9. Labadie EL. Cerebrospinal fluid alterations associated with central nervous system infections. *In:* Wood JH, Ed. Neurobiology of Cerebrospinal Fluid. New York and London: Plenum Press, 1982; 433-448.

10. Reimers JI. Interleukin-I beta induced trasient diabetes mellitus in rats. A model of the initial events in the pathogenesis of insulin-dependent diabetes mellitus? Dan Med Bull 1998; 45: 157-180.

11. Dinarello CA. Biology of interleukin-1. FASEB J 1988; 2: 108-115.

12. Lange CH, Cooney R, Vary TC. Central interleukin-1 partially mediates endotoxin-induced changes in glucose metabolism. Am J Physiol 1996; 271: E309-316.

Efficacy of Twice Weekly Iron Supplementation in Anemic Adolescent Girls

S. Shobha and D. Sharada

From the Department of Foods and Nutrition, Post Graduate and Research Center, Acharya N.G. Ranga Agricultural University, Rajendranagar, Hyderabad-500 030, India.

Correspondence to: Dr. S. Shobha, Department of Foods & Nutrition, Post Graduate & Research Centre, Acharya N.G. Ranga Agricultural University, Rajendranagar, Hyderabad 500 030, India.

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Two hundred and forty four girls with different hemoglobin levels were selected, of which forty-one were non-anemic. The rest were graded as mildly, moderately or severely anemic and supplemented with 60 mg of iron daily or twice weekly for twelve weeks. There was no significant difference in the increase in hemoglobin levels between daily and twice weekly-supplemented subjects at the end of the study. Unpleasant side effects of supplementation were experienced by 57.8% of the daily supplemented subjects as against 5.9% of twice weekly-supplemented ones. Twice weekly supplementation could be recommended for overcoming anemia in adolescent girls.

Key words: *Adolescent girls, Anemia, Iron supplementation, Hemoglobin.*

Iron deficiency anemia is the most prevalent micronutrient deficiency among humans all over the world. Among Indians, FAO and WHO, 1993(1) reported an incidence of iron deficiency in 65% of adult women, 45% of adult men and 77% of children under five. The percentage of Indian adolescent girls who were anemic was reported as 73.7% by Chaturvedi, *et al*.(2) and 61.9% in urban areas and 85.4% in rural areas(3).

Adolescent girls are a particularly vulnerable group as their requirements of iron as well as its losses from the body are high. Anemia during adolescence limits growth and delays the onset of menarche, which in turn may later lead to cephalopelvic disproportion(4). Very often, in India, girls get married and pregnant even before the growth period is over, making anemia doubly risky. Few programes for anemia control have targeted adolescent girls and health care of adolescent girls all over the world has not been given priority(4). Since the anemic status of these adolescent girls is bound to affect their offspring, care during this period is likely to pay rich dividends.

Recent studies have indicated that iron supplements given weekly once or twice can be as effective as daily supplements, cost less, are better accepted and may have fewer side effect(5). Such an intermittent supplementation would be of particular use in a public health program if proved to be effective.

This study examined the comparative effectiveness of a twice a week supplementation program to a daily supplementation program in enhancing the hemoglobin levels of adolescent girls with different grades of anemia and in reducing side effects.

Subjects and Methods

The study was conducted in an Andhra Pradesh Social Welfare Residential School for girls located in Ranga Reddy district. The school caters to girls from a low socio economic background. On the whole 244 girls belonging to the 13-15 years age group were selected and their ages were confirmed from school records. A pin prick blood sample was obtained from each student. A sterile disposable lancet was used and 20mL of the blood sample was accurately delivered using a standardized hemoglobin pipette, on to a Whatman No.1 filter paper which was air dried and stored for analysis of hemoglobin in the laboratory by the Cyanmethemoglobin method of Dacie and Lewis(6). Based on their initial hemoglobin levels, subjects were then classified as normal (>12g/dL), mild (10-11.99 g/dL), moderate (8-9.99g/dL) or severely (8 g/dL) anemic as per the WHO standard(7).

Subjects belonging to each grade of anemia were further randomly divided into two subgroups and allotted to either a daily or a twice weekly supplementation regimen.

The subjects were de-wormed with a single dose of 400 mg albendazole (Zentel tablet obtained from Smith-Kline Beecham) one week prior to supplementation. The supplement used consisted of 60 mg of iron and 0.5 mg of folic acid and was obtained from UNICEF. Supplementation was carried out under the strict supervision of the investigator and the supplement was administered around 4.00 p.m., three hours after lunch and three hours before dinner. Subjects were given the supplement either daily or on every Wednesday and Saturday depending on the regimen they belonged to. The period of supplementation was 84 days (*i.e.*, 12 weeks). A record of the attendance, morbidity and side effects experienced by each subject was maintained.

