

Iron therapy in pregnant women with iron deficiency anemia – A Meta-analysis

Anusha Natarajan¹, Priyadarsini Baskaran², and A Surendiran³

¹Jawaharlal Institute of Post Graduate Medical Education

²Affiliation not available

³Jawaharlal Institute of Postgraduate Medical Education & Research

November 5, 2020

Abstract

Background: Pregnancy significantly increases the need for iron. The prevalence of anemia in pregnant women is high, affecting 41.8% of all pregnant women worldwide. In patients with low tolerance to oral iron, it is recommended to start them on parenteral iron therapy but with variable degree of efficacy. Hence this meta-analysis was done with the following aim. **Aim:** This study aims to assess the efficacy of various iron preparations in pregnant women with Iron deficiency anemia (IDA). **Methods:** Randomised controlled trials (RCTs) (available as full free text) which included iron therapy in pregnant women with iron deficiency anemia were retrieved from electronic databases viz. PubMed, Google scholar and IndMed, with specific search terms. Qualities of RCTs were assessed using JADAD score and four RCTs with high score were included for analysis using RevMan 5.3 software. Outcome measures were change in hemoglobin levels and serum ferritin concentration after one month of therapy. **Results:** In the four RCTs included, a total of 267 patients were treated with oral iron and 267 patients were treated with parenteral iron therapy. Change in the hemoglobin levels between the 2 groups had a standard mean difference of 0.73, 95% CI (-0.05-1.52), with the p-value of 0.07. To assess the change in the serum ferritin concentration a total of 188 patients in oral iron and 197 patients in parenteral iron therapy were included. There was a standard mean difference of 0.88, 95% CI (0.60-1.66), with a p-value of <0.00001.

Iron therapy in pregnant women with iron deficiency anemia – A Meta-analysis

Anusha Natarajan¹, Priyadarsini Baskaran, Surendiran Adithan

¹Assistant Professor, Department of Pharmacology, Jawaharlal Institute of Postgraduate Medical Education & Research (JIPMER), Puducherry.

Background: Pregnancy significantly increases the need for iron. The prevalence of anemia in pregnant women is high, affecting 41.8% of all pregnant women worldwide. In patients with low tolerance to oral iron, it is recommended to start them on parenteral iron therapy but with variable degree of efficacy. Hence this meta-analysis was done with the following aim.

Aim: This study aims to assess the efficacy of various iron preparations in pregnant women with Iron deficiency anemia (IDA).

Methods:

Randomised controlled trials (RCTs) (available as full free text) which included iron therapy in pregnant women with iron deficiency anemia were retrieved from electronic databases viz. PubMed, Google scholar and IndMed, with specific search terms.

Qualities of RCTs were assessed using JADAD score and four RCTs with high score were included for analysis using RevMan 5.3 software. Outcome measures were change in hemoglobin levels and serum ferritin concentration after one month of therapy.

Results:

In the four RCTs included, a total of 267 patients were treated with oral iron and 267 patients were treated with parenteral iron therapy. Change in the hemoglobin levels between the 2 groups had a standard mean difference of 0.73, 95% CI (-0.05-1.52), with the p-value of 0.07. To assess the change in the serum ferritin concentration a total of 188 patients in oral iron and 197 patients in parenteral iron therapy were included. There was a standard mean difference of 0.88, 95% CI (0.60-1.66), with a p-value of <0.00001.

Introduction:

Pregnancy is a state of increased iron demand. Iron deficiency, which depends on the nutritional state of the patient, is the principal cause.¹ This increased demand for iron subsequently places the mother and infant at risk of developing iron deficiency anemia (IDA), which can lead to gestational complications, as well as increased maternal and infant morbidity and mortality.² Prevalence of Iron Deficiency Anemia (IDA) in pregnant women worldwide is 41.8%.³ Oral iron therapy is routinely used to treat IDA in pregnant women. However this can have gastrointestinal adverse effects which eventually lead to loss of adherence and decreased efficacy of iron therapy.^{4,5} In patients with low tolerance to oral iron, parenteral iron therapy is recommended. IV preparations can deliver a larger iron supply more rapidly than oral iron and, because of the route of administration, bypass the risk of gastrointestinal side effects.⁶ However the efficacy of the different available parenteral iron compositions are variable. Hence this meta-analysis was done with the following objective:

Objective:

To compare the efficacy between oral and parenteral iron therapy in pregnant women with Iron Deficiency Anemia (IDA)

Methods:

Search strategy and study selection

We conducted electronic searches in PubMed, Google scholar and IndMed to identify relevant articles. RCTs (available as full free text) with no restriction regarding to language, publication period, patient age was included in this study. The search term that was used was

Search term:

Oral iron AND Iron deficiency anemia in pregnant females

Parenteral iron AND iron deficiency anemia in pregnant females

Two independent reviewers (AN and PB) performed initial scrutiny of primary titles and abstracts (when available) to select potential full text articles for further scrutiny. When the title and abstract cannot be rejected by any reviewer, the full text of the article was obtained. Inclusion or exclusion of each study was determined by discussion and consensus between the two reviewers.

