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Case Report

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Severe Hypermagnesemia Caused by Laxative Use in Patients without Pre-Existing Renal Disfunction

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Abstract

Hypermagnesemia is an uncommon but a serious clinical condition that can be fatal. Magnesium-containing products are widely used as antacids or laxatives. We report severe hypermagnesemia in two constipated patients treated with magnesium-containing laxatives. This report demonstrates that excessive use of magnesium-containing laxatives can cause severe hypermagnesemia even in patients with normal renal function, especially in those patients with advanced age and concomitant bowel disorders. Physicians should be aware of the effects of these medications in constipated patients.
Keywords: Constipation, hypermagnesemia, laxatives, magnesium hydroxide

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INTRODUCTION

Hypermagnesemia is a rare disorder in patients with normal renal function and usually iatrogenic. Serum magnesium (Mg) levels are increased in 5% of hospitalized patients, (1) and more than 70% of patients with hypermagnesemia have abnormal renal function (2). We report two cases of symptomatic hypermagnesemia without pre-existing renal dysfunction

CASE PRESENTATION

Case 1

A 91-year-old woman who had been treated for pneumonia a week ago presented with complaints of confusion, fever, shortness of breath, and generalized weakness. She had a history of hypertension. Three days ago, her serum creatinine (0.36 mg/dL), estimated glomerular filtration rate (CKD-EPI eGFR) (>90 mL/dk/1.73 m^2), and serum Mg level (1.91 mg/dL) were normal (Table 1). She was admitted to the hospital with an initial diagnosis of pneumonia. On arrival, she was normothermic (36.0°C), with respiratory rate 20 breaths/min, heart rate (HR) 78 beats/min, and blood pressure 95/50 mmHg. The patient was lethargic, and the physical examination was unremarkable except for a distended tender abdomen. According to her relatives, she was constipated for a week and was taking Mg-containing laxatives *(Magnesie Calcinee)* during this period. The neurological examination showed a symmetric decrease in muscle tone and deep tendon reflexes. The hemogram showed leukocytosis (white cell count 33.03×10^9/L) and elevated C-reactive protein (152.4 mg/L). The blood chemistry study showed the following: serum creatinine, 0.63 mg/dL; blood urine nitrogen, 15 mg/dL; sodium, 135 mEq/L; potassium, 4.6 mEq/L; magnesium, 5.71 mg/dL; calcium, 8.9 mg/dL; phosphate, 3.45 mg/dL; alanine aminotransferase, 40 U/L; aspartate aminotransferase 43 U/L. Her arterial blood gas analysis revealed that she had decompensated metabolic alkalosis with pH 7.46, bicarbonate ion, 28.6 mmol/L partial pressure arterial CO_2 (PaCO2) 39.9 mmHg; partial pressure arterial oxygen (PaO2) 71.5 mmHg, and O2 saturation 96.1% while on 3 lt/min oxygen through nasal cannula. Electrocardiography (ECG) showed a sinus rhythm with an HR of 58 beats/min and left bundle branch block (PR, 200 ms;

Table 1. Laboratory data on admission and during treatment

Parameter	Patient 1			Patient 2		
	Three days before diagnosis	Hypermagnesemia diagnosis	Third day of treatment	Three days before diagnosis	Hypermagnesemia diagnosis	Third day of treatment
Magnesium (1.6-2.6 mg/dL)	1.91	5.71	2.16	1.84	6.11	2.12
Peripheral leukocyte count ($4.5\text{-}11 \times 10^9$/L)	9.35	33.03	4.95	7.01	5.98	6.96
Serum creatinine (0.5-1.1 mg/dL)	0.36	0.63	0.42	0.76	0.89	0.67
CKD- EPI eGFR (>60 mL/dk/1.73 m^2)	>90	78	>90	82	68	>90
Blood urea nitrogen (8-23 mg/dL)	16	33	10	19	44	17
Sodium (136-145 mEq/L)	125	135	136	142	128	134
Potassium (3.5-5.1 mEq/L)	4.6	4.6	3.4	3.9	5.0	3.2
Calcium (8.7-10.4 mg/dL)	8.0	8.9	8.6	8.5	7.1	6.8
Phosphate (2.4-5.1 mg/dL)	2.17	3.45	1.94	4.23	4.42	3.34
ALT (10-49 U/L)	14	40	19	58	42	87
AST (<34 U/L)	30	43	30	33	27	76

