Original Article

Will iron supplementation given during menstruation improve iron status better than weekly supplementation?

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To investigate the efficacy of two different iron supplements administered either on a weekly basis or during menstruation, a 16-week community experimental study was carried out among postmenarcheal female adolescent students in Kupang, East Nusa Tenggara, Indonesia. Forty eight students received a placebo tablet weekly, 48 other students got an iron tablet weekly and 41 students took an iron tablet for four consecutive days during their menstruation cycle. All subjects were given deworming tablets before supplementation. Haemoglobin, serum ferritin, height, weight, mid-upper arm circumference and dietary intake were assessed before and after intervention. The supplementation contributed to a significant improvement in the iron status of the intervention groups compared to the placebo group ($P < 0.05$). In the menstruation group, the haemoglobin concentrations of the anaemic subjects improved significantly ($P < 0.05$) while for the non-anaemic subjects, serum ferritin concentrations also increased significantly ($P < 0.05$). In the weekly group for anaemic and non-anaemic subjects, there was a significant increase in both haemoglobin and serum ferritin concentrations ($P < 0.05$). This study revealed that weekly supplementation of iron tablets continued for 16 weeks contributed a higher improvement to haemoglobin concentration, compared with supplementing iron tablets for four consecutive days during menstruation for four menstrual cycles. This suggests that weekly iron supplementation is preferable.

Key words: adolescents, anaemia, East Nusa Tenggara, Indonesia, iron supplementation, Kupang, menstruation.

Introduction

Iron deficiency anaemia is still the most prevalent nutritional problem encountered worldwide. The populations most at risk are pregnant women and children.[1] Since the 1970s, iron supplementation programs have been established in many countries; however, the programs have not succeeded in satisfactorily reducing the prevalence of anaemia. Factors such as low coverage rates of public health care systems and insufficient tablet distribution have contributed to reduce the efficiency of supplemental iron programs.[2] Another major constraining factor is low compliance due to side-effects of the tablet.[3]

So far, iron supplementation programs have targeted pregnant women with a curative approach.[4] However, the depletion of iron stores in women starts during adolescence with the onset of menstruation.[5] Therefore, iron supplementation programs targeted at female adolescents as a preventive approach may have the advantage of building up and maintaining the iron stores before pregnancy.[6]

Iron requirements are high among adolescents due to the processes of growth spurts, sexual maturation and menstrual blood loss. Menstruation typically starts about a year after peak growth. The mean requirement for absorbed iron reaches a maximum of about 1.5 mg/day at peak growth and falls to only 1.3 mg/day due to menstrual loss.[7] The daily requirement of iron among female adolescents is about 1.2–1.68 mg, consisting of 0.65–0.79 mg/day basal iron loss[8] and 0.48–1.9 mg/day iron loss during menstruation.[9]

There is considerable variation in menstrual blood loss among women, but the loss for any given woman is very consistent.[9] This is related to body size, is probably genetically influenced and is independent of haemoglobin values.[10]

The effect of growth on iron requirements changes considerably during the teenage period, with a maximum at the growth spurt around the age of 13 years. Between the ages of 13–16 years, around 0.38 mg extra iron is required daily to cover growth requirements. The total iron requirements in menstruating teenage girls can then be calculated by adding basal losses, growth requirements and menstrual iron requirements and their variations.[10]

A study by Hallberg *et al.* in 1995[11] revealed that iron absorption from a 0.56 mg dose of ferrous iron (given in a fasting state) increased continuously with increasing iron requirements. Other studies in European countries[10] have shown that the probability of developing iron deficiency increases with increasing losses of menstrual blood and haemoglobin values

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Accepted 14 May 2001

become lower. The effects of iron supplementation have therefore been the subject of several studies.

