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Evaluation of iron metabolism indices and their relation with physical work capacity in athletes

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Abstract

***Objective*—To evaluate the relation between iron status and physical working capacity, and to assess the effect of oral iron treatment on these variables, in athletes with borderline iron status.**

***Methods*—Blood haemoglobin (Hb), packed cell volume (PCV), red blood cell count (RBC), serum iron, total iron binding capacity (TIBC), and ferritin determinations were compared in 71 male and 18 female athletes participating in various sports and in matched male (n = 11) and female (n = 8) controls. The first aim was to assess the relations between these variables and performance in a physical work capacity test (PWC_{170}). Oral iron treatment (175–350 mg ferrous fumarate daily) was provided for three weeks to six male and five female athletes with borderline Hb concentrations, to determine the effects of such treatment on both iron status and performance.**

***Results*—Among females, handball players had the lowest serum ferritin concentrations ($P < 0{\cdot}05$), the highest TIBC values, and lowest PWC_{170} scores ($P < 0{\cdot}01$); runners had the highest ferritin concentrations and PWC_{170} scores ($P < 0{\cdot}01$). There were significant correlations ($P < 0{\cdot}01$) between PWC_{170} and PCV, serum ferritin, and transferrin saturation of female athletes. Hb, serum iron, serum ferritin, and transferrin saturation increased with iron treatment in both males ($P < 0{\cdot}01$) and females ($P < 0{\cdot}05$).**

***Conclusions*—Serum ferritin determination may prove a valuable addition to the screening of athletes and may indicate the need for iron treatment, even though a causal effect on improvement of work capacity may not be present.**

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Key terms: exercise; exertion; iron deficiency; sports anaemia; serum ferritin

Iron deficiency occurs as a result of an imbalance between iron absorption and excretion.[1] Absorption is in inverse relation to body iron stores,[1 2] and the serum concentration of ferritin is considered to be an index of these stores, 1 $\mu g{\cdot}litre^{-1}$ corresponding to 8–10 mg of body iron.[1-3] The aetiology of exercise related iron deficiency includes intravascular haemolysis, increased iron loss, and inadequate dietary iron intake.[4 5] Though no significant difference between the haematological status of athletes in various sports is reported,[6] iron loss is known to be increased in endurance activities.[3] Haemodilution by a relative increase in resting plasma volume in runners is an important reason for low haematological values, especially in highly trained athletes.[4 5 7-9] In the long run, the increase in blood volume may become more equally distributed between the plasma volume and the red cell mass.[9] Furthermore, in some studies[8 10] no differences were observed between the distribution of iron indices in runners and controls.

Single haemoglobin (Hb), serum ferritin, and transferrin saturation measurements are not sufficient to determine the phases of iron deficiency.[5] In the prelatent deficiency phase, as serum ferritin decreases to 30–60 $\mu g{\cdot}litre^{-1}$, other indices are not yet affected. In latent deficiency serum ferritin falls below 30 $\mu g{\cdot}litre^{-1}$, transferrin saturation decreases to 15–20%, serum iron concentrations may decrease, and total iron binding capacity (TIBC) may increase.[2 11 12] In overt iron deficiency anaemia, serum ferritin concentration is less than 12 $\mu g{\cdot}litre^{-1}$, and Hb is below 130–140 $g{\cdot}litre^{-1}$ in males and below 120 $g{\cdot}litre^{-1}$ in females.[2 8 11 12] Based on serum ferritin values, iron stores of athletes are reported to be about 30% less than normal, and in young women with low dietary haem iron, the incidence of iron deficiency may reach 50%.[12]

