Iron Supplementation: Oral Tablets Versus Intramuscular Injection

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Non-anemic, iron depleted women were randomly assigned to an injection group (IG) or oral group (OG) to assess which method is more efficient for increasing iron stores over a short time period. IG received a course of 5 × 2 mL intramuscular injections over 10 d, and OG received one tablet daily for 30 d. Fourteen, 21 and 28 d after commencing supplementation, ferritin concentration in OG significantly increased from baseline (means ± standard error: 27 ± 3 to 40 ± 5 to 41 ± 5 µg/L; \( P < 0.01 \)). Similarly, on days 15, 20, and 28 post the first injection, ferritin concentration in IG significantly increased from baseline (means ± standard error: 20 ± 2 to 71 ± 17 to 63 ± 11 to 63 ± 7 µg/L; \( P < 0.01 \)), and was also significantly greater than OG at day 15 and 28 (\( P < 0.05 \)). Iron injections are significantly more effective (both in time and degree of increase) in improving ferritin levels over 30 d than oral tablets.

Key Words: ferritin, hemoglobin concentration, iron stores

Iron deficiency is one of the most prevalent nutritional disorders in the world, particularly in females (4, 6). Ranging from depleted iron stores to the more severe form that results in anemia, iron deficiency has been frequently observed among various groups of trained athletes (3, 7, 8, 19, 20). There are several reasons why athletes may have low iron levels: plasma volume expansion, low dietary iron intake, bioavailable iron is low and/or excretion of iron is high (15). However, female athletes are at greater risk of iron deficiency than male athletes due to menstrual blood loss, as well as frequent sub-optimal dietary intake of iron (17, 24).

Further, in athletes, regular exercise can create a greater strain on body iron reserves due to increased losses through gastro-intestinal bleeding, urinary loss (hematuria), hemolysis of red blood cells and sweating (3, 5, 23). These avenues of iron loss, in combination with an inadequate dietary intake, and/or malabsorption of this mineral can easily result in iron deficiency developing in athletes (8, 15).

Iron status may be determined by measuring the body’s iron content in blood or tissue samples, particularly in the bone marrow. However, bone marrow biopsy...
requires an invasive procedure. Therefore, analysis of blood serum ferritin concentration is currently the preferred method used by medical practitioners to detect the first stage of iron deficiency (3, 18). A low serum ferritin level usually indicates a decrease in body iron stores, with iron supplementation and/or increased dietary intake of iron usually being prescribed when an athlete’s serum ferritin concentration is below 30 to 40 µg/L. (15, 17, 22). This level is higher than commonly applied to non-athletes, who are often characterized as being iron deficient when ferritin concentration is 12 to 20 µg/L (3).

Oral iron supplementation has been proven to increase iron stores over time, yet it is a slow process (commonly 4 to 8 wk to produce a 30 to 50% increase in serum ferritin levels) (9, 11). Therefore, if an important competition is imminent, supplementation through intramuscular injection is considered a preferable alternative by some sports physicians when serum ferritin is < 30 to 40 µg/L as it is thought that by injecting iron directly into the muscle, the iron levels will increase at a faster rate. Indeed, Chatard et al. (3, p. 238), stated “intramuscular iron injections could be given if the oral treatment is inadequate, as an injection is more efficient than oral supplementation.” However, little experimental evidence, particularly in athletes, is available to support this statement.

Therefore, the purpose of this study was to examine and compare the effect that the two commonly administered forms of iron supplementation (i.e., oral tablets and intramuscular injections) have on returning iron stores to a “normal” range over a short time period, attempting to confirm the widely held view that supplementation via intramuscular injection increases body iron stores at a faster rate than oral supplementation.