In Indonesia, studies of different population groups have shown that weekly administration of iron supplements successfully reduces anaemia. This is as effective as daily administration in preschool children,[12] adolescent girls[13] and in non-pregnant[14] and pregnant women.[15] However, low compliance is a major weakness of using weekly iron supplementation.[3] On the other hand, menstruation serves as a unique time for taking oral medicines. Supplements administered during the menstrual cycle may increase compliance and therefore, could be used as an alternative approach in treating anaemia. It was the aim of this study to compare the efficacy of weekly and menstrual period iron supplementation among adolescents.

Subjects and methods

This single blind community experimental study was undertaken from August to December of 1998 in Kupang, East Nusa Tenggara, in the eastern part of Indonesia.

Subjects

One hundred and fifty postmenarcheal female adolescent students were chosen from two different junior high schools in Kupang. One hundred of them were recruited from one school and allocated randomly to placebo or weekly groups. The other 50 students were recruited at random from a different junior high school and allocated to the menstruation group. This allocation method was chosen for practical reasons to avoid confusion in the field. Both schools were public schools that were located in relatively similar urban areas. The study protocol was approved by the Human Ethics Committee of the Faculty of Medicine, University of Indonesia, Jakarta, Indonesia. This protocol was fully explained to the subjects and informed consent was obtained from each subject and their parents before the study was implemented.

Methods

Sample size was calculated based on a standard formula for comparing two means.[16] Assumption on the difference in haemoglobin level before and after the intervention was 5.6 g/L with the standard deviation of 7.8, based on the previous study carried out by Angeles-Agdeppa *et al*.[17] Type I and type II errors were set at 0.05 and 0.1, respectively. After allowing for a 20% dropout rate, the total number of subjects to be included from each group was 50.

The study compared three groups that received either a placebo tablet weekly, an iron tablet weekly or an iron tablet taken for four consecutive days during menstruation to ensure the subjects received the same number of tablets per month. Weekly supplementation was implemented every Wednesday for both placebo and iron groups. Subjects in the menstruation group were given an iron tablet each day for four consecutive days, only when they were menstruating. For subjects attending morning classes, the tablets were taken in the morning. Subjects attending afternoon classes took the tablets in the afternoon.

The iron tablet used in this study contained 60 mg elemental iron and 0.25 mg folic acid in the form of 200 mg ferrous sulphate and was produced by PT Indo Farma, Jakarta, Indonesia. To control parasitic infestation, all subjects were given a single dose of 500 mg mebendazole three days before supplementation. The supplementation was conducted over 16 weeks under the supervision of teachers appointed from the participating schools and the first author. Due to unfavourable environmental conditions in the study area during late November 1998, the 16th week tablets for the placebo and weekly groups were taken in the 17th week. The second blood collection was done around five days after. In the menstruation group, the second blood collection was taken 1–19 days after taking the 16th tablet.

The weight, height, and MUAC of the subjects were measured at the beginning and the end of the study using an electronic weighing scale (SECA 770, SECA, Hamburg, Germany), microtoise and measuring tape, respectively.[18]

Venous blood samples of 2.5 mL were collected at the beginning and end of the intervention by laboratory technicians. Immediately after venipuncture, around 20 µL of blood was collected with a micropipette and transferred onto filter paper (Whatman no. 1, Balston, Maidstone, UK) for haemoglobin determination using the cyanmethemoglobin method[19] (Merck-test 3317, Merck, Darmstadt, Germany). The blood spots were collected in duplicate, air-dried for about 30 min, put into small plastic bags and stored at 4°C. The rest of the samples were centrifuged within 1 h of blood collection. The serum was collected and stored at –25°C for serum ferritin determination using a commercial kit (Imx System, Abbott, Abbott Park, IL, USA) for the enzyme immunoassay method.[19] The haemoglobin analysis was done after one month. Therefore, a correction factor of 1.1 (based on unpublished data from the Bogor Nutrition Research and Development Center) was set in determining the haemoglobin concentration. All haematological analyses were done in duplicate and conducted at the SEAMEO-TROPMED laboratory within one month of blood collection.

