Exercise, nutrition and iron status

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Abstract Iron deficiency is still a problem in developing countries as well as developed countries. Moreover, an athletic population has a high rate of iron deficiency anemia; most of whom participate in aerobic exercise. Therefore, most studies which have been conducted to investigate the effect of exercise on iron status have used aerobic exercise. A considerable number of studies suggest that aerobic exercise has harmful effects on the iron levels in the body. Therefore, most of the studies on improving iron deficiency focus on the effect of nutrition. However, mild resistance exercise improves iron status in the body. These results suggest the possibility of a difference in the effect of different types of exercise on iron status. Exercise would be economically advantageous as a measure to improve iron deficiency in developing countries that have a high rate of iron deficiency. Future studies might thus be needed to clarify the relationship between iron status and physical activity.

Keywords: iron deficiency, exercise, hemoglobin, heme synthesis, nutrition, anemia

Introduction

Iron deficiency is one of the most common nutritional problems in the world. The World Health Organization (WHO) estimated the prevalence of iron deficiency to be 15-20% of the world’s population. Iron deficiency is defined as a low level of internally stored iron and an insufficient supply of iron to various tissues.

Iron deficiency is thought to be caused by low iron intake, some relevant diseases, and, in women, blood loss by menstruation. Anemia (iron deficiency anemia) results from decreasing hematopoiesis in the hematopoietic tissues due to iron deficiency. Iron deficiency in tissues occurs either quickly or slowly depending on the balance between iron intake (or stockpile) and iron requirement. The developmental rate of iron deficiency in individual tissues and cell organelles depends on the turnover rate of iron-containing proteins.

Iron is associated with several metabolic processes, including mitochondrial electron transport, neurotransmitter synthesis, protein synthesis, organogenesis, and others. Therefore, iron deficiency results in several deleterious effects including decreases in work performance, immune function, sympathetic, endocrinological metabolism, and thermoregulatory performance. In addition, the reduction in hemoglobin due to iron deficiency causes changes in physical capacity through the decrease of an oxygen transporter in muscle. The content of iron-sulfur and cytochrome in mitochondria and the oxidative capacity of mitochondria are also decreased by iron deficiency. In short, the decreased exercise capacity occurs in association with the decrease in oxygen-carrying capacity, oxygen diffusing capacity in tissue and oxidizing capability in muscle. There is a change in the metabolic function associated with non-anemia iron deficiency. A sufficient level of iron in tissue as well as hemoglobin has therefore been reported to be important to enhance maximal oxygen uptake.

There has been a considerable amount of research on the effect of exercise or nutrition on iron status. Most of the studies on improving iron deficiency focus on the effect of nutrition. Few studies have so far investigated the effect of exercise on the prevention and/or improvement of iron deficiency. Therefore, this short review will demonstrate the effect of the type of exercise and the combination of exercise and nutrition on iron status.

Effect of exercise on iron status

Previous studies have shown that exercise itself can change the iron status in the body. Studies of athletes suggest that athletes tend to have a low serum ferritin level. These results are seen especially in long distance runners. Iron deficient anemia is a type of malnutrition that is frequently seen in female athletes. The primary cause is a lack of iron in the diet. The requirement for iron in a high-performance athlete is exacerbated by profuse perspiration (containing decidual epidermal cells), reduced fractional absorption of iron from the digestive tract, erythrocyte destruction by physical impact on the feet and...
iron hypermetabolism by erythrocyte destruction. Many of these studies investigated the impact of aerobic exercise. Studies on the effect of resistance exercise suggest a possible difference in the effect of exercise on iron status associated with the type of exercise (aerobic exercise vs. resistance exercise).

