Original Article

Effect of Iron and Folic Acid supplementation among nutritionally anemic women of reproductive age in rural Maharashtra: A community-based intervention study

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Abstract

Background: In the context of the limited effectiveness of daily iron supplementation in national programs, intermittent iron supplementation is currently under debate as a possible alternative. **Objective:** To study the outcome of twice weekly iron supplementation compared to daily supplementation. **Methods:** A community-based interventional study was carried out in 283 women of the 15-49 years age group who were not pregnant and not lactating at the initiation of the study. For intervention purpose, women with mild and moderate anemia were taken. In two schedules, an interventional drug (100 mg elemental iron with 0.5 mg folic acid) was given for three months. In the daily schedule, one tablet every day; and in the weekly schedule, two tablets once a week on a fixed day were given. **Result:** Out of 283 anemic participants, 141 received daily while 142 received weekly iron and folic acid supplementation. Post intervention, the weekly iron supplementation group revealed that, proportion of anemia cases reduced to the tune of 32.4% and the mean increase in hemoglobin level was 1.42 gm/dl (SD ± 0.77). In contrast, in patients who had a daily supplementation regimen, the mean increase in hemoglobin level was 1.78 gm/dl (SD ± 0.83). **Conclusion:** Result of present study shows that, effect of daily Iron and Folic Acid (IFA) supplementation to raise hemoglobin level was higher as compared to weekly IFA supplementation. But weekly supplementation when considered separately also had significant effect to raise the hemoglobin level. It is observed that, there is no statistically significant difference in the rise of hemoglobin in both the groups, signifying weekly iron therapy as effective role as daily iron therapy in reducing anemia.

Keywords: nutritional anemia, non pregnant non lactating, rural area, intervention trial.

Introduction

Anemia is one of the world's most widespread health problems. It is defined as a low level of hemoglobin (HB) in the blood. As per World Health Organization (WHO)[(1)], hemoglobin levels indicative of anemia at sea level in non-pregnant women are no anemia ≥ 12 gm/dl, mild 11-11.9 gm/dl, moderate = 8.0-10.9 gm/dl and severe <8 gm/dl. It is the only nutrient deficiency significantly prevalent in industrialized countries. Globally, 24.8%[(2)] people are anemic. In accordance with National family Health Survey - 5 (NFHS-5)[(3)] data, the prevalence of anemia in different age groups in Maharashtra was highest in children aged 6-35 months (68.9%), followed by ever-married women aged 15-49 years (54.5%), pregnant women aged 15-49 years (45.7%), and men aged 15-49 years (21.9%).

Women in their reproductive life have an exceptionally high demand for hemopoietic nutrients. When not pregnant or lactating, regular menstrual losses constitute a continuing loss of iron, which needs to be replaced[(4)]. In countries where the feasibility of general dietary improvement is limited, iron supplementation for vulnerable groups and food fortification are the most cost-effective means of addressing iron-deficiency anemia[(5)].

Daily supplementation with Iron and Folic Acid (IFA) for three months has been the standard approach for preventing and treating iron deficiency anemia among women of reproductive age. Despite its proven efficacy, there has been limited success with the daily regimen in public health programs, which is thought to be primarily due to low coverage rates, insufficient tablet distribution, and low adherence due to its side effects (e.g., constipation, dark stools or metallic taste)[(6)].

Intermittent use of oral iron supplements (i.e., once, twice, or three times a week on non-consecutive days) has been proposed as an effective alternative to daily iron supplementation to prevent anemia among women in the reproductive age group. The proposed rationale behind this intervention is that intestinal cells turn over every 5–6 days and have limited iron absorptive capacity. Thus the intermittent provision of iron would expose only the new epithelial cells to this nutrient, which should, in theory, improve the efficiency of absorption[(6)]. Intermittent supplementation may also reduce oxidative stress and the frequency of other side-effects associated with daily iron supplementation like blockage of absorption of other minerals due to the high iron levels in the gut lumen and the

intestinal epithelium. Experience has shown that intermittent regimens may also be more acceptable to women and increase compliance with supplementation programs[6].