Information on socioeconomic background, health condition, eating patterns and environmental sanitation were obtained using a structured questionnaire. A semiquantitative food frequency questionnaire was administered to obtain usual food intakes before and after the intervention. Food models were used to estimate portion size. The Indonesian Food Composition Tables were used to convert foods into nutrients. Nutrient analysis was carried out using the World Food Program version 2.0 (University of California, Berkeley, CA, USA).

Statistical analyses

Statistical analyses were carried out using SPSS for Windows, version 7.5 (SPSS, Chicago, IL, USA). Descriptive analyses were used to present subjects' characteristics. The chi-squared test was employed to assess associations between groups and socioeconomic backgrounds, health conditions, eating patterns and environmental sanitation. The normality of the data was checked using the Kolmogorov–Smirnov test.

The paired *t*-test was used to show differences before and after the intervention. Analyses of variance (ANOVA) were used to identify differences in continuous factors between groups. When adjustment for possible confounders was required, analyses of covariance (ANCOVA) were used. *P*-values of less than 0.05 were considered significant.

Results

The final data set consisted of 48 subjects in each of the placebo and weekly groups (4% dropouts in each group), and 41 subjects in the menstruation group (18% dropouts). Common reasons for dropping out were refusal to undergo blood collection, absent from class on the day of blood collection, transfer to another school and no menstruation during the fourth month of supplementation. After excluding extreme values (serum ferritin changes of more than 50 μg/L), a complete data set of serum ferritin levels covered 34 subjects in the placebo group, 31 subjects in the weekly group and 30 subjects in the menstruation group.

The mean age of the subjects was 14.6 ± 1.1 years and the mean age at menarche was 12.6 ± 1.0 years. Over 50% of the subjects experienced more than three days of menstruation. To estimate how heavy the subjects' blood loss was during menstruation, number of tampons used per day was employed as the indicator. Around 50% of the subjects in each group used more than two tampons. The initial nutritional status of the subjects indicated by height, weight, and MUAC measurements was homogeneously distributed among the three groups. None of these characteristics were statistically different among the three groups (Table 1).

The prevalence of anaemia in the placebo, weekly and menstruation groups was statistically different ($P < 0.05$) at 47.9, 72.9 and 24.4%, respectively. The initial haemoglobin concentration was lowest in the weekly group. The serum ferritin concentration of the placebo group was significantly higher than in the menstruation group (Table 1).

As for the subjects' iron status, the intervention significantly improved the haemoglobin concentration and serum ferritin level of the weekly and menstruation groups. In the menstruation group, anaemic subjects improved their haemoglobin concentrations significantly while non-anaemic subjects significantly improved their serum ferritin concentrations. The anaemic and non-anaemic subjects in the weekly group showed increases in both haemoglobin and serum ferritin concentrations (Table 2).

Among the anaemic subjects, the change in haemoglobin concentration of the weekly group was higher than those of the menstruation and placebo groups. However, among the non-anaemic subjects, the change in haemoglobin concentration of the weekly group was only slightly higher than that of the menstruation group. While the changes in serum ferritin level among the anaemic subjects were statistically similar between the three groups, the placebo group was found to have the lowest change in serum ferritin concentration among non-anaemic subjects (Table 3).

The subjects' socioeconomic background, health condition, eating patterns and environmental sanitation were distributed almost homogeneously among the three groups. Less than 20% of the subjects admitted to having experienced malaria, without any further confirmation. None of the subjects were smokers or multivitamin users. Most of the subjects claimed to always take plain water with their daily meal; however, the food frequency questionnaire showed that over 80% of them drank tea at least once a day.

