REVIEW ARTICLE

Fatal Hypermagnesemia Due to Laxative Use: Case Report and Review of the Literature

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ABSTRACT

Q3 We report a case of fatal hypermagnesemia in a 53-year-old woman admitted for acute exacerbation of chronic obstructive
Q4 pulmonary disease and with a history of chronic constipation treated regularly with magnesium-containing laxatives.
Q5 On admission, her magnesium level was 2.0 mg/dL, which rose to a peak of 10.8 mg/dL despite hydration and diuresis in the
Q6 presence of a normal kidney function. Continuous renal replacement therapy was promptly initiated, which reduced her serum magnesium levels, but her condition continued to deteriorate precipitously progressing to shock leading to oligoanuric renal failure, and she died 2 days later. A review of the literature shows that though rare and often unsuspected, severe hypermagnesemia frequently results in death even in individuals with normal renal function despite renal replacement therapy. In patients with constipation, retention of magnesium-based laxative in the gut apparently serves as a reservoir for continuous
Q12 magnesium absorption and contributes to mortality. [Am J Med Sci 2017;▮(▮):▮▮▮–▮▮▮.]

INTRODUCTION

We, recently, encountered a case of fatal hypermagnesemia in a 53-year-old woman who initially had normal kidney function but developed severe hypermagnesemia, acute renal failure and circulatory shock after ingesting large amounts of magnesium oxide (MgOx) and magnesium citrate (MgCit). She developed severe symptomatic hypermagnesemia with confusion and acute decline in her kidney function. Despite rapid lowering of her serum magnesium (Mg) levels with continuous renal replacement therapy (CRRT), the patient's condition deteriorated precipitously and she died 2 days later. Here we provide the details of this case and summarize the findings on similar cases previously published in the medical literature. The clinical and laboratory data associated with severe hypermagnesemia, and the treatment modalities adopted to reverse the fatal effects of this disorder are discussed.[1-15]

CASE REPORT

A 53-year-old Caucasian female with past history of chronic obstructive pulmonary disease, bipolar disorder on lithium, distant history of stroke and chronic constipation was admitted at Tulane Medical Center with chronic obstructive pulmonary disease exacerbation and constipation for 3 days. Her home medications included MgOx, MgCit, lactulose, lithium and sodium phosphate enemas. During the early part of her hospital stay, she received an additional 3.6 g of elemental magnesium in the form of MgOx (800 mg) and MgCit (2.8 g). Her initial laboratory results showed a normal serum creatinine (0.9 mg/dL), a normal lithium serum level (1.2 mmol/L) and a serum Mg level of 2.0 mg/dL (Figure 1). The next morning, approximately 15 hours after admission, the patient developed altered mental status and quickly became confused and lethargic. By that afternoon, she started vomiting, developed respiratory distress requiring intubation, and went into shock (blood pressure = 70/56 mmHg; pulse of 97 beats per minute; respiration of 30/minute). Subsequent laboratory studies showed a normal complete blood count, serum potassium of 3.1 mEq/L, blood urea nitrogen of 29 mg/dL, serum bicarbonate of 29 mmol/L and serum creatinine of 1.7 mg/dL. The serum magnesium level rose to 9.9 mg/dL after 2 days and peaked at 10.8 mg/dL despite vigorous hydration with intravenous normal saline. Nephrology was consulted for management of symptomatic hypermagnesemia. On physical examination, the patient was intubated; her pupils were dilated bilaterally and her extremities were cold and clammy. Her abdomen was hard and distended with diminished bowel sounds. Additional studies included a chest radiograph, which showed no remarkable changes. A radiograph of abdomen showed distended bowel loops, and ECG showed first-degree heart block although the prior ECGs were normal. Urine and blood cultures were negative.

The patient became anuric and eventually required 4 vasopressors (vasopressin, norepinephrine, epinephrine and dopamine) to maintain perfusion. She was given intravenous calcium gluconate and CRRT was quickly initiated, which improved the serum Mg levels to a nadir of 2.9 mg/dL. Despite the marked improvement of serum magnesium levels, her condition and hemodynamic status continued to worsen with prolonged hypotension and decreased perfusion leading to oligoanuric acute kidney injury, hypoxic encephalopathy and death.

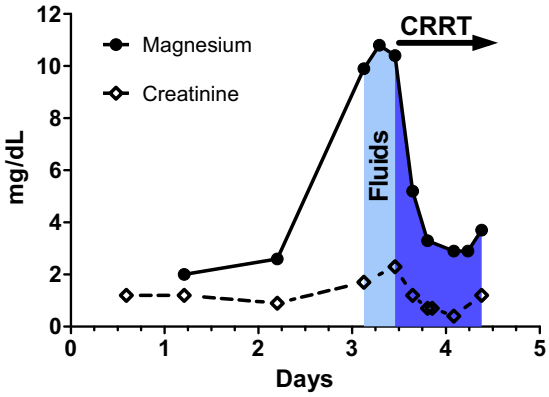

FIGURE. Timeline of serum creatinine and magnesium with corresponding treatments.