In iron deficiency anaemia, along with other clinical findings, work capacity and $\dot{V}O_2max$ decrease as a result of lowered Hb levels.[1-3 12] Iron related enzyme activities of athletes with iron deficiency are found to be only as low as values in sedentary people and the primary effect is on Hb.[13] The observation that $\dot{V}O_2max$ and total exercise duration values return to normal when serum iron, transferrin saturation, and serum ferritin stay low in subjects who have undergone venesection once their Hb levels are restored by transfusion shows that the fall in endurance in the anaemic state is associated with lower Hb, and not lower skeletal muscle enzyme activities.[14] In fact, Hb has been found to be an important determinant of O_2 diffusion rates into the working muscle, and a reduction in Hb results in decreased $\dot{V}O_2max$ because of depressed O_2 delivery and diffusing capacity.[15] Furthermore, total body Hb is found to influence $\dot{V}O_2max$ principally, whereas low Hb concentration has a greater effect on performance time.[16]

The iron status of women distance runners was found similar to that of sedentary people, with only serum ferritin concentration having the tendency to decrease in elite athletes.[17]

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Serum ferritin concentrations in female hockey players tended to fall below 20 $\mu g \cdot litre^{-1}$ following three to four seasons.[18] In contrast, swimmers were reported to have better haematological status than sedentary people.[19]

Some studies have shown that both Hb and serum ferritin levels improved following oral iron treatment.[20 21] Others found that only serum ferritin levels were corrected upon treatment of iron depletion without overt anaemia.[11 22 23] Investigators who gave a daily iron supplement of about 100 mg to female runners for 8 to10 weeks observed that, while serum ferritin levels increased rapidly, blood lactate and $\dot{V}O_2max$ or work capacity was unchanged,[21 24 25] whereas running time could improve[26] or remain stable[23 27] with a similar treatment. Restored oxygen utilisation and postexercise lactate following repletion of iron stores is also reported.[22]

In view of these conflicting reports, our aim in this study was to compare several haematological indices in athletes performing different sports, to evaluate the relationship between iron status and physical work capacity, and to assess the effect of oral iron treatment on these indices in athletes with borderline iron status.

Methods

SUBJECTS

Male athletes (n = 71) included 17 professional and 11 amateur soccer players, six national level wrestlers, seven swimmers, 11 middle distance runners, 12 second league basketball players, and seven body builders. Female athletes (n = 18) comprised 11 national league handball players, four swimmers, and three short or middle distance runners. The control groups consisted of 11 male and eight female university students not actively participating in sports. The subjects had no iron medication for the previous three weeks and had not accomplish any physical activity for the previous 24 hours.

PROCEDURE

Subjects reported to the laboratory at 9:30 am, at least three hours after a light breakfast, and their physical measurements were taken. After a sitting rest of 15 min, blood samples were withdrawn with minimum stasis from a forearm vein. Finger prick blood samples were also obtained for RBC, packed cell volume (PCV), and Hb measurements. Upon centrifuging the blood samples after a period of 30 min for clotting, clear sera were kept at –4°C for 48 h for serum iron and TIBC measurements and another portion was kept at –20°C for up to two months for serum ferritin determinations.

PWC_{170} TEST PROTOCOL

The subjects performed a physical work capacity test (PWC_{170}) on a mechanically braked Monark 868 bicycle ergometer (Varberg). They warmed up for 5 min at a speed of 60 rpm against a resistance of 1·0 kp and rested for 2 min. Then, while the speed was kept constant, the resistance was increased by 0·5 to 1·0 kp every 2 min. Heart rates were monitored using a Hellige Cardiotest EK 41 ECG apparatus and the test was completed upon approaching a heart rate of 170 $beats \cdot min^{-1}$.

HAEMATOLOGICAL TESTS

RBC and PCV measurements were performed by standard techniques and Hb levels were determined using Zijlstra's cyanomethaemoglobin method. Serum iron and TIBC analyses were performed using the semi-micro bathophenanthroline method (Merckotest 3307 and 3313, Merck) with an LKB K 4053 spectrophotometer. Transferrin saturation was calculated as the percent ratio of serum iron to TIBC. Serum ferritin measurements were done using a radioimmunoassay method (Amerlex Ferritin RIA, Amersham).

