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Session OR13 - OR13. Rare Bone Diseases and Mineral Metabolism

Add To Itinerary

OR13-3. Effects of Iron Isomaltoside versus Ferric Carboxymaltose on Hormonal Control of Phosphate Homeostasis: The PHOSPHARE-IDA04/05 Randomized Controlled Trials

March 24, 2019, 11:30 AM - 11:45 AM | Room 267

Authors

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Disclosures

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Abstract

Abstract: Iron isomaltoside (IIM) and ferric carboxymaltose (FCM) are newer intravenous iron preparations that can be administered in high-doses to rapidly correct iron deficiency anemia (IDA). FCM can cause hypophosphatemia due to fibroblast growth factor 23 (FGF23) mediated renal phosphate wasting, which has been associated with osteomalacia, but the comparative effects of IIM are unknown. In two separate, identically designed, open label randomized controlled trials, we 1:1 randomized 245 adults with IDA to receive IIM (single infusion of 1000 mg) or FCM (FDA-approved dosing schedule: 2 infusions of 750 mg administered 1 week apart). We compared the incidence, severity and duration of hypophosphatemia, and effects on renal phosphate excretion, FGF23, PTH, vitamin D, and biomarkers of bone turnover measured in blood and urine samples collected at study visits at baseline (day 0) and on days 1, 7, 8, 14, 21, and 35.

In pooled analyses of both trials, the incidence of hypophosphatemia <2 mg/dL was higher in the FCM versus IIM group (74.4% versus 8.0%, p<0.0001). Hypophosphatemia persisted at day 35 in 43.0% of FCM-treated patients compared to 0.9% of IIM-treated patients (p<0.0001). Severe hypophosphatemia ≤1 mg/dL occurred in 11.3% of FCM-treated patients compared to 0.0% of IIM-treated patients (p<0.0001). FCM significantly increased intact FGF23 compared to IIM (p<0.0001): on day 1, which was one day after the first infusion, FCM increased mean intact FGF23 from 49.9 pg/mL

at baseline to 149.5 pg/mL; by day 8, which was one day after the second infusion, FCM increased intact FGF23 to 327.9 pg/mL; the corresponding figures for IIM were 59.9 pg/mL at baseline, 58.3 pg/mL by day 1 and 66.9 pg/mL by day 8. Compared to treatment with IIM, FCM significantly: increased urinary fractional phosphate excretion; decreased serum 1,25-$(OH)_2$ vitamin D; decreased ionized calcium; and increased PTH, which persisted through day 35. These changes after FCM treatment were accompanied by significant increases in both total and bone specific alkaline phosphatase that also persisted through day 35. Correction of IDA was comparable between the two treatments. Serious or severe hypersensitivity reactions occurred in 0.8% in the IIM group and 1.7% in the FCM group.
Compared to IIM, FCM induced high rates of FGF23-mediated hypophosphatemia, which was frequently severe and often persisted for >35 days. FCM but not IIM also induced changes in vitamin D and calcium homeostasis that triggered secondary hyperparathyroidism, which likely contributed to persistence of hypophosphatemia. Consistent with case reports of pathological fractures following FCM use, FCM also induced significant elevations of biomarkers of bone turnover that are associated with osteomalacia.