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RESEARCH ARTICLE

Comparison of the Prophylactic Use of Iron Polymaltose Complex and Ferrous Sulfate Iron Preparations in Terms of Efficacy and Side Effect Profile in Pregnant Women

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Abstract

Introduction: Pregnancy is a physiological process in which the need for iron increases. We aimed to compare the effectiveness and side effects of different oral iron supplements on pregnant women. **Methods:** 100 pregnant women between the ages of 18-45 who used Fe+2 (ferrous sulfate) valent iron supplementation during their pregnancy were included in the study as group 1. 100 pregnant women in the same age range who used Fe+3 (iron polymaltose complex) valent iron supplementation during their pregnancy were determined as group 2. Response to anemia treatment was evaluated with the results of laboratory parameters (Hgb, Hct). The side effects of the preparations used in oral iron replacement were questioned retrospectively with a questionnaire applied to the patients. **Results:** 16 of 100 patients (16%) had side effects with oral iron polymaltose complex supplementation. 43 of 100 patients (43%) had side effects with oral ferrous sulfate supplementation. The overall side effect was higher in those taking oral ferrous sulfate supplementation ($p<0.001$). Hb and Hct values measured at 3-month periods were found to be similar between the groups ($p>0.05$). The most common side effect was nausea and vomiting with 12%. **Conclusion:** Both oral ferrous sulfate and iron polymaltose complex supplementation have similar effects on hemoglobin and hematocrit levels in pregnant women without iron deficiency anemia. However, oral ferrous sulfate supplementation causes more side effects compared to iron polymaltose complex.

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Introduction

Physiological changes in pregnancy can cause difficulties in the diagnosis of hematological diseases. While the plasma volume increases by approximately 40-50% in singleton pregnancies, the amount of erythrocytes increases by approximately 15-25%, so the need for iron increases during pregnancy. Anemia in pregnancy can be defined as hemoglobin levels below 11 g/dL in the first trimester; 10.5 g/dL in the second trimester; and 11 g/dL in the third trimester.[1] Iron supplementation is commonly recommended during pregnancy to prevent and treat iron deficiency anemia, a condition that can occur due to increased demands for iron during pregnancy. Pregnant women need approximately 27-30 milligrams (mg) of iron per day, compared to 18 mg per day for non-pregnant women.[2] Iron deficiency anemia in pregnancy has been associated with increased risks such as preterm birth, low birth weight, postpartum hemorrhage and perinatal mortality. Iron deficiency anemia should be treated with anti-anaemic iron supplements in addition to prenatal vitamins.[3]

However, iron supplements can cause side effects such as metallic taste, gastric irritation, diarrhea, constipation, nausea, vomiting, or stomach discomfort.[4] Patients may also be bothered by itching and by black/green or tarry stools that stain clothing or cause anxiety about bleeding. Taking the supplement with food or using a slow-release formulation may help reduce these side effects. In a systematic review, gastrointestinal adverse effects were seen with all oral formulations but extended-release ferrous sulfate with mucoproteins appeared to be the best tolerated.[5] It's important to note that not everyone will experience side effects from iron supplementation, and the benefits often outweigh the risks when iron deficiency anemia is present. In this study, we aimed to compare the use of different oral iron supplements in pregnant women in terms of efficacy and side-effect profile.

Material and Methods

This study was designed as a retrospective observational cohort study. 100 pregnant women between the ages of 18-45 who used Fe+2 (ferrous sulfate) valent iron during their pregnancy were accepted as group 1. 100 pregnant women in the same age range who used Fe+3 (iron polymaltose complex) valent iron during their pregnancy were determined as group 2. Pregnant women who were followed up in Ankara City Hospital's perinatology outpatient clinic regularly from the first trimester were included in the study. The questionnaire was applied to pregnant women between 32-40 weeks of gestation. Pregnant women with iron deficiency anemia, multiple pregnancies, and pregnant women with systemic or pregnancy related diseases were excluded from the study. Demographic characteristics and medical and obstetric histories of the pregnant women were reviewed and noted from the hospital records. The hemoglobin (Hb) and hematocrit (Hct) parameters of the patients, which were measured at 3-month intervals, were compared. Response to anemia treatment was evaluated with the results of laboratory parameters (Hgb, Hct). The side effects of the preparations used in oral iron replacement were questioned retrospectively with a questionnaire applied to the patients. The study protocol was performed in line with the Declaration of Helsinki. This study was approved by the Ankara City Hospital institutional review board (12.07.23/ E2-23-4487).