IRON TREATMENT

Following the first test, six of the male athletes with Hb concentrations below 140 $g \cdot litre^{-1}$ and PCV values below 43%, and five of the female athletes with Hb concentrations below 130 $g \cdot litre^{-1}$ and PCV values below 40% were treated for three weeks, using 350 mg and 175 mg of ferrous fumarate daily, respectively, equivalent to 112 mg and 56 mg of elemental iron. These subjects had no apparent parasitic or bacterial infections. All measurements were repeated one week after completion of the treatment.

STATISTICS

Means and standard deviations were calculated for all variables. Analyses of variance (ANOVA) were performed to compare the results of different groups. Unpaired Student's t tests were applied to compare the results of pairs of groups, and paired t tests to evaluate the effect of iron treatment, and correlation coefficients for within-group variables were obtained, all using the Minitab program.

Results

Mean values of the physical, haematological and serum indices for the male subjects are presented in table 1, and those for the female subjects are given in table 2. The pre- and post-treatment values of the subjects treated with oral iron are compared in table 3.

Blood RBC and PCV counts, and Hb and serum iron concentrations were found to be within the expected normal range for all subjects. Mean TIBC values of the male subjects were at the lower limit of the normal range of 54–71 $\mu mol \cdot litre^{-1}$. For the male athletes, only the runners' RBC counts were observed to be lower than the controls' ($P < 0·01$) – with no significant differences in iron indices ($P > 0·05$) – when comparing different sports. Runners had significantly higher PWC_{170} scores ($P < 0·01$) compared with other disciplines.

Female handball players who had lower serum ferritin concentrations ($P < 0·05$) than the controls had also the highest TIBC values and lowest working capacity ($P < 0·01$) among all female athletes. Female runners had the

Table 1 Physical, haematological, and serum indices of male subjects. Values are mean (SD)

Discipline	*Professional football (n = 17)*	*Wrestling (n = 6)*	*Swimming (n = 7)*	*Running (n = 11)*	*Basketball (n = 12)*	*Amateur football (n = 11)*	*Body building (n = 7)*	*Total athletes (n = 71)*	*Controls (n = 11)*
Age (years)	23·0 (3·1)	23·2 (5·3)	16·1 (1·1)	21·6 (3·7)	22·7 (1·2)	21·2 (1·4)	21·1 (1·9)	21·6 (3·3)	22·8 (1·0)
Height (cm)	174·1 (6·6)	173·8 (12·6)	177·0 (4·6)	174·3 (7·2)	191·6 (7·5)	175·0 (6·2)	172·9 (9·4)	177·4 (9·8)	175·5 (5·7)
Weight (kg)	71·0 (6·1)	79·3 (15·7)	71·4 (6·3)	65·9 (6·9)	85·5 (9·9)	69·9 (7·8)	78·6 (11·8)	74·0 (10·7)	70·6 (9·6)
PWC (W·kg^{-1})	3·00 (0·38)	2·59 (0·70)	3·07 (0·56)	3·62* (0·54)	3·31 (0·47)	3·13 (0·38)	2·66 (0·27)	3·11 (0·54)	2·20 (0·46)
RBC (10^{12}·litre^{-1})	–	4·67 (0·57)	4·54 (0·42)	4·09† (0·45)	4·64 (0·54)	4·42 (0·57)	4·52 (0·34)	4·45 (0·53)	4·48 (0·60)
PCV (%)	43·5 (2·4)	45·8 (1·2)	46·3 (2·4)	45·2 (2·8)	45·7 (1·6)	44·4 (3·5)	45·6 (2·6)	44·9 (2·6)	45·5 (2·5)
Hb (g·litre^{-1})	146·7 (10·9)	145·0 (8·5)	154·9 (7·8)	146·6 (9·9)	153·3 (5·4)	152·6 (7·5)	153·6 (10·8)	149·9 (9·3)	153·6 (9·1)
SI (μmol·litre^{-1})	19·2 (5·9)	18·7 (5·4)	18·0 (4·2)	19·1 (7·1)	18·5 (8·8)	16·7 (4·1)	20·8 (8·9)	18·7 (6·4)	18·8 (11·6)
TIBC (μmol·litre^{-1})	50·2 (7·7)	52·4 (4·7)	53·2 (7·3)	51·0 (7·2)	54·9 (13·4)	58·6 (9·0)	60·9 (9·0)	54·0 (9·3)	58·6 (10·1)
TS (%)	38·2 (12·6)	35·7 (5·4)	33·8 (6·1)	37·2 (11·9)	32·6 (11·7)	28·7 (6·4)	34·5 (14·0)	35·0 (10·0)	34·9 (15·2)
SF (μg·litre^{-1})	60·4 (31·3)	79·5 (52·0)	58·4 (22·4)	64·5 (45·4)	77·9 (41·0)	75·6 (34·2)	81·1 (54·5)	70·4 (39·1)	87·3 (42·4)

