Original Article

Once Weekly Versus Daily Iron Therapy on Prevention of Iron Deficiency Anemia in Non-Anemic Pregnant Women

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Abstract

Objectives: To evaluate the efficacy of weekly versus daily oral iron supplementation in non-anemic pregnant women in terms of the mean change in hemoglobin levels and the frequency of reported side effects.

Methodology: This randomized controlled study was conducted at the Department of Obstetrics & Gynecology, Maternal and Child Health Centre (MCH Unit 1), PIMS, Islamabad, from March 20 to September 19, 2021. A total of 266 women, aged 16 to 40 years, at a gestational age of 12 to 22 weeks, were included using a predetermined random allocation sequence. Participants in Group A took a weekly supplement of Tablet Ferrous Sulphate 200 mg along with 5 mg of Folic Acid twice on a designated weekday (totaling 120 mg of elemental iron). Patients in Group B continued with their daily supplements: Tab Ferrous Sulfate 200 mg once daily (60 mg of elemental iron) along with 5 mg of Folic Acid. Hemoglobin and Serum Ferritin levels were measured at the beginning and upon completion of the study, and any side effects reported by the patients were recorded. Data were entered into SPSS version 22.0 for analysis. An independent sample t-test was applied to compare the Hemoglobin and Serum Ferritin levels of the two groups to determine the significance of the difference between the two groups. The Chi-Square test was applied to compare the side effects in the two groups, with a p-value < 0.05 considered as significant.

Results: The mean Hemoglobin and Serum Ferritin levels were comparable at the end of the study period. Patients in Group A had a mean post-treatment Hb (g/dl) of 10.96 ± 0.27, while those in Group B had a post-treatment mean Hb of 11 ± 0.31 (p = 0.233). Patients in Group A had a mean Serum Ferritin level of 32.33 ng/ml ± 2.77, and in Group B, the mean Serum Ferritin level was 32.47 ng/ml ± 3.2 (p = 0.698). Patients in Group A reported significantly fewer side effects compared to patients in Group B.

Conclusion: Weekly iron therapy is as effective as daily iron therapy in preventing iron deficiency anemia in non-anemic pregnant women and is associated with fewer side effects.

Keywords: Iron Deficiency Anemia, Serum ferritin, Iron supplement, Hemoglobin

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Introduction

In developing countries, many women who are not anemic at the beginning of pregnancy develop anemia as the pregnancy progresses. Daily oral iron supplementation is prescribed to manage anemia. However, it has been observed that most women eventually become non-compliant.

Iron-deficiency anemia is a significant nutritional problem in developing countries, with pregnant women being especially at risk.[1,2] The amount of dietary iron absorbed often does not meet the increased demands during pregnancy, which include supporting expanded cell mass in the mother and iron deposition in the baby and placenta. Iron requirements increase, particularly during the second half of pregnancy, necessitating iron supplementation.[3,4] Even women who are not anemic at the beginning of pregnancy may develop anemia during the course of their pregnancy, as diet alone is insufficient to meet their iron needs. Iron deficiency usually develops gradually and may not be symptomatic or clinically apparent at first.[3] Anemia is associated with poor pregnancy outcomes, which is why pregnant women are prescribed iron supplementation, with the

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recommendation that women should take the tablets daily throughout the second and third trimester of pregnancy to prevent or treat anemia.[1,5] World Health Organization (WHO) guidelines also recommend a daily oral dose of 60 mg of iron and 400 µg of folic acid supplements throughout pregnancy, starting as early as possible as part of antenatal care (ANC) programs in developing countries with a high prevalence of anemia. Despite these recommendations, the prevalence of anemia remains high.[1,6]

Several factors can limit the effectiveness of iron supplement interventions. Among these, important factors include the cost and logistics affecting the supply of iron tablets and the reluctance of pregnant women to take iron supplements.[7,8] Health facilities may not have adequate supplies of iron supplements, or they may not consistently provide supplements to women during antenatal visits, while women may not be able to purchase iron preparations from the market. Even when provided with sufficient iron tablets for the remainder of the pregnancy, regular intake is often neglected due to the undesirable side effects associated with the form, amount, and frequency of supplement ingestion.[7-9] Therefore, alternative strategies are needed to reduce the rate of anemia.

