CASE REPORT

Lansoprazole-induced hypomagnesaemia

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SUMMARY

The introduction of proton pump inhibitors (PPIs) in the late 1980s optimised the medical treatment of acid-related disorders. They are potent medications and have a good safety profile. However, long-term therapy with PPIs may carry undesired side effects, one of which is hypomagnesaemia. This entity is likely to be under-reported. We present a clinical case which illustrates this important clinical problem. We present the case of a 73-year-old woman who was admitted to the hospital with supraventricular tachycardia due to hypomagnesaemia while using lansoprazole, followed by the literature review on this subject. In our patient after the intravenous magnesium replenishment, her arrhythmia resolved. After stopping her PPI her serum magnesium remained within reference values without oral supplementation. We believe that more attention towards this underdiagnosed side effect is required. Serum magnesium concentration should be checked in patients on PPIs if they are unwell or present with arrhythmia.

BACKGROUND

Proton pump inhibitors (PPI)-induced hypomagnesaemia is likely to be under-reported. We believe that more attention towards this underdiagnosed side effect of PPIs is required. Serum magnesium concentration should be checked in patients on PPIs if they are unwell or present with one of the potential manifestations of hypomagnesaemia.

CASE PRESENTATION

A 73-year-old woman presented at our accident and emergency department with a 1-week history of lethargy and palpitations. In the previous days she had felt unsteady on her feet and had noticed a generalised feeling of weakness. She also reported of nausea and vomiting for 2 days and was witnessed to vomit what looked like coffee grounds suggesting an upper gastrointestinal bleed.

Her medical history included non-ST elevation of myocardial infarction 2 years ago; hypertension, chronic kidney disease and hypocalcaemia since May 2010. Her medication consisted of: bisoprolol 5 mg once daily, aspirin 75 mg once daily, lansoprazole 30 mg once daily started 5 years ago, atorvastatin 20 mg once daily and calcichew D3 T twice daily.

She was independent, lived alone and had a normal exercise tolerance. She was a non-smoker and drank 1 unit of alcohol per week.

Physical examination revealed regular tachycardia of 150 bpm. Arterial blood pressure was 141/80 mm Hg. The heart sounds and respiratory examination were normal. Abdominal examination was unremarkable.

INVESTIGATIONS

The ECG showed supraventricular tachycardia.

On admission, laboratory results showed mild normocytic anaemia (haemoglobin 11.3, white cell count 14.3, platelets 179), chronic renal impairment: Na 141 mmol/L (134–145), K 4 (3.6–5) mmol/L urea 20.9 (1.7–7.1) mmol/L, creatinine 174 (55–125) μ mol/L.

She was found to have hypocalcaemia—calcium 1.93 mmol/L (2.10–2.60), albumin 39.0 g/L (35–50), phosphate 0.85 mmol/L (0.80–1.45), adjusted calcium 1.97 mmol/L (2.10–2.60). The liver function tests were normal and troponin I was negative.

On the second day the patient was found to have Mg <0.27 mmol/L, adjusted calcium 1.84 mmol/L (2.10–2.60) and phosphate 0.86 mmol/L (0.80–1.45). A gastroscopy did not show any evidence of an upper gastrointestinal bleed and she only had small benign cystic gland gastric polyps. Distal duodenal biopsies were normal.

TREATMENT

An additional dose of bisoprolol was administered. Intravenous magnesium Sulfate was given (16 mmols) and the patient was reverted to sinus rhythm within a few hours.

OUTCOME AND FOLLOW-UP

The patient was discharged home on the sixth day with ranitidine 150 mg twice daily and magnesium glycerophosphate ii twice daily (= 16 mmol magnesium per day). Lansoprazole was stopped. A 24 h urine collection for magnesium was requested.

She was reviewed 6 weeks later in the outpatient clinic where she reported feeling well and had remained in sinus rhythm. Her serum magnesium concentration was 0.53 mmol/L (0.7–0.9); parathyroid hormone and vitamin D were in normal range. The 24 h urine Mg collection which was collected while she was on intravenous and oral magnesium supplementation was 1.7 mmol/24 h (0.0–5.0) with urine magnesium—2.22 mmol/L. The results were consistent with very low 24 h urine magnesium excretion in keeping with poor intestinal absorption.

The patient was then followed up in the outpatient clinic 10 weeks postdischarge when her magnesium was 0.71 mmol/L (0.70–0.90), Na 141 mmol/L (134–145), K 4.8 mmol/L (3.6–5.0), urea 13.2 mmol/L (1.7–7.1), creatinine 159 μ mol/L (55–125), corrected calcium 2.55 mmol/L (2.10–2.60), albumin 38 g/L (35–50), phosphate 1.15 mmol/L (0.80–1.45) and her magnesium supplementation was discontinued. Her magnesium level remained normal following cessation of the PPI.

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DISCUSSION

We present a case of an adult patient presenting with a severe complication of hypomagnesaemia while using a PPI. Discontinuation of the medication resulted in resolution of hypomagnesaemia and hypocalcaemia. Over 50 cases of PPI-induced hypomagnesaemia have been reported in the literature, but the problem is likely to be more widespread.

The effect of PPIs on intestinal magnesium transport is poorly understood. Intestinal magnesium absorption occurs in two ways: active saturable mechanism and in passive paracellular. Approximately 90% of the absorption happens in a passive way and is linear with the dietary content of magnesium.¹

The active transcellular pathway has become clearer since the discovery of TRPM6 and TRPM7 channels, which conduct magnesium (and calcium) into the cell following transmembrane gradient.¹ TRPM6 is present along the entire gastrointestinal tract, lung tissue and testis, while TRPM7 is omnipresent in tissues.

Several hormonal and other factors have an influence on TRPM6/7 expressions and their magnesium transport.

Li *et al*² proved that the activity of TRPM6/7 channel increases in the presence of external protons. They also demonstrated in their in vitro study that glutamates in the pore-forming region of TRPM6/7 are responsible for pH sensitivity.³ Users of PPIs have a reduced amount of intestinal protons, that is, they have a more alkaline intraluminal pH.

Paracellular Mg²⁺ transport is facilitated by a passive mechanism and is responsible for about 90% of intestinal Mg²⁺ absorption.¹ Thogon *et al*⁴ demonstrated in an in vitro study the effect of omeprazole on the passive mechanism of Mg²⁺ transport. They suggested that omeprazole selectively inhibited the non-saturable passive component, but not the saturable active component.

The exact mechanism of PPI-induced hypomagnesaemia remains an area of research. It is well recognised that this

condition may lead to important and often life-threatening events. The Food and Drug Administration announced in March 2011 that PPIs may cause low serum magnesium if taken for a prolonged period.⁵

Learning points

- We suggest that the side effects of proton pump inhibitor use should be considered in the differential diagnosis of hypomagnesaemia at any age.
- Serum magnesium concentration should be checked in patients on PPIs if they are unwell or present with one of the potential manifestations of hypomagnesaemia.
- This entity is likely to be under-reported and is likely to become recognised more commonly because of increased awareness.

Competing interests None.

Patient consent Obtained.

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