ALT: alanine aminotransferase; AST: aspartate aminotransferase; eGFR: estimated glomerular filtration rate

QT interval, 473 ms). Urinary ultrasonography showed normal renal parenchymal echogenicity and thickness (10 mm). Computed tomography of the abdomen revealed that the rectum was filled with feces and fluid, which suggested the presence of ileus. Intravenous hydration with normal saline, intravenous calcium infusion and broad-spectrum antibiotics were started. Gastrointestinal decontamination was performed. Twelve hours after the patient's admission, magnesium level was rechecked, with a result of 7.18 mEq/L. Because of the patient's hemodynamic instability (blood pressure, 60/40 mmHg; HR, 60 beats/min) and oliguria, she was transferred to intensive care unit and was started on vasopressor support with norepinephrine and dopamine, intravenous hydration, and furosemide infusion. Three days after the cessation of Mg intake and supportive treatment, serum Mg level decreased (2.16 mg/dL), the patient was weaned from vasopressors, and urine output was restored with no need to perform hemodialysis. Subsequently inflammatory markers (leukocyte count, C-reactive protein, and procalcitonin) decreased; and the patient was discharged with a full recovery.

Case 2

A 65-year-old woman with a history of metastatic thymoma was admitted to the hospital with bicytopenia and urinary tract infection. She had not taken any chemotherapy drugs for the last three months. Her initial laboratory results showed a normal serum creatinine (0.78 mg/dL, CKD-EPI eGFR:82 mL/dk/1.73 m^2), and a serum Mg level of 2.02 mg/dL (Table 1). Abdomen imaging showed no findings of renal parenchymal disease. During her hospital stay, she received Mg-containing laxatives *(Magnesie Calcinee)* for chronic constipation. She became confused and lethargic on the seventh day of medication, although inflammatory markers were decreasing. Her blood pressure was 85/44 mmHg and pulse was 65 beats/min. The physical and neurological examination was unremarkable. The serum Mg level was elevated to 6.11 mg/dL and peaked at 7.04 mg/dL (normal range, 1.6-2.6). Concurrent laboratory studies showed serum creatinine 0.89 mg/dL, blood urea nitrogen 44 mg/dL, and serum calcium 7.1 mg/dL. Results of arterial blood gas analysis in room air [pH, 7.52; PaO_2, 84.9 mmHg; $PaCO_2$, 42 mmHg; bicarbonate ion, 34.4 mmol/L; base excess, 10.8 mmol/L; lactate, 1.6 mmol/L) indicated decompensated metabolic alkalosis. ECG showed a sinus rhythm with an HR of 62 beats/min. Intravenous hydration with normal saline, loop diuretics, and intravenous calcium administration was promptly initiated. Blood pressure improved with intravenous hydration (110/67 mmHg), and urine output was 3 L/day. Subsequently the serum Mg level decreased and was 2.12 mg/dL after three days. Patient was diagnosed with irritable bowel syndrome, and her treatment was planned with dietary modification and other laxatives. Informed consent was received for this study.

DISCUSSION

Mg is the fourth most common mineral and second most abundant cation in the human body, which is regulated by the intestine and the kidney (3). Because of its role in physiological processes, alteration in serum Mg concentration is associated with important

clinical symptoms. The kidney has a crucial role in maintaining the normal plasma Mg concentration in the narrow range of 1.6-2.3 mg/dL (0.66-0.94 mmol/L). Approximately, 15%-20% of the filtered Mg is reabsorbed in the proximal tubule, and most of the filtered Mg (50%-70%) is passively reabsorbed in the cortical segment of the thick ascending limb of the loop of Henle with paracellular mechanisms (4). In circumstances of increased dietary intake or excessive Mg administration, kidneys increase Mg excretion. Hypermagnesemia is rare because of this renal ability (5).

