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Annals of Sports Medicine and Research

Research Article

Combined Heme Iron Supplementation and Nutritional Counseling Improves Sports Anemia in Female Athletes

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Submitted: 13 April 2015
Accepted: 14 June 2015
Published: 17 June 2015

Keywords
- Sports anemia
- Female athlete
- Heme iron
- Protein consumption
- Nutritional counseling

Abstract

Athletes frequently suffer from anemia due to rigorous training, reduced food intake (for weight control), and destruction of erythrocytes. Menses can also render anemia improvements problematic. We investigated the effects of a combined supplementation and nutritional counseling intervention in female athletes exhibiting anemic symptoms. Capsules containing heme iron were used for supplementation (Fe at 14 mg/day). Nutritional counseling was based on indices of iron status (blood hemoglobin [Hb], serum ferritin [Fer], and soluble transferrin), nutrient status, and energy expenditure based on food intake and activity logs and training loads. Thirty female participants (mean age = 20.2 ± 1.3 years; Hb, 12.4 ± 0.7 mg/dL; Fer, 17.8 ± 13.7 ng/mL) who engaged in fencing, long jump, handball, or volleyball, were supplemented with capsules every day for 2 months but received no nutritional counseling. Participants in whom initial Hb and Fer values were >11.5 mg/dL and 10 ng/mL, respectively (n = 20), exhibited improved iron status. This was not observed in the remaining 10 participants, all of whom trained excessively and exhibited low Hb and Fer levels; these individuals received daily capsules for a further 2 months in addition to nutritional counseling. Heme iron supplementation and increased levels of food-derived minerals and proteins following nutritional counseling significantly increased blood iron levels, with a concomitant decrease in negative mood and an increase in "vigor" without constipation. In conclusion, long-term heme iron supplementation, in combination with nutritional counseling, could improve sports anemia in highly trained female athletes.

ABBREVIATIONS

Hb: Hemoglobin; Fer: Serum Ferritin

INTRODUCTION

Anemia occurs frequently in female athletes and represents a major cause of reduced performance [1]. In almost all cases, sports anemia results from a lack of dietary iron intake due to failure to increase intake commensurate with the increased demands for iron that result from heavy exercise [2]. To prevent or improve anemia, physicians should provide dietary guidance encouraging the intake of iron-rich food or iron supplements [3]. However, in female athletes suffering from mild anemia, [4,5] dietary guidance from doctors is not always followed due to incompatibility with strict dietary regimens designed for figure maintenance, e.g., in rhythmic gymnasts. Furthermore, long-distance runners have markedly elevated iron requirements that cannot be addressed through diet alone [6-8]. Hospital visits may be required to receive iron medication, leading some athletes to avoid seeking treatment unless symptoms are severe. In general, iron which is used for supplement is known to be an inorganic iron and poor absorption efficiency [5]. These iron supplementation also frequently causes constipation, which can impinge upon training. To increase medication compliance and thus reduce anemia incidence, medications conferring less burden on athletes are required. Heme iron is one of pigments derived from animal and is known to be absorbed better than sulfate iron [9]. In addition, the use of heme iron is hard to cause gastrointestinal problems. However, human intervention focused on athletes using heme iron supplementation has been reported less and the availability is not well evaluated. Improved iron status can provide marked benefits to female athletes. To reduce anemia, increased iron intake, which subsequently increases the pool of available iron, is important. Greater intake of other nutrients may also be necessary to increase iron availability [10,11], particularly protein, which acts as an iron transporter [12]. The degree of improvement in anemia symptoms in female athletes appears strongly associated with their nutritional status. [13]

We herein assessed improvements in iron status in female athletes following heme iron supplementation and also evaluated other nutritional components that appear to influence this relationship. The athletes' nutritional status was monitored during the trial; athletes were aware of the association between anemia and insufficient iron intake. We aimed to advance understanding of the most effective dietary guidelines for anemic female athletes, and we hypothesized that a combination of iron supplementation and nutritional counseling would result in optimal health outcomes.

