Eur J Appl Physiol (2003) 89: 500–502
DOI 10.1007/s00421-003-0839-x

SHORT COMMUNICATION

Michalis G. Nikolaidis · Yannis Michailidis
Vassilis Mougios

Variation of soluble transferrin receptor and ferritin concentrations in human serum during recovery from exercise

Accepted: 28 February 2003 / Published online: 24 April 2003

Abstract Serum soluble transferrin receptor (sTfR) has been proposed as a more stable index of iron status than serum ferritin in athletes. However, the variation in sTfR concentration during recovery from acute exercise is unknown. The aim of the present study was to examine the effect of prolonged moderate exercise on ferritin and sTfR concentrations, as well as on several hematologic variables up to 24 h post-exercise. Fifteen young, untrained men exercised on a cycle ergometer for 45 min at a heart rate of 150–155 beats min^{-1} and provided blood samples before as well as immediately, 6 h, and 24 h after exercise. Ferritin and sTfR values did not change significantly with time. sTfR levels exhibited lower variation during the observation period, the median intra-individual coefficient of variation being 5.2%, as opposed to 10.9% for ferritin. In conclusion, serum ferritin concentration is not affected by prolonged moderate exercise and can be used as a reliable index of iron status, at least for athletes not involved in extreme physical activities. Serum sTfR concentration seems to be more stable and could replace ferritin as the preferred index of iron stores if problems associated with the novelty of the assay were overcome.

Keywords Ferritin · Iron status · Exercise · Soluble transferrin receptor

Introduction

Serum ferritin has been the most frequently used index of iron stores in the body. However, normal ferritin levels do not always reflect adequate iron stores; being an acute phase protein, ferritin increases in various infections and inflammatory states, which may thus mask an iron deficiency. This is of concern to athletes, since strenuous exercise may induce inflammatory-like reactions, which in turn may induce an acute phase response (Malczewska et al. 2000).

According to most relevant studies, the concentration of the soluble transferrin receptor (sTfR) in serum appears to be of particular value for detecting iron deficiency. sTfR levels increase when iron stores diminish. Unlike ferritin, however, sTfR is not an acute phase protein; hence, its concentration is not affected by infections and inflammatory states (Malczewska et al. 2000). However, this by no means implies that sTfR levels remain stable after exercise.

Despite the importance of sTfR in the diagnosis of iron deficiency, to our knowledge, only two studies have tested the hypothesis that serum sTfR levels remain stable after acute exercise (Schumacher et al. 2002) or after a brief training period (Malczewska et al. 2000). Likewise, few studies have examined the influence of an exercise bout on ferritin levels in a thorough fashion. In contrast, most have collected a limited number of blood samples, usually immediately after strenuous exercise (e.g., ultramarathon; Fallon 2001). Measuring the levels of blood parameters immediately after acute exercise produces results of limited clinical value, since it is known that during the hours following an exercise bout the concentration of many blood parameters changes. This is the reason that blood sampling for the evaluation of an athlete's health status is usually performed after 1 day of abstinence from exercise training.

In view of the lack of data on the variation of serum sTfR levels during recovery from exercise and the limited relevant evidence regarding ferritin, the aim of the present study was to examine the effect of prolonged moderate exercise on their concentrations and on several hematologic variables up to 24 h post-exercise.

M. G. Nikolaidis · Y. Michailidis · V. Mougios (✉)
Department of Physical Education and Sport Science, TEFAA, Aristotle University of Thessaloniki, 541 24 Thessaloniki, Greece
E-mail: mougios@phed.auth.gr
Tel.: +30-2310-992238
Fax: +30-2310-992183

Methods

Subjects

Fifteen young healthy males participated in the study. They were non-smokers and non-obese (body mass index < 30 kg m^{-2}), and trained up to two times per week. Their age [mean (SD) throughout] was 22.6 (2.3) years. Their body mass and height were 74 (9) kg and 1.79 (0.05) m, respectively. The study was carried out according to the guidelines of the University of Thessaloniki Ethics Committee and all subjects gave informed consent prior to participation.

