Original Article

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Efficacy of daily versus intermittent administration of iron supplementation in anemia or blood indices during pregnancy

Abstract

Background: Pregnant women take iron supplements in order to prevent iron deficiency anemia which may have undesirable effects for both the mother and fetus. This study aimed to compare the daily and intermittent dose of iron supplementation in blood and iron indices in healthy pregnant women.

Methods: In this clinical trial study, 145 healthy pregnant women were selected with Hb≥11g%. The participants were randomly divided into two groups. Group 1 received daily iron supplement at 50 mg/day and group 2 received an intermittent dose of 3 times per week. Blood samples were assessed for complete blood count (Hb, Hct, RBC), iron, ferritin and zinc at baseline in the first trimester in all participants and the two groups were compared in regard to mean changes from baseline to the end of the study period in the third trimester. This clinical trial was registered in the Iranian Registry of Clinical Trials (www.irct.ir) with registration number ID: 2012082810682N1.

Results: The incidence of iron deficiency anemia was 2.7% in both groups. The mean levels of Hb, Hct and RBC in the first trimester were 13.3 g/dl, 39.4% and 4.5 mil/ml^3, respectively. At the end of the study, Hb, Hct, and RBC reduced significantly in both groups compared with baseline values ($p<0.05$). The difference from baseline in Hb and other blood indices did not differ significantly across the two groups.

Conclusion: These findings indicate that daily or intermittent administration of iron supplement to pregnant women has the same outcome. Regarding the side effects of iron in pregnancy, intermittent method seems preferable to daily intake.

Keywords: Iron deficiency, Ferritin, Zinc, Pregnancy, Iron supplement

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Iron deficiency anemia is one of the main causes of public health problems. A high proportion of women in both industrialized and developing countries become anemic during pregnancy (1). This can affect delivery and leads to low birth weight (2-6). The benefits of iron supplementation during pregnancy have been shown in several previously published studies (7). Maintaining hemoglobin and serum iron at adequate level during the second trimester exerts beneficial effects on mother and her child (8). On the other hand, increased serum iron concentration and accumulation of iron in different tissues may result in stillbirth or prevent fetus development (6-11). Increased storage of iron has also a negative influence on the absorption of other bivalent metals such as zinc which is the most important trace elements for normal metabolism (11). Additionally, these metals have important role in the synthesis of some proteins and expression of some genes and fetus maturation (12). Nevertheless, the benefits of iron supplementation for the mother and fetus during fetal or postnatal period have not been shown yet (4). In developed countries, a selective iron supplementation program is used during pregnancy based on hemoglobin and ferritin concentration in the first and second trimesters (13).

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However, in developing countries like Iran, all pregnant women receive daily iron supplements irrespective to hemoglobin status. With these reasons, the present study was conducted to compare the impact of daily versus intermittent administration of iron supplements on hemoglobin, red blood cell and iron indices in healthy pregnant women.

Methods

Study population: An interventional clinical trial study was performed on 145 healthy pregnant women at 20 week's gestation. All participants were enrolled in the Gynecology and Obstetrics Clinic, Babol, Iran, from October 2002 to September 2005.

Randomization: The subjects were randomly divided in to two groups on the basis of number given them at first visit. Even numbers entered in a group (group1=73 cases) received daily dose of iron supplement (50 mg/day) and odd numbers entered in another group (group 2=72 cases) received intermittent dose of iron supplement (three times /week) (50 mg/each time) from the 20th week of pregnancy.

Then, blood samples were taken from all the subjects in two trimesters (26-28 weeks) and three trimesters (34-37 weeks) to repeat the examination of blood indexes and measure the serum level of iron, ferritin and zinc as explained.

Enrollment: The purpose and design of the study was explained to each eligible participant and was given information consent of procedure and random allocation. The study participants were at 20 to 40 years of age with equal socio-economical condition. The subjects with β minor thalassemia, hemoglobin less than 11 g/dl, more than one delivery and diagnosed with internal and infectious diseases were excluded. Initial blood samples (5 ml) were drawn at 10-14 weeks of pregnancy (first trimester) and each volunteer was given an appointment for first visit within 15 days of enrollment. The participants should be visited at 26-28 and 34-37 weeks of gestation. They were also visited monthly at the clinic and asked about consumption of tablets and their side effects.

Iron, zinc and hematologic measurements: Iron, zinc and hematologic examination, including complete blood count and ferritin, were preformed on the blood samples at enrollment, 26-28 and 34-37 weeks of gestation. Blood samples were sent to the diagnostic laboratory and serum was immediately separated and stored at -20 °C. Complete blood counts were carried out within 3 hours of receipt. Serum iron, ferritin and zinc measurements were preformed weekly after the first thawing of previously frozen specimens. Complete blood count was measured with automatic cell counter (Hycell, France). Serum concentration of iron and zinc was measured by colorimetric assay using Zist-Shimi kit and Organ Tek kit, Iran, respectively. Serum concentration of ferritin was measured by enzyme-linked immunosorbent assay (ORG5Fe, Bngomtak, Germany).

Statistical analysis: In the statistical analysis, both groups were compared in regard to mean changes from baseline in Hb, Hct, serum iron, zinc and other parameters at the second trimester and the end of the study period by student t test or paired-t test using SPSS software, version 13.