Blood samples were obtained from each subject by pin prick method at the beginning of the study, and at the end of the third, sixth, ninth and twelfth weeks. No squeezing or compression, were employed and free flowing blood was collected from the punctured finger tip(8). Hemoglobin(6) was then estimated.

Group means and standard deviations were calculated and Student's 't' test and paired 't' tests were carried out to test the significance of difference between means of values of different groups as well as within the group at different periods of supplementation.

Results

Among the 244 subjects screened, 203 (83%) were anemic while the remaining 41 were non anemic. The anemic subjects were supplemented with iron either daily or weekly twice and changes in their hemoglobin levels were studied. The increase in hemoglobin of subjects belonging to all three grades of anemia and both regimens of supplementation is given in *Table I.*

The hemoglobin level increased steadily in all supplemented subjects as the period of supplementation increased. By the end of 21 days of supplementation, all categories of both

groups showed significant improvement from base line hemoglobin level. For the moderately and severely anemic subjects the difference between the two groups was not statistically different. In the mildly anemic girls the daily groups had significantly higher hemoglobin level than the weekly group. The same trend was seen by the 41st day of supplementation. By the 63rd day mildly anemic subjects supplemented daily reached normal levels of hemoglobin while weekly supplemented had near normal hemoglobin levels.

At the end of the study period, all mildly and moderately anemic subjects given either daily or weekly twice iron supple-mentation became normal (12 g/dL). Majority of the severely anemic subjects also reached near normal levels, though perhaps they would require a slightly longer period of supple-mentation to become completely normal. Severely anemic subjects showed maximum overall increment (58.78% in daily and 52.64 in weekly) followed by moderately (33.44% in daily and 29.69 in weekly) and mildly anemic subjects (23.22% in daily and 18.95% in weekly).

Table II gives the undesirable side effects experienced by subjects receiving the supplement.

Discussion

The high anemia prevalence of 83% observed in this study is similar to that reported by Chaturvedi, *et al.*(2) in Rajasthan and Vijayalakshmi(9) in Andhra Pradesh.

UNICEF/WHO JCHP(15) recommends iron supplementation for all females between 10-49 years in countries where over 30% of the population is anemic. While this would put additional financial burden on the government, the benefits in future would far outweigh the expenditure incurred. Recent studies by Liu, *et al.*(11) and Gross(12) have suggested that a supplement given weekly twice or even once would be as effective as a daily supplement in raising hemoglobin levels. In such a case, the cost of supplementation would also be cut to one third. In this study, supplementation with iron either daily or weekly twice brought about a significant increase in the hemoglobin levels of the subjects and there was no significant differ-ence between the increase brought about by both types of supplementation. At the end of 84 days of supplementation, the hemoglobin status of weekly twice-supplemented subjects was as good as daily supplemented subjects. As seen from the data, even for shorter periods of time this improvement holds good.

When the total mean increment in hemoglobin was examined, the severely anemic subjects showed the maximum increase. It is observed that lower the initial hemoglobin level, the greater the increase on supplementation. It is a fact that the body dictates the amount of iron to be absorbed depending on its own iron status(13). Even in the case of weekly twice-supplemented subjects of all categories, this trend was observed.

One of the problems of iron supplementation is that it causes unpleasant gastrointestinal side effects like epigastric pain, nausea, vomiting, diarrhea *etc*. This could be one of the reasons why many subjects discontinue the intake of the supplement. Weekly twice supplementation seems to have a definite advantage over daily supple-mentation in this aspect. In this study while 57.84% of the daily supplemented subjects suffered unpleasant side effects, only 5.94% of the weekly twice-supplemented subjects had adverse effects. This could probably be due to the avoidance of iron overload in the stomach of the subjects due to intermittent

