Antenatal Iron Supplementation: Only Thrice a Week

I.M.R. Goonewardena[1] and C. Liyanage[2]

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Summary

Objective: To study the effectiveness of an oral iron supplement administered only three times a week in improving the iron status of pregnant women.

Design: A longitudinal prospective cohort study.

Setting: University antenatal clinic, Galle.

Patients & Methods: Serum ferritin (SF), haemoglobin (Hb), and haematocrit (Hct) were measured in 77 pregnant women before and 12 weeks after an oral iron supplement given three times a week. An anthelmintic (mebendazole) followed by haematinic capsule containing *inter alia* 117mg of elemental iron as ferrous fumarate and 75mg vitamin C was used. Comparisons were made of the proportions of subjects with anaemia and iron deficiency before and after supplementation, and the change in mean SF, mean Hb and mean Hct levels.

Results: The mean Hb increased by 0.6 g/dL (SED 0.22, $p<0.01$) in spite of a mean decrease of Hct by 2% (SED 0.7, $p<0.01$). The number of subjects who presented with Hb<8g/dL and SF<12ng/mL decreased from 13(19%) to 1(1.2%) after supplementation ($p<0.05$). The mean Hb and mean SF increased significantly in the subjects who presented with an initial Hb<11g/dL and SF<12ng/mL ($p<0.001$). However the mean Hb and mean SF decreased in those who presented with an initial Hb>11g/dL and SF>12ng/mL ($p<0.01$).

Conclusion: Antenatal iron supplements given only thrice a week meets the additional iron requirements of pregnancy and improves the iron status of both anaemic and iron deficient pregnant women.

Introduction

The regimen of antenatal iron supplementation as practised today needs review. Daily oral iron supplements not only cause distressing side effects which result in poor compliance but also a substantial proportion of the supplement remains unabsorbed (1,2,3,4,5). Less frequent oral iron supplementation may be equally beneficial to a subject as daily supplements (6).

A study on non pregnant females has suggested that an iron supplement given once a week is equally effective in improving haemoglobin(Hb) levels as a daily iron supplement (7). However a study carried out by us suggested that weekly iron supplements were inadequate to meet the additional requirements of iron during pregnancy, especially in women with borderline or latent iron deficiency (8).

Studies on rats have shown that iron absorption is suppressed after an oral iron supplement. This suppression apparently lasts throughout their mucosal cell turnover time (9,10). It has also been shown that an oral iron supplement given every 2nd or 3rd day was equally effective as daily iron supplements in improving the iron status of anaemic rats (11).

Hence this study was designed to assess the effectiveness of an antenatal oral iron supplement given three times a week in improving the iron status of pregnant women.

1 Senior Lecturer, Department of Obstetrics & Gynaecology, Faculty of Medicine, University of Ruhuna, Galle.
2 Senior Lecturer, Department of Community Medicine, University of Ruhuna, Galle.

Patients and Methods

All women between 14 and 16 weeks period of gestation (POG) presenting themselves for antenatal care at the University Clinic, Galle, between 19 April and 14 June 1994 (n = 77) were recruited for the study. Informed written consent was obtained from all the subjects and ethical approval for the study was obtained from the Medical Faculty, Galle.

During venepuncture for the other routine antenatal investigations an additional 2mL of mixed venous blood was taken. The haematocrit (Hct) was estimated using haematocrit tubes, the haemoglobin (Hb) was estimated by cyanmethaemoglobin method and the serum ferritin (SF) by immunoradiometric assay technique using IRMA Ferritin Kits (Diagnostic Products Corporation, Los Angeles). This assay has a sensitivity of detecting 0.1 ng of SF/mL.

All subjects were given mebendazole 100mg twice daily for 3 days followed by a haematinic capsule containing approximately 117mg of elemental iron in the form of ferrous fumarate together with, folic acid 1.5mg, cyanocobalamin 15mcg, calcium carbonate 200mg, cholecalciferol 400iu and ascorbic acid 75mg. They were advised to take the haematinic with water at 11.00 a.m. (approximately one hour before lunch) on three stipulated days (monday, wednesday and friday) of each week for a period of 12 weeks.

