EFFECT OF DIETARY HEME-IRON INTAKES ON THE PREVENTION OF IRON-DEFICIENCY ANEMIA

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Abstract

Purpose : This study was undertaken to clarify the effect of heme-iron supplementation on the prevention of iron-deficiency anemia in male collegiate distance runners.

Methods : Forty-one male collegiate runners were divided into three groups, consisting of a heme-iron group(HI), a citrate-iron group(CI) and a non-iron group(NI). Iron tablets(heme-iron or citrate-iron)were administered at a dose of 7 mg per day for two months. The blood components and nutritional intakes were estimated before and after the intervention.

Results : The nutritional intakes did not differ among the three groups. The red blood cell, hemoglobin, hematocrit, ferritin, Glutamic-Pyruvate Transferase and γ -Glutamyl Transpeptidase levels were unchanged throughout the experimental periods. After the intervention, the serum iron levels significantly decreased in the NI group but not in the iron-supplemented groups, while the reticulocytes counts increased among the three groups.

Conclusion : The small amount of heme-iron supplementation was thus found to have a preventive effect on iron deficiency anemia without causing any negative side effects.

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key word : runner, heme-iron, nutritional intake, liver function

Introduction

The decreased work capacity due to iron deficiency anemia in men has been well documented. Iron deficiency sometimes impairs the adaptive response to aerobic performance and it may impair the ability to sustain physical performance at 65~85% of maximal O_2 utilization capacity($\dot{V}O_{2max}$), i. e., endurance^{1,2}). To reduce the impairment of aerobic performance induced by iron deficiency, many iron supplementation programs have been conducted for women using nonheme-iron. However, there have so far been few such reports on male runners. Telford et al.³) indicated that footstrike is the major contributor to haemolysis during running. If it is the main factor in the development of iron-deficiency anemia,

then the prevention of footstrike haemolysis might be an extremely important concern for athletes, such as long distance runners.

It is well accepted that the bioavailability of dietary iron has a greater impact on the body iron status than does the ingested amount of iron or the composition of meals ; the difference in absorption between heme and nonheme-iron is therefore important^{4,5}). The effects of heme-iron supplementation on iron depletion without anemia have not yet been fully characterized in male runners.

In this study, we examined the effect of oral heme-iron supplementation for two months on the prevention of iron-deficiency anemia in male collegiate runners.

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Methods

Subjects : Forty-one collegiate male runners participated in this study for two months. Each participant gave their signed informed consent before the study began. The Tokyo University of Agriculture's Ethics Committee on Human Subjects approved this study.

Study design : Based on their basal body iron status, the subjects were assigned to three groups : including a non-supplement group(NI group, $n=13$), a heme-iron supplement group(HI group, $n=13$), and a citrate iron supplement group(CI group, $n=15$). All subjects completed an 8-week supplementation period. The heme- and citrate-iron tablets were kindly provided by Itoh Hamu Life Science Co., Japan ; they contained 3.5 mg elemental iron and were taken two times a day by each subject. The subjects were instructed to consume the tablets with their breakfast and dinner. They were also instructed to avoid the consumption of any other multivitamin and mineral supplements during the study period. All subjects recorded their tablet intake, consumption of medication, illness, gastrointestinal symptoms, physical activity, and musculoskeletal problems.

At baseline(Before)and at the end of the 8-wk intervention(After), all participants were instructed to refrain from strenuous activity for 24 hours and were asked to fast overnight before the day of blood sampling.

Dietary assessment : All subjects completed a semi-quantitative food frequency questionnaire(FFQ)for the last 2—3 weeks using the EXCEL computer software program EIYOU KUN, consisting of a questionnaire based on the Standard Tables of Food Composition for Japanese⁶).

Blood collection and measurements : Blood samples were taken at baseline(May)and at 8 wks after the start of the iron intervention(July). Blood samples were collected via a venepuncture of the antecubital vein in a sitting position on an empty stomach and the samples were drawn and kept in two evacuated

tubes at the time the sample was obtained: one contained EDTA, while the other was empty. Hemoglobin(Hb)and hematocrit(Ht)were assayed in whole blood immediately after sampling. Hematological parameters, including red blood cell counts(RBC), Hb, Ht, white blood cell counts(WBC), the mean corpuscular volume(MCV), the mean corpuscular hemoglobin level(MCH), and the mean corpuscular hemoglobin concentration(MCHC), were estimated using a hematological Coulter CBC5 analyzer(Remed, Poland). The levels of reticulocytes, iron, ferritin, total iron binding capacity(TIBC), erythropoietin(EPO), haptoglobin(hp), albumin(Alb), blood urea nitrogen(BUN), uric acid(UA), glutamic oxaloacetic transaminase(GOT), glutamic pyruvic transaminase(GPT)and γ -glutamyl transpeptidase(γ -GTP)in serum were analyzed by Medical Laboratory Co. Ltd.(Kanagawa, Japan)

Statistical analysis : All data were expressed as the mean $\pm$ standard deviation(SD). The statistical analysis was performed using the Statistical Package for Social Sciences(SPSS for Windows, version 12.0J, SPSS Inc., Japan). Values of $p < 0.05$ were considered to be statistically significant. The following statistical methods were used for comparisons between the groups.

