointestinal symptoms. We report a case of lithium toxicity in a patient with bipolar disorder probably due to dehydration and decreased intake of food and fluids. Frequent monitoring of serum lithium level while maintaining hydration and electrolyte balance successfully treated the lithium toxicity.

Keywords: case report, lithium toxicity, neurotoxicity.

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Introduction

Lithium is one of the commonly used mood stabilizers. It is primarily used in patients with bipolar disorders. One study from Nepal showed that 58% of patients with bipolar disorders were taking sodium valproate and 34% of patients were taking lithium. Lithium comes as lithium carbonate and is administered orally. It comes in two formulations: immediate release and sustained release. The commonly used dose is 300 to 1200mg/day. Lithium has a narrow therapeutic index of 0.6 to 1.2 meq/L and levels above 1.5 meq/L cause toxicity, thus requiring regular monitoring. Interaction with various medicines as well as medical conditions predisposes patients to acute or chronic lithium toxicity. We present a unique case of lithium toxicity in a patient with bipolar disorder due to inadequate fluid and food intake.

Case Report

A 73-year-old female was brought to the emergency department with complaints of increasing restlessness, agitation, and irrelevant talking for two days. She had decreased her food and fluid intake four days prior to the presentation. She then developed an altered sensorium gradually. She was also having multiple episodes of watery, non-bloody loose stools and multiple episodes of non-bilious non-bloody vomiting, containing food particles. At the emergency department, her vitals were stable, she was not responding to questions, and couldn’t identify her family members. She had decreased self-care and was self-muttering. She also had bilateral horizontal nystagmus, and tremors in both hands. She was a known case of type I bipolar disorder, diabetes, and hypothyroidism. She was under lithium 300mg twice a day and olanzapine 2.5mg at night for the last 30 years. She was also taking metformin 500 mg twice a day and thyroxine 25 mcg for the last 15 years.

Her initial investigations were random blood glucose level: 131mg/dl, total leukocyte count: 11,100/mm³ (neutrophils: 69%, lymphocytes: 27%, basophils: 4%), urea: 42 mg/dl, creatinine: 0.6 mg/dl, sodium: 129 mEq/L and potassium: 4.6 mEq/L. Her electrocardiogram and non-contrast computed tomography (NCCT) scan showed normal findings. The initial serum lithium level was 3.2mmol/L, suggesting of lithium toxicity. Then she was admitted to the intensive care unit and was managed with intravenous fluids. Her serum lithium level, blood urea nitrogen creatinine, and electrolytes were monitored frequently. Her lithium level on the third and fifth day of admission was 2.03 mmol/L and 1.78 mmol/L respectively. After normalization of lithium level, she was transferred to the medical ward where she developed a hospital-acquired urinary infection and was successfully treated for the same.

Discussion

Acute Lithium toxicity occurs due to accidental or intentional intake of excessive amounts of lithium, chronic overdose and toxicity might be due to the accumulation of high levels during ongoing chronic therapy. Concomitant use of medicines such as psychotropics, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, diuretics, and nonsteroidal inflammatory drugs might reduce the excretion of lithium from the kidney, increasing the risk of toxicity. Comorbid conditions like cardiovascular disease, neuropsychiatric disease, renal disease, and hypothyroidism increase the predisposition to toxicity by influencing the ingestion, absorption, or excretion of lithium. Though lithium toxicity is common worldwide, it has not been reported in Nepal yet.

Patients with Lithium toxicity most commonly show neurological symptoms such as altered mental status, lethargy, seizure, pyramidal, extrapyramidal, and cerebellar signs. Musculoskeletal symptoms include coarse tremors, and muscle twitching. Gastrointestinal manifestations can be nausea, vomiting, and diarrhea. Renal toxicity presents as elevated serum creatinine, blood
urea nitrogen, decreased glomerular filtration rate, and nephrogenic diabetes insipidus.\textsuperscript{4} Cardiovascular toxicity manifests as tachycardia or bradycardia, hypotension, ST segment changes, QTc changes, T-wave inversion, etc. Chronic toxicity might cause electrolyte disturbance and endocrine effects such as hypothyroidism and goiter. There can be dermatological, ophthalmological, and hematological system involvement as well.