Hence, the purpose of this study is to evaluate whether a daily regimen of antenatal oral iron supplementation can be replaced with a weekly regimen in non-anemic pregnant women for the prevention of anemia with minimal side effects and patient morbidity.

Methodology

This was a randomized comparative study conducted at the Department of Obstetrics & Gynecology, Maternal and Child Health Centre (MCH Unit 1), PIMS, Islamabad. It was conducted from March 20th to September 19th, 2021, following the approval of the Ethical Review Board. The sample size of 266 patients (133 patients in each group) was calculated using the OpenEpi calculator, based on the following assumptions: Level of Significance 5%, Confidence Interval = 95%, Power of the test = 80%, Group A Hb ± SD 12.9 ± 6.09, and Group B Mean Hb ± SD 12.6 ± 9.89.[10]

A total of 133 cases were included in each group. Patients were recruited from the MCH OPD through non-probability consecutive sampling. Women who met the inclusion criteria, i.e., women between 12 to 22 weeks gestation with singleton pregnancy and Hemoglobin >10.5g/dl, were invited to participate in the study after giving informed consent. Women with hematological disorders such as Thalassemia, Sickle Cell Disorder, Hemolytic Anemia, Thrombocytopenia were excluded. Additionally, women with any chronic diseases, including Connective Tissue Disorder, Renal Disease, Hypertensive Disorders, Tuberculosis, and Cardiac disease, were also excluded. Detailed histories were obtained from enrolled patients, followed by a general systemic examination, along with all routine investigations.

All women were advised to take a single course of 100 mg of Mebendazole twice daily for three days. A total of 266 non-anemic pregnant women at 14-22 weeks gestation were assigned to the two arms of the randomized comparative study using a predetermined random allocation sequence. Participants in Group A took a weekly supplement of Tab Ferrous Sulphate 200mg plus 5mg Folic Acid twice on a designated weekday (amounting to 120 mg elemental Iron). Participants were instructed to take the Iron supplement approximately 1 hour before lunch or dinner and at least 2 hours after a previous meal or tea for a duration of three months. The participants in Group B continued with their daily supplements: Tab Ferrous Sulfate 200mg once daily (60mg elemental iron) plus 5mg Folic acid. Their Full Blood Count and Serum Ferritin levels were measured at the beginning and again at completion (after 12 weeks), and side effects reported by patients at the study's completion were also noted. Two Patients were lost to follow up in group B.

Data was entered into SPSS version 22.0 for analysis. Mean and SD were calculated for quantitative variables such as age, gestational age, Hemoglobin, and Serum Ferritin. Frequency and percentages were calculated for qualitative variables like side effects, including nausea, vomiting, and constipation. An independent sample t-test was applied to compare Hemoglobin and Serum Ferritin levels between the two groups at the beginning of the study and at the 12-week completion. A chi-square test was applied to compare side effects between the two groups, with a significance level set at P value < 0.05.

Results

Both groups are comparable in terms of age, parity, gestational age at enrollment, BMI, Hemoglobin level and Serum Ferrtin level at enrollment as seen in Table I.

Table I: Comparison of both groups in demographics, pre treatment Blood Hemoglobin and Serum Ferritin levels.

Demographic and pre iron therapy Parameters	Group A Intermittent Iron therapy (N=133)	Group B Daily Iron therapy (N=133)	P value
Age (years)	25.25±3.89	25.74±4.21	0.333
Parity	1.7±1.34	1.56± 1.35	0.392
BMI (kg/m^2)	25.59±2.08	26.11±1,99	0.1
Gest age at enrollment (weeks)	17.87±2.6	18.15±2.7	0.388
Pre treatment Hemoglobin (g/dl)	10.59±3.28	10.62±0.14	0.124
Pre treatment Serum ferritin (ng/ml)	29.87±3.28	29.71±3.41	0.705

Two patients were lost to follow up in group B while all patients completed study in group A. Patients in both groups had comparable Hemoglobin and Serum Ferritin levels at end of study implying that patients in both groups did not suffer from fall in Hemoglobin and Serum Ferritin at end of study. (Table II)

Table II: Post Treatment Comparison of Blood Hemoglobin & serum Ferritin levels.

