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DAILY VERSUS WEEKLY IRON SUPPLEMENTATION AND PREVENTION OF IRON DEFICIENCY ANAEMIA IN LACTATING WOMEN
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ABSTRACT

Objective: **To demonstrate the effectiveness and social feasibility of weekly versus daily iron supplementation in preventing and treating iron deficiency anaemia among anaemic mothers.**
Design: **A longitudinal in nature.**
Setting: **Seven urban slum communities in *Teklehaimanot Wereda,* Addis Ababa, Ethiopia.**
Subjects: **Two hundred seven eligible mothers were assigned to the daily supplementation, weekly supplementation or control groups following randomisation between March and May 2001. The daily supplemented groups (n=71) received 60 mg of elemental iron containing 300 mg ferrous sulphate and 400 µg folic acid from monday to friday. The weekly group (n=68) received one tablet once a week every monday supervised while the control group (n=68) was advised to take no medications without the knowledge of the investigators until the completion of the study. To eliminate a major source of variation, subjects participating in the study were de-wormed at the beginning of the study.**
Main outcome measures: **Haemoglobin and serum ferritin concentrations were compared before and after the intervention among the groups.**
Results: **The mean haemoglobin (Hgb), and serum ferritin concentration (SFC) at baseline were practically similar among the groups. Haemoglobin levels significantly increased at the end of the study in all the groups and the proportion of anaemia decreased from 6.9% to 1.6% in the daily, 6.7% to 1.7% in the weekly supplemented and 6.7% to 6.1% in the control groups. The difference noted between the daily and weekly supplemented groups was not significant. The improvement of SFC concentration was better in the daily than the weekly group but not statistically significant. Daily supplementation schedule caused more side effects and lower compliance level than the weekly supplementation schedule.**
Conclusion: **Weekly supplementation is simple, comparable to daily supplementation and economically advantageous. Thus, it is recommended to adopt the strategy for controlling anaemia. Further because of higher compliance rate and lower side effects, it is deemed to be socially feasible.**

INTRODUCTION

Iron deficiency anaemia (IDA) was recognised to be a problem and highly prevalent in many developing countries as early as 1967 (1-2). It is the most common type of nutritional anaemia, affecting young children and women of reproductive age(3-9). Many causes of iron deficiency anaemia have been identified. Nutritional deficiency due to lack of bioavailable dietary iron accounts for over 50% of the cases(10-12). Preventing and correcting IDA among women is crucial because of its negative consequences which includes increased morbidity, and decreased immunity among others(13).

ln Ethiopia, about eighteen out of a hundred of the pregnant and lactating women surveyed between 1985 and 1984 suffered iron deficiency anaemia(14). As an immediate measure, a daily iron tablet was supplied to those women who had access to proper antenatal check-ups. The daily iron supplementation regime seems to reach few women even in the urban settings and ignores the majority of the rural women in the country. In addition, compliance is low. The continuing high prevalence of anaemia is an indication that the efforts being made are not working well because of several major constraints such as inadequate supplies of iron supplements, and poor coverage of the rural population. As an immediate measure, therefore, the only hope of reaching the vulnerable groups as shown by a few studies is through a weekly iron supplementation intervention programme, which is economically advantageous and causes fewer complaints of side

effects(15). The present study is the first step in this direction and tests the hypothesis that weekly iron supplementation is equally as effective as daily supplementation in urban slum communities of Ethiopia.

MATERIALS AND METHODS

The study was conducted in *Teklehaimanot Wereda* (district) in Addis Ababa, Ethiopia, which purposively selected, between March and June 2001. Six *Kebeles* (villages) of the *Wereda*, which were amongst the less privileged(16) and most affected by macro and micronutrient malnutrition were enrolled in the study.

The study design was longitudinal in nature, which is comparing the effect of daily versus weekly iron supplementation schedule before and after intervention.

The sample size was calculated based on the expected prevalence of anaemia as inferred from the various sources(12,14) using the formula recommended by Pocock(17) for such an intervention trial. To achieve significant results at the 7% with a 5% dropout rate at a power of 90%, a total of 207 anaemic subjects (non-pregnant but lactating women) were required. For those procedures, which require serum ferritin analysis, a sub-sample of one in four subjects (25%) was selected systematically.