Statistical analysis

IBM SPSS version 25 software (Armonk, NY) was used for statistical analyses. The variables were investigated using the Kolmogorov-Simirnov test to determine whether or not they are normally distributed. Student's T-test was used to compare two normally distributed independent variables. Descriptive analyses were presented using mean±SD for the normally distributed variables. The chi-square test was used for categorical variables and values were presented as N (%). A p-value of less than 0.05 was considered to show statistically significant results.

Results

A comparison of demographic and clinical characteristics of pregnant women using iron polymaltose complex and ferrous sulfate iron supplements were shown in Table 1. Maternal age, gravida, parity, BMI, and gestational age at birth were similar between the groups ($p>0.05$). It was observed that the gestational week at which supplementation was started was earlier in pregnant women using ferrous sulfate iron preparations ($p=0.005$). The mean duration of oral iron preparation use was 18.1±8.4 in the iron polymaltose complex group and 21.5±8.5 in the ferrous sulfate group. The usage time was statistically longer in the ferrous sulfate group ($p=0.005$).

Table 1. Comparison of demographic and clinical characteristics of pregnant women using Fe+3 and Fe+2 valence iron supplements

Variables	Fe+3 (n=100)	Fe+2 (n=100)	p
Maternal age (year)	28.3±6.1	27.8±5.3	0.58
BMI (kg/m^2)	28.4±4.3	28.2±3.5	0.71
Gravida	2.1±1.2	2±1.2	0.65
Parity	0.8±0.9	0.7±0.9	0.88
Abortion	0.3±0.6	0.3±0.7	0.34
Gestational age (week)	36.3±2.1	36.7±2.1	0.21
duration of iron supplement use (week)	18.5±7.8	15.2±8.2	0.005
Usage time (week)	18.1±8.4	21.5±8.5	0.005

BMI: Body mass index.
Student's T-test; Results were presented as mean±SD. p<0.05 values were presented in bold

A comparison of the side effect profile in pregnant women using iron polymaltose complex and ferrous sulfate iron supplements was shown in Table 2. 16 of 100 patients (16%) had side effects with oral iron polymaltose complex. 43 of 100 patients (43%) had side effects with oral ferrous sulfate. The overall side effect was higher in those taking oral ferrous sulfate (p<0.001). The most common side effect was nausea-vomiting at 12%, and the second most common side effect was constipation at 10%.

Table 2: Comparison of the side effect profile in pregnant women using Fe+3 and Fe+2 valent iron supplements

Variables (n, %)	Fe+3 (n=100)	Fe+2 (n=100)	p
Presence of side effects	16 (16%)	43 (43%)	**<0.001**
Nausea-vomiting	4 (4%)	12 (12%)	
Stomach discomfort	3 (3%)	7 (7%)	
Diarrhea	0 (0%)	4 (4%)	
Bloating	0 (0%)	2 (2%)	**0.005**
Color change in stool	3 (3%)	6 (6%)	
Constipation	6 (6%)	10 (10%)	
Metallic taste	0 (0%)	2 (2%)	

Chi-Square Test; results were presented as number (%). p<0.05 values were presented in bold

First, second, and third trimester Hb and Hct values of pregnant women using iron polymaltose complex and ferrous sulfate iron supplements were compared in Table 3. Hb and Hct values measured at 3-month periods were found to be similar between the groups. No statistically significant difference was detected (p>0.05).