Post treatment parameters	Group A Intermittent Iron therapy (N=133)	Group B Daily Iron therapy (N=131)	P value
Post treatment Hemoglobin (g/dl)	10.96±0.27	11±0.31	0.233
Post treatment Serum ferritin (ng/ml)	32.33±2.77	32.47±3.2	0.698

Patients in Group A reported significantly higher side effects. All except number of patients reporting vomiting reached statistical significance (Table III)

Table III: Comparison of side effects amongst the two groups.

Side effects		Group A Intermittent Iron therapy	Group B Daily Iron therapy	P value
Nausea	Yes	1	6	0.043
	No	133	125	
Vomiting	Yes	0	3	0.072
	No	133	128	
Diarrhea	Yes	4	18	0.025
	No	129	113	
Constipation	Yes	13	17	0.492
	No	120	114	
Abdominal Pain	Yes	1	7	0.034
	No	132	124	

Discussion

Both supplementation regimens prevented a decrease in hemoglobin levels and the development of anemia. In our study, both treatments resulted in similar and significant increases in hemoglobin concentration and serum ferritin levels from baseline levels. However, a study conducted in Iran showed that daily iron intake was more effective than intermittent intake in preventing anemia in pregnant women. Their study included a twice-weekly dose of 45g of elemental iron. In contrast, our study employed a single 120 mg once-weekly dose in the intermittent group. Additionally, in that study, many women had lower ferritin levels at the beginning of the study.[11] Saxena et al., in their study, concluded that weekly iron supplementation is an effective option for anemia prophylaxis in non-anemic women; however, it was insufficient to raise hemoglobin levels in anemic women.[12] Conversely, a study in Sri Lanka revealed that non-anemic pregnant women found a weekly oral iron regimen to be as effective as a daily iron regimen in preventing anemia and iron deficiency during the third trimester.[10]

The women in both groups consumed the tablets in a real-life, unsupervised setting. However, they received detailed counseling on the importance of iron supplementation, correct intake, and dietary modifications. This suggests that the results are reproducible outside of a research context. It is worth noting that the results might have been different had the patients been directly supervised in their iron intake.

Similar to hemoglobin, serum ferritin levels increased in both groups, which has important implications for the ability of patients to maintain hemoglobin levels as pregnancy progresses.[13,14] Additionally, fewer side effects were reported with intermittent therapy compared to daily iron intake, consistent with findings in other studies.[10-12] Our study showed similar results. Taking iron on an intermittent basis has also been shown to have no oxidative stress in a study conducted in Mexico on non-anemic pregnant women. In the same study, both daily and intermittent therapy effectively prevented anemia, similar to our study.[15]

One possible explanation for the efficacy and lower side effects of intermittent iron therapy may be as follows: in humans, intestinal cells turnover every five to six days. Consuming iron on an intermittent basis exposes the iron to new mucosal cells, improving absorption. This approach also decreases the iron load in the gut lumen and intestinal cells, which in turn reduces oxidative stress and side effects. It might also alleviate absorption blockages.[16,17] Therefore, intermittent regimens lead to

better absorption with fewer side effects, improving tolerability and adherence to supplementation.[8-10]

Weekly supplementation can have significant implications for the organization and efficiency of iron supplementation programs for pregnant women. This would result in reduced costs and better availability, as fewer doses would be required

Conclusion

Weekly Iron supplementation is as effective as daily iron supplementation in preventing anemia in non-anemic pregnant women. Weekly Iron therapy is associated with lesser side effects. Hence intermittent (once weekly) iron supplementation is effective, needs lesser doses and is likely to have better patient compliance resulting in better success of Iron supplementation programmes.

Strengths & Limitations: The patients received supplementation in `real life` like situation and hence can be replicated outside research context. Due to cost constraints of producing a similar looking placebo blinding was not possible.

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