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Pre-pregnancy iron reserves, iron supplementation during pregnancy, and birth weight ☆

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ABSTRACT

Background: Early iron supplementation in women with sufficient reserves could provoke iron excess resulting in haemoconcentration and low infant birth weight (IBW).
Aim: To clarify the influence of early iron supplementation on maternal iron status and the IBW, taking into account pre-pregnancy iron deposits.
Study design: Longitudinal, prospective study.
Subjects: Healthy women volunteers (n = 82) intending to become pregnant.
Outcome measures: Women were grouped as a function of their pre-pregnancy (low or present) iron stores (serum ferritin (SF) < or ≥ 20 μg/L) and time of commencement of iron supplementation during pregnancy; "early" (<20 weeks) or "late" (≥20 weeks). Obstetric and clinical history, smoking habit, dietary intake and iron biochemical parameters were obtained at pre-pregnancy as well as at 1st, 2nd and 3rd trimesters. Haemoglobin, MCV, SF and transferrin saturation (TS) were measured.
Results: Overall, 36% of the women had low iron stores at pre-pregnancy. The mean early supplementation with iron was 140.7 mg/d and the mean of late supplementation was 99.01 mg/d. Early supplementation improves the biochemical status of the mother and does not provoke a significant increase in haemoconcentration relative to late supplementation independently of the pre-pregnancy iron levels.
Supplemental iron had a positive effect on birth weight among women with pre-pregnancy low iron stores ($\beta = 4.37$; SE = 1.8; $p = 0.038$) and did not affect birth weight among women with present iron stores ($\beta = -0.008$; SE = 3.03; $p = 0.998$).
Conclusion: Early iron supplementation with doses ~100 mg/d improves the biochemical status of the mother independently of her pre-pregnancy iron status. Supplementation with iron improves newborn birth weight in those women who start pregnancy with iron deficiency, and makes no significant difference to those women who are not iron deficient.

1. Introduction

Iron deficiency is the world's most common nutritional deficiency and is the major cause of iron deficiency anaemia in pregnancy [1]. The World Health Organisation (WHO) reported anaemia in an average of 18% of pregnant women in industrialised countries [1,2]. Most of these women were anaemic prior to conception.

More than 30% of fertile women in developed countries do not have adequate iron stores [2–7]. This situation carries risks for mothers during pregnancy, and for newborns. Further, iron deficiency and iron deficiency anaemia during pregnancy increase the risk of premature birth, and are associated with low birth weight together with delayed maturation, and low cognitive and motor capacity of the child [2,8,9].

In this context, the WHO recently recommended preventive weekly iron–folic acid supplementation where the prevalence of anaemia is above 20% among women of reproductive age and where mass fortification programs of staple foods with iron and folic acid are unlikely to be implemented within 1–2 years [10]. This complements the WHO's recommendation for antenatal supplementation with iron for all pregnant women to ensure their adequate iron supply and to

Abbreviations: BMI, body mass index; CRP, C-reactive protein; Hb, haemoglobin MLR, multiple linear regression; SF, serum ferritin; TS, transferrin saturation; VCM, mean corpuscular volume; WHO, world health organisation.

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avoid iron deficiency and its consequences for mother and child as pregnancy advances [1,2].

The overall quantity of iron necessary during pregnancy is high due to increases in the red cell mass; mostly in the 2nd trimester, accompanied by 50% expansion of the plasma volume and by the requirements of the growing foetus and placenta [11–13]. Even though mobilization of iron deposits and increased iron absorption [14] occur during pregnancy, iron requirements are difficult to cover by diet alone [11], especially when the supplement is provided late or when the woman commences pregnancy with an iron deficiency risk (serum ferritin<20 μg/l) [15–17]. Hence it is important that the women commence gestation in a good iron status so as to avoid the risks produced by high antenatal doses of iron, even if considered preventive or therapeutic [18,19].

The benefit of the early iron supplementation in women with insufficient reserves is well documented [20,21] but there is contradictory evidence regarding the effect of iron supplementation during gestation in women who are not iron deficient. While some authors have observed that the supplementation with iron in these women is beneficial for the newborn [22–24], others have indicated that it could provoke an excess of iron which can induce oxidative stress and haemoconcentration; factors that can negatively influence the health of the mother and the development of the foetus [7,16,25–33].

Hence, we proposed analysing the relationships between iron supplementation administered early or late in gestation, the haematological and biochemical parameters of the mother during pregnancy and the weight of the newborn. The relationships were assessed as a function of iron reserves (present or low) at the pre-pregnancy stage.