There are two major mechanisms of hypermagnesemia: renal function impairment and excessive magnesium intake (6). The serum Mg levels rise as renal function declines, but through the renal adaptation to increase magnesium excretion, serum Mg levels are well maintained until the creatinine clearance falls below 20 mL/min. Significant hypermagnesemia is rare unless the patient has received exogenous Mg. Although most commonly seen in patients who had parenteral Mg for preeclampsia, hypermagnesemia has been reported in patients receiving Mg-containing antacids, laxatives, or enemas even with normal renal functions (7-9). When Mg load exceeds renal excretion capacity, it causes hypermagnesemia as in both of our patients who were taking Mg-containing laxatives for chronic constipation. Clark and Brown (10) reported that hypermagnesemia is common in patients with bowel disorders that may enhance Mg absorption, and advanced age is an important risk factor. The patient in Case 1 with ileus was 91-year-old; and although she had apparently normal renal function, a decline in GFR was possibly accompanying her age.

Manifestations of hypermagnesemia are closely related to serum Mg concentration. Initial symptoms are observed when serum Mg level exceeds 4 mg/dL. Neuromuscular symptoms range from lethargy, drowsiness, and diminished deep tendon reflexes to somnolence, loss of deep tendon reflexes, and muscle paralysis. Bradycardia and hypotension are the earliest cardiovascular manifestations of hypermagnesemia. ECG changes, like prolongation of the P-R interval, an increase in QRS duration, and an increase in Q-T interval, are common. If untreated, it may progress to complete heart block and asystole, which can be fatal. Our patients had complaints of drowsiness and lethargy. In Case 1, oliguric acute renal injury contributed to hypermagnesemia that caused severe hypotension and shock.

Treatment of hypermagnesemia is based on cessation of Mg intake and volume repletion. Loop diuretics can enhance renal excretion of Mg. For cardiac arrhythmias thought to be secondary to elevations in serum Mg, infusion of calcium can stabilize the cardiac membrane. The patients with advanced renal insufficiency and/or severe hypermagnesemia manifestations often require dialysis.

CONCLUSION

We described two patients without pre-existing renal dysfunction who developed severe hypermagnesemia after oral ingestion of Mg-containing laxatives and were treated successfully. These cases suggest that severe hypermagnesemia can occur in the absence of pre-existing renal dysfunction, especially in patients with bowel disorders and advanced age. Routine measurement of serum Mg level, especially in high-risk patients, and initiating appropriate treatment promptly can ameliorate patients' course.

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REFERENCES

1. Whang R, Ryder KW. Frequency of Hypomagnesemia and Hypermagnesemia: Requested vs Routine. J Am Med Assoc 1990; 263: 3063-4. [CrossRef]
2. Crook M. A Study of Hypermagnesaemia in a Hospital Population. Clin Chem Lab Med 1999; 37: 449-51. [CrossRef]
3. Smogorzewski MJ, Stubbs JR, Yu ASL. Disorders of calcium, magnesium, and phosphate balance. In: Skorecki K, Chertow G, Marsden P, Yu A, Taal M, eds. Brenner & Rector's The Kidney. 10th ed. Philadelphia: Elsevier Inc.; 2016: 193-6.
4. Rouffignac C, Quamme G. Renal Magnesium Handling and Its Hormonal Control. Physiol Rev 1994; 74: 305-22.[CrossRef]
5. Touyz RM. Magnesium in clinical medicine. Front Biosci 2004; 9: 1278-93. [CrossRef]
6. Smogorzewski MJ, Stubbs JR, Yu ASL. Disorders of Calcium, Magnesium, and Phosphate Balance. In: Skoreck K, Chertow G, Marsden P, Yu A, Taal M, eds. Brenner & Rector's The Kidney. 10th ed. Philadelphia: Elsevier Inc.; 2016: 625-6.
7. Bokhari SR, Siriki R, Teran FJ, Batuman V. Fatal Hypermagnesemia Due to Laxative Use: Case Report and Review of the Literature. Am J Med Sci 2017; 355: 390-5. [CrossRef]
8. Weng YM, Chen SY, Chen HC, Yu JH, Wang SH. Hypermagnesemia in a constipated female. J Emerg Med 2013; 44: e57-60. [CrossRef]
9. Tatsumi H, Masuda Y, Imaizumi H, Kuroda H, Yoshida S, Kyan R, et al. A case of cardiopulmonary arrest caused by laxatives-induced hypermagnesemia in a patient with anorexia nervosa and chronic renal failure. J Anesth 2011; 25: 935-8. [CrossRef]
10. Clark B, Brown R. Unsuspected morbid hypermagnesemia in elderly patients. Am J Nephrol 1992; 12: 336-43. [CrossRef]