CASE REPORT

Recurrent confusional episodes associated with hypomagnesaemia due to esomeprazol

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SUMMARY

In February 2011, the Food and Drug Administration informed that prescription of proton pump inhibitor (PPI) drugs may cause low serum magnesium levels if taken for prolonged periods of time. We present an ex-smoker, 76-year-old man, with high blood pressure, diabetes mellitus and Barrett's oesophagus (treated with esomeprazole since 2003) admitted due to fluctuating aphasia. Neurovascular and neuroimaging studies were normal. Dyslipidemia and atrial arrhythmia were discovered. The patient was discharged with the diagnosis of left middle cerebral artery transient ischaemic attack and anticoagulation treatment was recommended. The patient returned to the emergency department on further two occasions (confusional episodes) and was admitted in order to complete the neurological study that was normal. The patient was discharged with the diagnosis of probable epileptic seizures. After a week, he was admitted due to generalised temblor and unsteadiness. A complete blood test was performed and showed a severe hypomagnesaemia (not previously performed).

BACKGROUND

In February 2011, the Food and Drug Administration informed that the prescription of proton pump inhibitor (PPI) drugs may cause low serum magnesium levels if taken for prolonged periods of time.

CASE PRESENTATION

A 76-year-old man was admitted on 10 December 2011 due to language disturbances. He was an ex-smoker and presented with high blood pressure and diabetes mellitus as cerebrovascular risk factors. These were being treated with valsartan, manidipine and metformin. He was diagnosed as having Barrett's oesophagus and had been treated with esomeprazole since September 2003. The patient suffered a confusional episode interpreted as fluctuating aphasia over a period of 30 min. Neurological status at admission was normal. A CT of the cranium showed leukoaraiosis. Blood test revealed glucose 133 mg/dL (70–110) and calcium 2.16 mmol/L (2.19–2.54). Magnesium determination was not performed. Neurovascular study was normal. Electrocardiogram monitoring showed an atrial arrhythmia with several ectopic foci and ventricular extrasystoles. The patient was discharged on the 12 December with the diagnosis of left middle cerebral artery transient ischaemic attack. Anticoagulation with low-molecular-weight heparin was initiated. Dyslipidemia was discovered (total cholesterol 220 mg/dL, low-density lipoprotein cholesterol 138 mg/dL, triglycerides 254 mg/dL) and atorvastatin was also added to the treatment.

After discharge, the patient returned to the emergency department (ED) on a further two occasions due to confusional episodes similar to the previous episode (19 and 21 December). On the 22 December, the patient was admitted after consultation in order to complete the neurological study. Blood test showed a slight hypocalcaemia 2.09 mmol/L (2.19–2.54) with a normal phosphate determination. Magnesium was not determined. Neurological studies were normal (cranial MRI, extra/intracranial angio-MRI, lumbar puncture and EEG being repeated twice). Atrial arrhythmia was persistent. The patient was discharged on the 5 January with the diagnosis of probable epileptic seizures. Levetiracetam was added to the previous treatment.

On the 19 January, the patient was referred to the ED after consultation due to generalised temblor, restlessness and unsteadiness. In the ED, the patient had a confusional episode like a delirium improving partially with intravenous clonazepam. EEG which was performed the following day was normal. A complete blood test was performed and showed a severe hypomagnesaemia 0.11 mmol/L (0.66–1.07) with calcium 1.85 mmol/L (2.19–2.54). Esomeprazole and levetiracetam were stopped and intravenous magnesium sulfate was initiated. On the 25 January, the magnesium blood level was normal (0.91 mmol/L). The intravenous treatment was modified to oral magnesium lactate. The patient's clinical status had progressively improved with the disappearance of symptomatology described previously.

Other causes of hypomagnesaemia were discarded; on the 31 January, omeprazole was initiated in order to confirm its relationship with the hypomagnesaemia. The patient was discharged with magnesium oral treatment. After a week, magnesium blood level decreased to 0.63 mmol/L. Omeprazol was stopped. We also stopped atorvastatin, oral antidiabetic and antihypertensive treatments due to good glycaemia and blood pressure control, with normal lipids levels.

The patient reported that since he began with esomeprazole magnesium blood levels had not been determined. He referred to the onset of some unspecific memory problems, irritability, restless and motor troubles (described as difficulties of doing some tasks) for 4 years. The patient's wife reported that he had recovered the quality of life he had had years earlier.

DISCUSSION

The main mechanisms of hypomagnesaemia are urinary (diuretics) and bowel loses (diarrhoea); other causes of hypomagenesemia include aminoglycosides, foscarnet, cisplatin, ethanol, malnutrition and hyperthyroidism. None of the previous was present in our patient. However, he had been taking esomeprazol for 8 years. In February 2011, the Food and Drug Administration (FDA) informed that prescription proton pump inhibitor (PPI) drugs may cause low serum magnesium levels if taken for prolonged periods of time.[1] The recommendation of the FDA is to consider PPIs as a possible cause of hypomagnesaemia, particularly in patients who are clinically symptomatic[1] such as our case, where surprisingly magnesium blood levels had never been determined.

Most patients with hypomagnesaemia are asymptomatic.[2] The clinical manifestations are asthenia, nauseas, vomits and muscle weakness. But patients with hypomagnesaemia may also present many further neurological symptoms such as seizures, paraesthesias, myoclonus, fasciculations, ataxia, dysarthria, irritability, disorientation, psychosis, vertigo and confusion.[3] Recurrent symptomatology[4] and even focal cerebral deficits such as hemiparesis[5] has been described.

On the other hand, magnesium has important effects on the cardiovascular system. It affects myocardial contractility by influencing the movement of ions such as sodium, potassium and calcium, and may also affect the vascular smooth muscle tone. Magnesium has a key role in many other important biological processes,[6] so preliminary evidence suggests that insulin sensitivity, hyperglycaemia, diabetes mellitus and dyslipidemia may be improved with increased magnesium intake, as presented in this case.[7]

Learning points

- Recurrent confusional episodes could be provoked by severe hypomagnesaemia.
- Owing to its wide range of neurological complications, magnesium blood levels should be performed in all patients with unexplained neurological symptomatology, above all in those with proton pump inhibitors.
- Hypomagnesaemia has also important effects on the cardiovascular system (high blood pressure, arrhythmias) and other biological processes (hyperglycemia, dyslipidemia).

Contributors MGD was involved in the study concept and design(), acquisition of data, drafting of the manuscript. SC, LS, JP were involved in critical revision of the manuscript for important intellectual content.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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