**Aerobic exercise and iron status.** Several studies have reported that decreases in hematocrit, hemoglobin, and serum iron and an increase in erythrocyte fragility may occur in individuals that participate in extreme aerobic exercise\(^\text{16-18}\). Several investigators have proposed mechanisms by which iron balance could be affected by intense physical exercise\(^\text{16-18}\). Explanations include increased gastrointestinal blood loss after running and hematuria as a result of erythrocyte rupture within the foot during running. The possibility of increased red cell turnover in athletes is supported by the ferrokinetic measurements conducted by Ehn et al.\(^\text{19}\). They demonstrated that the whole-body loss of radioactive iron occurred 20% faster in female athletes than in non-athletes, and both were faster than that in adult men. In addition, they reported that hemoglobin and serum iron were normal, while bone marrow showed non-anemic iron deficiency. The red cell turnover of iron deficient rats with exercise was increased in comparison to that in sedentary rats\(^\text{20}\).

On the other hand, aerobic exercise improves or mitigates deteriorated iron status in iron deficient rats. Perkkio et al. reported that the hemoglobin concentration, endurance capacity and \(\text{VO}_2\text{max}\) of iron deficient rats are significantly increased by aerobic exercise (treadmill) in comparison to that in sedentary rats\(^\text{21}\). However, the hemoglobin concentration of iron sufficient rats was not decreased by exercise in comparison to that in sedentary rats. Willis et al. reported that the hemoglobin concentration of iron deficient rats was significantly increased by aerobic exercise (treadmill) in comparison to that in sedentary rats\(^\text{22}\). Gagne et al. observed that the hemoglobin concentration and hematocrit were not decreased while the stainable bone marrow iron was lowered significantly by exercise\(^\text{23}\). They suggested that this phenomenon was most likely due to an increased iron turnover as well as the rate of hemoglobin synthesis and release from cells induced by exercise. Qian et al. reported that the rate of hemoglobin synthesis and the amount of iron uptake in the bone marrow erythroblasts were increased in the strenuously exercised rats (swimming), while the iron content of the liver, spleen, kidney and heart were decreased\(^\text{24}\). The iron deficiency in tissues is thought to be due to increased iron acquired by bone marrow cells and used for increased hemoglobin synthesis. Exercise could lead to a shift of iron from storage sites to bone marrow cells for increased hemoglobin synthesis. Similarly, lower iron stores were observed in the tissue of the exercised rats in comparison to sedentary rats. Strause et al. demonstrated that exercised rats had less total iron in the liver and spleen than sedentary rats\(^\text{25}\). Ruckman et al. observed the hemoglobin of trained rats was increased in comparison to sedentary rats\(^\text{26}\). However they suggested that there was an overall trend toward iron depletion in the liver and spleen of the exercised rats and that trend of decreased iron level in organs could be related to increased hemoglobin levels.

**Resistance exercise and iron status.** Few studies have investigated the effect of resistance exercise on iron metabolism in comparison to aerobic exercise. Mild resistance exercise improves the iron status in young women with non-anemic iron deficiency without iron supplementation\(^\text{27}\). The levels of serum ferritin, hemoglobin, number of red blood cells and total iron binding capacity increased significantly after 12 weeks of resistance exercise (dumbbell exercise) in young women with non-anemic iron deficiency. These findings revealed that daily mild resistance exercise can improve non-anemic iron deficiency and prevent iron deficient anemia. Serum iron levels did not increase. Mild exercise did not increase iron absorption from the gastrointestinal tract\(^\text{28}\). Therefore, these observations suggest the possibility that dumbbell exercise did not enhance iron absorption, but it did improve the iron status in the body due to an increased expression of iron binding proteins.

The effect of resistance exercise on iron status was investigated using voluntary resistance training (climbing) equipment developed for rats. An experiment with severely iron deficient rats observed that the hemoglobin concentration of rats exercised for 8 weeks significantly increased in comparison to sedentary rats\(^\text{29,30}\). Moreover, as shown in Figure 1, resistance exercise (climbing) was associated with a greater increase in the hemoglobin concentration in comparison to aerobic exercise (swim-
Exercise was not changed by acute exercise (33). ALAS activity in rats participating in habitual running increased after a single bout of running exercise, whereas the ventricles of rats not participating in regular exercise exercised rats.