PWC = physical work capacity; PCV = packed cell volume; Hb = haemoglobin; SI = serum iron; TIBC = total iron binding capacity; TS = transferrin saturation; SF = serum ferritin.
*P < 0·01 *v* other disciplines; †P < 0·01 *v* controls; two-sample Student test.

highest PWC_{170} scores and the highest serum ferritin concentrations (P < 0·01).

For all female athletes, PWC_{170} levels correlated (P < 0·01) with PCV (r = 0·60), serum ferritin (r = 0·55), and transferrin saturation (r = 0·53). When the relation of different variables with PWC_{170} was assessed in different disciplines, significant correlations were found for transferrin saturation in female swimmers (r = 0·96, P < 0·05) and for Hb in body builders (r = 0·75, P < 0·05).

Following iron treatment, Hb, serum iron, and serum ferritin concentrations increased both in males (P < 0·01) and females (P < 0·05). Male subjects responded with a significant increase in transferrin saturation (P < 0·01) as well. While females increased their PWC_{170} scores by 11% (P > 0·05), no such effect was recorded for the males.

Discussion

Group means for most of the iron metabolism indices were within the normal range, conform to the observations of Balaban *et al*,[10] Durstine *et al*,[17] and Weight *et al*.[8] The slightly raised serum iron concentrations obtained for most of the subjects may be explained by the fact that the exercise test was carried out about three hours after a light breakfast, to obtain a better performance in the ergometer test, thus adding to the biological variation of this index, which is already reported to be high.[3] Mean TIBC values close to the lower limit of the normal range may indicate some form of transferrin deficiency.

Being more endurance trained, male runners had higher PWC_{170} scores compared with other athletes. While most of their indices were comparable with the observations of Weight *et al*,[8] a higher plasma volume expansion may explain their somewhat lower RBC values.[5 8 20] This observation parallels those of Hallberg and Magnusson[7] and Weight *et al*.[28] Though not significant, the higher PCV and Hb values of the male swimmers, and the higher RBC and PCV levels encountered in their female counterparts, are in agreement with the observations of Pelliccia *et al*.[19] Otherwise, there were no significant differences in haematological status of the male athletes in various sports, in agreement with Biancotti and coworkers.[6] Female handball players, who have been competing in the national league for at least three seasons, had the lowest mean serum ferritin concentrations of 13·6 μg·litre^{-1}, in agreement with the results of Diehl *et al*[18] for female hockey players. This low value may be explained by poor dietary habits of the players as a team. Again, high PWC_{170} scores in the female athletes is a result of their being more highly trained.