Table 1. Specific characteristics of Indonesian female adolescent students in the three groups for administration of iron supplements

Characteristics	Placebo (n = 48)	Weekly (n = 48)	Menstruation (n = 41)	Total (n = 137)
Age (years)	14.5 ± 1.2	14.7 ± 1.0	14.7 ± 1.1	14.6 ± 1.1
Age of menarche (years)	12.4 ± 1.0	12.6 ± 1.2	12.7 ± 0.8	12.6 ± 1.0
Duration of menstruation (%)				
1–3 days	45.8	37.5	36.6	40.1
> 3 days	54.2	62.5	63.4	59.9
Number of tampons used per day (%)				
1–2 tampons	35.4	50.0	53.7	46.0
> 2 tampons	64.6	50.0	46.3	54.0
Anthropometric data				
Height (m)	1.47 ± 0.1	1.48 ± 0.1	1.48 ± 0.1	1.48 ± 0.1
Weight (kg)	38.5 ± 4.5	38.0 ± 4.6	40.0 ± 5.2	38.8 ± 4.8
MUAC (cm)	21.2 ± 1.6	20.9 ± 1.9	21.2 ± 1.8	21.1 ± 1.8
Haematological data				
Prevalence of anaemia (%)	47.9	72.9[a]	24.4	49.6
Haemoglobin (g/dL)	11.9 ± 1.3[b]	11.3 ± 1.3	12.5 ± 1.1[c]	11.9 ± 1.3
Ferritin (μg/L)	21.3 ± 2.2[d]	18.7 ± 3.2	16.7 ± 3.3	19.5 ± 1.7

P-values < 0.05 were considered significant [a]between menstrual and weekly administration (Chi-squared test), [b]between placebo and weekly administration (ANOVA test), [c]between menstrual and weekly administration (ANOVA test) and [d]between placebo and menstrual administration (Mann–Whitney test). All values are given as mean ± SD, except ferritin (μg/L) which is given as median ± SE. MUAC, mid-upper arm circumference.

Table 2. Haematological values of Indonesian female adolescent students before and after administration of supplements

Groups	*n*	Before	After
Placebo			
Anaemic			
Haemoglobin (g/dL)	23	10.85 ± 0.89	10.95 ± 1.03
Ferritin (μg/L)	17	23.06 ± 10.69	26.57 ± 16.46
Non-anaemic			
Haemoglobin (g/dL)	25	12.94 ± 0.67	13.04 ± 0.82
Ferritin (μg/L)	17	22.76 ± 11.11	24.63 ± 9.79
Weekly			
Anaemic			
Haemoglobin (g/dL)	35	10.76 ± 1.07	12.38 ± 1.47[a,b]
Ferritin (μg/L)	23	23.05 ± 15.76	30.88 ± 23.39[b]
Non-anaemic			
Haemoglobin (g/dL)	13	12.67 ± 0.44	13.27 ± 0.73[b]
Ferritin (μg/L)	8	27.97 ± 25.18	45.45 ± 30.87[a,b]
Menstruation			
Anaemic			
Haemoglobin (g/dL)	10	11.03 ± 0.90	11.64 ± 0.65 [b]
Ferritin (μg/L)	8	14.48 ± 19.96	14.94 ± 14.45
Non-anaemic			
Haemoglobin (g/dL)	31	12.97 ± 0.62	13.24 ± 0.50 [b]
Ferritin (μg/L)	27	23.56 ± 16.04	36.46 ± 19.86 [b]

P-values < 0.05 were considered significant [a]between weekly and placebo (ANOVA test) and [b]between before and after administration (paired *t*-test). All values are given as mean ± SD.

