CASE REPORT

Lithium toxicity after Roux-en-Y bariatric surgery

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SUMMARY

A 61-year-old woman with medical history significant for morbid obesity, type II diabetes mellitus, nephrogenic diabetes insipidus and bipolar disorder, had been stable on lithium carbonate therapy for several years. She had undergone a Roux-en-Y bypass surgery and, at the time of her surgery, her lithium level was found to be 0.61 mEq/L on a maintenance dose of 600 mg orally twice per day. She was discharged 8 days postoperatively on the same lithium dose, but presented to the emergency department 12 days postoperatively with signs of lithium toxicity. Her lithium level was elevated to 1.51 mEq/L and she was treated for lithium toxicity with supportive care and, ultimately, reduction of her lithium dose. Clinicians should be aware that dramatic and poorly understood changes in drug absorption may occur after bariatric surgery.

BACKGROUND

Obesity is a chronic illness with profound medical complications. The WHO estimates the number of obese people worldwide as being over 600 million, with a greater prevalence in developed countries.¹ Regular exercise and diet as a way of tempering weight gain is not achievable for many patients. Gastric bypass surgery as an alternative method of weight loss has become an acceptable strategy for weight loss in patients with obesity and specific comorbidities, and can lead to improved glycaemic control and even resolution of diabetes mellitus and cardiovascular disease.²⁻³ The surgical alterations to the stomach and intestinal tract are well-known to affect vitamin and mineral absorption, however, they may also affect drug absorption. As the number of patients having bariatric surgery increases, it is important for physicians to recognise that changes in medication formulations and dosing of many common drugs may be necessary.⁴

Frequently, patients being evaluated for bariatric surgery have psychiatric comorbidities. In one study, by Kalarchian *et al*,⁵ 66% of patients presenting for bariatric surgery had a history of a clinical psychiatric disorder and 38% of these had an active mood disorder. As lithium salts are one of the mainstays of treatment for bipolar disorders, a large number of morbidly obese patients undergoing evaluation for weight loss surgery may be on lithium for its mood stabilisation effects. It is therefore important to be aware of the altered pharmacokinetics of lithium in bariatric surgery patients, especially given lithium's narrow therapeutic index.

CASE PRESENTATION

We present the case of a 61-year-old woman with medical history significant for morbid obesity, type II

diabetes mellitus, recently diagnosed nephrogenic diabetes insipidus and bipolar disorder, stable on lithium carbonate therapy, who had undergone a Roux-en-Y gastric bypass 12 days prior to admission. At the time of surgery, her lithium level was found to be 0.61 mEq/L (upper limit of normal is 1.3). Prior to her bariatric surgery, all her medications had been converted to liquid formulations and she was discharged postoperatively 4 days prior to her emergency presentation. Due to her diagnosis of diabetes insipidus and concern for inadequate fluid intake, she had been discharged on intravenous D5 water at 150 mL/h until her planned follow-up at day 10 post-discharge. However, she presented to the emergency department prior to this planned visit with complaints of lightheadedness, dizziness, weakness and fatigue. On readmission, she was found to have a heart rate of 48 bpm, blood pressure of 74/38 mm Hg and an oxygen saturation of 99% on room air. She was alert and oriented, and the remainder of her neurological examination was unremarkable.

INVESTIGATIONS

Initial laboratory investigations demonstrated serum sodium of 128 mEq/L and a lithium level of 1.51 mEq/L. Her ECG demonstrated a regular sinus bradycardia with junctional escape rhythm. Her cardiac troponin I was below the cut-off for acute myocardial infarction. The patient was admitted to the intensive care unit, for hypotension and bradycardia and a diagnosis of lithium toxicity was made.

DIFFERENTIAL DIAGNOSIS

The patient was admitted with bradycardia and hypotension. Dehydration from poor oral intake and septic shock, from possible pneumonia, urinary or intra-abdominal source after her recent surgery were also considered.

TREATMENT

The patient received intravenous fluids and supportive care. The sodium and lithium levels corrected with intravenous hydration, and after 2 days of haemodynamic support with dopamine, she stabilised without further need for intervention. She initially received intravenous vancomycin and piperacillin/tazobactam, but these were discontinued after 48 h when culture data from blood and urine showed no growth.

OUTCOME AND FOLLOW-UP

The patient remained in the intensive care unit for 3 days before being transferred to the ward, on a lower dose of lithium of 300 mg orally twice per

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day. When she was discharged from the hospital, her lithium level was 0.54 mEq/L. She has not experienced lithium toxicity since the incident, but has continued to require lower dosages of lithium. Her current dose is 450 mg of extended release lithium carbonate once per day.