Ethical clearance was obtained from the research and ethical clearance committees of Ethiopian Health and Nutrition Research Institute, Ethiopia.

A census of all households with lactating women, aged 15 to 45 years within one to two kilometre radius of the working centre was made. Households, which had a lactating mother who was pregnant, were excluded, and those with lactating women were retained. The total number of households with lactating women identified by the census was 1017. A total of 227 of these were found to be anaemic. However, only 207 of them were considered for the study because twenty were excluded for ethical reasons. The study subjects were then assigned either of the different supplementation schedules (daily or weekly) or control group following randomisation. To eliminate a major source of variation, subjects participating in the study were dewormed with 120mg levamisole tablets before the intervention and advised to avoid taking any form of supplementation except what was given to them throughout the study period.

The daily supplemented group received one or 60 mg of elemental iron tablet (300mg ferrous sulphate and 400 µg folic acid manufactured in Cyprus, Greek) monday to friday while the weekly supplemented group received one tablet once a week every monday for three consecutive months with supervision by the fieldworkers. The tablets were administered in the morning between 8.00 and 9.00 hrs to make sure that the subjects swallowed the tablets in both supplemented groups. Any complaints aroused in the process were recorded in the follow-up sheet.

Serum ferritin and haemoglobin levels were measured at baseline, and repeated after three months to assess and compare the effect of the different supplementation group and control group (18). The serum ferritin concentration was measured by ELISA technique using fully automated ES 300 analyser (Roche, Boerrhinger Manheim). Roche, Boerrhinger Manheim, Germany, supplied the reagents used throughout in the study in the ELISA technique. A value below 12 is considered iron deficient. Haemoglobin was measured using Cyanmethaemoglobin Method(19-21). Haemoglobin below 12 gm/dl is considered anaemic.

Data were analysed for changes in haemoglobin and serum ferritin using the Statistical Package for Social Science (SPSS), version nine. To detect difference among groups ANOVA was used and Chi test was used for detecting differences in dichotomous outcomes. Altitude adjustments for haemoglobin was based on an increase of 0.3 gm/dl per 1000 meters at sea level to determine the prevalence of anaemia according to the age specific cut-offs for initial haemoglobin values(22).

RESULTS

Out of the 207 eligible mothers, eight of them stopped participating in the study, due to side effects of the drugs administered, and three due to change of residence. Overall, the dropout rate was 5.3% for the entire group. The dropout rate was slightly higher in the daily supplemented (3.4%), than the weekly supplemented (0.48%) and the control group (1.4%). Compliance was significantly higher in the weekly supplemented group (98.5%) than the daily (90.1%) supplemented group ($p=0.04$). The eight (3.9%) non-compliant cases due to the side effects of iron therapy, seven (9.8%) of the cases were in the daily supplemented group and one (1.5%) in weekly supplemented group. Three of mothers (4.4%) who were enrolled in the control group dropped out due to change of residence.

Table 1 shows the selected baseline demographic characteristics of the eligible lactating mother. Though, the individuals were randomly allocated to groups, the similarity of the distribution of subjects by characteristics among the groups was assessed by comparing the variables age, marital status, education, parity, household size, employment status. The distribution was not significantly different among the three groups ($p>0.05$).

Table 2 shows the distribution of anaemic mothers by various indices between the different supplementation and control groups before and after supplementation. The overall prevalence rate of anaemia for the entire groups of lactating women was 22.3% at baseline. The proportion of subjects with haemoglobin below 12 gm/dl was almost equally distributed among the groups (i.e., about 7%). After supplementation, the haemoglobin concentration improved, and prevalence of anaemia significantly reduced from 22.3% to 9.5% in the entire group distributed as follows: 6.9% to 1.6 %, in the daily 6.7% to 1.7% in the weekly and 6.7% to 6.1% in the control groups indicating that the reduction was 5.31 %, 5.0% and 0.6% in the daily, weekly and control groups respectively. When the daily and weekly supplemented groups were compared, the proportion of mothers with normal haemoglobin was slightly higher in the daily than the weekly group. The difference however, was statistically insignificant ($p=0.76$). On the other hand, when both supplemented groups were compared with the control groups, it was evident that the improvement in haemoglobin concentration was significantly higher in the supplemented groups than the control groups especially when the baseline haemoglobin values are considered ($p=0.000$).