DISCUSSION

Magnesium is the second most common and important intracellular divalent cation after calcium, and is an essential mineral for all cells and normal physiological functions.[16-18] Mg is necessary for oxidative phosphorylation, DNA and RNA synthesis, glycolysis, energy metabolism and bone health.[16,19,20] One of the key functions of this divalent cation is regulating the active transport of calcium and potassium with significant effects on neuromuscular junction, the central nervous system and the cardiovascular system.[17-19,21] Normal serum Mg concentrations are between 1.7 and 2.4 mg/dL (0.7–1.1 moL/L) and the kidney plays a vital role in maintaining Mg levels within this range.[17,22] Approximately, 10% of the filtered load of Mg is reabsorbed by the proximal tubule and approximately 50%-70% of the filtered load is reabsorbed passively in the cortical segment of the thick ascending limb of the loop of Henle.[17,19,23] Incidence of hypermagnesemia is very low in individuals with normal kidney function as healthy kidneys eliminate excessive Mg by abrupt reduction in tubular reabsorption to nearly negligible amounts. The major causes of hypermagnesemia are listed in Table 1.

Magnesium compounds are widely used medicinally as common laxatives and antacids (e.g., milk of magnesia) and are sometimes prescribed intravenously for the treatment of hypertension and hyperexcitability of eclampsia.[13,22,24] Hypermagnesemia is a rare condition that is usually iatrogenic or self-induced and severe hypermagnesemia often results in death.[1,2,4-14] The elderly individuals, patients with bowel disorders, and persons with renal impairment who take Mg-containing cathartics or antacids are particularly at high risk of developing hypermagnesemia.[13,14,25] Magnesium-based cathartic ingestion by chronically constipated patients sometimes leads to prolonged colonic retention aggravated by hypermagnesemia-induced paralytic ileus and continuous absorption contributing to sustained hypermagnesemia.[26-28] There are a number of cases in the published literature of patients developing hypermagnesemia in the setting of underlying renal insufficiency.[6,29-31] Although the development of hypermagnesemia is relatively rare in the presence of normal kidney function, there are a number of reports of severe hypermagnesemia in patients with normal renal function.[5,12,25,26,32-34]

Severe hypermagnesemia (serum levels > 8-9 mg/dL) is characterized by progressive loss of neuromuscular, respiratory and cardiovascular functions, decreased bowel motility due to myenteric neuronal block and interference with excitation-contraction coupling of smooth muscle cells, which further aggravates the underlying intestinal motility disorder allowing continued absorption of ingested magnesium. The systemic manifestations related to dose and serum levels of Mg are summarized in Table 2. Severe hypermagnesemia often ends in death despite vigorous attempts to lower serum magnesium levels (Table 3).[1,2,4-14,38]

A number of treatments are available for hypermagnesemia, such as saline diuresis, loop diuretics that can be used to enhance magnesium excretion in patients with normal kidney function and reverse mild symptoms.[25] However, patients with renal failure and life-threatening symptoms should be treated with hemodialysis using magnesium-free dialysate because of its high efficiency in removing magnesium. CRRT can be helpful in the setting of continuous absorption and it can protect against rebound hypermagnesemia. As magnesium acts as a calcium channel blocker, administration of intravenous calcium can help reverse cardiac arrhythmia, respiratory depression and hypotension.[39,40]

Symptoms of hypermagnesemia mimic various other medical conditions such as respiratory failure or septicemia; hence the clinician should keep in mind and watch closely for the possibility of life threatening electrolyte imbalance to avoid adverse outcomes.

TABLE 1. Major causes of hypermagnesemia.

Decreased renal excretion of Mg (GFR < 30 mL/min)
Excessive oral intake
Large doses of Mg-containing enema
Intravenous administration of $MgSO_4$
Addison's disease
Lithium intoxication
Theophylline intoxication

TABLE 2. Systemic effects related to serum Mg levels.

Serum Mg level (mg/dL)	Dose related systemic effects
1.7-2.4	Normal serum levels
5-8	Nausea, vomiting, headache and light headedness
9-12	Absent deep tendon reflexes, somnolence and hypotension
12-15	Sino-atrial and atrioventricular node block, muscle paralysis and hypoventilation
>15	Cardiac arrest, respiratory arrest, coma and death