Methods

Subjects

After initial screening of iron status in 40 club-level athletes, 22 females, from a range of sports (triathlon, distance running, swimming, road cycling, field hockey, netball, and softball) volunteered as subjects. They were classified as iron depleted without anemia, having a hemoglobin concentration of > 115 µg/L and a serum ferritin concentration of < 40 µg/L (13). They also met the exclusion criteria of current or recent (last 12 months) pregnancy, recent fever or illness (last 2 wk), recent blood donation and iron therapy (last 6 months), and severe asthma, as certain asthma medications can interfere with iron absorption (22). To lessen the chance of an acute phase response affecting the results (12), all blood tests were made at least 12 h after prior exercise training. All subjects gave their informed consent and the study was approved by the Human Ethics Committee of the University of Western Australia.

Experimental Protocol

The subjects were randomly assigned to either an injection group (IG; n = 11) or oral group (OG; n = 11), after being matched for age, height, mass, and sport. One of the OG subjects later withdrew from the study due to unrelated illness. The physical characteristics of the two groups (IG and OG) were respectively age: 21
± 6 y and 25 ± 11 y; height 167.3 ± 4.5 cm and 166.8 ± 5.8 cm and mass 61.3 ± 6.1 kg and 58.5 ± 4.4 kg.

Subjects in the IG received a course of five intramuscular iron injections (over 10 d), as used in our previous study (2) and was designed to produce a rapid rise in serum ferritin levels. Each injection (into the gluteus maximus) consisted of 2 mL of Ferrum H (Sigma Pharmaceuticals, South Croydon VIC, Australia), containing the equivalent of 100 mg of elemental iron. Subjects in the OG were given one Ferro-gradumet (dried ferrous sulphate) tablet containing the equivalent of 105 mg of elemental iron daily for 30 d. To assist absorption, tablets were taken with food and a 200 mL glass of orange juice (and were not to be consumed with milk, tea, coffee, caffeinated soft drinks, or bran). Subjects were regularly reminded of these requirements over the 30-d period and self-reported compliance with the supplementation protocol was excellent, with no tablets being returned.

Blood samples (for serum iron, transferrin, transferrin saturation, ferritin, and hemoglobin concentration) were taken from the IG 15, 20, and 28 d post the first injection and from the OG 14, 21, and 28 d after commencing supplementation. These times were chosen to allow a comparison of the effect over 1 month of supplementation by both methods. Subjects were asked to maintain their training levels and normal diet for the 1 month duration of the study.

Iron measures and hemoglobin concentration were respectively made on BM/Hitachi model 917 and Beckman Coulter Counter model STKS analyzers, with coefficients of variation being 1.5% (serum iron), 3.3% (serum transferrin), 6.8% (serum ferritin), and 0.8% (hemoglobin concentration).

The subjects were also required to compile a 4 d dietary record (including one weekend day) and menstrual history over the duration of the study, so that estimates of normal iron intake (Diet/1, version 4, Xyris, Brisbane, Australia) and iron loss due to menstruation could be made. The estimated total average amount of heme and non-heme iron consumed (mg/d) was determined by the procedures of Monsen et al. (14). To estimate the degree of menstrual blood loss, a score was created by multiplying the number of sanitary napkins/tampons used on the heaviest flow day by the number of days of menses, according to the method of Rowland and Kelleher (20).

**Statistical Analysis**

Paired *t*-tests were used to analyze within-group changes in iron status. A repeated measures MANOVA was used to assess any between-group changes, with post hoc unpaired *t*-tests used where appropriate. Statistical significance was accepted at *P* < 0.05.

**Results**

The iron measures and hemoglobin concentration for the IG and OG before and after supplementation are shown in Table 1. No significant differences existed between the two groups at baseline, and, with the exception of serum ferritin values, all measures were within normal ranges.

Supplementation significantly increased (*P* < 0.05) serum ferritin from baseline in both groups at all time points, but the resulting ferritin levels were significantly
higher \((P < 0.05)\) in the IG at the second (day 14/15) and final (day 28) measurements. The percentage increases in ferritin (from baseline) were significantly greater \((P < 0.01)\) at all time points in the IG, ranging from 224 to 260\%, compared to 51 to 52\% in the OG. No other iron measures, nor hemoglobin concentration, recorded any change in either group as a result of iron supplementation.