The subjects were reviewed at 4 weekly intervals and a structured interview was used to obtain information regarding compliance and side effects. Each subject was given only 15 haematinic capsules at a time. The number of tablets remaining was checked at each visit. At the end of 12 weeks a second sample of mixed venous blood was obtained for repeat Hb, SF and Hct estimations.

In the study, anaemia was defined as Hb less than 11g/dL and iron deficiency as SF less than 12ng/mL. Analysis of variance was used to assess any differences in age, parity or POG when the subjects were grouped according to their initial Hb and SF levels. The difference in proportions of subjects with anaemia and iron deficiency before and after supplementation was assessed using the chi square test. The change in mean Hb levels and mean SF levels after supplementation, in subjects with different initial Hb levels and SF levels, was assessed using the paired t test. Since the SF levels did not have a normal distribution (they had skewed distribution with a large number of low values) the paired test was carried out on their log values. The effectiveness of the thrice weekly regimen in improving iron stores was evaluated using the Mc Nemar's test.

Results

All the subjects were Sinhalese. There were 37 (48%) primigravidae. Their ages ranged from 15 to 43 years with a mean of 27 (SD 6.8). There were 47 (61%) subjects who presented with POG between 13 to 19 weeks and the rest had 20 to 26 weeks of gestation. Of the subjects only 19 (25%) had a monthly family income of Rs. 3000/- or more. There were 60 (87%) who had been educated above grade 6.

Of the subjects 33 (43%) had taken some form of haematinic prior to being included in the study. All except one of the 33 had obtained the haematinic from a family health worker in her local antenatal clinic.

There were no significant differences in age, parity or POG among the subjects when they were grouped according to their initial Hb and SF levels (Table 1). At the commencement of the study, 66 (86%) were anaemic and 27 (35%) had gross iron deficiency (Tables 2&3). Forty women (52%) had a Hct below 34% (Table 4). Every one of the subjects took all the capsules given and no significant side effects were reported.

In the total sample (n=77) the mean Hct decreased by 2% (SED 0.7, $p<0.01$). However the mean Hb increased by 0.6g/dL (SED 0.22 $p<0.01$). There was a reduction of mean SF by 6.4ng/mL which was statistically not significant (SED 3.75, $p<0.05$) (Table 5).

The mean Hb increased by 0.9g/dL (SED 0.21, p<0.001) and the mean SF increased by 7.9 ng/mL (SED 2.6, p<0.001) in the subjects who had initial Hb<11g/dL (n=66) and SF <12ng/mL (n=27) respectively (Tables 6 & 7). The number of women who presented with Hb <8g/dL and SF <12ng/mL decreased from 13(19%) at the start of the study to 1(1.2%) after supplementation (p<0.05) (Tables 1 & 8). Using the McNemar's test, evaluation of the effectiveness of the thrice weekly regimen showed a highly significant beneficial effect in grossly anaemic and iron deficient women who had Hb<8g/dL and SF<12ng/mL (p<0.001).

The mean Hb decreased by 1.2g/dL (SED 0.31, p<0.05-not significant) and the mean SF decreased by 14.1 ng/mL (SED 4.87, p<0.05) in the subjects who had an initial Hb>11g/dL (n=11) and SF>12ng/mL (n=50) respectively (Tables 6 & 7). There was also a reduction of mean Hct by 1.7% (SED 1.95, p>0.05-not significant) and 2.3% (SED 0.92, p<0.05) in these women who had Hb >11g/dL and SF>12ng/mL respectively.

Table 1

Haemoglobin (Hb) and serum ferritin (SF) levels according to age, parity and period of gestation (POG) (n=77); Hb in g/dL and SF in ng/mL

		Hb<8 (n=16)	Hb 8-10.9 (n=50)	Hb≥11 (n=11)	SF<12 (n=27)	SF≥12 (n=50)
Age	Range	17-41	15-41	21-43	17-41	15-43
	Mean	27.4	26.3	29.4	27.3	26.8
	SD	7.8	6.4	6.7	6.6	7.0
Parity	Range	1-5	1-5	1-5	1-4	1-5
	Mean	2.1	1.7	1.7	2.0	1.7
	SD	1.3	1.0	1.1	0.9	1.1
POG	Range	14-23	9-24	9-22	9-23	9-24
	Mean	18.8	18.0	16.4	17.6	18.1
	SD	3.0	3.6	3.4	3.7	3.5