MATERIALS AND METHODS

Subjects

Thirty female college students (mean age: 20.2 ± 1.3 years) who participated in a competitive sport and complained of anemia symptoms were recruited. Blood analysis showed mean hemoglobin (Hb) of 10–13.4 g/dL and ferritin (Fer) 2.8–40 ng/mL, indicative of the normal to mild anemia not requiring urgent treatment. The mean duration of sports participation was more than 9 years, in sports including volleyball, basketball, handball, sprinting, long jump, triathlon, swimming, working as a life guard, and badminton. All participants provided informed consent. This research was approved by the ethics committee of the College of Humanities and Science of Nihon University.

Intervention

In accordance with blood test results, 20 participants with Hb and Fer levels >12.0 g/dL and 10 ng/mL, respectively, were assigned to the normal group; the remaining 10 participants were assigned to the mild anemia group. These categorizations of these groups are referenced to WHO criteria [14]. Hb and Fer means across the entire sample were 12.4 ± 0.7 g/dL and 17.8 ± 13.7 ng/mL, respectively. Each group received two heme iron capsules (ILS, Inc., Japan) daily, each containing 7 mg, to be taken every morning and before the evening meal for 2 months. In an initial trial, no participants received nutritional guidance; in a second trial, the mild anemia group continued to receive supplementation for an additional 2 months and also received nutritional guidance at 2-week intervals (Figure 1). Blood tests, a food intake frequency survey, measurement of body composition and physical condition, and a psychological test (Profile of Mood States, POMS; Japanese version [15]) were administered before and after intervention, and iron status was also evaluated.

Measurement

Levels of albumin (Alb), red blood cells (RBC), serum iron (Fe), Fer, zinc (Zn), and Hb, as well as hematocrit (Ht), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), total iron binding capacity (TIBC), and unsaturated iron binding capacity (UIBC) were measured. Body weight, body fat percentage, and muscle mass were measured using the impedance method (InBody 520, Biospace Co., Ltd., CA, USA). Food intake frequency was indexed using the Excel Eiyo-kun Food Frequency Questionnaire (FFQ; ver. 6.0, Kenpakusha, Japan) in conjunction with the Food Frequency Questionnaire Based on Food Groups (FFQg; ver. 3.5, Kenpakusha, Japan). Total intake of calories, carbohydrates, protein, fat, Fe, and Zn and of food groups such as grains, meat, and vegetables, were compared between groups. The frequency of listlessness, dizziness, headache, general nausea, nausea upon waking, and upset stomach were assessed on a 5-point scale ranging from 1 (never) to 5 (always), as symptoms indicative of anemia. Breathlessness, listlessness, headache, and muscle ache were assessed as indices of aesthesia. Constipation and diarrhea were also quantified. Total training time per week, also subdivided by technique, endurance (to enhance cardiorespiratory function), and strength training (to increase muscle strength or mass), was also recorded. The influence of anemia on psychological state was evaluated using the POMS (Kaneko-Shobo, Japan). [15]

Nutritional guidance

Following the initial trial, only 10 mild anemia participants received nutritional guidance based on the results of their blood tests, FFQ data, physical condition, and training regime. Guidance was provided for 30 min at 2-week intervals. Individualized

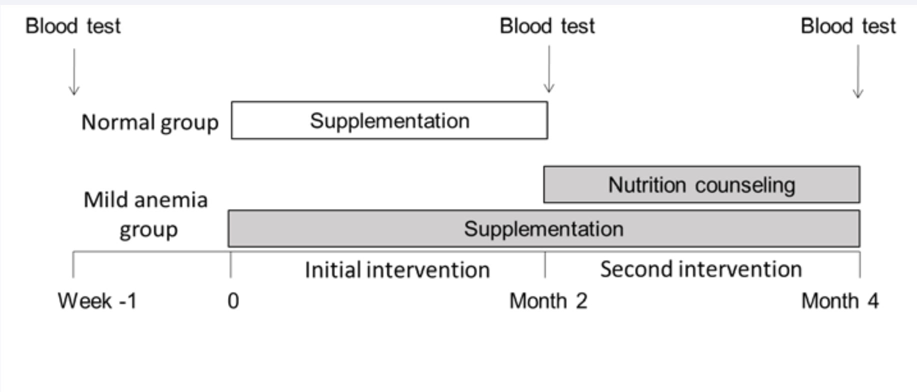

Figure 1 Study design.

guidance was based on the "Dietary Reference Intakes for Japanese–2010." [16] The importance of breakfast, of increased intake of protein, vegetables, and meats containing iron, and of restricting consumption of coffee, tea, and green tea (all of which contain tannin) was emphasized. Advice was tailored to the individual's lifestyle, thereby taking account of living arrangements (dormitory, living alone, or living with family), training regimen, and constipation and diarrhea status.