With regard to serum ferritin concentrations, only three (17%) of the female athletes were in the normal range, another three were in a state of prelatent iron deficiency, having serum ferritin levels less than 60 μg·litre^{-1}, and the remaining 12 (67%) were within the range of latent iron deficiency, with serum ferritin below 30 μg·litre^{-1} and transferrin saturation below 20%,[2 11 12] which supports the observations of Nickerson and coworkers[11] and Parr *et al*,[12] but not those of Risser *et al*[20] and Weight *et al*.[8] Hb concentrations were between 120 and130 g·litre^{-1} for three athletes whose serum ferritin levels were below 20 μg·litre^{-1}, whereas for two female athletes, Hb concentrations were below 120 g·litre^{-1} and serum ferritin was below 12, which are accepted as being critical levels indicating iron deficiency anaemia.[2 11 12] Though the female

Table 2 Physical, haematological, and serum indices of female subjects. Values are mean (SD)

Discipline	*Handball (n = 11)*	*Swimming (n = 4)*	*Running (n = 3)*	*Total athletes (n = 18)*	*Controls (n = 8)*
Age (years)	21·5 (1·7)	16·0 (0·8)	24·3 (4·9)	20·7 (3·5)	22·3 (1·0)
Height (cm)	168·7 (4·0)	162·8 (5·3)	162·3 (2·5)	166·3 (5·0)	161·8 (4·7)
Weight (kg)	60·6 (5.8)	54·8 (3·5)	55·8 (3·8)	58·5 (5·6)	54·2 (5·7)
PWC_{170} (W·kg^{-1})	2·25* (0·51)	2·82 (0·57)	3·20 (0·77)	2·54 (0·66)	1·98 (0·40)
RBC (10^{12}·litre^{-1})	4·08 (0·41)	4·38 (0·53)	4·05 (0·52)	4·14 (0·44)	4·09 (0·45)
PCV (%)	39·3 (2·8)	41·0 (1·2)	40·0 (2·0)	39·8 (2·4)	39·5 (2·2)
Hb (g·litre^{-1})	130·1 (12·0)	129·8 (9·2)	142·7 (4·0)	132·1 (11·2)	133·2 (7·9)
SI (μmol·litre^{-1})	18·5 (6·6)	14·3 (5·0)	22·1 (4·8)	18·2 (4·6)	18·0 (8·6)
TIBC (μmol·litre^{-1})	65·3* (9·3)	50·8 (4·9)	48·6 (5·3)	59·3 (10·9)	57·9 (10·0)
TS (%)	28·9 (10·2)	28·7 (14·0)	45·2 (5·0)	31·6 (11·7)	31·0 (14·8)
SF (μg·litre^{-1})	13·6† (8·4)	35·7 (24·5)	97·7* (67·1)	32·6 (40·7)	33·2 (19·4)

Abbreviations as in table 1.
*P < 0·01 *v* other disciplines; †P < 0·05 *v* controls; two-sample Student test.

Table 3 Physical, haematological, and serum indices of athletes on iron therapy. Values are mean (SD).

Group	Males, pre-treatment (n = 6)	Males, post-treatment (n = 6)	Females, pre-treatment (n = 5)	Females, post-treatment (n = 5)
Age (years)	22·3 (2·9)	22·3 (2·9)	18·6 (3·8)	18·6 (3·8)
Height (cm)	171·5 (2·7)	171·5 (2·7)	166·0 (5·7)	166·0 (5·7)
Weight (kg)	65·5 (6·6)	65·4 (6·8)	57·8 (3·3)	57·4 (3·2)
PWC_{170} ($W \cdot kg^{-1}$)	3·44 (0·58)	3·45 (0·78)	2·26 (0·43)	2·51 (0·18)
RBC ($10^{12} \cdot litre^{-1}$)	–	3·83 (0·29)	4·06 (0·41)	4·12 (0·51)
PCV (%)	42·3 (1·5)	43·0 (2·0)	39·0 (2·4)	40·6 (1·7)
Hb ($g \cdot litre^{-1}$)	137·7 (8·5)	150·8* (10·4)	126·2 (3·8)	129·8† (3·5)
SI ($\mu mol \cdot litre^{-1}$)	14·9 (4·9)	18·4* (4·0)	10·5 (3·4)	12·7† (3·4)
TIBC ($\mu mol \cdot litre^{-1}$)	44·6 (8·3)	51·0 (9·1)	60·7 (11·8)	62·9 (9·7)
TS (%)	34·2 (12·6)	54·9* (11·3)	18·1 (7·2)	20·3 (4·4)
SF ($\mu g \cdot litre^{-1}$)	44·0 (17·3)	57·2* (14·2)	17·6 (12·2)	22·0† (10·1)