Holloszy et al. reported that ALAS activity in the red portion of the vastus lateralis muscle in comparison to control rats at 17h (hours) after exercise, while the same activity returned to a level equal to the control by 40h after exercise (32). Abraham et al. reported that ALAS activity in the ventricles of rats not participating in regular exercise increased after a single bout of running exercise, whereas ALAS activity in rats participating in habitual running exercise was not changed by acute exercise (31).

Bone marrow ALAD activity in rats that perform habitual climbing exercise was increased by a single exercise bout (34). In addition, the time-dependent changes in the ALAD activity of the bone marrow were measured after resistance exercise as an index of heme biosynthesis capacity. Bone marrow ALAD activity was increased post-exercise, but decreased over time during the post-exercise period (34). Holloszy et al. reported that ALAS activity in the red portion of the vastus lateralis muscle is increased by treadmill running for 3 months (35). Bone marrow ALAD activity in iron deficient rats increased after 3 weeks of climbing exercise in comparison to sedentary rats (Fig. 2) (31,35). In addition, the bone marrow ALAD activity was not increased by swimming exercise in iron deficient rats that performed climbing exercise or swimming exercise for 3 weeks; whereas it was increased by climbing exercise (35). This increase in ALAD activity appears to be associated with a greater increase in hemoglobin concentration in climbing-exercised rats than in swimming-exercised rats.

Effect of exercise on heme synthesis

δ-aminolevulinic acid dehydratase (ALAD) and aminolevulinic acid synthase (ALAS), which are the rate-limiting enzymes in heme synthesis are often measured to examine the impact of exercise.

Holloszy et al. reported that acute running exercise in rats that did not perform habitual running exercise, led to a two-fold increase in ALAS activity in the red portion of the vastus lateralis muscle in comparison to control rats at 17h (hours) after exercise, while the same activity returned to a level equal to the control by 40h after exercise (32). Abraham et al. reported that ALAS activity in the ventricles of rats not participating in regular exercise increased after a single bout of running exercise, whereas ALAS activity in rats participating in habitual running exercise was not changed by acute exercise (31).

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Plasma iron is used for hemoglobin synthesis (36). Baltaci et al. reported that the plasma iron concentration was increased 24 h after an acute swimming exercise that lasted for 30 min (37). Both the bone marrow ALAD activity and plasma iron concentration were higher post-exercise than pre-exercise (34). The hemoglobin concentration of iron deficient rats trained by resistance exercise increased in comparison to sedentary or swimming-trained rats (38,39). Therefore, these findings suggest that resistance exercise is superior for improving the iron status in comparison to aerobic exercise because it leads to concomitant increases in both the plasma iron concentration and bone marrow ALAD activity after resistance exercise which, thus, facilitates hemoglobin synthesis in iron deficient rats engaged in resistance training.

Nutrition

The absorption of heme iron is higher than non-heme iron. Protein from a meat factor source promotes iron absorption, but not all protein has this effect. Moreover, a meat factor increases the absorption of non-heme iron twofold; yet not all animal protein has this effect (38). However, protein is a component of hemoglobin and myoglobin involved in the storage and transportation of iron, respectively; and the intake of a high protein diet is often recommended to prevent anemia. In fact, previous studies reported that a diet low in protein leads to anemia (39,40). A study investigated whether a high protein diet could enhance the anemia mitigating effects of resistance exercise in rats fed a moderately iron deficient diet. The results showed that a high protein diet has no effect on bone
Iron is an essential trace element for biological functions. However, excess intake causes gastrointestinal problems such as nausea, vomiting and diarrhea. In addition, consumption of iron in large amounts for the long term has potential health risks. One should therefore be cautious when using iron supplements.

**Conclusion**

Iron is an essential trace element for biological functions such as oxygen transport and enzymatic activity. However, excess iron can also be toxic to cells since it is associated with free radical production. Therefore, the intravital iron balance must be deftly regulated. Intravital iron metabolism forms a semi-closed circle of absorption, storage and recycling of iron. The recycling capability of iron may be enhanced by resistance exercise. Such exercise may therefore be a potentially effective and economical measure to improve the iron status in developing countries that have a high rate of iron deficiency. Further studies are needed in order to clarify the relationship between the iron status and physical activity.

**References**


