Combating Iron Deficiency Anemia among School Going Adolescent Girls in a Hilly State of North India: Effectiveness of Intermittent Versus Daily Administration of Iron Folic Acid Tablets

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ABSTRACT

Background: National surveys in India have documented an increasing number of adolescent girls suffering from anemia. Efforts to build iron stores in adolescent girls will help them improve their prepregnancy hemoglobin level. To assess the effectiveness of school-based supervised weekly, bi–weekly, and daily regimen of iron folic tablets in the treatment of anemia among adolescent girls.

Methods: This randomized clinical trial included 331 anemic school going adolescent girls of Shimla district of North India. Study subjects were randomized to once weekly, bi–weekly, and daily iron folic acid regimen group. An intent-to-treat approach was used to analyze the change in hemoglobin level and serum ferritin levels at the end of the trial period.

Results: The rate of change of hemoglobin and serum ferritin levels from baseline to the end of the intervention was found to be similar in all the three groups (P = 0.64 and 0.98 for change in hemoglobin and serum ferritin). Bi-weekly treatment regimen results in comparatively more increase in hemoglobin levels (3.1 g/dl) as compared to once weekly (2.4 g/dl) and daily groups (2.3 g/dl) (ANOVA F statistics = 6.08, P = 0.003). Among the study subjects who reported side effects, more were from daily regimen group (55%) as compared to intermittent regimen group (25% in bi-weekly group; 18% in weekly group; $P < 0.001$).

Conclusions: In Shimla hills of North India, school-based intermittent iron-folic acid therapy is a feasible and effective intervention for increasing hemoglobin and serum ferritin levels of anemic adolescent girls.

Keywords: Adolescent girls, anemia, intermittent, iron folic acid

Brief Communication

INTRODUCTION

Iron deficiency is a common and widespread nutritional public health disorder in India. All ages are vulnerable for this nutritional epidemic; however, adolescent girls are at a higher risk due to rapid growth and higher iron needs. For many

decades, physicians have been advising daily iron pharmacotherapy for treating mild and moderate anemia. This approach has been met with limited success as is evident from the trend of increasing or stable prevalence of adolescent anemia reported in various national surveys across India.[1,2]

Researchers have studied the effects of daily and intermittent weekly iron in improving hemoglobin levels. Intermittent administration of iron has been proposed to be safer and cost-effective.[3-6] However, most of these studies have been done among young children or pregnant women; and in them study participants are randomized into two study groups comprising of weekly and daily iron dosing. To the best of our knowledge, no previous study has compared weekly, bi-weekly, and daily iron dosing in treating adolescent anemia. With this background, the present study aimed to assess the effectiveness of school-based supervised weekly, bi–weekly, and daily regimen of iron folic tablets in the treatment of anemia among adolescent girls.

METHODS

Study design and participants

The study was a randomized controlled trial. Sample size estimate was based on the expected mean difference for hemoglobin between the study groups. To detect a mean difference of 1 g/dl hemoglobin between the intervention and control groups with 80% power and 5% significance (two-tailed), assuming a standard deviation of 2.0 g/dl; 63 subjects/group are required. Assuming a loss to follow-up of 20%, the final sample size is 70 subjects/group.

For selecting the required sample size, a total of 1596 adolescent school girls in nine selected schools of Shimla district of Himachal Pradesh were screened for anemia. Out of them, 340 study subjects were found suffering from mild and moderate anemia. After excluding nine study subjects owing to the refusal, a total of 331 anemic adolescent school girls aged 10-19 years were enrolled in the study. Study subjects were assigned in the three intervention groups by lottery method. They were asked to choose a sealed envelope from a basket, which contained handwritten tickets. This process resulted in enrolling 108 study subjects in once weekly group, 112 in bi-weekly, and 111 in daily group [Figure 1].

Study procedures

An orientation workshop was held in the Department of Community Medicine, Indira Gandhi Medical College, Shimla; wherein head masters/head mistresses of the selected schools along with science teachers were called for 1-day workshop and apprised of the study design. The teachers then informed the parents of children about the purpose of the study and got their written informed consent.

