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EFFECT OF WEEKLY IRON SUPPLEMENTATION ON IRON INDICES IN PREGNANT WOMEN

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ABSTRACT

Introduction: The serum iron and ferritin concentrations decline after midpregnancy. The amount of dietary iron, together with that mobilized from stores, will be insufficient to meet the average demands imposed by pregnancy. Without supplementation, the haemoglobin concentration and hematocrit fall appreciably as the blood volume increases leading to iron deficiency anaemia (IDA). **Aims & objectives:** To compare effectiveness of weekly supplementation of 200 mg elemental iron with daily supplementation of 100 mg elemental iron on iron indices along with haemoglobin and hematocrit values in pregnant women. **Materials & Methods**: A prospective randomised longitudinal study was conducted at a tertiary care teaching hospital. Study included 100 pregnant women randomly allocated to two groups. Group I (n=50) received daily iron and group II (n=50) received weekly iron supplementation. During follow-up haemoglobin and hematocrit values were estimated at 4, 8 , 12 and 16 weeks of iron supplementation. Iron indices: serum iron, total iron binding capacity (TIBC) and serum ferritin were estimated before and after 12 and 16 weeks of iron supplementation**.** **Results**: Significant increase in haemoglobin, hematocrit and serum iron levels was ovserved in both the groups ($p < 0.001$) but on intergroup comparison it was significantly higher in group I than group II ($p < 0.001$). Serum ferritin improved in both the groups but improvement was not significant in weekly supplemented group. Compliance was better and side-effects were less in group II as compared to group I (11.36% versus 39.9%). **Conclusion:** The weekly supplementation with 200 mg of elemental iron of pregnant women had desired effect on iron indices except for the serum ferritin level which can be overcome by extending the supplementation to the post-partum period.

INTRODUCTION

Iron deficiency anemia is one of the most common nutritional disorders and presents as a widespread public health problem in the world and especially in developing countries including India[1]. In India 62-88% pregnant women suffer from anaemia [2,3]. Approximately 80% of all anemias in pregnancy occur due to iron deficiency [4]. Anemia is associated with poor pregnancy outcome[5,6], in the form of preterm birth, low birth weight, inability to tolerate haemorrhage during labour leading to increase incidence of infection *etc.*

In India despite the effort of the National anemia prophylaxis programme since 1970 to supplement all pregnant women with daily iron and folic acid, anaemia still continues unabated[2,3]. The reasons for the limited success of iron supplementation are unclear but poor compliance because of the related gastrointestinal side effects of medicinal iron is commonly cited as an important constraint.

In recent years, oral iron supplementation program has been focused from daily doses to intermittent doses (once or twice weekly). Many studies have been conducted in various parts of world and most of the studies showed that the increase in hemoglobin level were similar to daily supplementation.

The hypothesis behind intermittent iron supplementation has been based on “mucosal block” theory of iron absorption[7]. The gut has a mechanism to prevent entry of excess iron in the body. The mucosal cells absorb iron on the basis of iron requirement of the body. The iron reaching inside the mucosal cell is either transported to plasma or oxidized to ferric form and complexed with apoferritin to form ferritin. This ferritin generally remains stored in the mucosal cells and is lost when they are shed (gut mucosal turnover rate 3-4 days). This is called the ferritin curtain [4]. The iron status of body and erythropoietic activity govern the balance between these two processes.

Though iron requirement during the first trimester is reduced but in the second and third trimesters it rises to between 4 and 6 mg, respectively [8]. During the last 6-8 weeks of pregnancy the iron requirement may rise up to 10 mg/d because of significant change in the red blood cell mass that starts in the middle of the second trimester [9- 11].

The phenomenon of hemodilution during pregnancy results in reduced hemoglobin concentration. As a result of increased requirement during pregnancy both serum iron and ferritin concentrations decrease and TIBC increases [12-14].

There is a moderate drop in the concentration of serum iron that stabilizes in the middle of pregnancy [15]. However there is steady rise in total iron-binding capacity

during pregnancy to approximately 50% above normal. There is some evidence that serum ferritin rises modestly early in pregnancy, presumably because of reduced erythropoietic activity; thus, iron is diverted to store [9,15]. Thereafter, however, the serum ferritin concentration drops steadily to approximately 50% of normal at midterm. These changes reflect hemodilution and the mobilization of iron from stores to meet the increased demands of pregnancy.

The present study was conducted to determine and compare the effects of daily versus weekly iron supplementation on iron indices at different duration of supplementation.

MATERIALS AND METHODS

Study design: This was a randomized prospective longitudinal study.

Ethical approval: Study was conducted in the department of Obstetrics and Gynaecology for one year duration; it was approved by ethical committee of research department of our institution. Inform consent was taken from the participants.

Inclusion criteria: apparently healthy pregnant women of 16 to 22 weeks of gestation with haemoglobin level between 9.0 g/dl to 11.0 g/dl were included in the study.

Exclusion criteria: Women with multiple pregnancy, haemoglobin level < 9.0 g/dl or > 11.0 g/dl, with chronic systemic disorder or with any high risk factor were excluded.