2. Materials and methods

This is a longitudinal and prospective study conducted in a group of healthy women volunteers who were intending to become pregnant soon, and who were between 18 and 35 years of age. They were residents of Reus, a city on the Mediterranean coast of Catalonia in North-Eastern Spain. This study was conducted in the Unit of Preventive Medicine, Faculty of Medicine, Rovira i Virgili University in collaboration with the Unit of Obstetrics and Gynaecology of the St Joan Hospital, Reus. All the haematological and biochemical analyses were done in the clinical laboratories of the Hospital (Laboratory Certification ISO 9001-2008).

The exclusion criteria included: if the woman was suffering from any chronic illness (chronic anaemia included) that would alter her nutritional or inflammation status, needing specific dietary/nutritional treatment, and multiple pregnancy (pregnancies with more than a single foetus). The study was approved by the Ethics Committee of the *Hospital Universitari Sant Joan de Reus*. All the individuals signed informed consent according to the requirements of the Helsinki Declaration.

There were 141 women recruited into the study and they were scheduled for 3 assessments over 9 months. There were 29 women who did not conceive within that period and were referred to the infertility clinic; 16 decided not to continue with the study mainly because of a change in gynaecologist, delivery in another hospital or change of address; 13 were excluded by the investigators for having incomplete biochemical data and 1 for having twins. Hence, complete data from pre-pregnancy to delivery were obtained in 82 women. Socioeconomic data were similar among these women and those who had been excluded from the study. All women had a socioeconomic level typical of the “middle class”.

The design of the study is shown schematically in Fig. 1. At the first pre-pregnancy clinical visit, the volunteers filled-in a general clinical history. Information recorded included medications, smoking habit and socio-demographic characteristics. They were also asked to maintain a 7-day dietary history before each pre-pregnancy visit. Blood was taken for biochemical analyses in all the pre-pregnancy visits (every three months until pregnancy was achieved, but for no more than one year) and the clinical visits at gestational weeks 8, 20, 32 and at birth. Smoking habit and dietary intake data were obtained at gestational weeks 6, 10, 26 and 38. Birth weight and gestational age were recorded at delivery.

Blood analyses included haemoglobin, mean corpuscular volume (MCV) using Beckman Coulter analyzer (Fullerthon S.A, California, USA), serum ferritin (SF) by immunoassay as described [34] and serum iron and transferrin by standard methods (ITC Diagnostics S.A and Biokit S.A. respectively, Barcelona, Spain). The transferrin saturation (TS) index was calculated as reported [35].

All the samples were measured in duplicate, and the means were used in the statistical analyses.

Since inflammation and infection can elevate SF levels, we analyzed C-reactive protein levels (CRP) (Biokit S.A., Barcelona, Spain) which was considered a potentially confounding variable in the statistical analyses.

Presence of iron stores at pre-pregnancy was defined as SF levels>20 μg/L and low iron stores as SF<20 μg/L [36].

Iron deficiency was defined as two or more of the following parameters being altered: depleted iron stores (serum ferritin levels ≤12 μg/L), low TS (<16%) and mean corpuscular volume (<80 fl) [1,2].

Anaemia was defined as Hb<12 g/dL at pre-pregnancy, Hb<10.5 g/dL at week 20 and Hb<11 g/dL at weeks 8, 32 and at birth [1].

Haemoconcentration was defined as Hb>13 g/dL at the 2nd and 3rd trimesters and as Hb>13.5 g/dL at term [33].

At the 10th week visit, the obstetrician recorded if the patient had taken any type of supplement, and recommended to all the women an iron supplementation of between 60 and 120 mg/d ferrous sulphate.

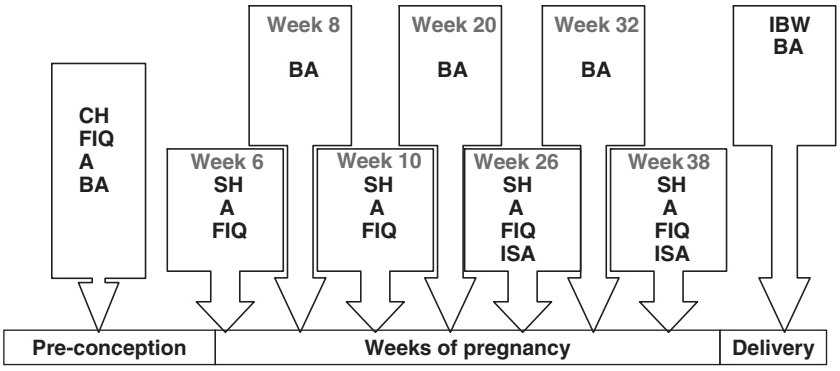

Fig. 1. Study design. CH = clinical history; SH = smoking habit; FIQ = food intake questionnaire; A = anthropometry; BA = biochemical analyses; IBW = infant birth weight; ISA = iron supplementation adherence.