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Iron Status Markers of Pregnant Women Receiving Iron Treatment and Iron

Nilüfer Yiğit Çelik[1], Barış Mülayim[1], Sema Mülayim[2], Elif Durukan[3], Filiz Yanık[4]

[1]Başkent Üniversitesi Tıp Fakültesi, Alanya Uygulama ve Araştırma Merkezi, Kadın Hastalıkları ve Doğum Kliniği, Antalya,
[2]Alanya Devlet Hastanesi, Kadın Hastalıkları ve Doğum Kliniği, Antalya
[3]Başkent Üniversitesi Tıp Fakültesi, Biyoistatistik, Ankara
[4]Başkent Üniversitesi Tıp Fakültesi, Kadın Hastalıkları ve Doğum Anabilim Dalı, Ankara

Abstract

Objective: To investigate the effectiveness of iron treatment and iron prophylaxis in the regard of iron status markers during pregnancy.

Methods: Two-hundred twelve pregnant women admitted to Baskent University Alanya Medical Center included the study.The pregnant women in the hemoglobin group treated with one iron hydroxide polymaltose complex tablet (containing 100 mg of elemental iron= Fe+++) per day throughout pregnancy when hemoglobin (Hb) level was <11g/ dl. In the ferritin group, pregnant women received iron prophylaxis with one the same tablet based on ferritin values early in pregnancy.

Results: All Hb,hematocrit (Hct), ferritin, iron and iron binding capacity values were found significantly different between trimesters of pregnancy in both groups. And except the mean decrease of Hb values between the first and third trimester of pregnancy, the other markers were not found significant between the two groups. Differences in Hb, Hct, ferritin, iron and iron binding capacity values between first and third trimester in the hemoglobin and ferritin groups were as follows; 1.6±0.9 vs. 1.3±1.1 g/dl, 4.4±3.1 vs. 3.8±2.8%, 20.7±30.4 vs. 20.7±26.0 İg/L, 24.6±41.9 vs. 24.1±37.8 µg/ dl, -138.1± 84.4 vs. -119.1±84.4 µg/ dl.

Conclusion: Even iron recommended to pregnant women when only if their Hb level was less than 11g/dl during pregnancy; those have similar changes in the regard of iron status markers throughout pregnancy when compared to iron recommended according to ferritin levels early in pregnancy.

Keywords: Hemoglobin, hematocrit, ferritin, iron and iron binding capacity.

Demir tedavisi veya demir profilaksisi alan hastalarda serum demir belirteçleri

Amaç: Gebelik süresince demir tedavisi veya demir profilaksisinin serumda demir durumunu gösteren belirteçlere etkisini araştırmak.

Yöntem: Başkent Üniversitesi Alanya Uygulama ve Araştırma Merkezinde takip edilen 212 gebe ilk başvuruda randomize olarak iki gruba ayrıldı. Birinci gruba (hemoglobin (Hb) grubu) kontrolleri sırasında Hb düzeyi <11 g /dl tespit edildiğinde günde bir tablet demir hidroksi polimaltoz kompleksi alması önerildi. İkinci gruptaki (ferritin grubu) hastalara ise erken gebelikteki ferritin düzeylerine göre aynı demir preparatını yine tüm gebelik boyunca alması önerildi.

Bulgular: Grupların kendi içinde Hb, hematokrit (Hct), ferritin, demir (fe) ve demir bağlama kapasitesi değerlerinin (febk) hepsi tüm trimesterler için anlamlı ölçüde farklı bulundu. Hb seviyesinde üçüncü ve birinci trimesterler arasındaki ortalama düşüş dışındaki diğer tüm belirteçlerin farkları istatistiksel olarak anlamsızdı. Hb, hct, ferritin, demir ve demir bağlama kapasitesinin birinci ve üçüncü trimesterlerdeki değerlerinin arasındaki farklar hemoglobin ve ferritin grupları için sırasıyla: 1.6±0.9 vs. 1.3±1.1 g/dl, 4.4±3.1 vs. 3.8±2.8%, 20.7±30.4 vs. 20.7±26.0 İg/L, 24.6±41.9 vs. 24.1±37.8 µg/ dl, -138.1± 84.4 vs. -119.1±84.4 µg/ dl idi.

Sonuç: Gebelikte demir tedavisinin Hb seviyesi 11 g/ dl altına düştükten sonra başlanmasıyla erken gebelikteki ferritin seviyelerine göre başlanmasının serum demir durumunu gösteren belirteçler açısından benzer etkileri olmaktadır.

Anahtar Sözcükler: Hemoglobin, hematokrit, ferritin, demir ve demir bağlama kapasitesi.