The theoretical framework for our study intervention is based on a published theory claiming a mechanism which induces better absorption of intermittent iron dosage as compared to daily dosing. The theory postulates that the first dose of iron causes saturation of intestinal cells and thus, inhibits further absorption. It is only after these cells detach and are replaced by new cells in next 5 or 6 days will the next dose of iron be absorbed.[7,8] Thus, we wanted to compare daily iron-folic acid dosing with intermittent dosing (both weekly and twice weekly spread). Hence, we formed three study groups. Study subjects in once-weekly group received a total of 52 doses spread over a period of 1-year. Similarly, bi-weekly group received 104 tablets spread over a period of 1-year. The daily treatment group received 100 iron folic acid tablets daily over a period of 3 months.

The iron folic tablets contained 335 mg ferrous sulfate (100 mg of elemental iron) and 500 μg of folic acid. These tablets were distributed by the class teacher immediately after school recess break to ensure they were not taken on an empty stomach. The consumption of each tablet along with any self-reported side effects (vomiting, loose stools, and constipation) was recorded in a register by the class teacher. For each study subject, 5 ml venous blood sample was collected. This was done at baseline and at the end of the intervention period.

Statistical analysis

The primary outcomes of the study consisted of changes in serum hemoglobin and serum ferritin levels. The secondary outcome was recording the side effects in each intervention group. ANOVA test was used to compare the intervention and control group mean hemoglobin and serum ferritin levels at baseline and at the end of the intervention period. Chi-square test was used to compare the

proportional change in hemoglobin and serum ferritin between baseline and end of the intervention. Intention to treat analysis was performed. All the analyses were done using Epi Info software for windows (version 7, CDC, Atlanta, USA). The Ethics Committee of Indira Gandhi Medical College, Shimla approved the study.

RESULTS

The mean age of the studied subjects was 14.3, 14.2, and 14.8 years in once-weekly, bi-weekly and daily dosing groups, respectively. At baseline, no significant differences were seen in hemoglobin and serum ferritin status between the three study groups (P = 0.23 and 0.09 for hemoglobin and serum ferritin, respectively) [Table 1].

At the end of the study period, hemoglobin increased in all the three groups. In once-weekly, it increased to 12.2 g/dl, in bi-weekly 12.9 g/dl, and in daily group 12.0 g/dl. Serum ferritin also increased in all the three intervention groups. In Once-weekly, it increased to 35.5 µg/l, in bi-weekly 34.3 µg/l, and in daily 34.8 µg/l [Table 1].

The rate of change of both biochemical values from baseline to the end of the intervention was found to be similar in all the three groups (P = 0.64 and 0.98 for change in hemoglobin and serum ferritin). The mean increase in hemoglobin levels was comparatively more in the bi-weekly group as compared to once weekly and daily groups (ANOVA F statistics = 6.08, P = 0.003) [Table 1].

Overall, more than three-fourth of the study subjects reported no side effects of the intervention. Only 23% (77 study subjects) reported side effects. Significantly, more study subjects enrolled in daily regimen group reported side effects (n = 43, 55%) as compared to bi-weekly group (n = 20, 25%) and once-weekly group (n = 14, 18%) (χ^2 = 28.2, $P \leq 0.001$). The common reported side effects were episodes of nausea/vomiting (n = 23, 6.9%), constipation (n = 13, 3.9%), diarrhea (n = 4, 1.2%) and epigastric pain (n = 3, 0.9%).

DISCUSSION

In the present study, all three study regimens of iron folic acid therapy (once weekly, bi-weekly, and daily) improved hemoglobin levels, but the proportion of change from baseline to end of the intervention was found to be similar. Similar to our finding, Kotecha *et al*. in their study among adolescent girls in India reported that supervised once a week iron-folate administration (IFA) supplementation in schools was an effective intervention to reduce anemia.[9] Agarwal *et al*. in their study on adolescent girls in India concluded that regular weekly iron-folic administration was effective and suitable for treating mild to moderate anemia.[10]

We observed that the mean increase in hemoglobin levels was comparatively more in the bi-weekly group as compared to once weekly and daily groups Similar to this finding, a study among adolescents noted hemoglobin increment to be the highest in the bi-weekly group.[11] School-based survey in Mozambique[12] and Egypt[13] among adolescent girls have also documented effectiveness of intermittent iron folic acid tablets in increasing

Table 1: Impact of weekly, bi-weekly, and daily iron-folate administration on hemoglobin in adolescent school girls

