International Journal of Sciences: Basic and Applied Research (IJSBAR)

ISSN 2307-4531
(Print & Online)

http://gssrr.org/index.php?journal=JournalOfBasicAndApplied

Iron- Deficiency in Pregnancy: Our Experience in Intravenous Iron Treatment with Ferric Carboxymaltose, Iron Sucrose and Ferric Hydroxid Dextran Complex

Diana Yordanova[a*], Asen Nikolov[b]

[a,b]*University Hospital of Obstetrics and Gynecology "Maichin dom" 2, Zdrave St 1430 Sofia, Bulgaria*

Abstract

Anemia is one of the most prevalent nutritional deficiency problems affecting pregnant women. The high prevalence of iron and other micronutrient deficiencies among women during pregnancy in developing countries is of concern and maternal anemia is still a cause of considerable perinatal morbidity and mortality. Severely anemic pregnant women may require blood transfusion, which is not always feasible in under- resourced settings, and it may even carry some risks for the woman. To avoid this, intravenous preparations are used in the management of moderate iron- deficiency anemia in pregnancy. Our data confirmed that intravenous administration elevated the hemoglobin and they were well tolerable. Iron sucrose is the preferred and it has demonstrated a high success rate. Recently, ferric carboxymaltose and ferric hydroxide dextran complex take place in the treatment of iron- deficiency anemia in pregnancy. There are no investigations in Bulgaria that compared the effectiveness of the three intravenous preparations for treatment of moderate iron- deficiency anemia during the second and third trimester of pregnancy.

Key words: iron- deficiency anemia; ferric carboxymaltose; iron sucrose; ferric hydroxide dextran complex.

---

* Corresponding author.

1. Introduction

Iron deficiency is the most widespread nutritional deficiency in the world [1]. It is the most common cause of anemia during pregnancy. The World Health Organization defines anemia in pregnancy as a hemoglobin level below 110 g/l in the first and third trimester and below 105 g/l in the second trimester [2].

Iron deficiency may be effectively diagnosed in most cases by serum ferritin level [3]. There are two types of iron deficiency: absolute (iron stores are reduced or depleted and serum ferritin levels are low, below 20 μg/l) and functional (when the mobilization of iron from the macrophages is not fast enough to fulfill the increased demands of bone marrow, despite adequate total body stores). When the functional iron deficiency is a result of the presence of inflammation, patients have normal or high serum ferritin levels and elevated serum hepcidine [4]. The last stage of absolute iron deficiency is the iron- deficiency anemia. It can be mild, moderate and severe according to the concentration of hemoglobin. The anemia is moderate when the hemoglobin level is between 99 g/l and 70 g/l. A number of oral and parenteral iron preparations have been used in the treatment of iron-deficiency anemia for many years [5]. Whereas oral preparations are adequate for the treatment of mild forms of iron- deficiency anemia, parenteral iron therapy is necessary in situations where there is need for rapid repletion of iron stores, anemia is moderate to severe, or in cases of malabsorption or intolerance to oral iron therapy [5, 6]. Iron formulations suitable for intravenous administration need to achieve a balance between effectiveness and safety [7].

Ferric carboxymaltose [8] is a new intravenous iron formulation promising to be more effective than ferric hydroxide dextran complex and as safe as iron sucrose. There isn't such an investigation of the intravenous management of iron- deficiency anemia in pregnancy in our country.

2. Materials and methods

It is a prospective analysis of 68 pregnant women, collected for a year. The inclusion criteria are: symptomatic iron- deficiency anemia unresponsive or intolerable to oral iron substitution; second to third trimester; moderate anemia. The exclusion criteria are: functional iron deficiency; multiple pregnancies; first trimester; mild and severe forms of iron- deficiency anemia (hemoglobin level > 100 g/l and below 70 g/l). The investigated pregnant women are divided in three groups: 30 who are treated with iron sucrose, 20 who are treated with ferric hydroxide dextran complex and 18 who are treated with ferric carboxymaltose.

The preparations are administrated as an intravenous infusion of 200 mg iron daily, three times a week. Data are collected on the pre- treatment serum hemoglobin and ferritin and same data collected at 24 and 72 post-infusion hours and at one week. Primary endpoint was to evaluate the maternal safety and tolerability. Secondary endpoint was to assess efficacy of the treatment.

3. Results and discussion

The mean rise of hemoglobin value was 23.1 g/l for ferric carboxymaltose, 15.5 g/l for ferric hydroxide dextran complex and 9.8 g/l for iron sucrose. Pre-infusion hemoglobin and ferritin levels were comparable in the three

groups. Mean pre- infusion values of ferritin were 13.3 µg/l. At 24 post- infusion hours there is no significant rise of the hemoglobin and ferritin values in the three groups. At 72 post- infusion hours, the mean hemoglobin and ferritin rise in the ferric carboxymaltose group was 8.4 g/l and 10.4 µg/l, 3.2 g/l and 7.1 µg/l in the ferric hydroxide dextran complex group and 2.9 g/l and 5.3 µg/l in the iron sucrose group.

