Abstract / Povzetek predavanja

Intravenous iron and hypophosphatemia: why it deserves attention

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Iron deficiency (ID) and iron deficiency anaemia (IDA) are major global health problems. Synthesis of haemoglobin is prioritised and before anaemia occurs, all other iron dependent processes related to energy-metabolism are already down-regulated. Thus, we need to consider that ID per se is an indication for diagnostic investigations and treatment, even in the absence of IDA.

The diagnosis of ID is straight-forward in the absence of systemic inflammation. Transferrin saturation (TSAT) below 16% and ferritin below 30 ug/L always means ID. In the context of systemic inflammation (CRP elevation), ferritin up to 300 may still be consistent with absolute ID if TSAT is below 20. Analysis of soluble transferrin receptor and reticulocyte haemoglobin equivalent (Ret-He) may be of further assistance when the interpretation is difficult.

The first-line treatment of ID and IDA is oral iron. However, oral iron is not absorbed in the setting of systemic inflammation due to increased hepcidin synthesis from the liver, resulting in blocking of absorption from the intestine. Also, oral iron is associated with many mainly gastrointestinal side effects resulting in lack of treatment compliance. Since treatment must continue up to 6 months to reach the goals of normalising haemoglobin levels and refilling iron stores, follow up is essential.

For these reasons, we often must rely on intravenous iron treatment to reach our treatment goals. The two drugs mainly used, ferric carboxymaltose (FCM) and ferric derisomaltose (FDI) are equally efficient and both are safe. They differ however in the amount that can be administered on each occasion and in the risk of causing hypophosphatemia.

Iron preparations differ

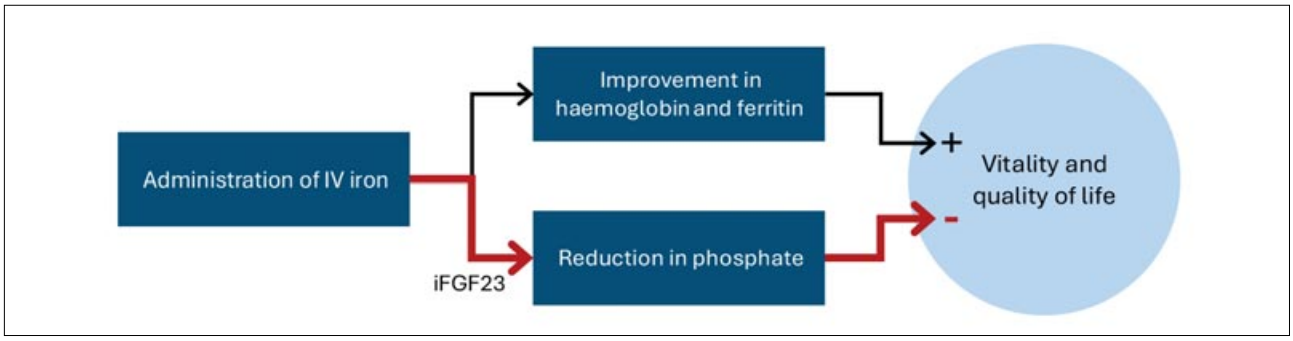

Figure 1. Iron preparations differ regarding the risk of developing hypophosphatemia and subsequent consequences

Phosphate growth factor 23 (FGF 23), synthesised by osteoblasts, is the main regulator of phosphate in the body. During repeated treatment with FCM, the levels of intact FGF 23 increases, with urinary loss of phosphate, hypocalcemia, increased levels of parathyroid hormone, lack of active vitamin D and increased activity of enzymes involved in bone metabolism as consequences. Fatigue is an early clinical symptom of hypophosphatemia, while osteomalacia and kidney stones may follow later. Since hypophosphatemia is difficult to treat due to rapid urinary losses, the best treatment is prevention through choice of treatment drug.

Controlled studies in females and patients with Inflammatory Bowel Disease have demonstrated a significantly higher degree of hypophosphatemia after treatment with FCM compared to FDI. The lowest phosphate levels occur 2 weeks after treatment, but hypophosphatemia persists in some patients even after one month. Elevation of enzymes involved in bone metabolism persist even longer. Hypophosphatemia counteracts the positive effect of iron on fatigue, and it also has negative impact on patient vitality. In addition, long term effects on bone such as osteomalacia and fractures have been demonstrated, together with an increased risk of kidney stones. Furthermore, long-standing high levels of FGF 23 might damage the myocardium.

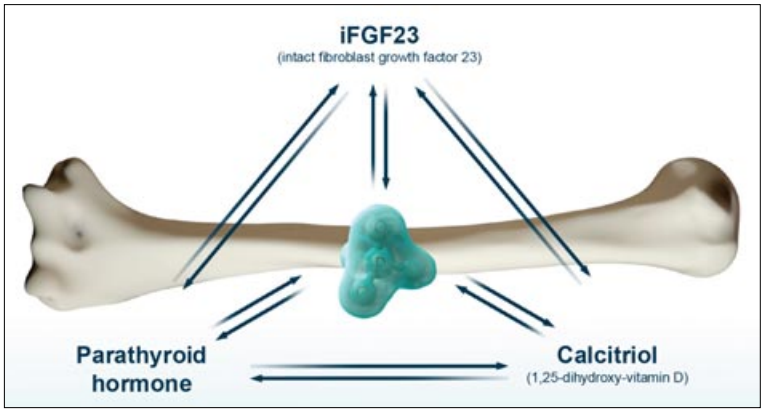

Figure 2. Persistent high levels of intact FGF 23 leads to urinary loss of phosphate and consequently negative effects on bone

The need to measure phosphate and the higher number of infusions required to meet iron defecits when FCM is used also has health economic consequences. When modelling this in different scenarios, FDI comes out as the most cost- effective treatment.

CONCLUSIONS

- Iron deficiency is a global health problem.
- Intravenous iron is often needed to treat anaemia and refill iron stores.
- Ferric carboxymaltose and ferric derisomaltose are both highly effective and safe.
- Ferric carboxymaltose carries a risk of hypohopshatemia with fatigue, reduced vitality and negative effects on bone metabolism as consequences.
- These negative effects of ferric carboxymaltose and the need for more infusions to meet iron requirements leads to higher treatment costs compared to ferric derisomaltose.

References:

1. Pasricha SR, Tye-Din J, Muckenthaler MU, Swinkels DW. Ion deficiency. Lancet 2021; 397: 233 - 48
2. Wolf M, Rubin J, Achebe M, et al. Effect of iron isomaltoside versus ferric carboxymaltose on hypophosphatemia in iron-deficinecy anemia: two randomized clinical trials. JAMA 2020; 323: 432 - 43
3. Zoller H, Wolf M, Blumenstein I, et al. Hypophosphatemia following ferric derisomaltose and ferric carboxymaltose in patients with iron deficiency anaemia due to inflammatory bowel disease (Phsophare-IBD): a randomised clinical trial. Gut 2023; 72:644 - 53
4. Lindgren S, Strid H, Hjortswang H, et al. A Swedish cost-utility analysis of ferric derisomaltose versus ferric carboxymaltose in the treatment of iron deficiency anaemia in patients with inflammatory bowel disease. J Med Econ 2025; 28:567-75