Table 3. Iron status change in Indonesian female adolescent students after supplementation[†]

Indicators	Placebo		Weekly		Menstruation	
	Mean ± SD	*n*	Mean ± SD	*n*	Mean ± SD	*n*
Haemoglobin change (g/dL)						
Anaemic	0.01 ± 0.65	23	1.62 ± 1.26[a,b]	35	0.61 ± 0.76	10
Non-anaemic	0.10 ± 0.51	25	0.59 ± 0.62[a]	13	0.27 ± 0.25	31
Total	0.01 ± 0.57	48	1.34 ± 1.21[a,b]	48	0.35 ± 0.45	41
Ferritin change (μg/L)						
Anaemic	3.51 ± 10.58	17	7.83 ± 14.51	23	0.46 ± 7.07	7
Non-anaemic	1.87 ± 11.66	17	17.46 ± 8.87[a]	8	12.90 ± 13.32[c]	23
Total	2.69 ± 10.99	34	10.32 ± 13.82[a]	31	9.99 ± 13.17[c]	30

[†] After controlling for initial haemoglobin values. *P*-values < 0.05 were considered significant using the ANCOVA test [a]between placebo and weekly administration, [b]between weekly and menstrual administration and [c]between placebo and menstrual administration.

Before the study and extending to during the intervention, nutrient intake was significantly lower in terms of energy, carbohydrate, protein, fat, folate, iron, vitamin A, vitamin C, phytate, calcium and zinc. However, no significant differences were found among the three groups in terms of the levels of these nutrients during the intervention. The dietary iron intakes indicated that less than 10% of subjects in the three groups consumed safe levels of iron, (i.e. 67–99.9% of the recommended daily allowance (RDA))[20] and the majority of the subjects (over 80%) consumed less than two-thirds of the RDA of iron.

Discussion

One of the main problems of the iron supplementation program was low compliance.[3] In 1996, the Ministry of Health in the Republic of Indonesia recommended giving iron tablets to women of reproductive age for as often as 10 days during menstruation.[21] As menstruation occurs at a specific time during each cycle, administration of iron tablets during this time may increase compliance. As there is not yet an efficacy study comparing exactly the same doses and amounts of iron tablets administered either on a weekly basis or during menstruation, doubts must persist. Since the existing program uses weekly supplementation, it is important to compare it with the new recommendation in order to increase compliance. In this study, four tablets were used instead of 10 to equalise the dosage of iron received. The validity of this approach was then confirmed by the fact that over 50% of the subjects' menstrual cycles took longer than 3 days (Table 1).

As has already been confirmed by earlier studies,[11–14,16] the present study revealed that weekly iron supplementation significantly improved the iron status of female adolescents. This was shown by increased haemoglobin concentrations and serum ferritin levels when compared with a placebo group (Table 2).

Another finding of this study was the presence of a similar effect when iron supplements were administered for four days during menstruation. In the anaemic subgroup, improvement was observed as an increase in haemoglobin concentrations whereas in the non-anaemic subgroup, improvement was observed as an increase in serum ferritin levels (Table 2). These data support the conclusion that in anaemic persons, absorbed iron is first used to normalise the haemoglobin concentration of the plasma so that it can function in its essential role of supplying tissues with oxygen. Only when the haemoglobin concentration is close to a satisfactory level are iron stores then replenished, as shown by a subsequent increase in serum ferritin levels.[22] The presence of iron deficiency increases iron absorption, even at times when depleted iron stores are not accompanied by changes in serum iron, haemoglobin levels or iron-turnover rates. Similarly, increased iron stores are associated with decreased iron absorption.[23]

More anaemic subjects were found in the weekly group, with the prevalence of anaemia being 72.9% in this group. The issue was that the placebo and weekly groups were composed of subjects from the same school whereas those in the menstruation group were from another school. This allocation was necessary to maintain the single-blind method implemented in the other two groups. Therefore, the initial haemoglobin concentration was considered statistically as a factor in the analysis of covariance. The initial anaemia status was coded as < 12.0 g/dL (anaemic) and ≥ 12.0 g/dL (normal). There was a significant association between treatment type and initial anaemia status for change in haemoglobin level ($P = 0.011$) but the change in serum ferritin level was not significant ($P = 0.077$).