Table 1

Selected demographic characteristics of groups

Type of Variables		Type of study subjects: Daily (No. = 71)	Weekly (No. = 68)	Control (No. = 68)	Total (No. = 207)
Age breakdown*(years)					
	15-20	4(1.9)	7(3.4)	6(2.9)	17 (8.2)
	21-25	23(1.1)	20(9.7)	23(11.1)	66 (31.9)
	26-30	23(11.1)	4(6.8)	22(10.6)	59 (28.5)
	31-35	13(6.3)	11(5.3)	8(3.9)	32 (15.5)
	36-40	7(3.4)	15(7.2)	9(4.3)	31 (15.0)
	41-49	1(0.5)	1(0.5)	-	2 (1.0)
	Mean±SD	28.62±5.73	29.0±7.05	27.75±5.48	28.46±6.12
Marital status*					
	Single	11(5.3)	15(7.2)	11(5.3)	37(17.9)
	Married	49(23.7)	45(21.7)	48(23.2)	142(68.6)
	Divorced	2(1.0)	4(1.9)	6(2.9)	12(5.8)
	Separated	6(2.9)	2(1.0)	3(1.4)	11(5.3)
	Widow	3(1.4)	2(1.0)	-	5(2.4)
Education status*					
	none	12(5.8)	19(9.2)	13(6.3)	44(21.3)
	1-4	8(3.9)	6(2.9)	5(1.9)	19(9.2)
	5-8	31(15.0)	23(11.1)	29(14)	83(40.1)
	Secondary	18(8.7)	17(8.2)	21(10.1)	56(27.1)
	Post secondary	2(1.0)	3(1.4)	-	5(2.4)
Parity*					
	Para one	11(5.3)	26(12.6)	22(10.6)	59(28.5)
	Para two	23(11.4)	10(4.8)	15(7.2)	48(23.2)
	Para 3-5	24(11.6)	21(10.1)	27(13.0)	72(34.8)
	Multipara (≥ 6)	3 (6.3)	11(5.3)	4(1.9)	28(13.5)
	Mean±SD	3.55±0.9	3.25±1.14	3.19±0.9	3.33±1.03
Household size*					
	<10 family members	67(32.4)	64(30.9)	46(31.9)	197(95.1)
	≥10 family members	4(1.9)	4(1.9)	2(1.0)	10(4.9)
	Mean±SD	6.14±2.8	6.6±2.6	6.29±2.6	6.34±2.7
Employment status*					
	Self	2(1.0)	9(4.3)	4(1.9)	15(7.2)
	Government	2(1.0)	2(1.0)	2(1.0)	112(54.1)
	Daily labourer	7(3.4)	7(3.4)	6(2.9)	20(9.7)

* P>0.05, Figures in parentheses are percentages

Table 2

Distribution of mothers by anaemia status as shown by various indices before and after three months of intervention

Indices	Treatment Groups	Before	After	SE	(95% CI)
Haemoglobin(hgb) (<12gm/dL)					
	Daily	71(6.98)	17(1.67)	0.37	0.16-0.31*
	Weekly	68(6.7)	18 (1.77)	0.38	0.14-0.30*
	Control	68(6.7)	62(6.09)	0.42	-0.061-0.11
	Total	207(20.38)	196(9.53)	0.23	0.1-0.19**
Serum ferritin (SF) (<12µg/l (deficient)					
	Daily	4(7.5)	1(1.8)	0.03	-0.18-0.11
	Weekly	5(9.4)	2(3.7)	0.03	-0.02-0.11
	Control	2(3.8)	0(0.0)	0.02	-0.01-0.07
	Total	11(20.7)	3(5.5)	0.04	0.01-0.1*
40-150µg/1(normal)	Daily	7(13.2)	11(20.7)	0.04	-0.12-0.04
	Weekly	6(11.3)	9(17.0)	0.04	-0.11-0.05
	Control	6(11.3)	6(11.3)	0.04	-0.08-0.08
	Total	19(35.8)	26(49.0)	0.04	-0.12-0.05

