

Severe Hypermagnesemia Resulting from Laxative Use in a Patient with Renal Insufficiency

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Normally, ingested magnesium is readily excreted in the urine. Hypermagnesemia is an uncommon laboratory finding, and symptomatic hypermagnesemia is rare.^{1,2} However, hypermagnesemia may develop in patients with impaired renal function or in those who are given a large dose of magnesium either intravenously or as an enema.³ This article describes the case of an elderly man with chronic renal failure who ingested magnesium-containing laxatives and developed confusion and severe symptomatic hypermagnesemia in the context of worsening renal function. The clinical and laboratory findings typical of hypermagnesemia and the management of the disorder are also discussed.

CASE PRESENTATION

Patient Presentation and History

A 76-year-old man came to the emergency department because of progressively worsening confusion, fatigue, weakness, numbness in all extremities, and lower abdominal fullness and discomfort of several weeks' duration. He had associated slurring of speech, along with nausea and anorexia. The patient had a 2-year history of chronic constipation, for which he took one or two 16-oz bottles of over-the-counter milk of magnesia daily. Initially, the milk of magnesia was effective, but with prolonged use, larger doses were required for relief of constipation. The patient's medical history included chronic renal failure caused by longstanding hypertension (baseline creatinine level of 2.3 mg/dL), peptic ulcer disease, thrombocytopenia, iron deficiency anemia, and emphysema caused by smoking. The patient had no history of alcohol abuse. His medications included milk of magnesia, an iron supplement, and ranitidine.

Physical and Neurologic Examinations

Physical examination revealed a well-developed elderly man in no acute distress. His blood pressure was 103/60 mm Hg, heart rate was 60 bpm, respiratory rate was 20 breaths/min, and temperature was 36.7°C (98°F). His pupils were equal, round, and reactive to light, and the extraocular muscles were intact. The patient's neck was supple, without any lymphadenopathy or jugular venous distention. The chest was clear to auscultation bilaterally, and the heartbeat was regular with a grade II/VI systolic ejection murmur. Abdominal examination was unremarkable.

On neurologic examination, the patient appeared confused. Cranial nerves II through XII were intact. The strength in the right upper extremity was diminished to grade 3/5 but was 5/5 in all other extremities. The deep tendon reflexes were 1+ and symmetrical; the plantar reflexes were equivocal.

Laboratory Measurements

The patient's laboratory measurements revealed the following values: leukocyte count, $26.7 \times 10^3/\text{mm}^3$; hemoglobin, 9.7 g/dL; hematocrit, 24%; platelet count, $754 \times 10^3/\text{mm}^3$; serum sodium, 126 mEq/L; serum potassium, 6.6 mEq/L; serum chloride, 85 mEq/L; serum carbon dioxide, 32 mEq/L; blood urea nitrogen, 85 mg/dL; serum creatinine, 4.8 mg/dL; plasma glucose, 166 mg/dL; serum magnesium, 9.4 mEq/L;

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Table 1. Causes of Hypermagnesemia

Addison's disease
Decreased renal excretion
Familial hypocalciuric hypercalcemia
Hyperparathyroidism
Hypothyroidism
Lithium intoxication
Renal failure (glomerular filtration rate less than 30 mL/min)
Theophylline intoxication
Tumor lysis syndrome

serum phosphorus, 9.1 mg/dL; serum calcium, 7.4 mg/dL; and serum albumin, 2.1 g/dL.

Additional Studies

Radiographs of the patient's chest and abdomen showed no abnormalities. A 12-lead electrocardiogram (ECG) revealed a 1-degree atrioventricular block, which was not seen on prior ECGs. Results of blood and urine cultures were negative.

Hospital Course

The patient underwent emergent hemodialysis for hyperkalemia and hypermagnesemia. Calcium was not used intravenously to treat the hypermagnesemia, because the patient's serum phosphorus level was very high and hemodialysis was readily available in the hospital.⁴ The patient underwent a computed tomography scan of the head, which showed no abnormalities. He developed upper gastrointestinal bleeding, with a decrease in hemoglobin to 6.5 g/dL, and received a blood transfusion. Upper endoscopy was performed, showing esophagitis. The patient developed respiratory failure, requiring mechanical ventilation and vasopressor administration for blood pressure support. He continued to require dialysis for acute renal failure. His magnesium level was less than 4 mEq/L after the initial dialysis treatment and remained between 2.9 and 3.7 mEq/L during his hospital stay. He also developed an intra-abdominal abscess involving the gallbladder, which also may explain the initial elevation in the leukocyte count. Because his overall condition and prognosis were poor, life support was withdrawn at the family's request, and the patient died within 24 hours.