Hence this intervention study, as a part of the thesis, was conducted to evaluate the effect of daily versus twice Weekly Iron and Folic Acid Supplementation (WIFS) among women of the 15 to 49 years age group who were Non-pregnant and Non-lactating (NPNL).

Material and Methods

This was an intervention study conducted in 2013 for a period of one year, among currently NPNL women of the reproductive age group of 15 to 49 years, using multistage sampling. We randomly selected one Taluka in the Kolhapur district in the first stage. In 2nd stage, we randomly selected one Primary Health Center (PHC) and randomly selected a Sub centre (SC) from that selected PHC for study.

We used absolute precision 13% and took sample size using below formula $N = (2Z1^2 S^2)/d^2$. From the referred study, we took Z at 95% CI, pooled SD as 0.35 [HB (11.62+-0.23, 11.57+-0.44)], and absolute precision 0.13, and calculated a sample size of 137 in each arm[7]. Considering non-responders in the study, we took 141 and 142 in two arms.

For proper assessment of the objectives, the study was conducted as follows:

All the villages from the selected SC were visited, and all NPNL women in the age group of 15 to 49 years were recorded as a sampling frame. Among all, 1239 women were identified as women in the age group of 15 to 49 years who were NPNL. Then by systematic random sampling, every 3rd woman was listed and got 413 women in the list. The anemia status of these women was also noted. Women with mild or moderate anemia were included; and a total of 283 women were included in the present intervention study. Attempts were made to establish a good rapport with this study group. Written informed consent was obtained from each participant for their participation after the nature of the study was fully explained to them in their local languages. Interview was taken using a structured questionnaire designed and validated through a pilot study under the following headings: general information, socio-demographic information, and personal history. Capillary blood was drawn by the finger prick method for hemoglobin estimation. Hemoglobin concentration was estimated by the Colorimetry-hemoglobin cyanide method.

These women were again followed up after 15 days. Based on hemoglobin levels done earlier, those with mild anemia (HB 11 gm/dl to 11.9 gm/dl) and moderate anemia (HB 8 gm/dl to 10.9 gm/dl) were stratified into subgroups according to their age and type of anemia. Then women within each subgroup (age and type of anemia) were randomly allocated into daily and weekly groups, as shown below in Table 1.

Table 1: Sample for Daily and weekly supplementation

Daily				Weekly			
Age Group	Type of anemia		Sample for Intervention	Age Group	Type of anemia		Sample for Intervention
	Mild	Moderate			Mild	Moderate	
15-19	5	21	26	15-19	5	22	27
20-24	5	20	25	20-24	4	20	24
25-29	2	23	25	25-29	2	23	25
30-34	2	22	24	30-34	3	22	25
35-39	2	20	22	35-39	1	19	20
40-44	0	13	13	40-44	0	14	14
45-49	0	6	6	45-49	1	6	7
Total	16	125	141	Total	16	126	142

Intervention

Thus, 141 participants were allocated to the daily group and 142 to the weekly group. Nutritional education regarding dietary and cooking practices was given to both groups.

Deworming was done using the tablet albendazole 400 mg stat and after 15 days to all study participants. The interventional drug was an IFA tablet. Each IFA tablet contains 100 mg elemental iron (Ferrous Ascorbate) with 0.5 mg folic acid. Interventional drug (IFA) was given for 3 months in two schedules: daily in one group and weekly in another group. One tablet was given every day in the daily schedule, and in a weekly schedule, two tablets were given once a week on a fixed day. At the time of medicine distribution, participants were counseled regarding probable adverse effects and how to overcome them. The help of Auxiliary Nurse Midwife (ANMs), Multi-Purpose Worker (MPWs), and Accredited Social Health Activist (ASHAs) were used taken to monitor the intervention, which was

recorded in a notebook provided to them. Monitoring was cross-checked monthly by the investigator by random checking of study participants. Fifteen days medicines were given at a time to check the compliance of participants to the medicine during follow-up visits. Compliance was checked with the help of ASHA during visits by checking empty tablet packets.

The women were again followed up at the end of three months for hemoglobin estimation, and post-interventional change in hemoglobin levels was recorded.