Grouping: A total of hundred women were recruited and randomly allocated to two groups: **Group I** (Daily iron Supplementation, n=50) and **Group II** (Weekly iron Supplementation, n=50).

Methodology: All the subjects were matched for age, parity, socioeconomic status and baseline anthropometry i.e. height, weight and BMI (body mass index). A detailed history was obtained and complete physical examination done on all the women.

group I were given daily dose of 100 mg elemental iron and 1.5 mg folic acid and **group II** received once a week 200 mg of elemental iron and 3.0 mg folic acid . Subjects were provided iron tablets every month according to group allocated. All women were advised to show empty blister packs before issuing the drug for next month to ensure proper compliance.

They were subjected to routine antenatal investigations along with baseline complete haemogram and iron indices (serum iron, total iron binding capacity, serum ferritin). Serum iron was measured using bathophenanthroline method[16] Estimation of Total Iron Binding Capacity (TIBC) was done using magnesium carbonate. Serum ferritin was measured using enzyme immunoassay method (Mfg. by Syntron Bioresearch Inc. USA).

All the women were given antihelminthics. Subjects in

Haemoglobin & hematocrit values were estimated 4 weekly upto 16 weeks of iron supplementation. Iron indices were estimated after 12 weeks and 16 weeks of iron supplementation. On every visit subjects were asked about any side effects related to iron intake, like heart burn, nausea, vomiting, diarrhoea, constipation *etc.*

Statistical analysis: For comparing difference in a variable at two different time intervals paired 't' test was used. For comparing the proportions Chi-square (χ^2) test was used. A difference between two groups was considered significant for ' p' value <0.05.

RESULTS

Initially 100 women were enrolled, 50 in each group. However complete data were available for 89 women; 45 in group I and 44 in group II. Majority of subjects belonged to 16-18 weeks, 19-21 weeks of gestational age and few patients of 22-24 weeks of gestation.

The base line haematological values including iron indices did not have any statistically significant difference in both the groups. Intergroup 'p' values for serum iron, TIBC, serum ferritin were 0.815, 0.724 and 0.333 respectively.

The haemoglobin (Hb) level increased to a significant level (Table 1) in weekly supplemented group after 12 weeks of supplementation (p=0.0015) and also at the end of supplementation *i.e.* After 16 weeks of supplementation (p<0.001). Though the increase in haemoglobin levels in daily supplemented group was significantly more than weekly group (p=0.008). The improved levels in weekly supplemented group could not be ignored.

The hematocrit (Hct) values increased in weekly group to a significant level as in daily group. Upto 12 weeks of supplementation there was no significant difference in both groups ('p' value 0.20) but after 16 weeks of supplementation, the increase in daily group was significantly higher than weekly group('p' value <0.001). This pattern depicts the effect of hemodilution on hematocrit values and inference is that even after iron supplementation the hematocrit values remained almost same (Group II) or there was slight increase (Group I).

The serum iron values have no significant difference (p=0.067) in both groups after 12 weeks of supplementation but after 16 weeks of supplementation there was significant difference (p<0.001) in Group I and Group II showing more increase in Group I.TIBC values increased after 12 weeks of supplementation in both groups. As TIBC increases when there is more iron demand than the amount of iron absorbed. Thereafter there was fall in both Group I and Group II after 16 weeks of supplementation. But the fall was more in Group I indicating more improvement in iron status of patients. As Table 2 shows, there was significant difference in TIBC values after 16 weeks of supplementation in both Group I (p=0.0004) and Group II (p=0.038).

Though there was increase in S. ferritin levels in both Group I and Group II but it was more in Group I and the difference was statistically significant both after 12 weeks of supplementation (p<0.001) and after 16 weeks of supplementation (p<0.001). Serum ferritin values increased to a significant level (p<0.001) only in Group I, there was no significant increase in Serum ferritin values in Group II (p value 0.0661).

Side effects and compliance was also tested in this study and it was found that 40% of patients in daily group experienced negative side effects like nausea/vomiting, diarrhoea, constipation and heart burn; contrary to only 11.36% in weekly group. The difference was significant (p=0.002).

Table 1: Hematological values at the beginning and after 12 weeks and 16 weeks of supplementation period

Study groups		Baseline	12 weeks of supplementation	16 weeks of supplementation	Difference*	't' value*	'P' value*
Hb (g/dL)	Group I (n=45)	10.22±0.59	11.04±0.45	11.45±0.55	1.23	9.76	<0.001
	GroupII (n=44)	10.29+0.71	10.76±0.69	11.07±0.64	0.78	5.064	<0.001
Hct (%)	Group I (n=45)	32.19±2.04	35.87±2.30	37.58±2.34	5.39	11.211	<0.001
	GroupII (n=44)	32.94±2.46	34.81±1.76	35.63±1.99	2.69	5.244	<0.001

** difference is between initial and 16 weeks values*

Table 2: Iron indices at the beginning and after 12 weeks and 16 weeks of supplementation period