Table 3: First, second, and third trimester Hb and Hct values of pregnant women using Fe+3 and Fe+2 valence iron supplements

Variables	Fe+3 (n=100)	Fe+2 (n=100)	P
First trimester Hb (g/dl)	12.8±1.2	12.6±1.3	0.33
First trimester Hct (%)	38.3±3.8	37.9±3.5	0.60
Second trimester Hb (g/dl)	11.5±1.1	11.4±1.1	0.35
Second trimester Hct (%)	35.2±2.8	34.7±3.1	0.17
Third trimester Hb (g/dl)	11.4±1.1	11.7±1.2	0.31
Third trimester Hct (%)	34.8±3.1	35.5±3.5	0.21

Hb: Hemoglobin, Hct: Hematocrit
Student's T-test; results were presented as mean±SD

Discussion

Iron is an essential mineral that plays a vital role in the production of hemoglobin, the protein in red blood cells that carries oxygen throughout the body. The iron requirements increase during pregnancy to support the growing fetus, placenta, and maternal blood volume expansion. In our study, we found that the type of different oral iron supplements did not affect the gestational age at birth. Side effects were more common in those using oral ferrous sulfate supplements. These side effects included nausea, vomiting, stomach discomfort, diarrhea, bloating, gastric irritation, constipation, and metallic taste. These findings were consistent with the literature.[4] None of the pregnant women in the study had anemia in the first trimester. First trimester, second trimester, and third trimester Hb Hct values did not change according to the oral iron supplement used.

In a retrospective cohort study from China, it was found that compared with no anemia, anemia severity during pregnancy was associated with increased risks of placental abruption, preterm birth, severe postpartum hemorrhage, and fetal malformation.[6] Conversely, a review noted that supplementation of iron, folic acid, or both to pregnant women, either anemic or not, did not increase the birth weight or gestational week.[3] We did not find any difference at gestational week at birth either. Another study stated that the prevalence of anemia overall and by pregnancy trimester was higher among African American (Black) women than among other ethnic groups. The prevalence of anemia was higher among women evaluated in the third trimester of pregnancy than among those evaluated in the first or second trimester.[7]

There are some studies in the literature comparing the efficacy and tolerability of oral Fe+2 (ferrous sulfate) and Fe+3 (polymaltose complex) supplementation in pregnant women. The Common view is that both oral supplement types were equally effective, but fewer side effects were seen with the polymaltose complex.[4,8,9] Similar results were found in some studies among non-pregnant adult groups, and it was stated that the frequency of gastrointestinal side effe-

cts of the ferrous product was significantly higher, but both supplements were well tolerated.[10] Numerous clinical trials in men, women, children, and infants have shown a lower rate of treatment interruption with polymaltose complex than with ferrous sulfate.[11] It was also shown that iron polymaltose complex improved the cognitive function, and scholastic performance of adolescents with and without iron deficiency and anemia.[12] However, among children who received ferrous sulfate therapy for iron deficiency anemia, higher hemoglobin levels of ferrous sulfate were found to have fewer side effects compared to children who received iron polymaltose complex.[13] In laboratory studies on rats and in vitro studies, it has been shown that the iron polymaltose complex does not interact with commonly used drugs such as acetylsalicylic acid, tetracycline hydrochloride, calcium phosphate, methyl-L-dopa, magnesium hydrochloride, and none of them has a significant effect on iron absorption.[14,15] The small number of cases was the major limitation of our study. In addition, iron deficiency anemia was not observed in any of the pregnant women in both groups at the beginning of iron supplementation. We performed this study on pregnant women without iron deficiency anemia who received prophylactic iron supplementation.

Conclusion

In conclusion, both oral ferrous sulfate and iron polymaltose complex supplementation in pregnant women have similar effects on hemoglobin and hematocrit levels in pregnant women without iron deficiency anemia. However, oral ferrous sulfate supplementation causes more side effects compared to iron polymaltose complex. Our findings were consistent with the literature. Further studies are needed to obtain definitive results.

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Conflict of interest
None

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