Experimental design

Subjects reported to the laboratory the morning after an overnight fast and at least 3 days after their last exercise session. At approximately 9 a.m., each subject, while seated, provided 5 ml of blood from an antecubital vein, which was collected into an evacuated test tube. Afterwards, he warmed up on a Kettler KX1 bicycle ergometer (Ense-Parsit, Germany), being subjected to stepwise increases in power until a heart rate of 150–155 beats min^{-1} was reached within 10–15 min. This power was then maintained for 45 min, while the heart rate was monitored continuously by a Polar Accurex monitor (Kempele, Finland). Immediately after exercise, a second blood sample was collected (0 h), followed by one at 6 h (with a light meal in the meantime), and one at 24 h post-exercise (after an overnight fast). For hematology, an aliquot of each blood sample was mixed with EDTA solution to prevent clotting. The rest of the sample was left to coagulate and was centrifuged at 1,500 *g* for 10 min in order to separate the serum for chemical analyses.

Assays

Hematocrit, hemoglobin concentration, erythrocyte count, leukocyte count, and platelet count were measured in a Sysmex K-1000 (Kobe, Japan) autoanalyzer. Ferritin and sTfR were determined using enzyme immunoassay kits from DRG (Marburg, Germany) and Orion Diagnostica (Espoo, Finland), respectively, in an Anthos 2000 (Salzburg, Austria) photometer. Each parameter was determined on a single day in order to eliminate inter-assay variability. Post-exercise changes in plasma volume were computed based on hematocrit and hemoglobin as described (Dill and Costill 1974).

Statistical analysis

Data were analyzed using the Statistica 5.1 software. Results are reported as means (SD). Comparisons among the four blood samples taken from each subject with respect to each parameter were performed by repeated measures ANOVA followed by the Scheffé post hoc test, if appropriate. Linear correlation analysis between ferritin and sTfR was carried out by Pearson's product moment correlation coefficient. The level of statistical significance was set at $\alpha = 0.05$. Intra-assay and intra-individual coefficients of variation (CV) for ferritin and sTfR were also computed. The intra-individual CV was computed from the values of the four samples taken from each individual and is used as an index of the variation of the measured parameters after exercise.

Results

Plasma volumes at 0, 6, and 24 h post-exercise were 0.96 (0.06), 1.00 (0.06), and 0.99 (0.06), respectively, relative to pre-exercise (not significant). When post-exercise leukocyte counts, platelet counts, ferritin concentrations, and sTfR concentrations were corrected for plasma volume changes, the results of the statistical comparisons were not different from those performed on the original values.

ANOVA revealed significant changes in hemoglobin ($P < 0.05$), leukocyte count ($P < 0.001$), and platelet count ($P < 0.001$). Hemoglobin decreased at 6 h compared with 0 h ($P < 0.05$). Leukocytes increased at 6 h compared with pre-exercise and 0 h, and decreased at 24 h compared with 6 h ($P < 0.001$). Platelets increased at 0 and 6 h compared with pre-exercise and decreased at 24 h compared with 0 h ($P < 0.05$). Hematocrit, erythrocyte count, ferritin, and sTfR values did not change significantly with time. The pre-exercise values of ferritin and sTfR were 53.8 (39.8) μg/l and 2.33 (0,65) ng/l, respectively. Compared with ferritin, sTfR values exhibited lower variation during the observation period, the intra-individual CV ranging from 1.6 to 23.0% (median 5.2%), as opposed to 2.2–38.0% (median 10.9%) for ferritin. The intra-assay CV (determined on samples of intermediate concentrations) was 1.9% for ferritin and 2.8% for sTfR. Finally, there was no significant correlation between ferritin and sTfR concentrations.

Discussion

There is recent evidence that serum sTfR is a more reliable index of the iron status of athletes than ferritin (Malczewska et al. 2000; Schumacher et al. 2002). However, the effect of an acute exercise bout on the kinetics of serum sTfR is unknown. In an effort to fill this gap, the present work measured seven biological parameters (with the emphasis on ferritin and sTfR) at three time points during recovery from exercise.

Our data show that neither serum ferritin nor serum sTfR concentrations were affected significantly by a moderate exercise bout for up to 24 h post-exercise. These findings agree with those of Schumacher et al. (2002), who found no significant changes in the ferritin or sTfR levels of untrained individuals after a treadmill running protocol with characteristics similar to ours (70% maximum oxygen consumption rate for 45 min), although ferritin (but not sTfR) increased significantly (by 6%) in trained individuals subjected to the same protocol. On the other hand, Malczewska et al. (2000) found no correlation between the training load of the preceding day and sTfR levels of athletes during a brief training period; however, there was a significant moderate positive correlation between training load and ferritin levels.

