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LETTER TO THE EDITOR

Intermittent use of pantoprazole and famotidine in severe hypomagnesaemia due to omeprazole

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Dear Editor,

We read with interest the article 'Hypomagnesaemia due to use of proton pump inhibitors- a review', by Kuipers *et al.*[1] We present here a patient with severe hypomagnesaemia due to omeprazole. We emphasise that the intermittent use of pantoprazole and a histamine H2-receptor antagonist may be an appropriate therapeutic alternative for normalising serum magnesium concentrations, without recurrence of gastro-oesophageal symptoms.

The patient is a 67-year-old man who presented in April 2010 with paresthesia, numbness and weakness in his limbs. His medical history included hypertension, chronic obstructive airways disease and ischaemic heart disease. In October 2006 and December 2006 he was hospitalised because of tetany, with severe hypocalcaemia and hypomagnesaemia, which was attributed to alcoholism, without further studies. In 2006 he was on omeprazole therapy for gastroprotection. The patient was followed up in the outpatient clinic until July 2007, with serum magnesium at the lower limit of normal range or slightly reduced despite oral magnesium supplements. After that, he was lost to follow-up; he continued treatment with omeprazole until his current hospitalisation. The laboratory findings showed hypocalcaemia (1.55 mmol/l), hypomagnesaemia (0.14 mmol/l) and a level of 25-OH-vitamin D at 27.45 nmol/l (our laboratory range, 29.9 to 134.7). The complete blood count, and serum levels of albumin, glucose, creatinine, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, gamma glutamyl transpeptidase, sodium, potassium, and phosphorus were normal. He denied alcohol use, and other causes of hypomagnesaemia were absent, including family history of genetic electrolyte disorders, diarrhoea, and use of laxatives, or diuretics. The slightly low level of 25-OH vitamin D coincided with extraction at the beginning of spring. His medications were aspirin, losartan, diltiacem, fluticasone/salmeterol inhalers and omeprazole 20 mg daily. Omeprazole was stopped and famotidine (40 mg/12 h) initiated. Likewise, he began receiving intravenous magnesium sulphate and calcium gluconate. Then, oral replacement therapy with magnesium supplements (12 mEq/day), calcium carbonate and vitamin D was prescribed. Seven days after admission, the fractional excretion of magnesium was 1.05 (urinary magnesium of 0.49 mmol/l). Fourteen days after admission, the fractional excretion of magnesium was 9.33 (urinary magnesium of 8.27 mmol/l), with a serum magnesium of 0.86 mmol/l. Several authors have raised the possibility that genetic factors might result in increased susceptibility to PPI-induced hypomagnesaemia, as might be the case with heterozygous carriers of TRPM6 mutations.[1-3] In our patient, we searched for mutations by sequencing of all 39 exons of the TRPM6 gene and did not find mutations that can be seen in patients with familial hypomagnesaemia with secondary hypocalcaemia.[4] The laboratory reported the presence of single-nucleotide polymorphisms, rs7018994 (homozygous), rs7859201 (homozygous) and rs11144089 (heterozigous), and to our knowledge, at present, it is unknown whether the combination of these polymorphisms might have a negative impact on protein activity.[5]

After stopping omeprazole, the patient complained of reflux dyspepsia. A gastroscopy showed peptic oesophagitis and thickening of the gastric folds. A distal duodenal biopsy was normal and the IgA anti-tissue transglutaminase antibodies were negative. The gastroenterologists recommended to resume treatment with omeprazole 40 mg daily, and seven days after resuming omeprazole (and continuing with 12 mEq daily of oral magnesium supplements) the level of serum magnesium decreased from 0.86 mmol/l to 0.70 mmol/l, and the fractional excretion of magnesium

decreased to 1.13 (urinary magnesium decreased from 8.27 mmol/l to 0.41 mmol/l). Given the inadequate control of the gastrointestinal discomfort with famotidine in high dosage, and malabsorption of magnesium with omeprazole, we chose alternate-day therapy with omeprazole and famotidine, combined with domperidone and magnesium supplements (12 mEq daily). With this therapeutic regimen the patient was asymptomatic but the fractional excretion of magnesium was low, indicating magnesium deficiency.[6] Some researchers have postulated that pantoprazole is the least potent PPI at suppressing gastric acid secretion.[7] Thus, we replaced omeprazole by pantoprazole 40 mg/24 hour, three days a week (on Monday, Wednesday and Friday), and famotidine 40 mg/24 hour, four days a week (on Tuesday, Thursday, Saturday and Sunday), combined with oral domperidone and magnesium (12 mEq daily). With this last therapeutic regimen, which reduces the administration of PPIs an extra day per week, the patient is asymptomatic and 20 days later the fractional excretion of magnesium had increased to 5.02.

REFERENCES

1. Kuipers MT, Thang HD, Arntzenius AB. Hypomagnesaemia due to use of proton pump inhibitors- a review. Neth J Med. 2009;67:169-72.
2. Broeren MA, Geerdink EA, Vader HL, van den Wall Bake AW. Hypomagnesemia induced by several proton-pump inhibitors. Ann Intern Med. 2009;151:755-6.
3. Cundy T, Dissanayake A. Severe hypomagnesaemia in long-term users of proton-pump inhibitors. Clin Endocrinol (Oxf). 2008;69:338-41.
4. Fernández–Fernández FJ, Sesma P, Caínzos-Romero T, Ferreira L. Hypomagnesemia related to the use of omeprazole. Negative result for mutation in the TRPM6 gene. Med Clin (Barc). 2010; in press.
5. Song Y, Hsu Y-H, Niu T, Manson JE, Buring JE, Liu S. Common genetic variants of the ion channel transient receptor potential membrane melastatin 6 and 7 (TRPM6 and TRPM7), magnesium intake, and risk of type 2 diabetes in women. BMC Med Genet. 2009, 10:4. doi:10.1186/1471-2350/10/4.
6. Fleming CR, George L, Stoner GL, Tarrosa VB, Moyer TP. The importance of urinary magnesium values in patients with gut failure. Mayo Clin Proc. 1996;71:21-4.
7. Kirchheiner J, Glatt S, Fuhr U, et al. Relative potency of proton-pump inhibitors-comparison of effects on intragastric pH. Eur J Clin Pharmacol. 2009;65:19-31.