Statistical analysis

Data are presented as mean + SE; the JMP 8 software package (SAS Institute Japan, Japan) was used for the analyses. Group means were compared using the Tukey–Kramer HSD test. To compare the pre- and post-intervention values in each group, Student's t-test was used.

RESULTS

Athletic career and training

An athletic career, the age when staring an athletic regimen, and training time (h/week) did not differ between the normal to mild anemia groups (Table 1). The time engaged in training did not change during the intervention period in all groups (data not shown).

Changes in body composition

No significant changes in body weight, body fat, or muscle mass were observed in either group throughout the testing period (Table 2).

Blood test

During the initial intervention, Alb, RBC, MCV, MCH, MCHC, Ht, Reti, Hb, TIBC, UIBC, and Zn values were unchanged by heme iron supplementation (Table 3). Fe and Fer levels were increased significantly post- vs. first-intervention in the normal group, but not in the mild anemia group. In the second intervention, heme iron supplementation was continued only in members of the mild anemia group whose second post-intervention iron concentration was elevated significantly compared with that pre-intervention. In the mild anemia group, the changes between pre- and post-Fe, -Hb, and –Fer were elevated significantly after the second intervention compared with pre-intervention levels, and almost reached the levels observed in the normalgroup (Figure 2).

Physical condition and training load

More than 80% of participants sometimes had a more chronic physical condition such as "feeling languid" and "giddiness" during the pre-intervention period. There was a trend toward a decrease in "feeling languid" and muscle fatigue after the intake of heme iron capsules, but the data were not significant (Table 4). No participants reported constipation or stomachache after the long-term oral intake of heme iron capsules.

Changes in psychological state

No significant change in psychological state was observed in either group after the initial intervention. Tension and uneasiness, dysphoria and depression, anger and hostility, and confusion were decreased significantly in the mild anemia group during the second intervention (Table 5), and vitality scores were increased significantly.

Dietary survey

The intake of energy, protein, iron, and zinc (indexed using the FFQ), particularly with respect to frequency, was increased in the mild anemia group following the second intervention, but

Table 1: Athletic career and training in the mild anemia group and the moderate anemia group.

	Normal group	Mild anemia group
Athletic career, years	9.1±1.8	9.1±1.6
Started athletic age	9.1±1.2	10.8±1.1
Technical training h/week	7.3±2.3	9.5±1.9
Endurance training h/week	4.7±1.6	4.8±2.0
Strength training h/week	2.8±1.2	1.9±0.7

Abbreviations: Values are represented as means ± SEM (n = 20 or 10). Statistical analyses were performed by one-way analysis of variance. A p-value ≤ 0.05 by a Tukey–Kramer test among the five groups was considered to indicate statistical significance. Values for the one-way ANOVA test are indicated as significant with different letters.

Table 2: Body weight and Body fat, Muscle mass in the normal group and the mild anemia group to oral feeding heme-iron at Pre and Post.

	Normal group		Mild anemia group		
	Pre	Post	Pre	1st- Post	2nd- Post
Weight, kg	56.5±2.3	57.2±2.5	53.4±1.3	53.9±1.3	54.7±1.4
Body fat, %	22.8±1.1	22.8±1.2	23.1±1.7	22.8±1.8	23.2±2.3
Muscle mass, kg	23.5±1.0	23.8±1.0	22.1±0.9	22.2±1.0	22.6±1.5

Abbreviations: Values are represented as means ± SEM (n = 20 or 10). Statistical analyses were performed by one-way analysis of variance. A p-value ≤ 0.05 by a Tukey–Kramer test among the five groups was considered to indicate statistical significance. Values for the one-way ANOVA test are indicated as significant with different letters.