In addition to the two aforementioned studies, many other investigators have studied the effect of acute exercise on serum ferritin. There are reports both of increased levels (e.g., Fallon 2001) and of no significant changes after one bout of exercise (e.g., Gray et al. 1993;

Ricci et al. 1988). The reason for this discrepancy is very likely to be the different exercise loads employed. In general, ferritin increases after exhausting exercise, such as judo training for 4.5 h day^{-1} (Malczewska et al. 2000) and ultramarathon (Fallon 2001). Such activities can induce extensive muscle damage and inflammatory reactions, both of which can increase serum ferritin levels. On the other hand, exercise loads, such as those employed in regular training and in the present study, do not seem to cause significant changes in ferritin.

Of interest is the intra-individual variation of serum ferritin and sTfR. In our study, the minimal, median, and maximal intra-individual CV for sTfR were lower than the corresponding values for ferritin, a finding that agrees, to some extent, with Malczewska et al. (2000). In view of the similar and low intra-assay CV of the two assays, it appears that sTfR is a more stable index of iron stores than ferritin.

Along with ferritin and sTfR, we monitored the major hematologic parameters, of which only the leukocyte and platelet counts varied significantly during the observation period. Their increase immediately after and/or 6 h after exercise, as well as their return to pre-exercise levels within 24 h is in agreement with most of the relevant literature (e.g., Gonzalez et al. 1996; Hoffman-Goetz 1998).

The use of reliable indices of iron status is a prerequisite for the correct evaluation of the health status of individuals. The results of the present study showed that serum ferritin did not vary significantly up to 24 h after acute moderate exercise. Therefore, it seems that, at least for athletes not involved in extreme physical activities, ferritin can be used as a reliable index of iron stores. sTfR levels were also not affected by the exercise protocol employed; moreover, they proved more stable than the ferritin levels. Thus, serum sTfR can be also recommended safely as a marker of iron deficiency in athletes. However, the absence of widely accepted reference intervals (Schumacher et al. 2002), the large variability among the results from different assay kits (Schumacher et al. 2002) and the high cost of analysis limit the use of sTfR for routine purposes in the near future.

In conclusion, the results of the present study show, for the first time, that serum ferritin and sTfR levels remain stable up to 24 h after acute prolonged exercise of moderate intensity. This renders both parameters reliable indices of iron status for amateur endurance athletes.

References

Dill DB, Costill DL (1974) Calculation of percentage changes in volume of blood, plasma, and red cells in dehydration. J Appl Physiol 37:247–248

Fallon KE (2001) The acute phase response and exercise: the ultramarathon as prototype exercise. Clin J Sport Med 11:38–43

Gonzalez F, Manas M, Seiquer I, Quiles J, Mataix FJ, Huertas JR, Martinez-Victoria E (1996) Blood platelet function in healthy individuals of different ages. Effects of exercise and exercise conditioning. J Sports Med Phys Fitness 36:112–116

Gray AB, Telford RD, Weidemann MJ (1993) The effect of intense interval exercise on iron status parameters in trained men. Med Sci Sports Exerc 25:778–782

Hoffman-Goetz L (1998) Immunocompetence in physical activity and sport. In: Wolinski I (ed) Nutrition in exercise and sport. CRC, New York, pp 645–657

Malczewska J, Blach W, Stupnicki R (2000) The effects of physical exercise on the concentrations of ferritin and transferrin receptor in plasma of female judoists. Int J Sports Med 21:175–179

Ricci G, Masotti M, De Paoli Vitali E, Vedovato M, Zanotti G (1988) Effects of exercise on haematologic parameters, serum iron, serum ferritin, red cell 2,3-diphosphoglycerate and creatine contents, and serum erythropoietin in long-distance runners during basal training. Acta Haematol 80:95–98

Schumacher YO, Schmid A, Konig D, Berg A (2002) Effects of exercise on soluble transferrin receptor and other variables of the iron status. Br J Sports Med 36:195–199