

## CASE REPORT

### Two Patients with Parathyroid Hormone Suppression Caused by Proton Pump Inhibitors

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Hypocalcemia can be associated with coexisting hypomagnesemia, which induces hypoparathyroidism as well as resistance to parathyroid hormone (PTH). Here, we present two patients with severe hypomagnesemia and associated hypocalcemia, caused by proton pump inhibitors.<sup>1</sup>

#### Patient A:

Patient A was 61-year-old female, who was referred to our endocrinology department for persistent hypocalcemia. She reported that her calcium had been low for the last couple of years and it was as low as 1.53 mmol/l earlier this year. She was taking calcium and vitamin D supplements for some time. Her other medications included lansoprazole, alendronic acid and tramadol. She was admitted to a hospital once for intravenous calcium. She experienced tingling, numbness of her fingers and leg cramps. Her past medical history included jejunal bypass for obesity in 1976, chronic diarrhea and rheumatoid arthritis. Since the jejunal bypass in 1976, she had ongoing intermittent chronic diarrhea. She never had any neck irradiation, surgery or thyroidectomy, which could explain her hypoparathyroidism. Her blood test taken after clinic showed an inappropriately normal PTH of 5.1 pmol/l, in view of the very low adjusted calcium level at 1.53 mmol/l, undetectable magnesium <0.25 mmol/l, and low 25-OH Vitamin D at 14nmol/l. She was admitted was treated

with intravenous magnesium, calcium and an intramuscular injection of ergocalciferol (vitamin D). After the magnesium replacement, PTH improved to 26.9 pmol/l. She was discharged, but unfortunately she resumed her lansoprazole and had to be readmitted to hospital for intravenous magnesium replacement.

#### Patient B:

Patient B was admitted to the hospital complaining of generalised malaise and twitching. On admission, she was found to be very hypomagnesemic and hypocalcemic. Her blood tests revealed an undetectable magnesium level of <0.25 mmol/l, adjusted calcium level at 1.67mmol/l, PTH of 5.7 pmol/l and urea of 16.8 mmol/l. She was treated with intravenous magnesium and calcium, which corrected her magnesium and adjusted her calcium levels. Her repeated PTH came back as 23.8 pmol/l. Prior to this admission, her doses of furosemide and perindopril were also increased contributing to her dehydration as evidenced by raised urea level at 16.8

mmol/l. Her vitamin D was normal at 102 nmol/l. Her past medical history included diastolic heart failure, hypertensive heart disease and dementia. She was taking donepezil 10mg once a day, furosemide 80 mg once a day, perindopril 4mg once a day, vitamin D3 supplements and omeprazole 20 mg once day.

## DISCUSSION:

Hypomagnesemia usually accompanied by hypocalcemia has been reported in patients taking PPIs, particularly if the duration of drug utilization has been more than 1 year. The combination of PPIs and diuretics leads to an increased incidence of hypomagnesemia.<sup>1</sup>

Like calcium, magnesium plays a crucial role in the regulation of PTH secretion. These cases demonstrate the blunted PTH secretion in patients with severe hypomagnesemia.<sup>3</sup> Profound hypomagnesemia decreases the release of PTH and induces skeletal resistance to PTH, which can result in severe hypocalcemia.<sup>2</sup> In the first case, hypomagnesemia was driven by diarrhea, and in the second case it was caused by concurrent use of diuretics with a recent dose increase.<sup>1</sup> The patients in both cases were taking long-term proton pump inhibitors, which are known to reduce intestinal magnesium absorption. The presumed mechanism is impaired absorption of magnesium by intestinal epithelial cells caused by PPI-induced inhibition of transient receptor potential melastatin-6 (TRPM6) and TRPM7 channels.<sup>2</sup>

PPI-induced hypomagnesemia (PPIH) leads to severe symptoms, such as fits, convulsions, cardiac arrhythmia and increased risk for concomitant secondary electrolyte disturbances like hypocalcemia. Patients have significant comorbidities and most of them are affected by polypharmacy.<sup>3</sup>

Hypomagnesemia interferes with parathyroid hormone (PTH) release in response to hypocalcemia. PTH levels in most hypomagnesemic - hypocalcemic patients have been either normal or low.<sup>2</sup> Our patients had a low initial PTH level, but it was back to normal after the correction of hypomagnesemia. The hypocalcemia is quite profound in these patients and cannot be solely explained by an impaired secretion of the parathyroid hormone. There is possible resistance of the parathyroid hormone that contributes to hypocalcemia. It is advised to check magnesium level in patients who are expected to be on PPIs for a longer duration and who are simultaneously taking other medication like dietetics and digoxin that impair magnesium absorption.<sup>2</sup>

The described metabolic abnormalities normalized in both patients upon withdrawal of the proton-pump inhibitors, and neither patient required further magnesium or calcium supplementation. We discharged them to their primary care.

## Notes

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## References

1. Danziger, J., William, J. H., Scott, D. J., Lee, J., Lehman, L., Mark, R. G., Howell M.D., Celi, L.A., Mukamal, K. J. (2013). Proton-pump inhibitor use is associated with low serum magnesium concentrations. *Kidney International*, 83(4), 692–699. <https://doi.org/10.1038/ki.2012.452>
2. Hess, M. W., Hoenderop, J. G. J., Bindels, R. J. M., & Drenth, J. P. H. (2012). Systematic review: hypomagnesaemia induced by proton pump inhibition. *Alimentary Pharmacology &*

- Therapeutics*, 36(5), 405–413.  
<https://doi.org/10.1111/j.1365-2036.2012.05201.x>
3. Broeren, M. A. C., Geerdink, E. A. M., Vader, H. L., & van den Wall Bake, A. W. L. (2009). Hypomagnesemia induced by several proton-pump inhibitors. *Annals of Internal Medicine*, 151(10), 755–756.  
<https://doi.org/10.7326/0003-4819-151-10-200911170-00016>
  4. Epstein, M., McGrath, S., & Law, F. (2006). Proton-Pump Inhibitors and Hypomagnesemic Hypoparathyroidism. *New England Journal of Medicine*, 355(17), 1834–1836.  
<https://doi.org/10.1056/NEJMc066308>