Keep an eye on the proton pump inhibitor

Suzanne Cauchi[1]
Stephanie Debono[1]
James Gauci[2]
Jurgen Gerada[2]
Author details can be found at the end of this article
Correspondence to:
Suzanne Cauchi;
suzanne.a.cauchi@gov.mt

Introduction

Proton pump inhibitors cause electrolyte disturbances, but there are very few reports of electrolyte imbalances resulting in electrocardiographic changes. This article reports the case of a 52-year-old man on omeprazole for gastro-oesophageal reflux disease who presented with symptoms related to hypokalaemia, hypomagnesaemia and hypocalcaemia and a prolonged QTc interval. These electrolyte imbalances could only be corrected once omeprazole was stopped. This case highlights the importance of periodic electrolyte surveillance in patients who have used proton pump inhibitors for a long time and the need for alternative effective antacids. The need to reassess indication for proton pump inhibitor use and avoid over-prescription is also emphasised.

Discussion

Proton pump inhibitors are known to cause electrolyte disturbances, but published reports on this side effect are minimal. The first case linking proton pump inhibitors with hypomagnesaemic hypoparathyroidism was published in 2006 (Epstein et al, 2006). This is probably an effect of impaired gastrointestinal magnesium absorption secondary to prolonged proton pump inhibitor use (Sivakumar, 2016). Proton pump inhibitor-induced hypokalaemia (Mackay and Bladon, 2010) and hypocalcaemia (Sivakumar, 2016) have

Case report

A 52-year-old man with a past medical history of gastro-oesophageal reflux disease presented to the emergency department with a 6-month history of worsening upper limb paraesthesiae and abdominal cramps. He had been started on 20 mg omeprazole twice daily by his GP around 5 years previously. The rest of his history was unremarkable and he was not taking any other medication. Clinical examination elicited bilateral carpopedal spasms and positive Chvostek's signs. Abdominal and neurological examinations were unremarkable. Initial parameters on presentation were within normal limits.

Initial serum biochemistry revealed a potassium level of 3.12 mmol/litre, magnesium level of 0.10 mmol/litre and calcium level of 1.46 mmol/litre (reference ranges 3.50–5.10 mmol/litre, 0.65–1.05 mmol/litre and 2.05–2.60 mmol/litre respectively). Parathyroid hormone level was low–normal at 12 pg/ml (reference range 11–16 pg/ml). Complete blood count, C-reactive protein, sodium, urea and creatinine levels were within normal limits.

No electrolyte abnormalities were noted on serum biochemical investigations taken in previous years. Baseline electrocardiogram at presentation revealed a QTc interval of 507 ms (normal QTc interval 350–440 ms in men) (Figure 1). The QTc interval on a previous electrocardiogram was within normal limits.

Immediate intravenous electrolyte supplementation with potassium chloride in 0.9% saline and magnesium sulphate was followed by an infusion of calcium gluconate. Supplementation was started while the patient was on continuous cardiac monitoring in view of the risk of significant cardiac arrhythmias. Despite initial intravenous electrolyte supplementation for 4 days, the electrolyte deficiencies did not correct completely while the patient was still taking omeprazole, but the electrolyte levels normalised once the proton pump inhibitor was stopped. The patient was discharged with full symptom resolution, on an alternative antacid containing magnesium and on oral calcium carbonate supplementation. The QTc interval on electrocardiogram normalised to 402 ms. On outpatient follow up, electrolyte levels remained within normal limits and oral electrolyte supplementation was stopped successfully. The parathyroid hormone level normalised to 15 pg/ml.

To the authors' knowledge, this is the first case of proton pump inhibitor-induced prolonged QTc interval secondary to an array of profound electrolyte disturbances.

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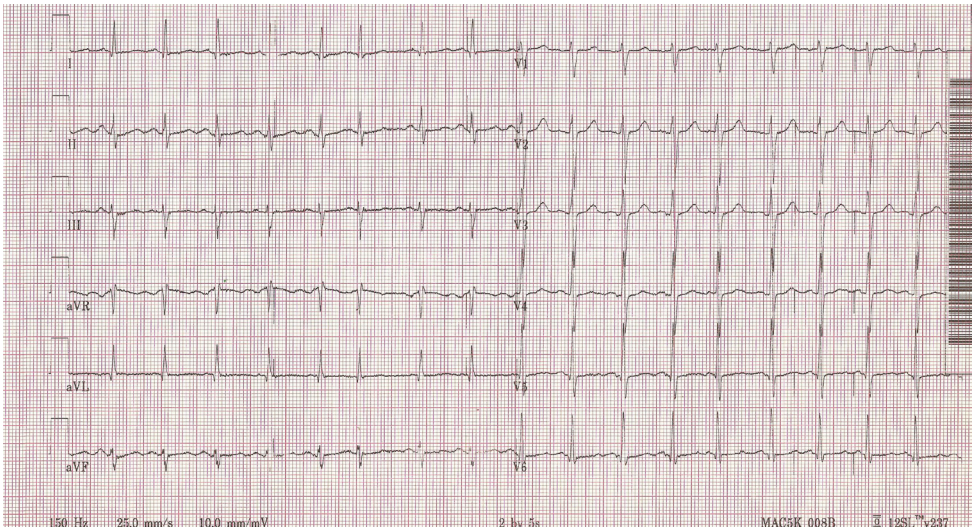

Figure 1. Electrocardiogram on admission with a prolonged QTc interval.

also been observed. The former results from increased renal potassium secretion owing to renal outer medullary potassium channel overactivity (Trottier and Gibson, 2015). The latter is a result of functional hypoparathyroidism caused by hypomagnesaemia. Moreover, the presence of achlorhydria also contributes to reduced calcium absorption (Sivakumar, 2016).

Such case reports prompted the Food and Drug Administration (2011) to issue a safety announcement regarding proton pump inhibitor use. In this patient, the temporal relationship between omeprazole, symptoms, lack of other causes for the electrolyte abnormalities and the rapid response on stopping the proton pump inhibitor, led the authors to strongly suspect that his electrolyte derangements were secondary to prolonged use of proton pump inhibitors.

Management of such cases includes cardiac monitoring, electrolyte supplementation and switching the proton pump inhibitor to an alternative agent. While discontinuation of the proton pump inhibitor allows rapid normalisation of electrolyte levels, recovery is often not seen if the drug is continued. The inability to prescribe proton pump inhibitor therapy in such patients poses a problem, for example, in patients prone to peptic ulceration.

This case emphasises the need for antacids with a similar therapeutic efficacy to proton pump inhibitors. It highlights the importance of electrolyte surveillance in patients with long-term proton pump inhibitor use and the need to reassess the indication for proton pump inhibitor use and avoid over-prescription because of the risk of life-threatening electrolyte disturbances.

Author details

[1]Department of Medicine, Mater Dei Hospital, Msida, Malta

[2]Department of Gastroenterology, Mater Dei Hospital, Msida, Malta

Learning points

- Prolonged use of proton pump inhibitors may be associated with electrolyte disturbances, predisposing patients to cardiac arrhythmias.
- Periodic electrolyte surveillance is indicated in patients on long-term proton pump inhibitors to avoid this complication.
- Correction of the electrolyte disturbance in such a situation often requires the proton pump inhibitor to be stopped.
- The continued indication for proton pump inhibitors should be assessed periodically to avoid over-prescription and unnecessary side effects.
- There remains a need for the development of alternative antacids with similar efficacy and a different side-effect profile.

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