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Hypophosphataemia Following Ferric Carboxymaltose Infusion

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Running head: Hypophosphatemia and iron infusion

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Informed written consent has been obtained from the patient.

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Dear Editor,

Hypophosphatemia following ferric carboxymaltose infusion

Intravenous iron therapy is used to treat iron deficiency anaemia when oral iron preparations are not tolerated, ineffective or contraindicated. Ferric carboxymaltose (FCM) (Ferinject®, Vifor Pharma UK) is an intravenous iron preparation approved for use in children over 14 years of age with a favourable reported safety profile, tolerability and efficacy and is used in paediatric centres, including in children less than 14 years.¹⁻²

Transient hypophosphatemia has been reported post iron infusion due to increased fibroblast growth factor-23 driving reduced tubular phosphate reabsorption and lasts for weeks to months.³ We have observed that frequent prescribers of FCM are not aware of hypophosphatemia as a possible adverse effect, however, this is an important differential to consider for severe refractory or symptomatic hypophosphatemia in patients following iron infusion.

We report a 17-year-old female with Crohns disease who presented with partial small bowel obstruction, bradycardia, hypotension and fatigue 12 days following FCM infusion. Bloods revealed severe hypophosphatemia (0.30mmol/L). Intravenous phosphate correction was prescribed and she was managed conservatively. Minimal serum phosphate increment was noticed the following day and she required daily intravenous phosphate corrections the next five days. On day 6 of admission her serum phosphate remained low (0.59mmol/L). Paired urine and serum samples showed elevated fractional excretion of phosphate (38%), confirming renal phosphate wasting. She was discharged on oral phosphate supplements and her serum phosphate normalised on day 22 post-FCM.

Current evidence on the clinical significance of iron-induced acute hypophosphatemia is conflicting. The vast majority of affected individuals in adult studies were asymptomatic however case reports describe otherwise unexplained fatigue, lethargy and muscle weakness.³

Chronic hypophosphatemia is documented in adults following repeated FCM doses, with case reports of osteomalacia and bone deformities, although confounding factors affecting bone homeostasis are likely.⁴ In children, there is currently inadequate information whether repeated FCM doses leads to recurrent acute or cumulative chronic hypophosphatemia.

Transient moderate to severe hypophosphatemia can occur following FCM but severe cases with clinical consequences are rare. Patients and clinicians should be alert for symptoms that may suggest hypophosphatemia in days to weeks following FCM (unexplained fatigue, muscle weakness, bone pain, fractures) and check serum phosphate level if hypophosphatemia is suspected. Concomitant risk factors for disorders of phosphate homeostasis may contribute to risk and should be identified and addressed, particularly in children requiring repeated infusions. Further quality research is needed to determine frequency of hypophosphatemia post-FCM in children and establish its clinical importance.

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