Abbreviations as in table 1.
*P < 0·01; †P < 0·05 *v* pre-treatment values; two-sample Student test.

controls scored better, with three (37%) in a state of prelatent and only one (12%) in a state of latent iron deficiency, female athletes had a similar hematological status, as also observed by Durstine *et al.*[17] Poor dietary habits and the high incidence of recurrent parasitic infections in Turkey may be partly responsible of the relatively low iron status of most of the subjects.

Of the male athletes, 30 (42%) were found to be in a state of prelatent iron deficiency, and two (3%) were already within the limits of latent iron deficiency, with another having only a serum ferritin below 30 $\mu g \cdot litre^{-1}$ and two more having only a transferrin saturation below 20%. Interestingly, Hb concentrations in two professional soccer players were between 130 and 135 $g \cdot litre^{-1}$, approaching the limit for iron deficiency anaemia. As judged by serum ferritin concentrations, three of the male controls (27%) were in a state of latent iron deficiency. Balaban *et al*[10] observed similar conditions in athletes and controls.

The correlations calculated for female athletes between their PWC_{170} levels and PCV values, serum ferritin concentrations, and transferrin saturation ratios ($P < 0.01$), and those between PWC_{170} scores and Hb concentrations for the body builders ($P < 0.05$) are interesting. Still, the small number of subjects suggests that these figures must be interpreted with caution.

The significant increases obtained in blood Hb, serum iron, and serum ferritin concentrations upon iron treatment, both in males ($P < 0.01$) and females ($P < 0.05$), and in transferrin saturation ratios in the males ($P < 0.01$), proved the presence of iron deficiency.[4 5] The relatively high pretreatment serum ferritin values observed in the males should be assessed with caution, since serum ferritin is an acute phase protein which increases with strenuous training.[29] The greater improvement in haematological status of the male subjects compared to the females may be explained by the higher oral iron doses they received. In fact, about 16 weeks of such treatment seem to be needed[25] for a gain of 45–50 $\mu g \cdot litre^{-1}$ in serum ferritin. These findings support those of Matter and co-workers[24] and Fogelholm *et al*,[21] who gave 50 mg per day of iron for 10 weeks and 100 mg per day of iron for eight weeks, respectively, to female runners, and those of Risser *et al*,[23] who also gave iron supplements to athletes with iron deficiency; but they disagree with those of Nickerson *et al*,[11] Lukaski *et al*,[22] Telford *et al*,[23] and Newhouse *et al*,[25] who did not observe increases in Hb levels. A reason for this may be the lower initial Hb concentrations in the present study compared to the ones they reported. No significant increases in PWC_{170}, an index of endurance capacity, was observed either, in agreement with various other investigators.[13 21 23–25 27] Training effect may be partly responsible of the rise in the females' PWC_{170} scores.

The evidence from this study suggests that for athletes participating in various sports, and especially for female athletes, serum ferritin may be the first indication of prelatent iron deficiency, at a time when Hb and serum iron concentrations, transferrin saturation ratios, and RBC and PCV counts are not yet affected. A significant linear relation was even observed between physical working capacity and serum ferritin concentrations for female athletes. There were no striking differences in iron status in athletes in various disciplines. Treatment of borderline iron status resulted in increased Hb, serum ferritin, serum iron, and transferrin saturation levels, but this was not accompanied by an increase in physical working capacity. The determination of serum ferritin concentrations, especially in the preseason period, may prove valuable as an indication for treatment, after ruling out bacterial and parasitic infections.

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