Statistical analysis

Pearson's chi-square test was applied to test the relationship between categorized independent and dependent variables. Fisher's Exact Test was used if the expected number in the cell was below 5 in a table. In order to analyse paired ordinal data (before and after levels of anemia), Wilcoxon Matched Pairs Signed Rank Test and Symmetry test (incorporating linear trend) were used as a test of significance. Unpaired 't' test was used to compare quantitative variables individually with anemia status. Paired 't' test was also used to compare pre and post-supplementation hemoglobin levels and to test hemoglobin differences by supplementation status. A p-value of < 0.05 was deemed statistically significant. Statistical Package for Social Science (SPSS) Version 20.0 was used to enter and code data. STATA SE 13.1 was used to analyse data.

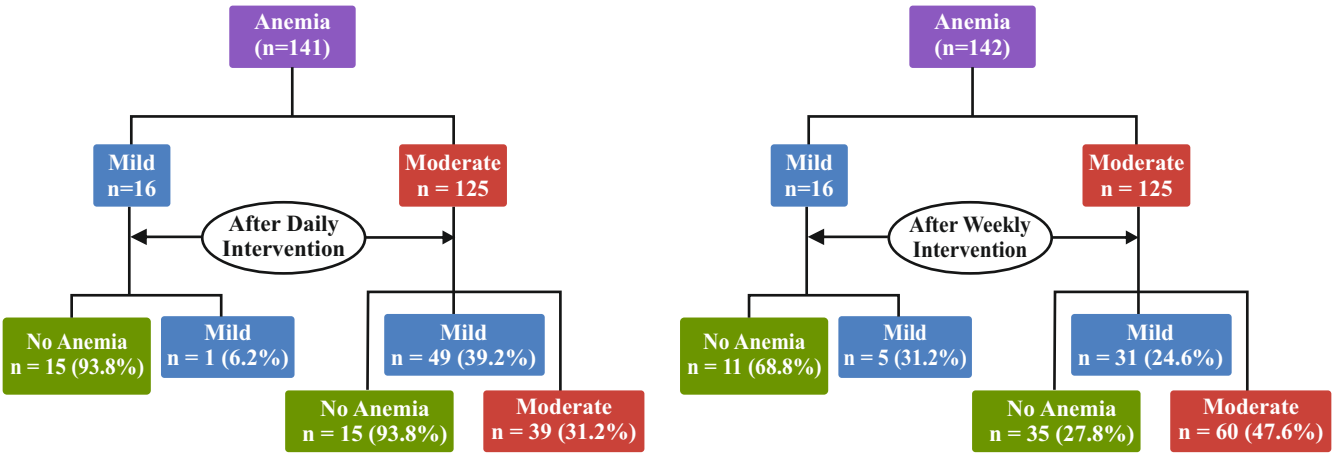
Ethical Consideration

The study was approved by the ethical review committee of the Grant Government Medical College and Sir JJ Group of Hospitals, Mumbai.

Result

A total of 283 NPNL women in reproductive age group were included in the present study. Out of 283 study population, 32 cases (11.3%) were mild anaemic, 251 (88.6%) were suffering from moderate anemia. Post-intervention hemoglobin level revealed that after three months of supplementation of IFA, there was a significant improvement in anemia status, particularly among participants with moderate anemia.

Figure 1 a showed that the overall proportion of anemia in daily IFA supplementation group was brought down by 36.8% (52 out of 141 recovered from anemia). The proportion of moderate anemia was brought down to 69.7% reduction (from 125 to 39 cases), while the proportion of mild anemia reduced to 6.2% (from 16 to 1). In the WIFS group, the overall proportion of anemia was brought down by 31.2% and proportion of moderate anemia was brought down to 47.6% (from 126 to 60) (Figure 1 b). After weekly intervention, out of 142 anemic cases, 46 recovered from anemia completely.



a) Daily schedule group **b) Weekly schedule group**

Figure 1: Comparison of anemia status before and after intervention among two group, daily schedule and weekly schedule