Time period	Weekly group (n=108)	Bi-weekly group (n=112)	Daily group (n=111)	Significance
Hemoglobin (g/dl)				
At baseline	9.9±0.8	9.8±0.9	9.7±0.9	ANOVA F statistics=1.45, P=0.23
At the end of trial	12.3±2.7	12.9±3.1	12.0±2.3	ANOVA F statistics=2.59, P=0.07
Mean change (baseline-end)	2.4±1.9	3.1±2.2	2.3±1.4	ANOVA F statistics=6.08, P=0.003
Percentage of change in values	19.5	24.0	19.2	χ^2=0.87, P=0.64
Serum ferritin (µg/dl)				
At baseline	15.0±1.4	14.8±2.1	14.5±1.5	ANOVA F statistics=2.40, P=0.09
At the end of trial	35.5±3.1	34.3±2.9	34.8±3.9	ANOVA F statistics=2.48, P=0.08
Mean change (baseline-end)	20.5±1.7	19.5±0.8	20.3±2.4	ANOVA F statistics=10.01, $P \leq 0.001$
Percentage of change in values	57.7	56.9	58.3	χ^2=0.404, P=0.98

ANOVA=Analysys of variance

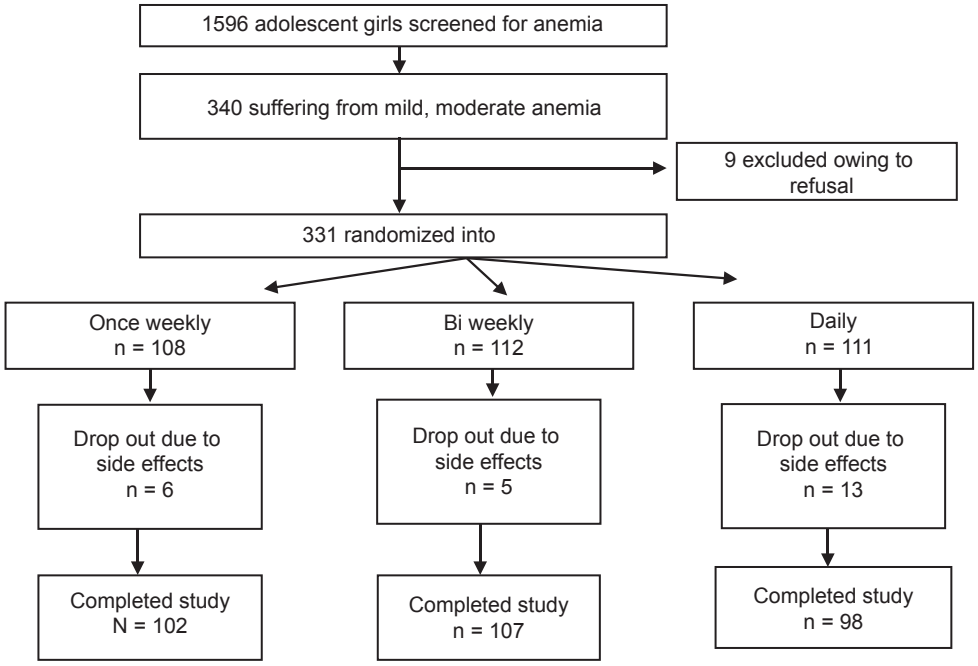

Figure 1: Patient distribution

hemoglobin levels. Contrary to our finding, a study done in Peru concluded that a daily schedule was better than the intermittent schedule in increasing hemoglobin values.[14]

In our study, the increment in serum ferritin was nearly equal in all the study groups. Similar to our finding, studies in Indonesia and Turkey comparing weekly and daily administration did not find any significant differences between treatment groups in serum ferritin concentration.[15,16] In contrast, Sungthong *et al*. reported higher serum ferritin in school children receiving daily doses of iron than in those receiving weekly doses.[17]

CONCLUSIONS

To conclude, our study has demonstrated that intermittent iron folic acid tablets have a similar response in increasing hemoglobin and serum ferritin levels compared to its daily administration. Further, weekly administration of IFA tablets has fewer side effects vis-a-vis daily administration. It is recommended that policy maker in India adapt intermittent regimens to tide over this adolescent public health problem in India.

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