To compare multiple independent groups(groups, time), two-way repeated measure analysis of variance(ANOVA)was performed as the initial step. If any differences were observed(main effect of group, interaction effect, $p < 0.05$) post hoc pairwise comparisons for the main effect on the time were by means of Friedman's nonparametric ANOVA. If a difference was observed in the main effect of the time, then the variables were analyzed by the Wilcoxon's signed-rank test. To compare these three independent groups, we checked the homogeneity of variance and tested for normal distribution in each group. If normal distributions were hypothesized in these groups, then a t-test was performed to compare the two means. If not, then the Mann-Whitney rank-test was performed. Statistical significance was accepted at a value of $p < 0.05$.

Results and Discussion

No main effect of group or time and no group x time interaction effect on the running distances were observed. The mean running distances ($\pm$ SD) in the NI, HI, and CI groups were 647 ± 197 km, 559 ± 141 km, and 708 ± 146 km in May and 648 ± 197 km, 560 ± 141 km, and 708 ± 145 km in July, respectively. There was no significant difference among the three groups; thus suggesting that the dietary iron supplementation did not affect the running distances.

No main effect of time or group and no time x group interaction effect were observed for the nutritional intakes or for the food intakes except for white vegetables (time, $p < 0.05$). The mean intakes of cereals in May and in July were 244 ± 82 g and 233 ± 70 g, respectively; potatoes 36.6 ± 10.1 g and 25.9 ± 7.1 g; beans 86.3 ± 17.9 g and 85.3 ± 15.2 g; fruits 66.6 ± 15.8 g and 76.2 ± 17.8 g; total vegetables including green and white vegetables 269.6 ± 108.8 g and 208.2 ± 75.4 g; beverages 250 ± 184 g and 309 ± 230 g; milk and dairy products 271 ± 79 g and 317 ± 77 g. Furthermore, there was no significant difference in the dietary iron intakes among the three groups during these experimental periods (mean dietary intake, 10.8 mg). Accordingly, the oral iron intakes were greater in both the HI and CI groups than in the NI group.

Although significant main effects of the time on RBC ($p < 0.05$), MCV ($p < 0.001$), MCHC ($p < 0.001$), and MCH ($p < 0.001$) were observed, no main effect of the group and no time x group interaction effect were observed. The levels of RBC ($p < 0.05$) and MCHC ($p < 0.001$) were significantly lower in July than in May, and levels of MCV ($p < 0.001$) and MCH ($p < 0.001$) were significantly higher in July than in May. The mean ($\pm$ SD) serum iron levels in May and in July were 156 ± 44 μ g/dl and 109 ± 22 μ g/dl in the NI group, 112 ± 33 μ g/dl and 89 ± 43 μ g/dl in the HI group, and 109 ± 28 μ g/dl and 99 ± 33 μ g/dl in the CI group, respectively. The mean ($\pm$ SD) transferrin saturation levels in May and in July were $37.1 \pm 10.8\%$ and $28.2 \pm 6.9\%$ in the NI group,

$26.4 \pm 8.1\%$ and $23.3 \pm 11.5\%$ in the HI group, and $26.6 \pm 7.1\%$ and $26.5 \pm 9.6\%$ in the CI group, respectively. A main effect of the group was observed in serum iron ($p < 0.01$) and transferrin saturation ($p < 0.05$). Main effects of time on TIBC ($p < 0.001$), erythropoietin ($p < 0.05$), serum iron ($p < 0.001$), transferrin saturation ($p < 0.05$), and reticulocytes ($p < 0.001$) were observed (Fig. 1). The mean erythropoietin concentrations of all three groups were significantly higher in July than in May, while the serum iron levels were significantly lower in July than in May, especially in the NI group. The mean transferrin saturation levels in the NI group significantly decreased in July, but not in either the HI or the CI groups. However, no time x group interaction effects were observed for any hematological parameters.

No main effect of the group, the main effect of the time and the group x time interaction effect on UA, GPT, and γ -GTP was observed (Table 1). These results suggested that dietary heme- or citrate-iron supplementation for 8 weeks at a level of 7 mg per day did not induce any negative side effects in the bodily functions. It seems likely that dietary iron supplementation under our experimental conditions does not have any harmful effect on the liver function, and therefore the consumption of 7 mg of iron per day for 2 months appears to be safe.

