

Lithium Toxicity Following Vertical Sleeve Gastrectomy: A Case Report

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We are presenting the first documented case of lithium toxicity after vertical sleeve gastrectomy surgery in an 18 year-old female with psychiatric history of bipolar disorder who was treated with lithium. This case illustrates the need for closer monitoring of lithium levels following bariatric surgery. Both psychiatrists and surgeons should be aware of the potential risk of lithium toxicity following bariatric surgery, as well as the need to judiciously monitor lithium level and possibly adjust the dose of some medications.

KEY WORDS: Lithium; Bariatric surgery; Gastric bypass; Gastrectomy; Intestinal absorption.

INTRODUCTION

There are more than 150,000 bariatric surgeries performed in the United States each year.¹⁾ About two-thirds of patients presenting for bariatric surgery have a history of some psychiatric disorder,²⁾ and around 4.0% of bariatric candidates suffer from bipolar disorder.^{2,3)} Over one-third of patients who undergo bariatric surgery take some psychiatric medication.^{2,4)} Lithium continues to be used as a first-line treatment for bipolar disorder and, given its narrow therapeutic window, changes in lithium pharmacokinetics following bariatric surgery is of particular interest.

We report a case of lithium toxicity after sleeve gastrectomy that illustrates the potential need for closer monitoring of lithium levels following bariatric surgery. The established association between morbid obesity and psychiatric disease^{2,3,5)} makes understanding how bariatric surgery affects the pharmacokinetics of psychotropic drugs of utmost importance.

CASE

An 18-year-old female with a history of bipolar disorder, anxiety disorder, and bulimia nervosa, initially pre-

sented to the Emergency Department complaining of fatigue, diarrhea, and tremors. The patient was taking 900 mg of lithium daily (300 mg morning, 600 mg evening). She was also taking citalopram 30 mg once daily and ziprasidone 160 mg once daily. The patient had undergone a vertical sleeve gastrectomy five weeks prior to presentation. The patient had lost 70 pounds since starting her bariatric surgery consultation program 6 months prior to presentation. Since her surgery, she had intermittent symptoms of vomiting and nausea, which contributed to poor fluid intake.

The patient was admitted for dehydration and acute kidney injury, and aggressive intravenous hydration was initiated. Lithium level was found to be 2.7 mmol/L, and lithium toxicity was diagnosed. Other laboratory findings upon admission included: serum sodium 133 mmol/L, potassium 3.1 mmol/L, chloride 96 mmol/L, bicarbonate 20 mmol/L, blood urea nitrogen (BUN) 53 mg/dl, creatinine (Cr) 2.19 mg/dl and hemoglobin (Hb) of 11.7 g/dl.

The patient's condition deteriorated dramatically on the second day of admission and she became very lethargic and obtunded. Despite having received 5 L intravenous fluid, the lithium level remained elevated at 2.6 mmol/L (BUN 44 mg/dl and Cr 1.50 mg/dl). Serum sodium, potassium, chloride and bicarbonate all normalized, while the Hb level declined to 10.3 g/dl. On examination, the patient was irritable and uncooperative. As the day progressed, she became more agitated, increasingly confused and disoriented. No coarse tremors or fasciculations were noted. She was given 5 mg intramuscular olanzapine for

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agitation and some improvement was noted. Nephrology consult recommended urgent dialysis. Two courses of hemodialysis were subsequently performed, and by the third day of her admission her serum lithium was 1.4 mmol/L. She continued to exhibit agitation, restlessness, and confusion with inability to follow 1-step commands. Chest and abdominal computed tomography (CT) scan showed no significant pathology; head CT showed no evidence of bleeding or stroke. Hospital course was further complicated by thyroid storm, nephrogenic diabetes insipidus, and pneumonia. Her mental status gradually improved as complications were treated. The patient was discharged 19 days after admission at which time no neurologic sequelae were noted.

DISCUSSION

We present the first documented case of lithium toxicity after vertical sleeve gastrectomy surgery. Although not well studied, concerns over alterations in the pharmacokinetics of lithium following bariatric surgery have been documented in the literature. Notably, there have been two cases of lithium toxicity following Roux-en-Y gastric bypass.^{6,7)}

The mechanism behind our patient's lithium toxicity is likely multifactorial. The patient had acute kidney injury, as evidenced by her increased creatinine, as well as likely secondary decreased fluid intake and dehydration. One study found the incidence of acute kidney injury in individuals who underwent bariatric surgery to be 5.8%.⁸⁾ Given that lithium is primarily renally excreted, it is clear that an alteration in hydration status affecting kidney function would lead to decreased lithium clearance. Dehydration occurs frequently during the six months following bariatric surgery, owing to the mechanically restricted stomach limiting fluid intake.

Additionally, weight loss itself can contribute to changes in the pharmacokinetics of lithium. In one study, the clearance of lithium in obese individuals was found to be significantly greater than that of a control group (33.9±7.0 ml/min versus 23.0±6.2 ml/min; $p=0.005$).⁹⁾ The 31.75 kg weight loss our patient experienced in just a few months may have impaired her lithium clearance.

Furthermore, the possibility of increased lithium absorption after bariatric surgery has been raised previously in the literature. In one *in vitro* model, investigators studied the dissolution of psychotropic drugs in media environments that mimic the gastrointestinal tract of a post-Roux-en-Y patient and compared to that of a preoperative

patient. While most of the drugs studied were found to have decreased or unaffected dissolution, the dissolution of lithium increased significantly (>200%) in the post bariatric surgery model.¹⁰⁾ Stomach pH increases significantly following both Roux-en-Y and vertical sleeve gastrectomy,¹¹⁾ which may facilitate the deprotonation of carbonate salt and result in an increased dissolution of lithium ions.

Given its narrow therapeutic window, lithium is a high-risk drug post bariatric surgery. Careful monitoring and perhaps dose reductions may be necessary for patients during the pre- and postoperative period.

Although some institutions have protocols in place to monitor lithium levels before and after bariatric surgery,¹²⁾ there are currently no widely accepted guidelines. A significant gap still exists in the literature concerning the pharmacokinetics of psychotropic medications following bariatric surgery. Further research on the pharmacokinetic changes of high-risk medications like lithium following bariatric surgery seems needed.

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