Correspondence: Nilüfer Yiğit Çelik, Başkent Üniversitesi Alanya Uygulama ve Araştırma Merkezi Saray Mah. Yunus Emre Cad. No:1 Alanya, Antalya
e-mail: niluferyigitcelik@yahoo.com

Introduction

Lack of convincing scientific support for choosing one or the other strategy in the regard of iron prophylaxis during pregnancy, it is generally prescribed based on selected knowledge, personal experience, tradition and economical considerations in Turkey and we believe as well as around the world. The debate concerning iron prophylaxis strategy to pregnant women has been controversial and no definite consensus has been reached. This is may be due to different prevalence of iron deficiency (ID) and iron deficiency anemia (IDA) around the world.

There are discrepancies between the recommendations from different health institutions like Food and Agriculture Organization of the United Nations,[1] The Nordic Nutrition Recommendations[2] or Department of Health in United Kingdom,[3] in the regard of iron prophylaxis during pregnancy but the common point, which they pay attention, is the iron reserves at the start of pregnancy. A ferritin concentration of 60 μg/L corresponds to iron stores of around 500 mg,[4] while iron deficiency is defined as empty iron stores with ferritin <12-15 μg/L.[5] It is possible to avoid unnecessary iron loading of women with adequate iron status, i.e., iron reserves of >500 mg as iron has a negative influence on the absorption of other essential divalent metals and causes an increase in the oxidative stress, as well.[6-12] Despite almost all pregnant women are advised for iron prophylaxis in Turkey those whom have not being taken iron prophylaxis for some reasons; encountered with low hemoglobin (Hb) levels during pregnancy and then after have to commence iron treatment. So we created the one-foot of our study with the pregnant women who received iron prophylaxis based on ferritin values early in pregnancy and the other-foot with the pregnant women who received iron only if their Hb level was less than 11g/dl during pregnancy. And then we evaluated the effectiveness of iron treatment and iron prophylaxis in the regard of iron status markers during pregnancy of Turkish women.

Methods

This clinical trial was conducted prospectively between January 2008- June 2008 at the Obstetrics and Gynecology Department of Baskent University, Alanya Medical and Research Center, in Alanya, Turkey. All women admitted to hospital for antenatal care recruited into this study. Two hundred sixty- eight pregnant women were admitted during this time. Of these 280 women, 54 were not eligible for the study. Each eligible participant gave written informed consent.

The institutional review boards of the Baskent University approved the protocol. Inclusion criteria for recruitment were as follows: who was at first trimester of pregnancy, had not taken supplements that contained iron in the last month, had a singleton pregnancy, had not known chronic illness (such as chronic hypertension, asthma, diabetes, gastrointestinal problems like ulcerative colitis or peptic ulcus), had not complicated pregnancy (threatened abortion history in present pregnancy etc), had not smoking. After excluding 54 women, 226 women were randomly allocated to either hemoglobin group or ferritin group by means of computer- generated number table. After randomization, fourteen women were subsequently excluded: 6 were lost to follow up, 5 women developed preeclampsia in second trimester, 3 patients did not give birth in the our hospital. Finally, the analysis was conducted on 100 women in the hemoglobin group and 112 women in the ferritin group.

The pregnant women in the hemoglobin group took one iron hydroxide polymaltose complex tablet (containing 100 mg of elemental iron= Fe+++) per day throughout pregnancy when Hb level was <11g/ dl. In the ferritin group, criteria to recommend iron supplementation were as follows: at the first prenatal visit[1]

if ferritin level was < 20 μg/L, one iron hydroxide polymaltose complex tablet per day throughout pregnancy was recommended at once to pregnant women immediately,[2] if ferritin level was 20- 60 μg/L, after 20 weeks of pregnancy women started to take one iron hydroxide polymaltose complex tablet per day,[3] if ferritin level was >60 μg/L, drug was not recommended to the pregnant women. For each woman, levels of hemoglobin, hematocrit, ferritin, serum iron and iron binding capacity were controlled in the first trimester (<14 gestational weeks), in the second trimester (20- 28 gestational weeks) and before delivery (32- 36 gestational weeks).

Administration of the drugs was in accordance with the manufacturers recommendations. A serum ferritin value of <12 μg/L was considered to indicate absent iron reserves and iron deficiency during pregnancy. The World Health Organization recommends a Hb of 11.0 g/ 100 ml as a cut off point for anemia throughout the whole pregnancy.[13] Iron deficiency anemia was defined as serum ferritin <12 μg/L in the presence of anemia. Incidence of iron deficiency and iron deficiency anemia was defined according to above criteria.

