e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2023; 15(1); 143-148

Original Research Article

# To Evaluate the Weekly Antenatal Oral Iron and Folate Supplementation is an Effective Alternative to a Daily Regimen in Non-Anemic Pregnant Women: A Comparative Study

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**Received: 25-10-2022 / Revised: 21-11-2022 / Accepted: 15-12-2022**

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**Conflict of interest: Nil**

**Abstract**

**Aim:** The aim of this study was to evaluate the weekly antenatal oral iron and folate supplementation is an effective alternative to a daily regimen in non-anemic pregnant women to prevent anemia and iron deficiency during the third trimester.

**Methods:** The present study was conducted in the department of obstetrics and gynaecology, Patna medical College and Hospital, Patna, Bihar, India for 1 year. Women having periods of gestation (POG) between 14 to 16 weeks were recruited for the study. All women were first given single dose of tab albendazole 400 mg. Then they were randomly allocated to the three treatment groups and given a haematinic capsule i.e. 200 mg of ferrous sulfate (60mg elemental iron) with 1mg folic acid tablet either weekly (n=25), thrice weekly (n=25) or daily (n=25).

**Results:** There were no significant differences in income, educational level, age, parity, POG, initial Hb and SF concentrations, Hct, and duration of previous haematinic prophylaxis between the three study groups. There is a reduction in the number of women with IDA in all three supplementation groups, but the number of women with ID is significantly increased in the weekly supplementation group and significantly decreased in the daily supplementation group.

**Conclusion:** Prophylactic oral iron supplements when given intermittently were not effective in preventing iron deficiency anaemia in pregnancy. In non-anemic pregnant women, a weekly regimen is an effective alternative to a daily regimen for antenatal oral iron and folate supplementation for preventing anemia and iron deficiency during the third trimester.

**Keywords:** Iron supplementation, pregnancy, serum ferritin, hemoglobin, haematocrit.



## Introduction

Iron-deficiency anemia (IDA) is the most common nutritional disorder in the world. Pregnant women are at particular risk of developing anemia because of the added iron requirements during pregnancy. Increasing the effectiveness of iron supplementation programs is the most practical short-term approach to alleviating

the problem. However, in India, a routine supplementation program has not led to much alleviation of the prevalence of IDA in pregnancy, due to multifactorial causes. [1] The main hazards of routine iron supplements are a high incidence of undesirable side-effects, leading to poor compliance. High doses of iron lead to gastrointestinal intolerance, suggesting some toxic effect on the gut mucosa that is probably mediated by iron related oxidative stress.

Iron requirements increase during pregnancy. [2,3] And this requirement may lead to anemia in pregnant women. [4,5] Lower hemoglobin cut off is 11.0 g/dL in the first and last trimester and 10.5 g/dL in the second trimester. Therefore, any level below 10.5 g/dL should be considered as anemia. [6] Iron consumption for pregnant women is undesirable, because of the side effects. The probable cause is the effect of oxidative stress of high doses of Iron, which leads to gastrointestinal intolerance. [4] As gut mucosal turnover rates is about three days, administering iron during these days may lead to lower iron absorption. Periodic iron supplementation may let the mucosa to heal and gets better iron absorption. [7-9]

Nutritional iron deficiency is highest in population segments that are at peak rates of growth, namely, infants, young children, and pregnant women. Pregnancy is a time in which the risk for developing iron deficiency anemia is highest, because iron requirements are substantially greater than average absorbable iron intakes.

The overall iron requirement during pregnancy is significantly greater than that in the nonpregnant state despite the temporary respite from iron losses incurred during menstruation. Iron requirements increase notably during the second half of pregnancy because of the expansion of the red blood cell mass and the transfer of increasing amounts of iron to both the growing fetus and the placental structures. Iron is also lost in maternal blood and lochia at parturition. The degree to which these increased requirements can be met depends on the size of iron stores at the start of pregnancy and on the amounts of dietary iron that can be absorbed during pregnancy. The fact that iron deficiency anemia frequently develops in pregnancy indicates that the physiologic adaptations are often insufficient to meet the increased requirements. As a result, iron supplementation during pregnancy is a common practice throughout the world.

The aim of this study was to evaluate the weekly antenatal oral iron and folate supplementation is an effective alternative to a daily regimen in non-anemic pregnant women to prevent anemia and iron deficiency during the third trimester.

## Materials and Methods

The present study was conducted in the department of Obstetrics and Gynaecology, Patna Medical College and Hospital, Patna, Bihar, India for 1 year. Women having periods of gestation (POG) between 14 to 16 weeks were recruited for the study. Informed written consent was obtained from all women.

## Methodology

During venipuncture for other routine antenatal investigations an additional 2 ml of mixed venous blood was taken. The haematocrit (Hct) was estimated using haematocrit tubes, the haemoglobin (Hb) was estimated by the cyanmethaemolgobin method and serum ferritin (SF) by an immuno-radiometric assay technique using IRMA Ferritin Kits (Diagnostic Products Corporation, Los Angeles).

All women were first given single dose of tab albendazole 400 mg. Then they were randomly allocated to the three treatment groups and given a haematinic capsule i.e. 200 mg of ferrous sulfate (60mg elemental iron) with 1mg folic acid tablet either weekly (n=25), thrice weekly (n=25) or daily (n=25). The women were advised to

take the supplement with water at 11.00 a.m (approximately one hour before lunch).