This study revealed that the different methods of iron supplement administration produced significantly different effects. Iron supplementation given weekly gave a greater difference in haemoglobin concentration after four months of intervention, compared with that given during menstruation. This may result from three different possibilities. Firstly, consuming the iron supplement over four consecutive days during menstruation may saturate the gut,[24] leading to a decrease in the iron absorption rate later on.[25] Secondly, menstruating subjects had physiologically high iron requirements due to additional iron loss from menstrual bleeding,[7] so supplementing 16 iron tablets may not be adequate for menstruating adolescents. And lastly, the presence of lower amounts of vitamin C (an iron absorption enhancer)[26] and higher amounts of calcium[27] and phytate (more than 500 mg/day among the three groups,[28] acting as iron absorption inhibitors) in the subjects' daily nutrient intakes may result in the low bioavailability of iron present in the body. This condition is actually the result of a vicious cycle where iron is absorbed well in an empty stomach but then stimulates the presence of gastrointestinal side-effects.[29] However, in the present study, the iron tablets were taken either in the morning (for subjects attending morning classes) or in the afternoon (for subjects attending afternoon classes) without further confirmation as to whether or not the tablets were taken after meals.

This study confirms that iron supplementation given either weekly or during menstruation for four months is more effective in improving the iron status of female adolescents than no iron supplementation. The four month iron supplementation program, which involves the consumption of 16 iron tablets given during menstruation, contributed a smaller effect in improving the adolescents' haemoglobin concentrations, compared with the weekly schedule. This suggested that weekly iron supplementation is still preferred. Furthermore, a study evaluating iron absorption during menstruation is required to get a clear picture of its mechanism in the bodies of menstruating women. Further investigations would then be needed to refine the dosage and the number of tablets given per menstrual cycle.

Acknowledgements. The authors wish to thank SEAMEO-TROPMED Regional Center for Community Nutrition in Jakarta for their financial support. We are grateful to all of the enumerators for their assistance in data collection, and to the teachers at SMPN 4 and SMPN 3 Kupang for their dedicated supervision during the study. We extend our deep appreciation to all the volunteers whose participation made this study possible.

References

1. Yip R. Iron Deficiency. Contemporary Scientific Issues and International Programmatic Approaches. J Nutr 1994; 124: 1479S–1490S.
2. Schultink WJ, Gross R. Iron deficiency alleviation in developing countries. Nutr Res Rev 1996; 9: 281–293.
3. Schultink WJ. Iron-supplementation programmes. Compliance of target groups and frequency of tablet intake. Food Nutr Bull 1996; 17: 22–26.
4. Gross R, Angeles-Agdeppa I, Schultink W, Dillon D, Sastroamidjojo S. Daily versus weekly iron supplementation. Programmatic and economic implications for Indonesia. Food Nutr Bull 1997; 18: 64–70.
5. MacPhail P, Bothwell TH. The prevalence and causes of nutritional iron deficiency anemia. In: Fomon SJ, Zlotkin S, eds. Nutritional Anemia. Nestlé Nutrition Workshop Series, Vol. 30. New York: Nestec, 1992.
6. Latief D. Iron supplementation of non-pregnant women prior to pregnancy. In: Krause VM, Yip R, eds. Improving Iron and Zinc Nutrition in Infancy and Early Childhood Proceedings of the Bali Consultation Meeting for the planning of multi-country iron and zinc intervention trials. Bali: UNICEF, 1997.
7. Dallman PR. Changing iron needs from birth through adolescence. In: Fomon SJ, Zlotkin S, eds. Nutritional Anemia. Nestlé Nutrition Workshop Series, Vol. 30. New York: Nestec, 1992.
8. Fairweather-Tait S. Iron Biochemistry. In: British Nutrition Foundation. Iron Nutritional, Physiological Significance. London: Chapman and Hall, 1995.
9. Aggett P. Iron and Women in Reproductive Years. In: British Nutrition Foundation. Iron Nutritional, Physiological Significance. London: Chapman and Hall, 1995.
10. Hallberg L, Rossander-Hulten L. Iron requirements in menstruating women. Am J Clin Nutr 1991; 54: 1047–1058.