Estimates of normal daily dietary iron intake for the IG were significantly higher \((P < 0.05)\) than for the OG, being respectively 17 ± 5 mg/d to 12 ± 4 mg/d, with the difference coming from a greater estimated non-heme iron intake. Estimates of daily heme iron intake and the amount of iron absorbed were not different between the two groups. Similarly, menstrual score, duration of menstruation, and total number of napkins/tampons used were not different between the two groups over the supplementation period.

**Discussion**

To the authors’ knowledge, this is the first study to directly compare the effects of iron supplementation via intramuscular injection and oral tablets on iron status in female athletes. Significant increases from baseline in serum ferritin were recorded...
in both groups as a result of the treatment, but at day 14/15 and day 28, the IG values were significantly greater than in the OG. These data confirm that iron supplementation via intramuscular injection is a more effective method of increasing iron stores than oral tablets over a short time period (1 month).

With regard to oral iron supplementation, the magnitude of increase seen from baseline to 28 days (~ 14 µg/L) here is in agreement with previous findings. Following similar dose regimes to those used here, Rowland et al. (21) and Zhu and Haas (25) reported that after 4 wk of supplementation, ferritin levels had increased by approximately 13 and 15 µg/L respectively. Recently Pitsis et al. (18) showed that 2 months of oral supplementation produced an increase of approximately 18 µg/L in female athletes, and Friedman et al. (8) found that oral supplementation for 12 wk with twice the daily intake of elemental iron (i.e., 200 mg) to that used in our study, increased ferritin levels by approximately 20 µg/L. Therefore, when iron depleted, but non-anemic females undertake oral iron supplementation, ferritin levels can be expected to improve by 10 to 20 µg/L over 4 to 12 wk, with most of the increase likely to occur in the first 4 wk. However, in all the aforementioned studies, baseline ferritin levels were < 20 µg/L and after supplementation did not in any case exceed 40 µg/L. Larger changes in ferritin levels appear difficult to achieve with oral supplementation, and even after 2 to 3 months of daily intake, many athletes may still be marginal with regard to ferritin levels and iron stores. Nielsen and Nachtigall (15) have previously suggested that all athletes with serum ferritin levels of < 35 µg/L should be supplemented.

In contrast to oral supplementation, intramuscular iron injections produced much larger increases in ferritin levels, of 43 to 51 µg/L. These changes also occurred quickly, being present 15 d after the first injection and remaining in place at both 20 and 28 d. Our previous study (2) also produced similar increases over the same time frame. The only other study to have investigated the effects of iron injections on ferritin levels was by Ashenden et al. (1) who found no changes were evident. However, in their study, only a single (2.5 mL) injection was given, rather than the course of five injections as used here. Also, they only re-measured ferritin levels 21 d after the injection, therefore their results cannot be considered in parallel with ours. Similarly, Kumar et al. (10) compared oral and intramuscular iron supplementation in anemic pregnant women over 12 wk, finding similar increases in ferritin levels and hemoglobin concentration, but only two iron injections were administered, in comparison to daily oral supplementation.

Lastly, it should be noted that intravenous iron administration may be superior to both intramuscular and oral supplementation, but this invasive route is generally reserved for severe cases of iron deficient anemia (16). For athletes who are non-anemic, but iron deficient, dietary intake of particularly heme iron should be increased initially, and if time permits, then a course of oral iron supplements may be taken in order to boost ferritin levels by 10 to 20 µg/L over 4 to 12 wk. However, if an important competition is imminent (1 to 2 wk), a course of intramuscular iron injections may be used to more quickly increase ferritin levels (2), in addition to instituting appropriate dietary modifications.

In conclusion, our results show that a course of intramuscular iron injections can quickly raise ferritin levels in iron depleted, but non-anaemic females, from approximately 20 µg/L to 60 to 70 µg/L, which is approximately twice the level at which supplementation is often recommended (15). These changes are larger
and more rapid than those which occur with oral supplementation over 30 d, but the effect of this change on iron storage and exercise performance remains unclear and awaits further study. It can also be reported that none of the subjects used here experienced any side effects from either form of iron supplementation.

References