Study groups		Baseline	12 weeks of supplementation	16 weeks of supplementation	Difference*	t' value*	'P' value*
Serum iron (µg/dL)	Group I (n=45)	79.06±33.55	105.16±25.01	134.50±19.37	55.44	9.599	<0.001
	Group II (n=44)	77.85±35.79	93.43±34.13	107.01±29.98	29.16	4.143	<0.001
TIBC (µg/dL)	Group I (n=45)	549.33±166.33	608.11±119.05	440.91±105.32	-108.42	3.6943	0.0004
	Group II (n=44)	528.75±146.98	629.85±175.37	464.54±139.52	-64.21	2.102	0.038
Serum ferritin (µg/dL)	Group I (n=45)	50.05±29.68	82.42±30.09	117.44±20.22	67.39	12.588	<0.001
	Group II (n=44)	58.82±36.36	58.92±26.49	70.70±24.08	12.21	1.861	0.0661

** difference is between initial and 16 weeks values*

DISCUSSION

The present study aimed to evaluate the effect of weekly compared with daily iron supplementation on iron indices along with haemoglobin and hematocrit values in pregnant women who attended the antenatal clinic, at our hospital.

Though in our study the haemoglobin rise was more significant in daily group, it increased to a significant level [Table 1 (p<0.001)] in weekly group too and was maintained to a safe level. In study by Mumtaz *et al.*[17] too, the hemoglobin rose to a significant level in weekly group (p=0.0037).

The serum iron values increased to a significant level in both groups but increase in daily group was significantly more than weekly group (p<0.001). Similarly the TIBC values increased up to 12 weeks of supplementation thereafter there was fall in TIBC values which was significant in both groups but in daily group the change was significantly more than weekly group (p<0.001).

Serum ferritin value which is a sensitive indicator of iron storage did not increase to a significant level (p=0.0661) in weekly group but in daily group the increase was significant (p<0.001). Similar results were found in the study by Mumtaz *et al.* [17] where the serum ferritin level increased to a significant level in daily group (p<0.001) whereas in weekly group it did not change (p=0.16). In the study by Sunil Gomber *et al.* [18] the ferritin values continued to be remain low during pregnancy irrespective of supplementation (p=0.63 within groups and p=0.40 between groups). In the study by A. Mukhopadhyay *et al.* [19] the baseline S. ferritin values were significantly different in both groups (p=0.027) with a lower value in weekly groups. There was no significant increase in S. ferritin values in both daily (p=0.477) and weekly group (p=0.680). Intergroup p values was 0.10. In study by Ridwan *et al.* [20], there were no significant within group changes in serum ferritin concentrations. But a small decrease in the weekly group together with a small increase in the daily group, however caused a small but significant difference between groups in treatment effect (p=0.049). In study by SMZ Hyder *et al.*[21] the baseline S. ferritin values were higher in weekly group (p=0.06). There was no significant difference in S. ferritin values at 6 weeks post-partum in both the groups. But in anaemic subset of women a significantly (p<0.01) larger increment in the daily regimen was observed than in the weekly at 6 weeks post-partum (Table-3).

Table 3: S. Ferritin levels in the two intervention groups in different studies

Study	Daily supplementation		Weekly supplementation	
	Initial S.ferritin (µg/dl)	Final S.ferritin (µg/dl)	Initial S.ferritin (µg/dl)	Final S.ferritin (µg/dl)
A. Mukhopadhyay *et al.*[18]	18.41+21.9	27.7+19.8	23.2+20.5	20.5+16.9
Sunil Gomber *et al.*[17]*	2.93	2.84	2.69	2.67
Ridwan *et al.*[19]	28.0+19.2	27.7+19.8	23.2+20.5	20.5+16.9
Mumtaz *etal.*[16]	23.8+29.7	41.6+34.9	23.0+33.7	27.6+31.5
SMJ Hyder *et al.*[20]**	12.4	57.6	20.3	57.3
Present study	50.0+29.7	117.4+20.	58.82+36.4	71.04+24

* The data in this study was provided after logarithmic conversion

** Final values were taken at 6 weeks postpartum

So, we can say that though Hb raised to a significant level in weekly supplemented group in most of the studies but S. ferritin values showed a variable change. S. Ferritin

values increased to a significant level in the daily group in most of the studies (except study of Sunil Gomber *et al.*[18] and Ridwan *et al*.[20]) but in weekly supplemented group it either did not change or decreased.

Though, under experimental conditions (as discussed earlier), the increase in haemoglobin or serum ferritin levels was lower with weekly supplementation than with daily supplementation, the positive implication for large-scale intervention may compensate for this.

CONCLUSION

It can be concluded from this study that supplementation of pregnant women once per week with 200 mg of elemental iron is an effective option for prophylaxis in mild anaemic or non-anaemic pregnant women in terms of hematologic response including iron indices under conditions resembling routine antenatal care. Although iron stores as indicated by S. ferritin were improved but the improvement was not significant in weekly supplemented group. This was probably because of increased demands during pregnancy which outstripped the supply. This can be overcome by extending the supplementation to the post-partum period.

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