Systematic review and network meta-analysis: Safety of different intravenous iron preparations for the treatment of iron deficiency anemia in inflammatory bowel disease

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Aim: To compare the tolerability of intravenous (IV) iron compounds (ferric carboxymaltose (FCM), ferumoxytol (FOX), iron sucrose/saccharate (IS), iron isomaltoside (ISM) and iron dextran (IDX)) used to treat iron deficiency anaemia (IDA) in patients with inflammatory bowel disease (IBD) in a systematic review and network meta-analysis (NMA).

Methods: PUBMED, SCOPUS, Web of Science and Cochrane databases were searched for randomised controlled (RCT) and other prospective trials analysing IV iron therapies for IDA in patients with IBD. Outcome was the total of drug-related AEs and SAEs. Bayesian NMA was performed after bias analysis and the MCMC method used to calculate relative tolerability of each therapy. Heterogeneity was tested with I^2. Analyses were conducted using Rgemtc. DIC was used to compare fixed and random effect models (REM). NMA was expressed as OR with 95% CrI.

Results: Of 2730 studies found, after duplication removal and detailed review, 4 RCTs (NMA) and 21 other trials (systematic review only) remained. No eligible studies for FOX and no RCTs for IDX were found. NMA was performed. The REM fit the data adequately with no evidence of inconsistency; all p-values were ≥5%. No statistically significant difference in AE rate was found between different IV iron products vs. oral iron (OR=0.87,95% CrI [0.43;1.7] for FCM; OR=0.80, 95%CrI [0.36;1.8] for IS; OR=1.5,95%CrI [0.64;3.7] for ISM). The systematic review (n=2619) showed AE rates of 83/1028(8.1%) for FCM, 78/481(16.2%) for IS, 89/475(18.7%) for ISM and 10/83(12%) for IDX. Drug-related SAEs occurred at pooled rates of 0.1%/2.2%/0.0%/1.1% for FCM/IS/IDX/ISM respectively. AE/SAE rates for oral iron were 22.6%/1.4%.

Conclusions: While the systematic review indicates FCM to be associated with fewer AEs, statistical significance is unproved due to lack of data from RCTs. Although hypophosphataemia has been reported to be associated with IV iron therapy, especially FCM, it was temporary and asymptomatic, if reported. There were no reports of hypophosphataemia-related bone manifestations. Further RCTs are needed to draw conclusions on the comparative safety of IV iron products.