The software SPSS version 17.0 (Statistical Package for the Social Sciences, version 15.0, SPSS Inc, Chicago, Ill, USA) was used to monitor progress and analyze the data. The continuous variables (Age, BMI, gravidity of the subjects, serum hemoglobin, hematocrit, ferritin, iron levels and iron binding capacity) were presented as mean ± SD (standard deviation), and were compared with regard to study groups using independent samples t-test. Within each group, to evaluate the variation of serum hemoglobin, hematocrit, ferritin, iron levels and iron binding capacity between first, second and third trimesters repeated measures variance analysis was used and to determine which trimester was significantly different from the others, bonferoni adjusted paired samples t-test was performed. Statistically significance was set at "$p \leq 0.05$ (in bonferoni adjusted tests, "$p<0.016$" was considered as statistically significant).

Results

In hemoglobin group 100 and in the ferritin group 112 pregnant women were followed during their pregnancies. The mean age of the pregnant women was 29.0±1.2 in the hemoglobin group and 28.7±1.3 in the ferritin group ($p>0.05$). As shown in Table 1, age, gestational age, gravidity and body mass index (BMI) of the pregnant women were not significantly different between groups. Venous blood samples were obtained on average at 7.7± 2.0 weeks and 8.0±2.2 weeks in the first trimester, 24.4±2.5 weeks and 27.0±2.8 weeks in the second trimester and 33.7±1.4 weeks and 33.5±1.7 weeks in the third trimester in hemoglobin and ferritin groups, respectively ($p >0.05$).

In Table 2, mean values of serum hemoglobin (Hb) hematocrit (Hct), ferritin, iron and iron binding capacity levels in two groups for each trimester was shown. The mean of serum

Table 1. Demographic characteristics of the pregnant women.

Variable	Hemoglobin group (n= 100)	Ferritin group (s=112)	p***
Age (year)*	29.0±1.2	28.7±1.3	>0.05
Gestational age at delivery (week)*	38.9±0.9	38.4±0.8	>0.05
Gravidity*	2.1 ±1.0	2.1 ±1.1	>0.05
Parity**	1 (0-1)	1 (0-1)	>0.05
Body mass index*	22.1±5.6	23.2±7.8	>0.05

*Data are given as mean± SD; ** Median (inter quartiles); *** Independent samples t- test

hemoglobin, hematocrit, ferritin, iron levels decreased and the iron binding capacity increased within the time in both groups (p< 0.0001). Within the hemoglobin group, the serum hemoglobin level decreased from 12.4±1.0 to 10.9±1.1 in second trimester and to 10.7±1.1 in the third; but in the ferritin group the decrease of hemoglobin level occurred significantly in second trimester (p<0.016), there was not statistically significant difference between the third and second trimester hemoglobin levels (p>0.016).

The decrease of serum hematocrit, ferritin and iron levels were significant in the second trimester in both of the groups (p<0.016). The mean of iron binding capacity increased in second trimester in both of the groups, and the increase continued also in third trimester. Mean differences between third trimester and first trimester values of the serum markers of the iron status (mean hb, htc, ferritin, iron, iron binding capacity) between the two groups were shown in Table 3. There was only in the mean decrease in Hb value was statistically different between groups, while for the all other markers, significant difference were not found. Prevalence of iron deficiency was 14%, 66%, 68% in the hemoglobin group in the first, second, third trimester, respectively while prevalence of iron deficiency anemia was 6%, 46% and 32%. In the ferritin group, prevalence of iron deficiency was 23% in the first trimester where as prevalence in the second trimester and third trimester of pregnancy were increased 68% vs. 86% in the second and third trimesters, respectively.

Prevalence of iron deficiency anemia for each trimester was as follows: 9%, 50% and 34% in the first, second and third trimester respectively in the ferritin group.

Discussion

In our study, all Hb, Hct, ferritin, iron and iron binding capacity values were found significantly different among trimesters of pregnancy in both groups. Except the mean decrease of Hb values between the first and third trimester of pregnancy, the other markers were not found significantly different between the two groups. But the difference in Hb values between two groups was clinically insignificant (1.6 ±0.9 vs. 1.3±1.1g/dl). Our study showed that

Table 2. Serum levels of pregnant women with respect to iron status markers in each group.