DISCUSSION

General Considerations

Magnesium is the fourth most abundant cation in the body and the second most abundant cation intracel-

lularly, after potassium. Bone and skeletal muscle are the major reservoirs for magnesium. Serum magnesium in healthy patients is closely regulated within a normal range of 1.40 to 1.75 mEq/L (0.7–0.9 mmol/L). Approximately 30% to 40% of the normal dietary intake of magnesium is absorbed by the gastrointestinal tract. Absorption occurs primarily in the distal portion of the small intestine, namely the jejunum and the ileum.^{2,5} Approximately 70% to 80% of magnesium is filtered at the glomerulus. Approximately 5% to 15% of its reabsorption occurs in the proximal tubule, 60% to 70% occurs in the thick ascending limb (TAL) of the loop of Henle, and 10% to 15% occurs in the distal tubule.

Etiology

Hypermagnesemia is an uncommon laboratory finding.⁵ Various disease states (Table 1) may either present with or result in mild increases in magnesium levels.^{6,7} Parathyroid hormone (PTH), calcitonin, glucagon, and vasopressin stimulate magnesium absorption in the TAL of the loop of Henle and the distal collecting tubule. PTH enhances both calcium and magnesium reabsorption in the loop of Henle by increasing sodium chloride reabsorption (thus generating a transepithelial potential difference) and increasing the permeability of the TAL to paracellular magnesium transport. Calcitonin increases magnesium reabsorption in the loop of Henle. The effects of calcitonin may be mediated by cyclic adenosine monophosphate (cAMP) generation in the TAL. Glucagon enhances magnesium reabsorption via a glucagon-sensitive adenylate cyclase. Vasopressin's action is mediated through stimulation of the sodium/potassium/chloride triporter, which increases lumen-positive voltage, thereby increasing magnesium and calcium transport.^{5,7} Corticosteroid hormones also stimulate sodium chloride and magnesium absorption in the TAL. Possible mechanisms of the absorption include an increase in luminal positive voltage, an increase in paracellular permeability, and, in some cases, mediation by cAMP.

Pathophysiology

Hypermagnesemia is accompanied by other concomitant laboratory and physiological abnormalities. In hypermagnesemia, calcium and magnesium reabsorption is decreased in the proximal tubule and then in the loop of Henle. Elevated magnesium levels also decrease total sodium and water reabsorption in the proximal tubule. Metabolic acidosis, hypercalcemia, hypokalemia, phosphate depletion, alcohol use, and volume expansion all produce an immediate increase in magnesium excretion in the urine. Therefore, hypomagnesemia may be

Table 2. Clinical Consequences of Hypermagnesemia

Magnesium level > 4 mEq/L

Inhibition of neuromuscular transmission
 Deep tendon reflexes abolished
 Inhibition of cardiac electrical conduction with prolongation of PR and QT intervals

Magnesium level > 7 mEq/L

Lethargy
 Hypotension

Magnesium level > 10 mEq/L

Paralysis of voluntary muscles
 Respiratory failure
 Heart block or asystole

Table 3. Over-the-Counter Antacid or Laxative Preparations

Drug	Contents	Preparation
Gaviscon*	Aluminum hydroxide	95 mg/15 mL (suspension)
	Magnesium carbonate	358 mg/15 mL (suspension)
Maalox*	Aluminum hydroxide	225 mg/5 mL (suspension)
	Magnesium hydroxide	200 mg/5 mL (suspension)
Milk of magnesia	Magnesium hydroxide	390 mg/5 mL (suspension)
		300 mg (tablet)
Mylanta*	Calcium carbonate	311 mg (gelcap)
	Magnesium carbonate	232 mg (gelcap)

*Brand name.

encountered in clinical conditions such as diabetic ketoacidosis, phosphate depletion, and alcoholism.