Table 2

Distribution of subjects according to haemoglobin (Hb) and serum ferritin (SF) levels before supplementation (n=77)

Hb g/dL \ SF ng/mL	<12	12-59.9	≥60	Total
<8	13	3	0	16
8 – 10.9	14	31	5	50
11 – 12.9	0	8	3	11
≥ 13	0	0	0	0
Total	27	42	8	77

Table 3

Levels of haemoglobin (Hb), serum ferritin (SF) and haematocrit (Hct) before supplementation (n=77)

	Range	Mean	SD
Hb(g/dL)	6.6 – 12.2	9.4	1.6
SF(ng/mL)	2.5 – 177.5	28.0	28.0
Hct(%)21	– 42	33.1	4.5

Table 4

Distribution of subjects according to haematocrit (Hct) and period of gestation (POG) before supplementation (n=77)

Hct% / POG (weeks)	<30	30 – 33	34 – 36	>36	Total
13 – 19	10	15	11	11	47
20 – 26	4	11	10	5	30
Total	14	26	21	16	77

Table 5

Change in mean values of haemaglobin (Hb), serum ferritin(SF) and haematocrit(Hct) after supplementation (n=77)

	Mean change	SED	p
Hb (g/dL)	+ 0.6	0.22	<0.01
SF (g/dL)	– 6.4	3.75	> 0.05*
Hct (%)	– 2	0.7	<0.01

(+) = Increase ; (–) = Decrease

*not significant

Table 6

Change in mean values of haemoglobin (Hb), according to Hb level before supplementation (n=77)

Initial Hb	Mean change	SED	p
< 11 g/dL (n=66)	+ 0.9	0.21	<0.001
> 11 g/dL (n=11)	− 1.2	0.31	> 0.05*

(+) = Increase (−) = Decrease

*not significant

Table 7

Change in mean values of serum ferritin (SF) according to serum ferritin (SF) level before supplementation (n=77)

Initial SF	Mean change	SED	t	p
< 12 ng/mL (n=27)	+7.9	2.60	2.52	<0.05
≥ 12 ng/mL (n=50)	− 14.1	4.87	2.33	> 0.05

(+) = Increase (−) = Decrease

Table 8

Change in distribution of haemoglobin(Hb) and serum ferritin(SF) after supplementation (n=77)

Hb g/dL \ SF ng/mL	<12	12-59.9	≥60	Total
<8	− 12*	− 1	0	− 13
8 − 10.9	+ 1	+ 15	− 5	+ 11
11 − 12.9	+ 6	− 2	− 2	+ 2
≥ 13	0	0	0	0
Total	− 5	+ 12	− 7	0

* p < 0.05

The mean Hct decreased by 2.1% (SED 0.75, $p<0.001$) and 1.6% (SED 1.01, $p>0.05$-not significant) in the subjects who had an initial Hb <11g/dL (n=66)and initial SF <12ng/mL (n=27) respectively.

Discussion

This study was designed only to assess the effectiveness of a thrice a week oral antenatal iron supplementation regimen and not to study its effects under controlled conditions.

Daily iron-folate supplementation and anthelmintic therapy has been found to be effective in improving the iron status of pregnant women in the plantation sector of Sri Lanka (3). Hence the anthelmintic mebendazole was given in our study to exclude the possibility of helminthiasis interfering with the results. However the prevalence of helminthiasis especially due to hookworm infestation is probably low in urban areas like Galle (12).

Many pregnant women prefer to take a haematinic capsule rather than the standard UNICEF tablet of ferrous sulphate and folic acid. Hence this particular capsule was selected for our study because it is freely available at a relatively low cost (<Rs. 1.50) and is one of those which is frequently prescribed by the medical practitioners in the country.

In the present study, the reduction of mean Hct probably reflects the physiological haemodilution of pregnancy. The reduction of mean Hb and mean SF in the non anaemic and iron replete subjects is probably a consequence of this and not due to the occurrence of anaemia or iron deficiency (13,14,15,16). It has been found that this reduction occurs even after antenatal iron supplementation (17), and it has also been suggested that attempts should not be made to try and prevent it (14,15,16).