Each woman was given either 6 (weekly group), 18 (thrice weekly group) or 42 (daily group) capsules at a time. The number of capsules remaining was checked at each visit. A second sample of mixed venous blood was obtained for Hb, SF and Hct estimations at 34 weeks of gestation. Hence the duration of supplementation varied from 20 weeks (in the women who had a gestation of 14 weeks at recruitment) to 18 weeks (in women who had a gestation of 16 weeks at

**Statistical analysis**

Data on all subjects were entered into a computer database and analysis was performed using SPSS 18 advanced statistics program. All variables fitted into normal distribution and parametric analysis using mean, standard error of mean and standard deviation were employed. The significance of the difference between the daily and weekly supplemented groups was assessed by the student's t-test for unpaired values and the chi-square test for non-parametric variables. Correlations were calculated using Pearson's coefficient of correlation recruitment).

**Results**

**Table 1: Analysis of variance**

| Characteristics | Mean±SD | P-value |
|---|---|---|
| Age (yrs) | 25.5±5.5 | 0.8 |
| Parity | 1.8±0.9 | 0.1 |
| Gestation (weekly) | 18.2±3 | 0.7 |
| Pre prophylaxis (weeks) | 3.7±2.3 | 0.8 |
| Duration (weeks) | 15.5±2.4 | 0.06 |
| Pretreatment Hb (g/l) | 8.2±18 | 0.6 |
| Pretreatment Hct (%) | 35.5±2.9 | 0.3 |
| Pretreatment SF (microg/l) | 19.1±13.5 | 0.1 |

There were no significant differences in income, educational level, age, parity, POG, initial Hb and SF concentrations, Hct, and duration of previous haematinic prophylaxis between the three study groups.

**Table 2: Results of supplementation**

| Supplementation | Pretreatment | Post treatment | P-value |
|---|---|---|---|
| Once a week (N=25) | 8 | 10 | <0.0001 |
| Thrice a week (N=25) | 9 | 25 | 0.800 |
| Daily (N=25) | 8 | 15 | <0.0001 |
| Total | 25 | 50 | |

Whole numbers indicate numbers of women in each group (SF<12microg/l)

**Table 3: Results of supplementation**

| Supplementation | Pretreatment | Post treatment | P-value |
|---|---|---|---|
| Once a week (N=25) | 17 | 2 | <0.0001 |
| Thrice a week (N=25) | 18 | 13 | 0.800 |
| Daily (N=25) | 20 | 5 | <0.0001 |
| Total | 55 | 20 | |

Whole numbers indicate numbers of women in each group (Hb<11.0g/l)

The results of supplementation are shown in Table 2 &3. There is a reduction in the

number of women with IDA in all three supplementation groups, but the number of women with ID is significantly increased in the weekly supplementation group and significantly decreased in the daily supplementation group.

## Discussion

Iron deficiency continues to be the leading single-nutrient deficiency in the world, affecting the lives of > 2 billion persons despite considerable efforts to decrease its prevalence for the past 3 decades. [10,11] Primary focuses have been to increase the amount and bioavailability of iron in the diet [12-14], to control infections that contribute to iron losses from the body [15], and to improve economic, educational, and social conditions that contribute to the high prevalence of iron deficiency. [16,17]

It is recognized that one of the major problems of daily supplementation schedule is lack of compliance because of the high incidence of gastrointestinal side effects. Added to this, are the recent concerns of molecular damage as a result of iron over-dosage. [18]

Contrary to our expectations only daily iron supplementation was effective in preventing iron deficiency. Although the sample size was small, highly significant increased risks of the subjects developing ID with the weekly and thrice weekly regimens were clearly seen. A significantly higher risk of developing IDA was seen in the weekly supplementation group. The possible higher risk of IDA in the thrice weekly supplementation group may have reached statistical significance with a larger sample. The risk of developing IDA or ID did not appear to be influenced by either the initial Hb and SF (before supplementation) or the duration of supplementation. These findings too may be a result of the small sample size.

Though in our study the haemoglobin rise was more significant in daily group, it increased to a significant level in weekly group too and was maintained to a safe level. In study by Mumtaz et al. too, the hemoglobin rose to a significant level in weekly group ($p=0.0037$). [19] 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 ($p<0.0001$). Similar results were found in the study by Mumtaz et al. where the serum ferritin level increased to a significant level in daily group ($p<0.0001$) whereas in weekly group it did not change ($p=0.16$). [19]

In the study by A. Mukhopadhyay et al. [18] 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 were 0.10. [4]

In study by SMZ Hyder et al. [20] the baseline S. ferritin values were higher in weekly group ($p=0.06$). A recent meta-analysis of eight studies could not find any evidence to justify changing the existing daily antenatal oral iron supplementation program to a weekly supplementation regimen. [21] Although there is a slight increase in the absorption of oral iron when the supplements are administered weekly this increase did not result in sufficient amounts being absorbed to meet the increased demand during pregnancy, especially in ID subjects. [22] Furthermore, there is no evidence to suggest that a weekly regimen would lead to improved compliance as most healthy subjects are poorly motivated to take prophylactic treatment. [23]

According to the evidence available at present daily oral iron supplementation is recommended for pregnant women in communities at risk of IDA. Intermittent iron supplementation appears to be inappropriate. [24]

## Conclusion

Prophylactic oral iron supplements when given intermittently were not effective in preventing iron deficiency anaemia in pregnancy. In non-anemic pregnant women, a weekly regimen is an effective alternative to a daily regimen for antenatal oral iron and folate supplementation for preventing anemia and iron deficiency during the third trimester. However, in anemic women, even those with mild anemia, daily supplementation appears to be superior to weekly. Considering the magnitude of the problem in India, a weekly schedule does not seem to be a suitable strategy for large-scale programs. However, in a hospital setting, it may be a suitable and welcome option for non-anemic women with good iron stores.

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