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Available online at: http://www.iajps.com ***A Case Report***

LONG TERM PPI USE: NOT SO BENIGN AFTER ALL

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Abstract:
Proton pump inhibitors (PPIs) potently inhibit gastric acid secretion and are widely used for treatment of acid-related diseases including gastroesophageal reflux disease and secondary prevention of aspirin/NSAID-induced ulcers. In the following case report, we present a 53-year-old male patient with convulsions caused by severe hypomagnesemia as an adverse effect of proton pump inhibitor (PPI) treatment. He also had hypocalcemia, hypokalemia, borderline vitamin D insufficiency, vitamin B12 deficiency & vertigo as a side effect of long-term PPI use.

Key Words: *Proton Pump Inhibitors (PPIs), Hypomagnesemia, Hypocalcemia, Hypokalemia, Vitamin B12 Deficiency*

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CASE REPORT:

The patient was a 53-year-old Caucasian male. He presented with incapacitating vertigo, confusion and vomiting for 3 days, was reluctant to mobilize because of the vertigo and his oral intake was minimal during this period. 3 weeks before hospital admission he had an episode of tonic-clonic seizure. Medical history was significant for mild glaucoma and essential hypertension. He was on 8mg perindopril, 5mg amlodipine, 20mg omeprazole & 20mg atorvastatin. He was on omeprazole for about 1 year.

On admission, the blood pressure was 186/88 mmHg, pulse was regular at 102 beats/minute and the respiratory rate was 19 per minute. On physical examination there was symmetrically brisk deep tendon reflexes with no focal neurology. He was reluctant to sit up or stand with considerable anxiety. Otherwise the rest of the physical exam was normal. He was cleared from an ENT view point. The laboratory tests showed magnesium 0.1 mmol/L (references: 0.6 - 1.1 mmol/L), adjusted calcium 2.1 mmol/L (references: 2.2 -2.6 mmol/L), potassium 2.7 mmol/ L (references: 3.5 - 5.3 mmol/L), vitamin D 62 nmol/L (borderline insufficiency), vitamin B12 162 pg/ml (180 - 914 pg/ml). Phosphate, PTH, renal profile, TSH and serum folate were within normal limits. The electrocardiogram (ECG) revealed sinus rhythm and the corrected QT interval was within normal limits. Magnetic resonance imaging of the head was normal.

The magnesium, calcium, potassium & vitamin D levels were corrected. Oral cyanocobalamin was prescribed to replenish vitamin B12 stores. All of his symptoms resolved following correction. His PPI treatment was stopped, and he is now under surveillance in the outpatient clinic with no electrolyte abnormalities.

DISCUSSION:

Hypomagnesemia is a common problem, occurring in nearly 12 percent of hospitalized patients and is especially more common in intensive care unit patients. The clinical manifestations of magnesium depletion can be varied and include neuromuscular hyperexcitability (tremors & convulsions), various cardiovascular manifestations including torsade de pointes (a specific form of polymorphic ventricular tachycardia) and other electrolyte abnormalities. The symptoms tend to depend on the rate of development and the actual serum levels.

The presumed mechanism by which omeprazole and other PPIs cause hypomagnesemia is impaired absorption of magnesium by intestinal epithelial cells caused by PPI-induced inhibition of transient receptor potential melastatin-6 (TRPM6) and TRPM7 channels. Renal losses are not likely to be involved, since urinary magnesium excretion is appropriately low in patients with hypomagnesemia due to PPIs.

An important cause of hypocalcemia is hypomagnesemia. The major factors resulting in hypocalcemia in hypomagnesemia patients are hypoparathyroidism, parathyroid hormone (PTH) resistance, and vitamin D deficiency. Low magnesium levels impair PTH release in response to hypocalcemia. PTH-induced release of calcium from bone is substantially impaired when the plasma magnesium concentration falls below 0.8 mmol/L. The main reason for low vitamin D levels is due to decreased conversion of 25-hydroxyvitamin D to 1,25-dihydroxyvitamin D by the kidney.

Hypokalemia is another common feature of patients with hypomagnesemia. Potassium secretion from the collecting duct cell into the lumen is mediated by luminal potassium channels, a process that is inhibited by intracellular magnesium. Hypomagnesemia is associated with a reduction in the intracellular magnesium concentration, which releases this inhibitory effect on potassium efflux resulting in enhanced urinary losses.

Medications that reduce gastric acid may decrease vitamin B12 absorption since gastric acid plays a role in dissociation of vitamin B12 from food proteins, which allows it to bind IF. Long-term use is more likely to cause clinically significant vitamin B12 deficiency. Periodic testing of vitamin B12 levels is often used in individuals receiving long-term gastric acid-suppressing medications, and unexplained macrocytosis and/or macrocytic anemia in these individuals should prompt testing for vitamin B12 deficiency.

CONCLUSION:

PPIs can cause hypomagnesemia due to reduced intestinal absorption. Long-term therapy with PPIs has been associated with vitamin B12 malabsorption. It is important to obtain serum magnesium levels prior to starting a PPI in patients who are expected to be on long term (≥1 year) treatment, or in patients who take PPIs in conjunction with other medications associated with hypomagnesemia. Monitoring magnesium and vitamin B12 levels in patients on long-term PPIs is good practice.

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