There is evidence to show that iron absorption is regulated by an individuals iron stores (18). Hence iron-deficient women will have an increased rate of iron absorption compared to iron replete women. This is probably the reason for the anaemic and iron deficient women in this study showing a marked increase of Hb and SF levels, resulting in a significant reduction in the number of grossly anaemic and iron deficient women.

The differences in effectiveness among iron-replete and iron-deficient subjects were not due to any influence of age, parity or gestational period.

The improvements of iron status in the anaemic and iron deficient women occurred in spite of haemodilution. This indicates that the thrice a week dose was not only adequate to meet the additional iron requirements of pregnancy but was also able to improve the iron status of the subjects.

As the subjects in the study complied with the thrice a week regimen of supplementation and did not report any significant side effects, this regimen should be more acceptable to pregnant women in Sri Lanka. To assess whether this regimen is as effective as daily supplementation, a controlled clinical trial is required. Such a trial is currently in progress in our department.

Conclusion

Antenatal oral iron supplements given only three times a week, meet the additional iron requirements of pregnancy. It is also effective in improving the iron status of both anaemic and iron deficient pregnant women. No significant side effects were reported and a good compliance was reported.

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References

1. Charoenlarp PA. WHO collaborative study on iron supplementation in Burma and Thailand. American Journal of Clinical Nutrition 1988;47:280-297.

2. Kurzon MD. Iron supplementation using different dose levels in Filipinos. Nutrition Research 1983;3:257-264.

3. Athukorala TMS, de Silva LDR, Dechering WHJC, Dassanayake TS de C, Perera RS. Evaluation of effectiveness of iron folate supplementation and anthelmintic therapy against anaemia in pregnancy – A study in the plantation sector of Sri Lanka. American Journal of Clinical Nutrition 1994;60:286-292.

4. O'Neill-Cutting MA, Crosby WH. Blocking of iron absorption by a preliminary oral dose of iron. Archives of Internal Medicine 1987;147:489-491.

5. Fairweather-Tait SJ., Minski MJ. Studies on iron availability in man using a stable isotope techniques. British Journal of Nutrition 1986;55:279-285.

6. Fairweather-Tait SJ. Iron availability – the implications of short term regulation. Nutrition Bulletin 1986;11:174-180.

7. Gross R, Shultink W, Juliawati. Treatment of anemia with weekly iron supplementation. Lancet 1994;344:821.

8. Goonewardene IMR, Liyanage C. Antenatal Iron Supplementation; once a week only. Sri Lanka Journal of Obstetrics & Gynaecology 1995;17:in press.

9. Wright AJA, Southon S, Fairweather-Tait SJ. Measurement of non haem iron absorption in non anaemic rats using ^{59}Fe: can the Fe content of duodenal mucosal cells cause lumen or radioisotope dilution or both, thus resulting in the underestimation of Fe absorption? British Journal of Nutrition 1989;62:719-727.

10 Fairweather-Tait SJ, Swindell TE, Wright AJA. Further studies in rats on the influence of previous iron intake on the estimation of bioavailability of Fe. British Journal of Nutrition 1985;54:79-86.

11. Wright AJA, Southon S. The effectiveness of various iron supplementation regimens in improving iron status of anaemic rats. British Journal of Nutrition 1990; 63:579-585.

12. Fonseka P, Wijewardene K, de Silva DGH, Wijesiri W. Community control of soil transmitted helminths in rural Sri Lanka. International Development & Research Centre (IDRC) Canada. IDRC File No: 3-P-87-0061.

13. Hall MH, Blood and neoplastic diseases; pregnancy anaemia. British Medical Journal 1974;1:661-663.

14. BMJ Leader. Do all pregnant women need iron? British Medical Journal 1978;2:1317-1319.

15. Cavetti NG, Esemita AG, Paternoster D, Pelliazani P, Grella P. Iron balance in pregnancy in relation to anaemia. Clinical Experiments in Obstetrics & Gynaecology 1992;19:218-221.

16. Holland S, Johansen KS. Adequate iron stores and the 'nil nocere' principle. Haematologia Budapest 1993;25:69-84.

17. Peck TM, Arias F. Haematological changes associated with pregnancy. Clinics in Obstetrics & Gynaecology 1979;22:785-792.

18. Gavin MW, MacCarthy DM, Garry PJ. Evidence that iron stores regulate iron absorption-set point theory. American Journal of Clinical Nutrition 1994:59:1376-1380.