Variable	1st trimester	2nd trimester	3rd trimester	p*
Hb level (g/ dl)				
Hemoglobin group	12.4±1.0	10.9±1.1	10.7±1.1	<0.0001
Ferritin group	12.2±1.2	10.9±1.1	10.9±1.2	<0.0001
Hematocrit level (%)				
Hemoglobin group	36.7±2.5	32.7±2.9	32.2±3.0	<0.0001
Ferritin group	37.1±3.3	33.5±2.9	33.2±3.2	<0.0001
Ferritin level (µg/ L)				
Hemoglobin group	39.0±28.3	16.1±18.1	18.2±22.7	<0.0001
Ferritin group	29.0±27.2	11.1±8.5	8.3±6.0	<0.0001
Serum iron level (µg/ dl)				
Hemoglobin group	73.9±35.6	55.4±37.4	49.3±38.8	<0.0001
Ferritin group	71.6±32.2	57.6±40.9	47.5±34.2	<0.0001
Serum iron binding capacity (µg/ dl)				
Hemoglobin group	325.8±67.1	421.8±74.7	420.6±60.5	<0.0001
Ferritin group	283.1±75.0	346.6±85.6	393.9±84.4	<0.0001

*Repeated measures variance analysis

Table 3. Differences in markers of iron status between first and third trimesters in each group.

Markers of iron status	Mean difference (± SD)	p*
Differences in Hb		
Hemoglobin group	1.6±0.9	<0.05
Ferritin group	1.3±1.1	
Differences in Hct		
Hemoglobin group	4.4±3.1	>0.05
Ferritin group	3.8±2.8	
Differences in ferritin		
Hemoglobin group	20.7±30.4	>0.05
Ferritin group	20.7±26.0	
Differences in iron level		
Hemoglobin group	24.6±41.9	>0.05
Ferritin group	24.1±37.8	
Differences in iron binding capacity		
Hemoglobin group	-138.1±84.4	>0.05
Ferritin group	-119.1±84.4	

*Independent samples t test.

either receiving iron when only if their Hb level was less than 11g/dl during pregnancy or receiving iron according to ferritin levels early in pregnancy had similar changes with respect to iron status markers during pregnancy. Iron deficiency prevalence was 68.0% and 86.0% in the third trimesters of pregnancy in the hemoglobin and ferritin groups, respectively.

Iron deficiency anemia prevalence was 32.0% and 34.0% in the third trimesters of pregnancy in the hemoglobin and ferritin groups, respectively. When we compared our results with Milman et al's results in the regard of ID and IDA, our results were very high. When they recommended 80-mg/day irons from 18th weeks of pregnancy, ID and IDA prevalence were found 12.3% and 0 in the 32 weeks of gestation respectively.[13] Also when we compared our study with Siega Riz et al's results, we can see this difference again, IDA was observed 10% among iron receiving group in the third trimester.[14] Prevalence of ID and IDA were high in our study, but definition of ID and IDA, prophylactic dose and duration of iron, and criteria for when prophylaxis should be given were different between these studies and our study. Factors such as socioeconomic status, lifestyle, eating habits could affect the prevalence of iron deficiency and iron deficiency anemia.[15-17] So may be every nation should have to find its own guideline for iron prophylaxis during pregnancy due to affecting reasons. To our knowledge, our study is the first one that such an evaluation has done in the literature. Gofin R et al published the one, which was similar to our study, in this study 478 pregnant women who received iron supplementation from the 4th month of pregnancy compared with 392 pregnant women who received iron treatment only if their Hb level was less than 12 g/dl, or had no supplementation.

The mean decrease of Hb and Hct levels between the second and third trimester of pregnancy was lower in the supplementation group (-0.9 g/dl Hb, -2.1% Hct) than in the treatment group (-1.1 g/dl Hb; -3.3% Hct).

The differences between the two groups were significant only for the Hct levels.[18] In another study, 429 of women who had hemoglobin levels of > or = 110 g/L and ferritin levels of > or = 40 μg/L and were assigned randomly to receive prenatal supplements with 30 mg of iron as ferrous sulfate or 0 mg of iron until 26 to 29 weeks of gestation. Daily prenatal supplements with 30 mg of iron that were given from about 12 weeks of gestation to the third trimester to initially non-anemic women with sufficient iron stores (ferritin, ≥40 μg/L) did not significantly improve iron status at the beginning of the third trimester.[14] In a randomized, double-blind, placebo-controlled trial, 244 women who had a hemoglobin concentration of 13.2 g/dl or greater and a serum ferritin level higher than 15 μg/L between the 13th and 18th week of pregnancy took either one 150-mg tablet of ferrous sulfate daily or placebo during their pregnancies. They concluded that if iron supplementation has not used, it did not cause a considerable decrease in markers of anemia in women with a hemoglobin concentration of

13.2 g/dl or greater in the second trimester of pregnancy.[19]

Conclusion

In conclusion, our study suggests that even iron recommended to pregnant women when only if their Hb level was less than 11g/dl during pregnancy; those have similar changes in the regard of iron status markers throughout pregnancy when compared to iron recommended according to ferritin levels early in pregnancy.

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