Table 3: The concentrations of blood iron status in the normal group and the mild anemia group to oral feeding heme-iron at Pre and Post.

	Normal group		Mild anemia group		
	Pre	Post	Pre	1st- Post	2nd- Post
Alb, g/dL	4.7±0.06	4.6±0.1	4.6±0.06	4.5±0.1	4.7±0.07
RBC, 10^4/μL	439.5±4.6	453.0±3.1	442.9±15.5	451.4±15.7	452.0±15.3
MCV, fL	90.1±0.9 ab	91.6±0.7 a	84.4±1.9 b	84.9±1.9 ab	86.0±1.7 ab
MCH, pg	29.8±0.3 a	30.0±0.2 a	27.0±0.9 ab	26.8±0.8 b	27.1±0.7 ab
MCHC, %	33.2±0.1	32.7±0.2	31.9±0.4	31.5±0.3	31.5±0.3
Ht, 10^4/μL	39.5±0.4 ab	41.5±0.3 a	37.1±0.6 b	37.5±1.1 ab	40.9±1.5 ab
Reti, $^0/_{00}$	11.0±0.5	11.2±0.9	8.3±0.6	8.7±0.6	8.3±0.5
Hb g/dL	13.1±0.1 ab	13.7±0.1 a	11.6±0.2 c	12.1±0.4 bc	12.6±0.3 abc
Fe, mg/dL	93.5±9.7 bc	151.3±11.4 a	49.2±7.0 c	72.1±12.5 bc	108.5±18.1 ab
TIBC, μg/dL	322.6±9.3 b	321.4±12.4 b	405.8±19.4 a	409.5±19.2 a	417.1±24.6 a
UIBC, μg/dL	210.6±18.3 b	197.8±16.9 b	356.6±22.3 a	337.4±20.3 a	308.6±24 a
Fer, ng/mL	31.4±1.9 b	41.9±3.1 a	6.3±0.9 c	9.6±2.9 c	11.7±1.5 c
Zn, μg/dL	89.9±7.7	84.5±4.6	85.8±2.5	82.4±5.0	92.9±2.2

Abbreviations: Values are represented as means ± SEM (n = 20 or 10). Statistical analyses were performed by one-way analysis of variance. A p-value ≤ 0.05 by a Tukey–Kramer test among the five groups was considered to indicate statistical significance. Values for the one-way ANOVA test are indicated as significant with different letters.

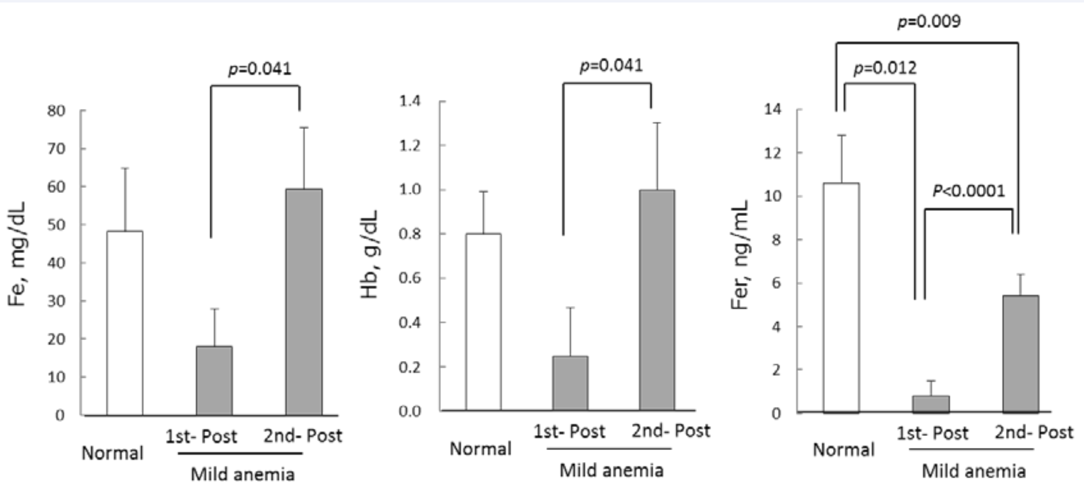

Figure 2 Pre- and post-oral heme iron supplementation changes in blood Fe, Hb, and Fer levels in mild (n = 20) and moderate (n = 10) anemia groups. Values are presented as means ± SE. Using Student's-t test, a value of $p < 0.05$ was taken to indicate statistical significance.

