

Severe Hypophosphataemia Induced by Intravenous Iron

Role of the Pharmacist in Searching For Alternate Treatments



Background

Hypophosphataemia is an uncommon adverse effect associated with intravenous iron.(1) This case reports the use of calcitriol to treat a patient with severe hypophosphataemia refractory to intravenous phosphate supplement.

Clinical Features

A 72-year-old female with a history of scleroderma and oesophageal strictures requiring frequent oesophageal dilatation presented to hospital with severe vomiting. She also presented with generalised weakness, fatigue, body aches and paraesthesia in both hands. Her medical history included iron deficiency anaemia managed by frequent iron infusions with the last infusion administered three weeks ago.

Laboratory results revealed severe hypophosphataemia (serum phosphate 0.18 mmol/L). Other results were consistent with intravenous iron induced hypophosphataemia mediated by elevated fibroblast growth factor 23 including:

- 1,25-dihydroxyvitamin D deficiency
- Phosphaturia
- Hypocalcaemia
- Elevated parathyroid hormone

Intravenous phosphate replacement (30 to 40 mmol/day) was insufficient in correcting serum levels.

Case Progress

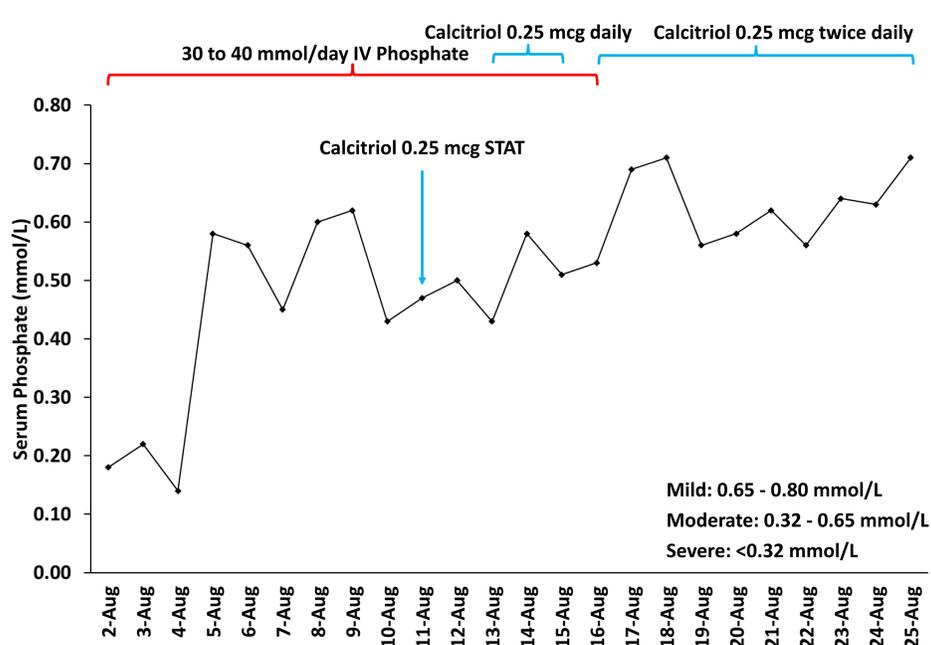


Figure 1. Changes in serum phosphate throughout admission.

The pharmacist performed a literature search to identify alternatives and recommended the use of calcitriol to the treating team as three case reports described the use of calcitriol with good effect.

Treatment with calcitriol 0.25 micrograms daily for three days, then twice daily thereafter resulted in a rapid increase in serum phosphate to 0.71 mmol/L within five days. Phosphate levels were maintained without the need for further intravenous phosphate replacement.

Parathyroid hormone levels also normalised by day five of calcitriol treatment. The patient displayed pronounced improvements in symptoms and was discharged 12 days after calcitriol started.

References

1. Wolf M, Koch TA, Bregman DB. Effects of iron deficiency anemia and its treatment on fibroblast growth factor 23 and phosphate homeostasis in women. *J Bone Miner Res.* 2013;28(8):1793-803.
2. Bishay RH, Ganda K, Seibel MJ. Long-term iron polymaltose infusions associated with hypophosphataemic osteomalacia: a report of two cases and review of the literature. *Ther Adv Endocrinol Metab.* 2017;8(1-2):14-9.
3. Pazirandeh S, Burns DL. Overview of vitamin D. *Mulder JE, ed. UpToDate.* Waltham, MA: UpToDate Inc. <http://www.uptodate.com.acs.hcn.com.au> (Accessed on October 29, 2018.)