Figures in parentheses are percentages and derived from the total recruited mothers for Hgb(No. = 1017) while the percentages for SF is calculated from 53 mothers. SEM=standard error of the mean
*=P< 0.05
**=P<0.01

The serum ferritin levels at baseline were not significantly different among the groups. After supplementation, the serum ferritin concentration (SFC) improved and the proportion of mothers with low SFC significantly decreased from 20.7 % to 7.5% in the *Wereda.* This was distributed as follows: 7.5% to 1.8% in the daily, 9.4% to 3.7% in the weekly supplemented groups and none in the control groups indicating that the reduction was 5.7% in daily, 7.6% in weekly and 0% in the control groups. The difference noted between the daily and weekly supplemented groups was not significant On the other hand, the proportion of mothers with normal SFC in the entire group was close to a half (49.1%) distributed as follows: 11(20.7%) in daily, 9(17.0%) in weekly and 6(11.3%) in the control groups indicating that the improvements were 7.2%, 5.7% and 0 % in the daily, weekly and control groups respectively. No significant difference was observed among the groups neither between the iron-supplemented groups. Interestingly, the maximum level of SFC attained were between 83 and 126 µgm/L in the entire group indicating that none of the supplemented groups had a feature of iron overload (SFC>300µgm/L).

Table 3 shows the 95% confidence interval, mean±SD and changes in haemoglobin and serum ferritin concentration of the groups before and after intervention in iron supplemented and control groups. The mean haemoglobin concentration was distributed as follows: 12.27±0.32 in daily, 12.2±0.39 in weekly and 11.01±0.65 in the control groups. It was significantly higher in the supplemented groups than the control groups (p=0.00). The mean changes in haemoglobin concentration were also 0.74±0.49 in daily, 0.83±051 in weekly and 0.37±0.76 in the control groups. The differences observed among the groups (both supplemented and control) was significantly higher in the supplemented groups; but were not significantly different from the control groups (p=0.00).

The mean serum ferritin concentration across the different groups ranged from 48.1 to 62.6 in the entire group distributed as follows: 62.6 in daily, 52.5 in weekly supplemented group and 48.1 in the control groups. The difference noted among the group was not statistically significant. The changes in SFC ranged from -8.6 to 18.4 in the entire group distributed as follows, 18.4 in daily, 18.3 in weekly and -8.6 in the control group indicating a significant improvement in the supplemented groups than the controls.

Although side effects such as nausea, vomiting, constipation and skin itching were more common in the daily than the weekly supplemented groups during the first two weeks of the therapy, the differences noted between groups were not significant. The above symptoms became milder in the sixth and eighth weeks in both groups, and gradually subsided except in eight women, who were forced to discontinue, seven in daily and one in weekly supplemented groups.

Table 3

Haemoglobin and serum ferittin concentration of mothers before and after three months of iron supplementation

Parameter	Treatment groups	Mean±SD(95% CI)	Mean±SD(95% CI)	Mean±SD(95% CI)	Paired t-test	
Haemoglobin		Before (No. = 207)	After (No. = 196)	Change(No. = 196)	T-value	P-value
(in gm/dL)	Daily	11.5±0.39(11.4-11.6)	12.27±0.32(12.1-12.4)	0.74±0.49(0.62 - 0.86)	-1.22	0.00
	Weekly	11.4+0.36(11.3-11.5)	12.2±0.39(12.1-12.3)	0.83±0.51(0.70-0.95)	-12.9	0.00
	Control	11.4±0.44(11.3-11.5)	11.01±0.65(10.8-11.2)	-0.37±0.76(-0.56)-(-0.18)	3.93	0.00
	F-value	2.4	144.7	80.3		
	P-value	0.09	0.00	0.00		
Serum ferritin		Before (No. = 53)	After (No. = 53)	Change (No. = 53)	T-value	P-value
(in µg/L)	Daily	44.3±28.36(30.6-57.9)	62.6±30-6(47.8-77.4)	18.4+8-7(14.1-22.6)	-9.14	0.00
	Weekly	42.4±28.7(28.6±56.3)	52.5+29.4 (38.3-66.71	18.3±8.7(14.1-22.6)	-7.27	0.00
	Control	48.2±38.5(26.9 -69.5)	48.1±38.5(26.7-69.4)	-8.6±0.7[(-0.48)-(0.31)]	0.46	0.64
	F-value	0.14	0.91	34.9		
	P-value	0.87	0.41	0.00		