11. Hallberg L, Hulten L, Bengston C, Lapidus L, Lindstedt G. Iron balance in menstruating women. Eur J Clin Nutr 1995; 49: 200–207.
12. Schultink WJ, Gross R, Gliwitzki M, Karyadi D, Matulessy P. Effect of daily versus biweekly supplementation in Indonesia preschool children with a low iron status. Am J Clin Nutr 1995; 61: 111–115.
13. Katelhut A, Schultink W, Angeles I, Gross R, Pietrzik K. The effects of weekly iron supplementation with folic acid, vitamin A, vitamin C on iron status of Indonesian adolescents. Asia Pac J Clin Nutr 1996; 5: 181–185.
14. Gross R, Schultink W, Juliawati. Treatment of anemia with weekly iron supplementation. Lancet 1994; 344: 821.
15. Ridwan E, Schultink W, Dillon D, Gross R. Effect of weekly iron supplementation of pregnant Indonesian women are similar to those of daily supplementation. Am J Clin Nutr 1996; 63: 884–890.
16. Hassard TH. Understanding Biostatistics. London: Mosby Year Book, 1991.
17. Angeles-Agdeppa I, Schultink W, Sastroamidjojo S, Gross R, Karyadi D. Weekly micronutrient supplementation to build iron stores in female Indonesian adolescents. Am J Clin Nutr 1997; 66: 177–183.
18. WHO. Physical status. The use and interpretation of anthropometry. Report of WHO expert committee. Geneva: WHO, 1995.
19. INACG. Measurement of Iron Status. A report of the International Nutritional Anemia Consultative Group (INACG). Washington DC, USA: The Nutrition Foundation, 1985.
20. Nguyen TL. Effects of vitamin A and iron fortified supplementary food on vitamin A and iron status of rural preschool children in Vietnam (PhD Thesis). SEAMEO-TROPMED RCCN, University of Indonesia, Jakarta, Indonesia, 1997.
21. Ministry of Health. The protocols of iron supplement administration for community workers. Republic of Indonesia: Directorate of Community Nutrition, Directorate General of Community Health, Ministry of Health, 1996.
22. Bothwell TH, Charlton RW. Iron deficiency in women. A report of the International Nutritional Anemia Consultative Group (INACG). Washington DC, USA: The Nutrition Foundation, 1981.
23. Lanzkowsky P. Iron Deficiency in Adolescents. In: Winick M, ed. Adolescent Nutrition. New York: John Wiley and Sons, 1982.
24. Goddard WP, Coupland K, Smith JA, Long RG. Iron uptake by isolated human enterocyte suspensions in vitro is dependent on body stores and inhibited by other metal cations. J Nutr 1997; 127: 177–183.
25. Viteri FE, Xunian L, Tolomei K, Martin A. True absorption and retention of supplemental iron is more efficient when iron is administered every three days rather than daily to iron-normal and iron-deficient rats. J Nutr 1995; 125: 82–91.
26. Hunt JR, Muller LM, Lykken GI, Gallagher SK, Nielsen FH. Ascorbic acid: effect on ongoing iron absorption and status in iron-depleted young women. Am J Clin Nutr 1990; 51: 649–655.
27. Fairweather-Tait S. Iron Absorption. In: British Nutrition Foundation. Iron Nutritional, Physiological Significance. London: Chapman and Hall, 1995.
28. Kim Y, Carpenter CE, Mahoney AW. Gastric acid production, iron status, and dietary phytate alter enhancement by meat of iron absorption in rats. J Nutr 1993; 123: 940–946.
29. Cook JD, Reddy MB. Efficacy of weekly compared with daily iron supplementation. Am J Clin Nutr 1995; 62: 117–120.