

ONLINE FIRST

Hypomagnesemia and Proton Pump Inhibitors

Below the Tip of the Iceberg

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Severe magnesium deficiency associated with proton pump inhibitors (PPIs) has been described recently with clinical presentations varying from life-threatening conditions to muscle cramps and paresthesias. Probably milder cases go undetected. We report an asymptomatic case of hypomagnesemia associated with chronic use of PPIs in a 67-year-old woman. She had had symptoms of gastroesophageal reflux disease for several years, which abated partially with PPIs, and denied any other symptoms or medications. Her initial evaluation showed an unexplained hypomagnesemia with a very low magnesium excretion rate in urine. Serum calcium, phosphorus, potassium, and glucose levels and renal function were normal. After PPI withdrawal, serum and urinary magnesium levels normalized.

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Severe magnesium deficiency associated with proton pump inhibitors (PPIs) was first described by Epstein et al in 2006.¹ Sixteen other cases were described subsequently with clinical presentations varying from life-threatening conditions, like collapse with anoxic encephalopathy, to muscle cramps and paresthesias.²⁻⁶ Probably milder cases go undetected. We report an asymptomatic case of hypomagnesemia associated with chronic use of PPIs.

REPORT OF A CASE

A 67-year-old female physician came to the office of one of us (T.W.F.) in May 2009, at the request of her surgeon, seeking advice for losing weight as a preparation for gastroesophageal reflux disease (GERD) surgery. She had had symptoms of GERD for several years, which abated partially with PPI use. She denied any other symp-

toms or medications. Her height was 158 cm, and her weight was 86.5 kg. Her body mass index, calculated as weight in kilograms divided by height in meters squared, was 34.7. Her initial evaluation showed an unexplained hypomagnesemia with a very low magnesium excretion in urine. Serum calcium, phosphorus, potassium, and glucose levels and renal function were normal. She was prescribed a low-calorie balanced diet, divided into 5 to 6 small meals daily, supplemental magnesium hydroxide, and an exercise program (at least 1 hour of exercise, 5 times a week). She lost weight gradually and decreased her PPI intake. After an uneventful surgery for GERD in July 16, 2010, she was able to discontinue PPI use. Serum and urinary magnesium levels normalized after PPI withdrawal (**Figure**).

COMMENT

Hypomagnesemia is usually caused by renal or intestinal loss, such as diuretic therapy, diarrhea, or heavy alcohol consumption. Clinical findings can be re-

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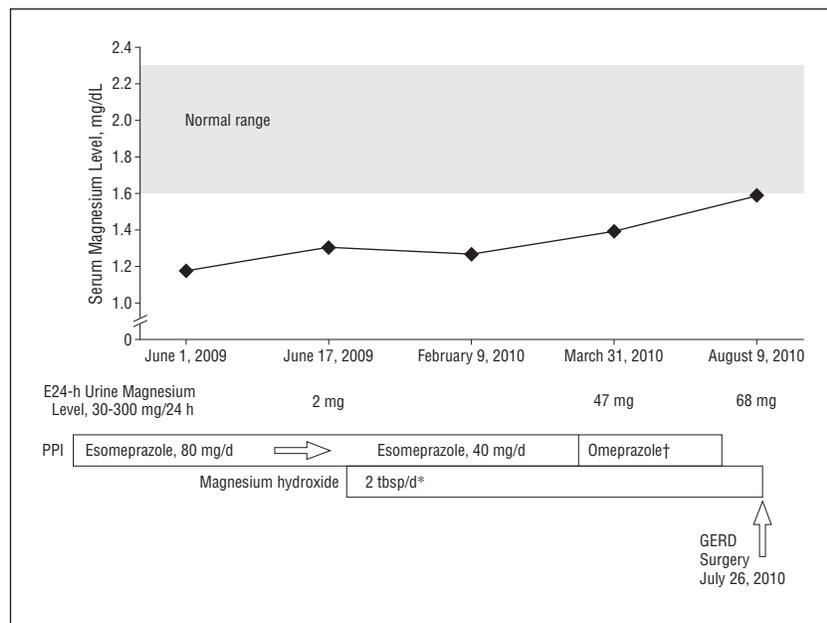


Figure. Serum and urinary magnesium levels and proton pump inhibitor (PPI) use. GERD indicates gastroesophageal reflux disease. *A dosage of about 1000 mg. †A dosage of 40 mg tapered to 15 mg. To convert serum magnesium levels from milligrams per deciliter to millimoles per liter and urine magnesium from milligrams per 24 hours to millimoles per day, multiply by 0.411.

lated to neurologic symptoms, like paresthesia, lethargy, or seizures; muscular symptoms, like cramps or tetany; and cardiovascular manifestations, like arrhythmias or electrocardiogram abnormalities (prolonged QT interval, ST depression, and U waves).¹⁻⁶ Use of PPIs have been recently associated with low magnesium levels, but the mechanism remains not fully understood. Low urinary magnesium excretion was observed in several cases described previously,¹⁻⁶ which suggests that it is likely related to reduced magnesium absorption from the intestine. Intestinal absorption of this ion proceeds in both a passive paracellular and an active transcellular manner.⁷ Cundy and Dissanayake² studied the renal magnesium handling in 2 patients with PPI-related severe hypomagnesemia and the effects of oral magnesium supplements while continuing the PPI. They

observed avid renal magnesium retention after intravenous magnesium infusion, implicating a failure of intestinal magnesium absorption. Because in their patients the hypomagnesemia could be partially corrected by high-dose oral magnesium supplementation, they suggested that PPI use can inhibit active magnesium transport in the intestine.

This drug class is currently widely used for many clinical situations, and many patients may be at risk for this complication. To our knowledge, this is the first case report of asymptomatic hypomagnesemia related to PPI use, which is probably an underreported situation. Mild hypomagnesemia is often asymptomatic but is associated with higher risk of developing dangerous perioperative arrhythmia.⁸ Monitoring magnesium levels in patients taking PPIs, especially in a preoperative setting, should be considered.

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