Results

The mean age of the studied subjects was 25.7 and 26.1 years in group 1 and group2, respectively. No significant differences were seen on blood indices, iron and zinc status between group1 and 2 at first trimester. Figure 1 shows that the amount of Hb, HCT, RBC in both groups decreased significantly at the second and third trimester of pregnancy compared with baseline in the first trimester ($p<0.05$) whereas MCV and MCH increased significantly in group1 ($p<0.05$) and nonsignificantly in group 2 ($p>0.05$).

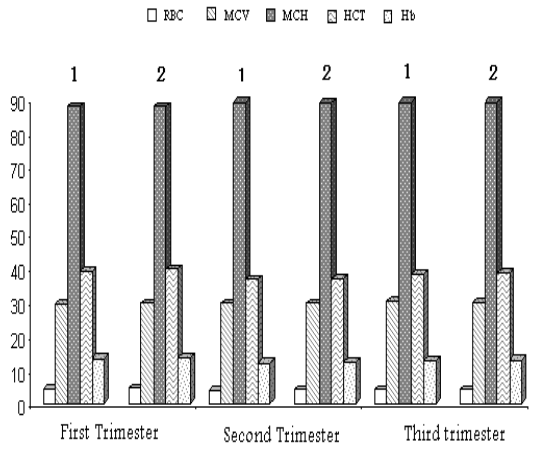

Figure1. Comparison of daily (1) and intermittent (2) dose of iron supplementation on mean of RBC, MCV, MCH, HCT and Hb in healthy pregnantwomen.

Moreover, at the end of the study period, serum iron nonsignificantly increased compared with baseline in both groups ($p>0.05$) while serum ferritin decreased significantly

in groups 1 and 2 (p=0.01, p=0.03, respectively) (table 1). Proportion of iron deficiency anemia was similar in both groups at 2.7%. In addition, serum zinc decreased nonsignificantly in both groups compared with baseline. In whatever way or manner, the magnitude of reduction in serum zinc was higher in group 1. Furthermore, the mean changes from baseline in serum iron and ferritin did not differ between the two groups (table 1)

Table 1. Comparison of daily and intermittent dose of iron supplementation on mean of iron, ferritin and zinc in serum of healthy pregnant women.

Indexes	First trimester			Second trimester			Third trimester		
	Iron	Ferritin	Zinc	Iron	Ferritin	Zinc	Iron	Ferritin	Zinc
Group	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD
1 (n=72)	86.9±28.9	40.9±36.4	94.4±41.7	88.5±36.9	31±31.3	81.7±37.7	90.2±30.8	30.3±27.3	84.7±32.6
2 (n=73)	97.6±37.3	42.4±32.8	98.1±31.6	104.5±62.6	22.7±18.4	83.7±2.2	94.4±47.8	30.4±63.4	78±30.4

Discussion

The findings of this study indicate that Hb, Hct, and RBC count reduce significantly in both groups at the time of delivery as compared with the baseline values. These changes along with significant reduction of serum ferritin indicate exacerbation of anemia over the study period despite iron supplementation. The laboratory features of anemia are consistent with iron deficiency anemia. These observations indicate that neither daily nor intermittent administration of 50 mg oral iron do not completely prevent iron deficiency anemia in pregnant women.

However, in group 1, the dosage of iron was two times higher than group 2, it was not resulted in greater improvement of mean corpuscular hemoglobin in group 1 suggesting inadequate acquisition of iron by RBC in both groups. On the other hand, the increased level of MCH was not associated with Hb improvement or correction of RBC indices indicating contribution of other factors including volume expansion in the development of anemia during pregnancy. For example, high MCV values in both groups do not correspond with iron deficiency anemia, but suggest zinc deficiency as observed in this study.

In addition, the contribution of vitamin B12 or folic acid deficiency in the development of macrocytic anemia in our patients.could not be ignored, since, the deficiency of these factors during pregnancy is common. All the same, we did not assess these parameters for documentation. Exacerbation of anemia in the third trimester of pregnancy should be attributed to the increased volume of plasma during the third trimester as compared with the first trimester. Even so, inadequate administration of iron to mother to compensate fetus requirement is also responsible for the occurrence of anemia. Nevertheless, an optimal dosage of iron for prevention of anemia has not been determined yet. Based on the available data, maintaining hemoglobin levels at 9 gr/ dl to 13 gr/ dl has been considered safe for the mother and fetus (14).

The results of this study are in contrast with the other studies which have addressed the effect of iron supplementation in pregnancy. In these studies, intermittent iron supplementation during pregnancy reduced the prevalence of anemia defined as Hb <110g/L or increased the level of Hb (14-16). However, our findings are in agreement with other studies (17-21).

This study indicates that both the daily method and intermittent administration of iron may be used for the correction of anemia. While the efficacy of intermittent administration despite the lower dosage, was similar to daily iron supplementation but its effect in the correction of RBC indices particularly the correction of cell hemoglobin was not sufficient to compensate iron requirement.

This study has limitation, with regard to inadequate sample size for the detection of a significant difference between the comparison groups. Another limitation may be referred to the dosage of iron or the time of starting iron supplement to increase Hb levels in the third trimester. Higher dose of iron or treatment earlier than the 20th gestational week could possibly be accompanied by further elevation of Hb. In conclusion, this study revealed that neither daily nor intermittent administration of iron supplementation at 50 mg dose was not adequate for the

compensation of iron requirement during pregnancy. Nonetheless, the independent effect of iron treatment on hemoglobin is cofounded by several factors including the time of commencing iron, duration and the dosage of iron, and volume expansion over the course of pregnancy. Intermittent administration of iron can be used as an alternative method for preventing of anemia during pregnancy.

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