In order to test whether the change in hemoglobin before and after intervention in the daily and weekly iron-folic acid supplementation groups, the symmetry (asymptotic) test was used as a test of significance. This was also borne out by Wilcoxon Matched Pairs Signed Rank Test. The analysis indicated that there was a statistically significant difference between the two groups ($p<0.0001$) (Table 2). Overall, the percentage of mild anemia increased after the intervention in both weekly and daily groups. In participants who had WIFS, mean hemoglobin increased from 9.72 gm/dl (SD±0.79) to 11.14 gm/dl (SD±0.96) that is, the mean increase in hemoglobin level was 1.42 gm/dl (SD ± 0.77). In contrast, for participants who had a daily supplementation regimen, a mean hemoglobin increased from 9.57 gm/dl (SD±0.899) to 11.36 gm/dl (SD±0.932); that is, the mean increase in hemoglobin level was 1.78 gm/dl (SD ± 0.83). Thus, participants on a daily supplementation regimen had significantly higher hemoglobin levels after three months

compared to a weekly supplementation regimen; however, participants on a weekly regimen also had a substantial increase in their hemoglobin levels. When compared the mean rise of hemoglobin in both the groups (unpaired t test, p-value 0.051), the difference was non-significant.

Table 2: Change in hemoglobin level after weekly/daily iron and folic acid supplementation

IFA supplementation type	Pre and post	Mean Hemoglobin (gm/dl)	Standard Deviation	95% CI	p-value
Weekly	Pre-intervention (142)	9.72	0.79	9.59-9.85	<0.0001 (VHS)
	Post-intervention (142)	11.14	0.96	10.98-11.3	
Daily	Pre-intervention (141)	9.57	0.90	9.42-9.72	<0.0001 (VHS)
	Post-intervention (141)	11.36	0.93	11.20-11.51	

IFA: Iron and Folic Acid, VHS: Very High Strength

Discussion

The current study attempted to assess anemia prevalence and the effect of daily versus twice a WIFS among NPNL women in the reproductive age group. The overall prevalence of anemia in study area was 74.3%. If the prevalence of anemia at the community level is more than 40%, according to WHO[2], it is considered a severe public health concern. The present study observed a very high prevalence of anemia and is similar to earlier studies[8-11].

From the present study, the change in hemoglobin level before and after WIFS for three months along with deworming, showed a significant reduction in the proportion of anemia and a rise in mean hemoglobin level in NPNL women of the reproductive age group. These findings are consistent with previous studies' findings[12-15]. The overall proportion of mild anemia increased and moderate anemia decreased after the intervention in both groups, due to the shifting of certain participants from moderately anemic groups to mildly anemic groups. The mean rise of hemoglobin in both the groups was non-significant, indicating that weekly iron supplementation is as efficacious as the daily supplementation of iron therapy for incremental effect of hemoglobin. WHO[6] also strongly recommend intermittent IFA supplementation as a public health intervention in reproductive age group women living in settings, where anemia is highly prevalent, to improve their hemoglobin concentrations and iron status and reduce the risk of anemia.

But when we compared the effect of daily versus WIFS, it was observed that participants on a daily regimen had significantly higher hemoglobin levels after three months than a WIFS regimen. These findings are inconsistent with findings of previous studies[16,17]. A study conducted by Agarwal et al.[18] on 2088 participants (with hemoglobin>7.9g/dl), including 702 on daily and 695 on weekly iron-folate administration, showed that weekly administration took longer time to raise hemoglobin, but was effective as well as practical for anemia prophylaxis in adolescent school girls. A current review conducted by Margetts[19] concluded that WIFS taken for at least 12 weeks improved iron status, as judged by increased hemoglobin and, in some studies, serum ferritin levels.

Conclusion

Thus, present study confirmed that anemia is a major public health problem in NPNL women in the study area. The data analysed in this study and available in the literature makes clear that though daily supplementation has a better effect on hemoglobin increase, weekly supplementation can be advocated in some cases as a preventive approach, especially for all women in the reproductive age group who loose iron due to regular menstrual cycle. It can also be advocated for participants of anemia treated with daily IFA supplementation for maintenance purposes, as it reduces the cost. This offers not only the reduction of cost, but a reduced frequency of side effects also, that would offer fewer disincentives and encourage compliance.

Conflict of Interest: Nil

Source of Support: Nil

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