Clinical Manifestations

The many clinical manifestations of hypermagnesemia include findings ranging from weakness and lethargy to coma. Other manifestations are outlined in **Table 2**. The majority of reported cases of hypermagnesemia have occurred in patients with impaired renal function and are iatrogenic in nature.⁸ In rare instances, magnesium levels may be elevated to toxic levels (ie, 5 mEq/L or greater).⁹ In the case patient, hypermagnesemia may not have directly caused his death, but it played a major indirect role by causing altered mental status, bradyarrhythmia, and hypotension, resulting in aspiration pneumonia and sepsis.

Neuromuscular toxicity has been frequently described in severe cases of hypermagnesemia, as occurred in this patient, resulting in somnolence, loss of deep tendon reflexes, and respiratory failure from muscle paralysis. The neurotoxicity of hypermagnesemia is caused by the inhibition of acetylcholine release from the neuromuscular end plate.

Hypotension results from cutaneous flushing and is mediated through vasodilatation of vascular smooth muscle and inhibition of norepinephrine release by sympathetic postganglionic nerves. Hypocalcemia has been reported in some patients because of suppression of PTH.⁵ However, calcium acts as a direct antagonist to magnesium, and the intravenous use of calcium can reverse the potentially lethal respiratory and cardiovascular effects of hypermagnesemia.^{4,10}

The case patient underwent dialysis because of his hyperkalemia and high phosphate levels. Hyperkalemia

is a rare finding in hypermagnesemia and occurs from the blockade of the potassium channels, resulting in impaired renal excretion of potassium.⁷ In the case patient, this disorder was further compounded by the acute decline in renal function and the inability to excrete potassium.

Diagnosis

A diagnosis of hypermagnesemia should be considered in any patient with renal insufficiency who has hyporeflexia, lethargy, prolonged PR and QT intervals on an ECG, ventricular arrhythmias, hypotension, and respiratory depression. The early recognition and treatment of hypermagnesemia may prevent life-threatening consequences.

Treatment

Initial assessment should focus on the patient's medications and diet (**Table 3**), followed by steps to minimize the intake of magnesium and expedite its removal (**Table 4**). Intravenous infusion of normal saline in volume-depleted patients enhances magnesium excretion. In severe cases, intravenous administration of calcium is indicated and can be life-saving by reversing respiratory depression, cardiac arrhythmia, and hypotension.^{7,11} Intravenously administered calcium induces magnesuria by inhibiting magnesium reabsorption in the TAL. This effect is mediated by the binding of calcium to the extracellular calcium-sensing receptor that is located on the basolateral membrane of this segment of the nephron.^{5,7} Renal excretion of magnesium may be enhanced by volume expansion with intravenous infusion of normal saline and administration of loop diuretics such as furosemide to inhibit reabsorption of magnesium

Table 4. Treatment for Hypermagnesemia

Therapy	Dose	Route	Effect(s)
Calcium chloride	1 g	Central line	Reverses acute cardiac, respiratory, and neurologic effects
Calcium gluconate	100–200 mg	Peripheral line	Reverses acute cardiac, respiratory, and neurologic effects
Intravenously administered saline	1–2 L	Peripheral or central line	Increases magnesium excretion
Furosemide	40–80 mg	Peripheral or central line	Inhibits reabsorption of magnesium in the thick ascending limb of the loop of Henle
Bumetanide	0.5–2 mg	Peripheral or central line	Inhibits reabsorption of magnesium in the thick ascending limb of the loop of Henle
Hemodialysis without magnesium	3–4 h	Central catheter	Removes magnesium
Peritoneal dialysis	12–24 h	Tenckhoff catheter	Removes magnesium

in the TAL. Intermittent hemodialysis was the only effective treatment for the case patient because he also had severe hyperkalemia, hyperphosphatemia, and significant renal failure. A single report exists in the literature of a patient undergoing continuous arteriovenous hemodialysis for hypermagnesemia.¹² Finally, magnesium-containing laxatives and antacids should be avoided in patients with renal insufficiency—even for short-term use—to prevent the serious complications of magnesium intoxication.

HP

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