Hinton et al.⁷⁾ investigated the effect of iron supplementation on the work rate in iron-depleted nonanemic women during a 15-km time trial and reported that iron supplementation (100 mg of ferrous sulfate) increased the serum ferritin level and decreased the level of transferrin receptors, and the decrease in the 15-km time was also greater in the supplemented group. These results in the hematological changes corresponded well with our ferritin levels (data not shown), thus suggesting that dietary iron supplementation might improve the running time.

Although many reports involve 100 mg iron supplementation, health problems resulting from an excessive intake of iron might occur at this high dose

A. Serum iron ($\mu\text{g/dl}$)

1) Control (NI)

2) Heme-Fe (HI)

3) Citrate-Fe (CI)

B. Transferrin saturation (%)

1) Control (NI)

2) Heme-Fe (HI)

3) Citrate-Fe (CI)

C. Reticulocytes (%)

1) Control (NI)

2) Heme-Fe (HI)

3) Citrate-Fe (CI)

Fig 1. The effect of dietary iron supplementation on the body iron status.

A : The serum iron concentration ($\mu\text{g/dl}$), B : Transferrin saturation (%), C : Reticulocyte counts (%)
 Abbreviations : a-b : significantly different from each other ($p < 0.05$), * : significant difference between the values obtained in May and in July ($p < 0.05$)

level. In our study, subjects consumed an additional 7 mg iron as either heme- or citrate-iron. If the prevention of iron deficiency anemia can be achieved with both small and larger amounts of dietary iron supplementation, then the small amount would thus be preferred because of the lower potential for

adverse effects, especially regarding long-term supplementation.

Further studies are needed to clarify the optimal dosage of dietary iron supplementation for the prevention of iron deficiency anemia.

Table 1. Comparison of the biochemical analysis data.

Intervention	Groups	May	July	ANOVA		
				Group	Int	Group × Int
TP	NI	7.68 ± 0.37	7.77 ± 0.31 a	0.048	0.906	0.486
	HI	7.54 ± 0.26	7.46 ± 0.37 c			
	CI	7.50 ± 0.28	7.47 ± 0.40 b			
	Total	7.57 ± 0.30	7.56 ± 0.38			
ALB	NI	4.73 ± 0.20	5.06 ± 0.26 a,**	0.214	0.000	0.237
	HI	4.71 ± 0.22	4.89 ± 0.25 *			
	CI	4.68 ± 0.14	4.88 ± 0.24 b,**			
	Total	4.71 ± 0.18	4.94 ± 0.26			
A/G	NI	1.62 ± 0.20	1.91 ± 0.26 **	0.855	0.000	0.738
	HI	1.68 ± 0.20	1.93 ± 0.30 **			
	CI	1.67 ± 0.15	1.91 ± 0.22 **			
	Total	1.66 ± 0.18	1.92 ± 0.25			
BUN	NI	17.2 ± 4.3 a	15.2 ± 5.2	0.126	0.000	0.540
	HI	19.8 ± 5.0	17.9 ± 3.3			
	CI	20.7 ± 3.7 b	17.4 ± 4.7 *			
	Total	19.4 ± 4.5	16.9 ± 4.5			
UA	NI	5.82 ± 0.95	5.92 ± 0.76	0.502	0.279	0.538
	HI	5.45 ± 0.82	5.74 ± 1.21			
	CI	5.47 ± 1.13	5.45 ± 0.97			
	Total	5.57 ± 0.96	5.69 ± 1.00			
GOT	NI	28.3 ± 5.1	23.3 ± 5.3 *	0.889	0.000	0.597
	HI	30.2 ± 13.9	22.1 ± 6.6 **			
	CI	27.9 ± 4.5	22.2 ± 5.1 *			
	Total	28.8 ± 8.9	22.5 ± 5.6			
GPT	NI	21.8 ± 4.5	21.8 ± 6.6	0.856	0.302	0.689
	HI	21.7 ± 7.9	19.5 ± 8.8			
	CI	21.7 ± 5.7	20.5 ± 6.2			
	Total	21.7 ± 6.2	20.5 ± 7.2			
γ-GTP	NI	12.9 ± 3.1	13.8 ± 3.5	0.052	0.620	0.391
	HI	10.9 ± 2.8	11.3 ± 1.8 a			
	CI	14.7 ± 6.7	14.0 ± 3.6 b			
	Total	12.8 ± 4.8	13.0 ± 3.2			

Means are significantly different from the May levels ; *p<0.05, **p<0.01.

Different letters indicate a statistically significant difference. all data are expressed as the mean±SD. NI : Control, HI : Heme-iron group, CI : Citrate-iron group.

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