Inclusion criteria

Types of participants

This review considers studies that include patients with iron deficiency anemia

Types of intervention

This review considers studies that evaluate oral iron preparations and parenteral iron preparations in patients with iron deficiency anemia

Types of outcomes

This review considers studies that included increase in hemoglobin levels after the use of either oral or parenteral iron preparations

Types of studies

This review considers only randomized controlled trials for inclusion

Data collection

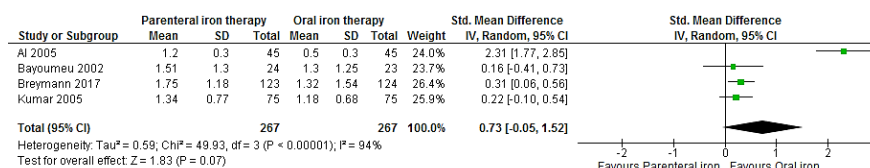
Quality of RCT and risk of bias was assessed using RevMan. Quality of the included RCTs were analyzed using JADAD score. Quantitative data was extracted from papers included in the review using the standardized data extraction tool from RevMan. The data extracted includes specific details about the interventions, populations, study methods and outcomes of significance to the review question and specific objectives.

Statistical analysis:

Quantitative data were pooled in statistical meta-analysis using Review Manager 5.3. Effect sizes were expressed as weighted standard mean differences for continuous data and their 95% confidence intervals were calculated. Heterogeneity was assessed statistically using the Chi-square test. $p < 0.05$ was considered statistically significant.

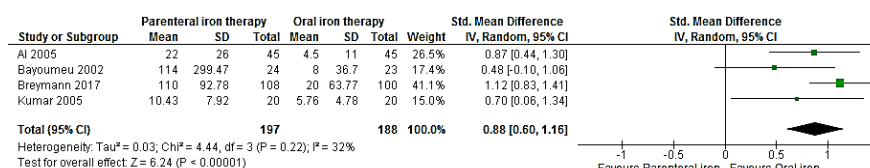
Results and Discussion:

Fig 1: Change in hemoglobin levels with oral vs. parenteral iron therapy in pregnant women with iron deficiency anemia



$P = 0.07$, figure 1 shows the change in the hemoglobin levels with oral iron therapy and parenteral iron therapy in pregnant women. This shows that there was no significant improvement in the hemoglobin levels between the two formulations

Fig 2: Change in serum ferritin levels with oral vs. parenteral iron therapy in pregnant women with iron deficiency anemia



$P < 0.00001$, figure 2 shows the change in the serum ferritin levels with oral iron therapy and parenteral iron therapy in pregnant women. This shows that there was a statistically significant improvement in the serum ferritin levels in the oral iron therapy than parenteral iron therapy.

Iron deficiency anemia during pregnancy is common and deserves special attention because of its potential consequences.⁸ The elevation in the hemoglobin levels were comparable in both the groups. Oral iron therapy had statistically significantly better efficacy in improving serum ferritin levels. Studies documenting adverse effects of oral and parenteral iron therapy will provide added evidence to the present findings.

Conclusion:

Oral and parenteral iron therapy showed similar efficacy. This suggests that wherever possible oral iron therapy is preferable owing to the lower cost and ease of administration and also being non-invasive administration it will be preferred over the parenteral iron therapy.

References:

1. Hercberg S, Galan P, Prual A, Preziosi P. Epidemiology of iron deficiency and iron deficiency anemia in the French population. *Ann Biol Clin* 1998;56:49-52.
2. Breymann C, Milman N, Mezzacasa A, Bernard R, Dudenhausen J. Ferric carboxymaltose vs. oral iron in the treatment of pregnant women with iron deficiency anemia: an international, open-label, randomized controlled trial (FER-ASAP). *Journal of Perinatal Medicine*. 2017;45(4).
3. de Benoist B, McLean E, Egli I, Cogswell M, (eds). Worldwide prevalence of anaemia 1993–2005: WHO global database on anaemia. 2008. Available at: http://whqlibdoc.who.int/publications/2008/9789241596657_eng.pdf.
4. Breymann C, Honegger C, Holzgreve W, Surbek D. Diagnosis and treatment of iron-deficiency anaemia during pregnancy and postpartum. *Arch Gynecol Obstet*. 2010;282:577–80.
5. Khalafallah AA, Dennis AE. Iron deficiency anaemia in pregnancy and postpartum: pathophysiology and effect of oral versus intravenous iron therapy. *J Pregnancy*. 2012;2012:630519.
6. Milman N. Prepartum anaemia: prevention and treatment. *Ann Hematol*. 2008;87:949–59.
7. Jadad Scale > Score Calculator [Internet]. *Tools.farmacologiaclinica.info*. 2020 [cited 20 May 2020]. Available from: <http://tools.farmacologiaclinica.info/index.php?sid=36287>
8. Bayoumeu F, Subiran-Buisset C, Baka N, Legagneur H, Monnier-Barbarino P, Laxenaire M. Iron therapy in iron deficiency anemia in pregnancy: Intravenous route versus oral route. *American Journal of Obstetrics and Gynecology*. 2002;186(3):518-522.