At a week, the total rise in hemoglobin and ferritin was 15.7 g/l and 13.1 µg/l in the ferric carboxymaltose group, 13.4 g/l and 10.5 µg/l in the ferric hydroxide dextran complex group and 8.5 g/l and 6.8 µg/l in the iron sucrose group (see table 1 and table 2).

Table 1: Mean values of hemoglobin in the ferric carboxymaltose, ferric hydroxide dextran complex and iron sucrose groups before and after intravenous infusions.

Intravenous preparation	Mean pre- infusion values of hemoglobin	Mean hemoglobin' values at 24 post-infusion hours	Mean hemoglobin' values at 72 post-infusion hours	Mean hemoglobin' values at a week
Ferric carboxymaltose	82.3 g/l	81.3 g/l	89.7 g/l	105.4 g/l
Ferric hydroxide dextran complex	86.2 g/l	85.1 g/l	88.3 g/l	101.7 g/l
Iron sucrose	87.4 g/l	85.8 g/l	88.7 g/l	97.2 g/l

Table 2: Mean values of ferritin in the ferric carboxymaltose, ferric hydroxide dextran complex and iron sucrose groups before and after intravenous infusions.

Intravenous preparation	Mean pre- infusion values of ferritin	Mean ferritin' values at 24 post-infusion hours	Mean ferritin' values at 72 post-infusion hours	Mean ferritin' values at a week
Ferric carboxymaltose	12.3 µg/l	13.2 µg/l	22.7 µg/l	25.4 µg/l
Ferric hydroxide dextran complex	13.2 µg/l	14.1 µg/l	20.3 µg/l	23.7 µg/l
Iron sucrose	14.4 µg/l	14.8 µg/l	19.7 µg/l	21.2 µg/l

The incidence of drug- related adverse events was low and mostly mild in the three groups. Mild adverse events (headache, flushing, chills, nausea, tachycardia, wheezing, myalgia) occurred in 2.2 % for ferric carboxymaltose, in 3.4 % for ferric dextran complex and in 2.9 % for iron sucrose (see table 3).

Table 3: The incidence of drug- related adverse events in the ferric carboxymaltose, ferric hydroxide dextran complex and iron sucrose group.

	Ferric carboxymaltose	Ferric hydroxide dextran complex	Iron sucrose
Headache	5.6 %	6.2 %	4.1 %
Flushing	3.4 %	5.8 %	6.3 %
Chills	1.2 %	2.1 %	2.8 %
Nausea	2.0 %	0.9 %	1.5 %
Tachycardia	2.7 %	4.3 %	3.5 %
Wheezing	0.2 %	3.2 %	1.2 %
Myalgia	0.6 %	1.0 %	0.7 %

4. Conclusion

Three preparations appear effective and safe, with low risk of serious adverse effects and side- effects. Ferric carboxymaltose administration in pregnant women is well tolerated and is not associated with any relevant clinical safety concerns. Ferric carboxymaltose has a comparable safety profile to iron sucrose but offers the advantage of a much higher iron dosage at a time reducing the need for repeated applications and increasing patients' comfort. Ferric carboxymaltose is the drug of choice, if intravenous iron treatment becomes necessary in the second or third trimester of pregnancy.

References

[1] Zimmermann M. B.. R. F. Hurrell. Nutritional iron deficiency (2007) Lancet 370: 511- 520.

[2] de Benoist B., E. McLean, I. Egli et al. Worldwide prevalence of anemia 1993- 2005: WHO global database on anemia (2008) Available at: http://whqlibdoc.who.int/publications/2008/9789241596657_eng.pdf.

[3] World Health Organization. Serum Ferritin Concentrations for the Assessment of Iron Status and Iron Deficiency in Populations. Geneva: World Health Organization (2011). Accessed at: http://www.who.int/vmnis/indicators/ferritin/en/

[4] Nemeth E., T. Ganz. Hepcidin and iron- loading anemias (2006) Haematologica; 91: 727- 732.

[5] Breymann C., C. Honegger C., W. Holzgreve et al. Diagnosis and treatment of iron- deficiency anemia during pregnancy and postpartum (2010) Arch Gynecol Obstet; 282: 577- 580.

[6] Reveiz L., G. M. L. Gyte, L. G. Cuervo, A. Casasbuenas. Treatments for iron-deficiency anaemia in

pregnancy (2011) *Cochrane Database Syst Rev*. 10: CD003094.

[7] Crichton R., B. G. Danielson, P. Geisser et al. Iron therapy with special emphasis on intravenous administration (2008) Uni- Med Verlag AG, London, Boston.

[8] Bernd F., J. Collingwood, N. A. Hodyl, G. Dekker. Intravenous ferric carboxymaltose for anemia in pregnancy (2014) *BMC Pregnancy and Childbirth*;14: 115 doi:10.1186/1471-2393-14-115