DISCUSSION

The significance of iron deficiency anaemia across different age groups and population has been widely reported(22-24). It suffices to note that, the effects are significant enough to cause long term retardation of national development through failure of individual to realise full genetic potential and to optimally exploit opportunities. Recently, developed algorithms for calculating economic loss due to iron deficiency in countries with high burdens of anaemia estimate losses in the order of billions of US

dollars every year(25). Cognisant of these facts, control and prevention of iron deficiency anaemia is a priority in the micronutrient intervention program.

This study shows a slightly higher prevalence of IDA than previous figures obtained from rural mothers in Ethiopia, which were found to be 18.4(14). This shows that the slum communities/*Kebeles* are at risk, and suggests the need for iron supplementation for the women as well as the other at-risk groups in the community.

The mean age of mothers in the entire group (28.4± 6.12 years) indicates that the problem of IDA to be mostly among the younger motherhood group in the community.

It is noted that significant increase in haemoglobin concentration and a fall in the prevalence of anaemia in both the daily and weekly supplemented groups were found after iron supplementation for three months. It is further noted that therapeutic effectiveness was equally significant whether 60mg of iron is supplemented once weekly or 60mg of iron is administered daily.

A small improvement was also seen in the control group suggested to be due to the positive effects of de-worming. Thus de-worming of the subjects in the community should be considered together with the weekly iron supplementation intervention for better results. Similar effect of de-worming also was reported previously in a study of pregnant women on a Sri Lankan plantation(13). In a sub-sample of the study subjects, daily administration of iron produced a slightly greater increase in serum ferritin than the weekly supplementation. However, the rise in serum ferritin with daily administration of iron is of no practical significance as long as the preventive weekly supplementation program is conducted and attains the referred haemoglobin increases. In addition, the slower response of serum ferritin in the weekly schedule seems an important advantage in lessening the chances of iron overload.

The reports of side effects observed in this study were related to the frequency of iron supplementation. The fewer side effects observed in the weekly supplemented groups than the daily supplementation group shows that weekly supplementation is better and should be adopted especially where the problem of iron deficiency anaemia is highly prevalent in the country.

A study from China and Indonesia also investigated the potential effect of intermittent compared with daily iron supplements(13,26). The study showed the haemoglobin responses to be similar in daily and weekly groups, although the group given the supplements daily had a substantially larger rise in serum ferritin than did the intermittently supplemented groups. Side effects were also reported to be more among the daily supplemented than the weekly group(27).

The commonly reported side effects such as nausea, vomiting, abdominal pain, constipation, skin itching and changes in stool colour which were reported by the supplemented groups have been reported during the first two weeks of the therapy(13). In the present study, side effects were more common in the daily supplemented groups than the weekly supplemented groups. However, the difference observed between the groups was not statistically significant (P=0.4).

In the present study, compliance was high, ranging from 92% to 97% compared with previous studies(13,26). It is evident that dropout rate due to side effects was slightly higher among the daily than the weekly supplemented groups suggesting that the weekly supplementation schedule programme is more favoured than the daily schedule in our setting. This finding is in conformity with the study from Sri Lanka(13).

In conclusion, the weekly supplementation is a simple intervention to increase haemoglobin concentration in anaemic women and it is economically advantageous; the unit cost of weekly supplementation per tablet was 0.16 Ethiopian Birr, equivalent to 0.02 $USD as compared to the daily cost of 0.80 Ethiopian Birr, equivalent to 0.10 $USD, which is five times higher than the weekly schedule.

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