When a patient presents to the emergency, the nature of ingestion (eg, acute or chronic, suicide attempt), and the drug formulation (standard formulation or sustained release) should be determined. History of recent illnesses causing dehydration (eg, vomiting, diarrhea, fever, anorexia) is taken. The patient is assessed for signs of dehydration and a focused neurologic examination is performed to look for alterations in mentation, ataxia, and neuromuscular excitability (eg, tremors, myoclonus).\textsuperscript{6}

Lithium concentration is obtained upon presentation and repeated every 2 to 4 hours during initial management; the normal range is 0.8 to 1.2 mEq/L (mmol/L). Drug concentration may not correlate with clinical severity. However, we monitored lithium levels less frequently as this test was not available at our center and the sample had to be sent to the outside lab. Other essential evaluation at the emergency includes an electrocardiogram, cardiac monitoring, assessment of oxygenation, and monitoring of urine output, serum electrolytes, calcium, renal function, glucose, and thyroid-stimulating hormone.\textsuperscript{7} For the acute onset of confusion with an unclear diagnosis, brain imaging may be required.\textsuperscript{8} This patient also had a normal NCCT scan.

The treatment plan starts with assessing and stabilizing the airway, breathing, and circulation. Sodium and water balance is restored with intravenous hydration with isotonic saline at twice the maintenance rate for a total of approximately 2 to 3 liters, depending upon the patient's fluid status and cardiac function. Since we suspected our patient was having dehydration and inadequate intake of food and fluids, we also gave normal saline as well as dextrose solutions for replenishment.

At the emergency department, charcoal should be administered if the co-ingestant is unknown. However, lithium by itself doesn’t bind to charcoal and may not be helpful. All patients with toxicity signs and symptoms, even those with normal serum lithium levels, should be admitted for monitoring in the hospital as the drug level might not correlate with severity. If symptoms are moderate to severe, the patient is admitted to an intensive care unit and serum lithium levels are obtained serially until the values start descending. Patients are discharged after symptoms resolution or serum lithium level less than 1.5 mEq/L.\textsuperscript{9}

Guidelines recommend hemodialysis for serum lithium concentration greater than 5 mEq/L (or mmol/L), regardless of the clinical status of the patient or if the Serum lithium concentration is greater than >4 mEq/L (4 mmol/L) in patient with impaired kidney function, and if patients have symptoms of severe lithium toxicity such as seizures, altered mental status, cardiopulmonary collapse, or life-threatening dysrhythmia irrespective of the lithium concentration.\textsuperscript{6} Though many articles report the use of hemodialysis to enhance the elimination of lithium in patients with lithium poisoning but there is no research from randomized controlled trials on its benefits and harms in patients with lithium poisoning.\textsuperscript{10} This patient's lithium level was below 4meq/l and she didn’t have any renal impairment thus she was managed conservatively with hydration and supportive measures.

Studies have demonstrated a positive correlation between lithium knowledge and lithium levels that were more stable. Thus, after successful treatment patient and her caregiver were counseled regarding the measures to prevent toxicity in the future as there is evidence that patients with knowledge regarding lithium have stable serum lithium levels.\textsuperscript{11}
This was a case of lithium toxicity in an elderly woman with multiple comorbidities, thus caution should be taken while generalizing the findings.

In conclusion, we report this case to highlight that simply continuing usual dose of lithium while patient has dehydration due to decreased fluid intake might cause lithium toxicity, requiring monitoring of serum lithium, and appropriate supportive measures.

Patient’s Perspective
I was not feeling well prior to presentation and was hardly taking any food or fluids however, I was continuing my usual dose of lithium, which I have been taking for long time. I was taken to hospital by my family members after my symptoms worsened and I was given intravenous fluids and other supportive measures, following which my condition improved gradually.

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Reference