TABLE I– *Changes in Hemoglobin of Anemic Subjects During Supplementation*

Degree of anemia	Regimen of Supplementation	Mean hemoglobin g/dL on					
		0 day	21 days	42 days	63 day	84 days	Net Increase in hemoglobin
Mild n=67	Daily Supplement (DS) n=33	10.42 ±0.36	11.16[a]* ±0.36	11.79[b] ±0.39	12.31[c] ±0.44	12.84[d] ±0.54	2.42 ±0.53
	Weekly Twice (WTS) n=34	10.51 ±0.35	10.95[a]* ±0.39	11.38[b]* ±0.43	11.91[c]* ±0.53	12.49[d]* ±0.65	1.99 ±0.63
Moderate n=75	DS n=39	9.18 ±0.48	9.99[a] ±0.51	10.85[b] ±0.49	11.57[c] ±0.52	12.25[d] ±0.53	3.08 ±0.69
	WTS n=36	9.33 ±0.43	10.07[a] ±0.51	10.65[b] ±0.61	11.32[c] ±0.52	12.10[d] ±0.43	2.77 ±0.53
Severe n=61	DS n=30	7.40 ±0.76	8.45[a] ±0.61	9.59[b] ±0.61	10.68[c] ±0.58	11.75[d] ±0.46	4.35 ±0.88
	WTS n=31	7.56 ±0.51	8.46[a] ±0.47	9.43[b] ±0.63	10.46[c] ±0.75	11.54 ±0.75	3.98 ±0.89

Total n=203 DS-n=102 WTS-n=101

a,b,c,d: Increase in Hb significant between 0-21,21-42, 42-63 & 63-84 days
* Increase in Hb significant DS & WTS

TABLE II–*Undesirable Side Effects of the Supplement*

Side effects of the supplement	No.of subjects with side effects		Total
	DS group n=102	WTS group n=101	n=203
Abdominal pain	42 (41.18)	5 (4.95)	47 (23.15)
Nausea	11 (10.78)	1 (0.99)	12 (5.91)
Vomiting	6 (5.88)	_ _	6 (2.96)
Total	59 (57.84)	6 (5.94)	65 (32.0)

Values in parenthesis indicate percentages.

Key Message

- Twice weekly supplementation of iron is as efficacious as daily supplementation in adolescent girls.

supplementation. Liu, *et al*.(11) reported that 37% of daily supplemented subjects complained of unpleasant side effects while only 7% of weekly twice supplemented subjects experienced them.

Supervised administration of weekly twice supplementation of iron to anemic subjects was found to be as advantageous as daily supplementation as far as raising the hemoglobin levels were concerned. It has an edge over the traditional supplementation method with regards to occurrence of unpleasant side effects, which could perhaps lead to better compliance among subjects to iron supplementation.

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REFERENCES

1. Chakravarthy I, Sinha R K. Prevalence of micronutrient deficiency based on results obtained from the national pilot programme on control of micronutrient malnutrition. Nutr Rev 2002; 60: S53-S58.
2. Chaturvedi S, Kapil U, Gnansekharan N, Sachdev H P S, Pandey R M, Banti T. Nutrient intake amongst adolescent girls belonging to poor socio-economic groups of rural Rajasthan. Indian Pediatr 1996; 33: 197-201.
3. Sharma A, Prasad K, Rao Vishweswara K. Identification of an appropriate strategy to control anemia in adolescent girls of poor communities. Indian Pediatr 2000; 37: 261-267.
4. Brabin L, Brabin B J. The cost of successful adolescent growth and development in girls in relation to iron and vitamin A status. Am J Clin Nutr 1992; 55: 955-958.
5. Schultink W, Gross R, Gliwitzki M, Karyadi D, Matulassi P. Effect of daily versus twice weekly iron supplementation in Indonesian pre-school children with low iron status. Am J Clin Nutr 1995; 61: 111-115.
6. Dacie J V, Lewis S M. Practical Hematology. Sixth edn Edinburg: Churchill Livingstone; 1984, pp 22-49.
7. World Health Organization. Nutritional anemia. WHO Technical Report Series no. 405 Geneva. WHO, 1968.
8. International Nutritional Anemia Consultative Group: Measurement of iron status. Washington DC. The Nutrition Foundation, 1985.
9. Vijaylakshmi V. Identification of field techniques to measure the physical work performance and to study the influence of iron deficiency in rural, school going adolescent children(13-15 years) PhD thesis submitted to ANGR Agricultural University, Hyderabad, 1997.
10. UNICEF-WHO Joint committee on Health Policy. Strategic approach to operationalizing selected end decade goals: Reduction of iron deficiency anemia. JCHP 30/95/4.5. Geneva, WHO, 1995.
11. LiuX N, Kang J, Zhao L , Viteri FE. Intermittent iron supplementation is efficient and safe. Food Nutri Bull 1995; 16: 139-146.
12. Gross R, Schultink W, Juliawati. Treatment of anemia with weekly iron supplementation. Lancet 1994; 344: 821.
13. Beard J L, Dawson H, Pinero J D. Iron Metabolism: A comprehensive review. Nutr Rev 1996; 54: 295-317.