DISCUSSION

The most common type of bariatric surgery is Roux-en-Y gastric bypass, which is the procedure that our patient underwent. In this surgery, a small stomach pouch is created and then reattached to the small intestine (the 'Roux' limb), bypassing the remaining stomach and duodenum. The resulting biliopancreatic limb is made up of the rest of the stomach and proximal small intestine, reattached to the jejunum (the 'Y') and contains the digestive enzymes from the stomach, bile and pancreas (figure 1). Weight loss is achieved by restrictive and malabsorptive processes.⁷ Postoperatively, patients who have undergone Roux-en-Y gastric bypass are at risk of a number of vitamin and mineral deficiencies.⁸ In order to minimise these deficiencies, recommended nutrient supplementation regimens are employed and vary depending on the specific operative procedures undertaken.⁹

Lithium carbonate is a commonly used drug for the treatment of bipolar depression and, less commonly, other mood disorders. It is quickly and almost completely absorbed from the gastrointestinal tract. Lithium has no appreciable protein binding, and its volume of distribution of total body water is 0.7–0.9 L/kg. It is almost entirely renally excreted, with 80% of the drug filtered by the glomerulus being reabsorbed in the proximal tubule and loop of Henle. The clearance of lithium is approximately 20–30% of the glomerular filtration rate (GFR). Therefore, decreases in GFR (which are expected to occur with weight loss) cause increased serum lithium concentrations, and, conversely, increases in GFR cause decreased serum concentrations.¹⁰

In an in vitro model of pre and post-Roux-en-Y gastric bypass surgery, Seaman *et al*¹¹ looked at the dissolution of a number of psychiatric medications. The model incorporated pH changes, temperature, transit time and the presence or absence of digestive enzymes. Ten of the 22 drugs studied demonstrated decreased dissolution rates in the postbariatric model while only two drugs (including lithium) showed clearly increased rates of drug dissolution. In a case report, Walsh and Volling¹² described a 53-year-old woman stable on lithium prior to Roux-en-Y surgery. Two weeks postsurgery, the lithium level had increased

Table 1 Drugs with known effects to absorption after gastric bypass surgery

Decreased absorption	Increased absorption
Phenytoin ¹³	Digoxin ¹⁴
Erythromycin ¹⁵	Atorvastatin ¹⁶
Ampicillin ¹⁷	Lithium ¹²
Levonorgestrel ¹⁸	Penicillin ¹⁹
Cyclosporine ^{20 21}	
Tamoxifen ²²	
Warfarin ²³	
Imatinib ²⁴	
Tacrolimus ²⁵	

by about 50% with a stable creatinine, and 1 month postsurgery, the patient was toxic with a level of 3.22 mmol/L and had a serum creatinine level of 3.41 mmol/L. It is unclear if the increased absorption of lithium caused the kidney injury or if dehydration caused the kidney injury and the resultant increase in lithium levels.

Unfortunately, the effects on absorption of most drugs is little studied and poorly understood.⁴ While in vitro drug dissolution is important when considering overall drug absorption, it alone cannot predict changes in absorption postgastric bypass. Other factors including reduction in surface area, changes in transit time and reduction in food ingestion all contribute and can neither be easily modelled nor predicted. In addition, various formulations of the same drug, for example, liquid, tablet or extended release, also likely affect drug absorption to an unknown degree.

The limited pieces of information available are often from case reports or small series, but the current effects of Roux-en-Y gastric bypass on the absorption of common drugs are summarised in table 1.

The patient described in this report presented with signs and symptoms of lithium toxicity shortly after gastric bypass surgery. Due to concerns regarding dehydration from the already established lithium-induced nephrogenic diabetes insipidus, she was discharged with intravenous fluids to avoid renal complications. There was no appreciable acute kidney injury present when she presented to the emergency department, so it is likely that changes in lithium dissolution and absorption played more of a role in the lithium toxicity than increased or decreased renal tubular excretion.

Bariatric surgery patients have a complex and largely unstudied physiology. A multidisciplinary approach should be employed preoperatively and postoperatively for these patients, to ensure haemodynamic and biochemical stability. While many drugs have decreased absorption postoperatively, it must be

Figure 1 Depiction of Roux-en-Y gastric bypass. Illustration by Emily Kim.

Learning points

- ▶ Bariatric surgery is now a common and acceptable strategy for weight loss in the morbidly obese.
- ▶ The absorption of drugs and nutrients by the gastrointestinal tract can be markedly affected by the alterations of bariatric surgery.
- ▶ Dosages of drugs need to be closely reconsidered and carefully monitored in patients who have undergone bariatric surgery.

recognised that there are certain medications, such as lithium carbonate, that are sensitive to gastric bypass surgery and have significant increases in dissolution and absorption causing previously stable plasma levels to become toxic without a change in the dose administered.

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