Mar 28, 2020

Comparative risk of hypophosphatemia following the administration of intravenous iron preparations: a network meta-analysis

Ioannis Bellos[1]

[1]National and Kapodistrian University of Athens

1 Works for me dx.doi.org/10.17504/protocols.io.bebyjapw

Ioannis Bellos

ABSTRACT

The administration of intravenous iron has been recently linked to increased risk of hypophosphatemia, as it induces the release of fibroblast growth factor-23, leading to increased urinary excretion of phosphate and reduced serum 1,25-dihydroxyvitamin D concentration. Severe hypophosphatemia represents a potentially serious complication since it may be associated with increased rates of heart and respiratory failure and rhabdomyolysis, as well as with chronic manifestations, especially osteomalacia. Nonetheless, it remains unclear which iron preparation is linked to higher rates of hypophosphatemia. As a result, the present network meta-analysis aims to accumulate current literature knowledge in the field in order to simultaneously compare the effects of different intravenous iron preparations (ferric carboxymaltose, ferumoxytol, iron isomaltoside, iron sucrose and iron dextran) on serum phosphate, by taking into account both direct and indiret evidence.

1 Review title: Comparative risk of hypophosphatemia following the administration of intravenous iron preparations: a network meta-analysis

2 Review question: To compare the incidence of hypophosphatemia following the intravenous administration of different iron preparations (ferric carboxymaltose, ferumoxytol, iron isomaltoside, iron sucrose and iron dextran).

3 Searches: No date or language restrictions will be applied. MEDLINE, Scopus, CENTRAL, Web of Science, ClinicalTrials.gov and Google Scholar databases will be systematically searched from inception. Literature search will include the terms: hypophosphatemia, phosphorus, iron, ferric, ferrous, carboxymaltose, ferumoxytol, isomaltoside, sucrose, dextran.

4 Participants/population Inclusion criteria: patients receiving any intravenous iron preparation for any indication (e.g. iron-deficiency, chronic kidney disease, inflammatory bowel disease or hemorrhage) Exclusion criteria: Administration of oral iron, intravenous iron preparation not specified, no definition of hypophosphatemia

5 Intervention(s), exposure(s): Administration of any iron preparation (ferric carboxymaltose, ferumoxytol, iron isomaltoside, iron sucrose and iron dextran).

6 Types of study to be included Randomized controlled trials (RCTs) will be held eligible. Cohort, case-control or cross-sectional studies, case reports, case series, animal studies, review articles and in vitro studies will be excluded.

7 Main outcome: Incidence of hypophosphatemia, defined as serum phosphorus below 2.0 mg/dl.

8 Additional outcome(s): Incidence of severe hypophosphatemia (serum phosphorus below 1.3 mg/dl) and persistent hypophosphatemia.

Citation: Ioannis Bellos (03/28/2020). Comparative risk of hypophosphatemia following the administration of intravenous iron preparations: a network meta-analysis. https://dx.doi.org/10.17504/protocols.io.bebyjapw

9 Data extraction (selection and coding): RCTs will be held eligible if they report the risk of hypophosphatemia among patients treated with intravenous iron. The following data will be extracted from each study: name of first author, date of publication, country, study design, inclusion and exclusion criteria, clinical setting, indication for iron treatment, presence of chronic kidney disease, definition of hypophosphatemia, iron dose, number of patients and patients' baseline characteristics (e.g. age, gender, renal function, comorbidities).

10 Risk of bias (quality) assessment: All studies will be assessed using the Cochrane risk of bias tool for randomized controlled trials, taking into account the domains of randomization, blinding, allocation concealment, withdrawals and dropouts.

11 Strategy for data synthesis: Network meta-analysis is planned to be conducted in order to simultaneously compare hypophosphatemia risk for all intravenous iron preparations. League tables, posterior density plots and cumulative ranking curves will be constructed. Consistency will be assessed both globally and locally, while transitivity will be tested by evaluating the distributions of potential confounding factors across studies classified by comparison.

12 Analysis of subgroups or subsets: Subgrouping is planned on the basis of treatment indication and presence of chronic kidney disease.

Citation: Ioannis Bellos (03/28/2020). Comparative risk of hypophosphatemia following the administration of intravenous iron preparations: a network meta-analysis. https://dx.doi.org/10.17504/protocols.io.bebyjapw