not significantly. The intake frequency of fish and dairy products (sources of protein and calcium) and of green and yellow vegetables (sources of vitamin C, fiber, and iron) was increased in the mild anemia group following the second intervention. In the normal group, nutritional intake remained unchanged post-intervention.

DISCUSSION

Before intervention, female athletes were divided into two groups (normal to mild anemia groups) according to Hb and Fer levels in an initial blood test. The blood test results for participants with the normal were within the normal range compared with individuals who required medical treatment for anemia [17]. However, because Hb>14 g/dL is recommended [18-20] in athletes to maximize athletic performance, heme iron supplementation should confer competitive benefits even in those with normal. In practice, 80% of athletes in all groups complained of sports anemia symptoms such as a headache or fatigue; thus, reduced performance was expected. Improving the iron nutritional status is expected to improve performance in female athletes.

Female athletes in both the normal to mild anemia groups were supplemented with heme iron for 2 months. Afterward, heme iron supplementation was continued for a further 2 months in only the mild anemia group together with nutritional guidance. Supplementation improved the blood levels of Fe and Fer significantly in the normal group. In the mildanemia group there was no change in first 2 months; however supplementation for a

Table 4: Chronic physical condition and physical condition in training in the normal group and the mild anemia group to oral feeding heme-iron at Pre and Post.

		Normal group		Mild anemia group		
		Pre	Post	Pre	1st- Post	2nd- Post
Chronic physical condition	Feel languid	3.5±0.3	3.1±0.1	2.8±0.2	2.8±0.3	2.9±0.2
	Hardships of morning	3.7±0.4	3.8±0.2	3.1±0.2	2.9±0.3	2.6±0.3
	Head feels heavy	2.9±0.5	2.8±0.5	2.5±0.3	2.1±0.4	2.1±0.2
	Headache	2.8±0.4	2.6±0.4	2.3±0.3	2.2±0.4	1.9±0.3
	Giddiness	3.3±0.5	2.6±0.2	3.2±0.3	2.9±0.3	2.4±1.5
	Nausea	1.6±0.3	1.3±0.2	1.7±0.2	1.6±0.3	1.5±0.3
	Total indefinite complaint*	17.8±1.7	15.9±0.6	15.4±1.2	14.5±1.1	13.7±1.5
Physical condition in training	Shortness of breath	2.6±0.3	2.4±0.3	3.3±0.3	2.7±0.3	2.5±0.2
	Tired feeling	3.1±0.4	2.3±0.4	2.8±0.2	2.5±0.3	2.5±1.9
	Muscular fatigue	2.8±0.5	2.8±0.3	2.7±0.2	2.0±0.3	1.9±0.3
	Headache due to lack of oxygen	2.6±0.4	2.5±0.4	1.9±0.3	1.7±0.2	1.6±0.3
	Total indefinite complaint*	14.0±1.1	13.0±1.3	13.9±1.1	12.6±1.0	11.9±0.8

Abbreviations: Values are represented as means ± SEM (n = 20 or 10). Statistical analyses were performed by one-way analysis of variance. A p-value ≤ 0.05 by a Tukey–Kramer test among the five groups was considered to indicate statistical significance. Values for the one-way ANOVA test are indicated as significant with different letters. *total indefinite complaint was shown in the total of each item in chronic physical condition or physical condition in training, respectively.

Table 5: Profile of Mood States in training in the normal group and the mild anemia group to oral feeding heme-iron at Pre and Post.