Mechanism of Hypophosphataemia

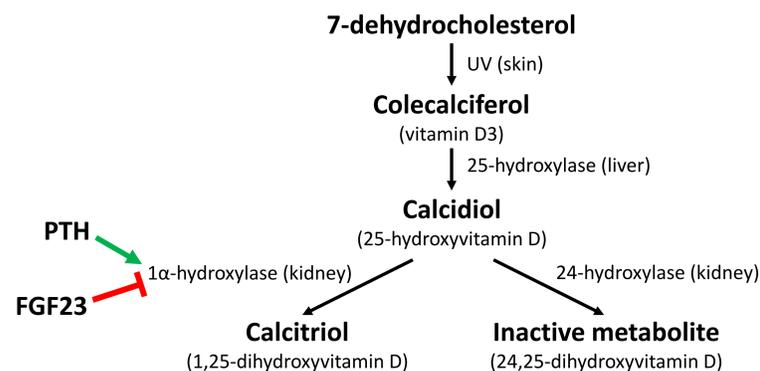
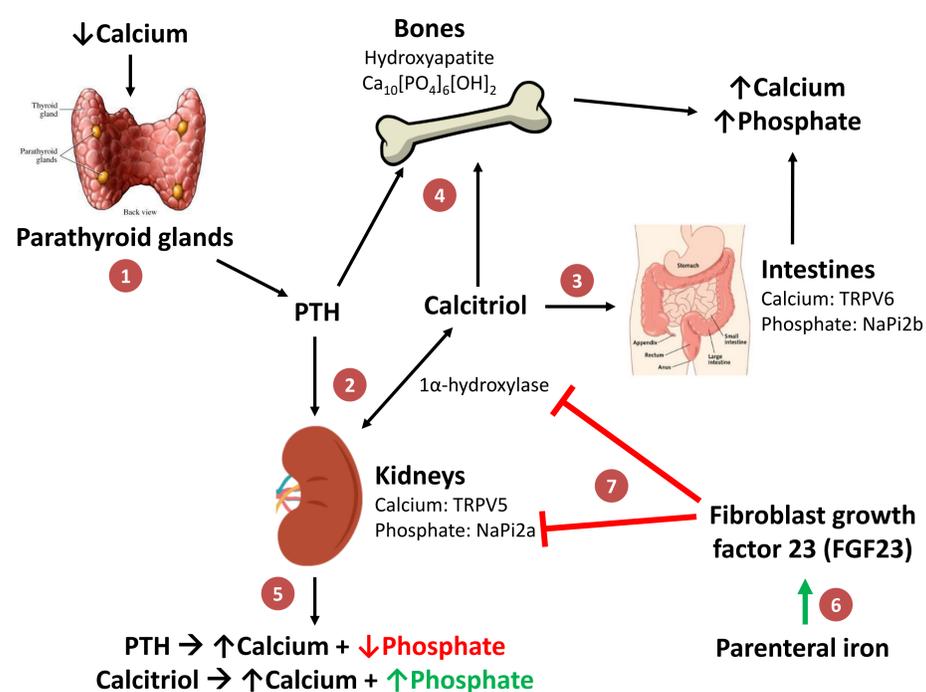


Figure 2. Vitamin D activation pathway adapted from (2,3).



	Intestines	Bones	Kidneys	
PTH	-	↑Ca ↑PO ₄	↑Ca ↓PO ₄	↑FGF23 [23.2-95.4 ng/L]
Calcitriol	↑Ca ↑PO ₄	↑Ca ↑PO ₄	↑Ca ↑PO ₄	↓Calcitriol [60-200 pmol/L]
				↓Phosphate [0.87-1.45mmol/L]
				↓Calcium [2.09-2.54 mmol/L]
				↑PTH [1.3-7.6 pmol/L]

- 1 Parathyroid glands secrete PTH during hypocalcaemia
- 2 PTH stimulates 1α-hydroxylase to increase calcitriol synthesis
- 3 Calcitriol increases dietary absorption of Ca and PO₄
- 4 PTH and calcitriol stimulate bone resorption to release Ca and PO₄
- 5 PTH and calcitriol increase renal reabsorption of Ca
Calcitriol increases renal reabsorption of PO₄ while PTH decreases it
- 6 Parenteral iron increases FGF23 level
- 7 FGF23 reduces renal reabsorption of PO₄ and increases urinary PO₄ excretion
Inhibits 1α-hydroxylase to decrease calcitriol synthesis
Acts directly on kidneys to reduce PO₄ transporters

Figure 3. Mechanism of hypophosphataemia induced by FGF23 with summary table of PTH and calcitriol's effect on target organs and expected trends in laboratory results adapted from (2,4-6).

Conclusion

Severe hypophosphataemia induced by intravenous iron is an uncommon complication and can be refractory to intravenous phosphate replacement. Calcitriol may be effective in correcting hypophosphataemia, particularly in cases refractory to intravenous phosphate replacement. This case highlights the role of the pharmacist to proactively identify alternate treatments.