Reviewer's report

Title: Meta-analysis of efficacy and safety of intravenous ferric carboxymaltose (Ferinject) from clinical trial reports and published trial data

Version: 2 Date: 2 July 2011

Reviewer: Manuel Muñoz

Reviewer's report:

In this paper, the authors performed a meta-analysis on the efficacy and safety of ferric carboxymaltose by summarising the available date from clinical trials using clinical trial reports and published reports. They identified 14 studies with 2,110 randomised patients exposed to ferric carboxymaltose, 875 to oral iron, 592 to placebo, and 145 to intravenous iron sucrose were identified. Additional data were obtained from cohort studies. Oral iron was the most common comparator. Intravenous ferric carboxymaltose improved mean Hb, serum ferritin, and transferrin saturation levels, whereas serious adverse events and deaths were similar in incidence in ferric carboxymaltose and comparators; rates of constipation, diarrhoea, and nausea or vomiting were lower than with oral iron. The authors concluded that this study increases the evidence available to support recommendations given for intravenous iron treatment, but direct comparison trials between different intravenous iron preparations are lacking.

Major compulsory revisions

1. They included data from unpublished clinical trial reports. How was the quality of these reports assessed? Why were they not published when some one were performed as far as 2004? This reviewer has some doubts on the use of data from unpublished, not peer-reviewed reports.

2. Time period for identification of studies is not given. However, there is an important study (FERGIcor) comparing ferric carboxymaltose with iron sucrose in more than 400 IBD patients which is missing (It was presented at the EUGW Barcelona October 2010, and just published in Gastroenterology June 12 PMID 21699794).

There is not any comment or analysis on the economical implications of the use of ferric carboxymaltose.

Minor essential revisions.

Abstract.

3. Intravenous ferric carboxymaltose was given up to the calculated iron deficit (up to 1,000 mg in one week) for iron deficiency anaemia ….
4. The final sentence of the conclusion (It increases the evidence available to support recommendations given for intravenous iron treatment, but direct comparison trials between different intravenous iron preparations are lacking) is not accurate.

Background

5. Page 4, paragraph 2. Cost of blood products, but not mention to cost of different IV iron preparations, nor comparison between IV iron and transfusion.

6. Page 5, paragraph 2. “Intravenous iron preparations typically involve iron as high or low molecular weight iron dextran, iron gluconate, or iron sucrose, and require multiple administrations of low doses to replenish iron stores”. This does not apply to HMWID, LMWID, or Ferinject.

7. Page 6, paragraph 2. Please, check reference 28 (Iron dextran or Ferinject?)

Methods

8. Which was the time period for identification of studies?

Discussion

7. The reader would benefit for a more complete discussion on death.

8. Why ferinject-induced hypophosphatemia, and its possible clinical consequences, has not been commented?

9. Again, some comments on comparative cost-effectiveness will be much well come.

Direct comparison between iron preparations are few, but not lacking

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

have received honoria and/or travel funds for lectures and /or consultacy from Vifor Pharma (Switzerland), Vifor Uriach Pharma (Spain), and PharmaCosmos (Denmark)