	Normal group		Mild anemia group		
	Pre	Post	Pre	1st- Post	2nd- Post
Tension-Anxiety	13.0±1.4 ab	8.5±1.5 ab	12.7±1.5 a	12.9±1.4 a	7.6±0.9 b
Depression-Dejection	10.6±2.1 ab	9.5±2.3 ab	16.0±1.3 a	13.8±1.4 a	5.8±1.5 b
Anger-Hostility	11.5±2.2 a	8.8±2.6 ab	16.0±1.8 a	15.0±1.4 a	4.4±0.9 b
Vigor	10.6±1.5 ab	10.4±1.4 ab	8.2±0.9 b	9.8±1.2 ab	13.1±0.9 a
Fatigue	9.7±0.6	7.9±1.8	12.5±1.9	9.7±1.2	8.9±0.7
Confusion	12.6±1.4 ab	9.3±1.7 bc	14.9±0.6 a	9.9±1.7 bc	6.5±0.9 b

Abbreviations: Values are represented as means ± SEM (n = 20 or 10). Statistical analyses were performed by one-way analysis of variance. A p-value ≤ 0.05 by a Tukey–Kramer test among the five groups was considered to indicate statistical significance. Values for the one-way ANOVA test are indicated as significant with different letters.

Table 6: Food intake and nutrients in the normal group and the mild anemia group to oral feeding heme-iron at Pre and Post.

	Normal group		Mild anemia group		
	Pre	Post	Pre	1st- Post	2nd- Post
Total energy, kcal	2381±252	2253±176	2090±120	1964±112	2111±176
Protein, g	75.4±9.4	75.2±5.2	66.5±6.0	67.7±5.8	72.3±5.0
Carbohydrate, g	314.7±28.4	290.4±25.1	263.9±17.0	254.0±12.8	307.9±21.2
Fat, g	81.6±10.2	80.3±5.8	66.2±4.9	68.8±5.8	75.7±7.2
Fe, mg	8.2±0.9	7.9±0.8	7.2±0.8	6.6±0.6	8.3±0.8
Zn, mg	9.5±1.3	9.2±0.7	7.9±0.8	7.9±0.7	8.7±0.6
Brightly colored vegetables, g	78.1±22.1 ab	74.0±21.2 ab	38.7±7.6 b	61.5±15.4 ab	101.8±12.6 a
hypochromic vegetable, g	147.9±28.9	149.7±35.5	78.4±18.3	102.9±19.5	132.4±22.1
Seafood, g	43.6±14.5	38.0±6.9	35.0±7.7	42.0±12.0	54.7±11.2
Meat, g	143.6±25.8	144.0±18.5	106.9±22.7	106.9±16.9	97.7±17.2
Egg, g	35.8±5.6	29.6±4.3	23.0±5.9	29.0±11.0	41.6±11.7
Dairy products, g	180.8±33.0	157.8±35.1	134.3±23.8	179.1±47.1	227.9±55.7
Small fish, g	2.8±1.6	2.7±1.2	2.0±0.9	2.4±1.2	3.8±1.2

Abbreviations: Values are represented as means ± SEM (n = 20 or 10). Statistical analyses were performed by one-way analysis of variance. A p-value ≤ 0.05 by a Tukey–Kramer test among the five groups was considered to indicate statistical significance. Values for the one-way ANOVA test are indicated as significant with different letters.

further 2 months improved the iron status, particularly regarding the blood levels of Fe and Hb. The range of their changes was the same as those observed in the normal group during the initial intervention. Because the levels of Fer increased slightly, it might take a longer time for iron storage to recover in individuals with mild anemia. In most previous reports, an intervention period >6 months of iron supplementation was in used athletes [21]. Thus, 2 months supplementation was insufficient to improve iron status in participants with mild anemia. However, supplementation for >2 months was needed in patients with mild anemia, such as those with a blood Fer level <10 ng/mL.

A dietary survey revealed that carbohydrate and protein intake, as determined using the FFQ, failed to reach the levels recommended for athletes during the whole intervention period [22,23]. A greater intake of other vitamins and minerals in addition to iron might also be important in patients with anemia [24]. For example, protein is particularly important for iron transportation and storage [25]. Thus, overall improved dietary habits, in addition to heme iron supplementation, are necessary, particularly in patients with severe symptoms of anemia. There was no significant change in total energy intake or the amount of each nutrient consumed during the initial intervention. However, the intake of brightly colored vegetables was increased significantly during the extra 2-month intervention period in the mild anemia group compared with during the initial 2-month period. Many brightly colored vegetables, such as spinach, contain high levels of iron; therefore, an increased the intake of these might increase iron intake [26]. This could be attributed to nutritional guidance that consequently led to an improved iron status.

Muscle mass before and after intervention was unchanged in both groups, probably because training regimens were also largely unchanged throughout this period, with few participants engaging in muscle training during the intervention. This was because the majority of the sports were in their off-season, so less marked changes in body fat and muscle mass would be expected. Nutritional guidance alone was not associated with significantly increased protein intake or with elevated levels of Alb. Athletes with sports anemia typically exhibit a diminished capacity to deliver oxygen to the muscles, with reduced blood flow and concomitantly impaired protein metabolism; these features render improvements in musculature more difficult [27,28]. This is important because athletes with sports anemia frequently exhibit a reduced capacity to deliver oxygen to the muscles and decreased blood flow, [29] which might explain difficulties in increasing muscle mass. Improved protein intake in conjunction with heme iron supplementation, nutritional guidance, and attention to the training regimen will likely confer marked benefits. A superior method of supplying protein is required for athletes, in combination with heme iron supplementation, training regimen monitoring, and nutritional guidance.

In the normal group, Hb and Fer values pre-intervention were too low for competitive athletes; therefore, heme iron supplementation was expected to enhance athletic performance. However, subjective anemia symptoms and psychological state did not exhibit marked improvements. This may have been due to individual differences in self-perceived symptoms. Guidance from a sports nutritionist can improve the psychological state and eating habits of athletes [30,31]. For example, in the initial intervention, heme iron supplementation without nutritional guidance was ineffective. During the second intervention, combining heme iron supplementation with nutritional guidance ameliorated anemia in the mild anemia group and also improved general and psychological health. This highlights the importance of nutritional guidance for anemia. Taken together, these data suggest that heme iron supplementation in conjunction with nutritional guidance is associated with improved mood and increased positive emotions such as “liveliness” in female athletes with mild anemia.

A dose of 14 mg/day heme iron did not exceed the recommended amounts [16,32]; if intake is excessive, adverse effects might occur due to increased oxidative damage. At the correct dose, the activity of hemeoxygenase, which is involved in transporting iron to the gut, is suppressed [33], reducing the likelihood of deleterious consequences. [9] Excessive athletic training can induce muscle inflammation and promote the expression of hepcidin, which suppresses iron absorption in the gut. [34]. Further research on the influence of hepcidin on heme iron absorption is required.

Gastrointestinal dysfunction and diarrhea are less common in response to heme iron supplementation compared with non-heme iron. [35] In the current study, no participant exhibited gastrointestinal dysfunction or diarrhea throughout the intervention period, indicating that heme iron supplementation is practical for athletes. Although iron sulfate supplementation has been frequently reported in athletes, heme iron supplementation is rarely reported.

CONCLUSION

The current study suggests that the intake of heme iron capsules improved sports anemia in female athletes effectively. However, long-term support with nutritional guidance and heme iron intake will be required to achieve a similar effect in female athletes with anemia who perform large amounts of exercise. Future studies should consider methods of increasing protein intake, monitor the content of training programs, and provide nutritional support including instruction regarding changing dietary habits. Finally, when the most effective method of applying heme iron capsules has been established it will be useful for all female athletes with sports anemia.

ACKNOWLEDGEMENTS

We received grant from “The Ito Foundation” and institute of humanities and social sciences in Nihon University. We are also grateful to ILS inc. for heme iron capsule offer. The authors would like to thank Ms R. Suzuki and J. Suzuki for their assistance with the experiments. We appreciate Prof. H. Kushi and Prof. F. Mizuochi for helpful suggestion.

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Cite this article

Matsumoto M, Hagio M, Katsumata M, Noguchi T (2015) Combined Heme Iron Supplementation and Nutritional Counseling Improves Sports Anemia in Female Athletes. Ann Sports Med Res 2(6): 1036.