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Iron Status in the Female Blood Donor

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Introduction

Iron deficiency is of important clinical significance because reduced iron stores compromise the body's ability to synthesize hemoglobin, an oxygen-binding protein. Clinical manifestations of iron deficiency include decreased hemoglobin or anemia, fatigue and decreased work performance, decreased regulation of body temperature, decreased immunity, and complications in neonates of iron-deficient mothers among numerous other symptoms (10). Hemoglobin level has been the traditional measure to screen for iron deficiency. This approach, however, detects only persons with severely depleted iron stores (4). Numerous sources agree that "serum ferritin concentration provides the single best and least invasive way to measure the size of the body's iron store (1,3)." Three stages of iron deficiency have been described. The first stage involves a decrease in iron stores without any clinical symptoms. The second stage of deficiency compromises erythropoiesis although hemoglobin concentrations are maintained within 95% of the reference range. The third stage of deficiency, the only stage detected by hemoglobin measurements, is iron deficiency anemia which leads to inadequate hemoglobin production (1,7,9,10). A measure of serum ferritin levels can detect the first stage of iron deficiency since ferritin is the storage form of iron that is depleted in this first stage. Monitoring the status of iron storage is of major importance in the early detection and prevention of iron-deficiency anemia and is also of importance in monitoring the changing iron status of female blood donors. For example, in one study 30% of women of childbearing age who were not blood donors and 48% of women who were blood donors had iron deficiency as measured by serum ferritin concentrations (4). Many blood donor sites continue to use the traditional method of hemoglobin level to assess the iron status of a potential donor. This continued practice erroneously determines that many iron deficient donors have adequate levels of iron.

Iron is found in the body in several forms. It can be stored as ferritin, associated with the blood transport protein transferrin, bound to hemoglobin and myoglobin, or associated with a number of iron dependent enzymes (7). Maintenance of total body iron is dependent on the absorption of ingested iron by the intestinal mucosa. Iron absorption is a complex process that is influenced by body stores, the rate of usage by the body, bioavailability of iron based on the chemical nature of ingested iron (9) and dietary factors that affect the bioavailability of iron (6,10). Not only is it important to understand the best method of detecting body storage of iron, it is important to understand how body stores can be increased by understanding the factors that effect the absorption of iron. The absorption of iron can be affected by a high concentration of other minerals, such as zinc (4). It has also been found that "the addition of heme iron to physiological doses of ferrous iron can strongly increase the amount of iron absorbed (3)." Iron bioavailability can vary from <1% to >50% depending on the regulatory mechanisms in the intestinal mucosa (10). These factors must be considered in the clinical setting because the mere prescription of non-heme iron supplements or increased dietary intake of iron may not be sufficient to increase iron stores to adequate levels in iron deficient patients.

Female blood donors must be particularly careful to monitor their total body store of iron. Because women of childbearing age lose a substantial amount of iron in monthly

menstruation, excess loss of iron from blood donations puts women at increased risk of iron deficiency anemia and its associated complications.

Effect of Iron Stores on Iron Absorption in Female Blood Donors

It has been demonstrated, in a study of thirty-four female blood donors, that reductions in iron stores are correlated with increases in iron absorption(6). If it is true that iron stores are negatively correlated with iron absorption, female blood donors should display increased absorption of ingested iron due to the increased erythropoietic demand caused by blood loss with each donation. One study of healthy elderly individuals (over age 65) found that there was a statistically significant increase in iron absorption in female blood donors compared to non-donors, $7.4 \pm 3.6\%$ and $2.5 \pm 1.4\%$, respectively (6). In another study of sixteen elderly women who were repeat donors, it was demonstrated that the mean iron absorption between the first and second donations was 0.85 mg/day. This value gradually increased to a mean of 3.55 mg/day at the end of the study and remained significantly higher than the mean iron absorption of the non-donor control group (5). The increase in iron absorption can be viewed as an adaptive response in which the intestinal mucosa increases the uptake of iron in response to a fall in storage levels. With each blood donation there was a concomitant decrease in serum ferritin concentration until the gradually increasing iron absorption reached an adequate level to replace iron lost by donation and by normal mechanisms (5). This evidence supports our original hypothesis that decreases in serum ferritin results in an increase in iron absorption. There is not, however, an initial one to one correlation.

The Setpoint Theory of Iron Absorption

As stated in the preceding section there was a delayed response in increased iron absorption due to decreasing serum ferritin as a result of blood donation. From this observation it can be assumed that the increased iron absorption does not occur until there is significant deviation from individual baseline iron stores. At that point the intestinal mucosa increases the absorption of iron. There is thought to be a "store regulator" mechanism by which the body signals this need for increased absorption (1). One fault in this system is that in individuals with low initial stores of iron the delayed response in iron uptake will not be sufficient to compensate for lost iron before the individual becomes anemic (5). In this case the increased absorption is believed to still take place although it occurs after body stores are at anemic levels.

The two previously mentioned research studies provide evidence for a setpoint theory of individual iron levels. This theory, as described by Gavin et al., claims that each individual has a setpoint at which the body attempts to maintain iron levels under normal conditions(6). In the study of eight healthy, elderly non-donor females there was not a significant change in iron stores over the course of two years, even in those taking oral supplements of iron. In this study sixteen healthy, elderly female blood donors reached a maximal mean absorption of iron at 3.55 mg/day regardless of iron intake and supplementation (5). There seems to be a level of iron storage that is reached, at which there is no further increase in serum ferritin although there is continuous supply of iron

supplements. This evidence shows that the size of individual iron stores alone does not determine the efficacy of iron absorption in blood donors. Since there is a setpoint for individual iron absorption the rate of absorption is changed to maintain each individually determined setpoint. It can be assumed that blood donors have a higher setpoint for iron storage than do non-donors because donors have increased absorption rates (5).

Reason for Increased Iron Absorption in Female Blood Donors

We have seen that there is a significant increase in the absorption of iron in donors versus non-donors. Evidence has been provided to support the claim that an increase in iron absorption occurs until the individual setpoint for iron stores has been achieved. We will now explore one reason behind this increase in iron absorption in female blood donors. Borch-Iohnsen et al. postulated that "one possible explanation is that blood donations result in a raised activity level of erythropoiesis" and thereby higher demands for iron (2). The increased formation of red blood cells increases the cellular demand for iron, which has been identified as a necessary inorganic element in hemoglobin. Female blood donors therefore absorb more iron to meet these increased needs.

Effects of Iron Supplementation in Female Blood Donors

A study of two iron supplements in female blood donors and non-donors indicate that iron supplementation may be beneficial in maintaining adequate iron stores. In a study by Borch-Iohnsen et al. there was a significant increase in serum ferritin and hemoglobin in female donors and non-donors taking two forms of iron supplements (2). One supplement contained 20 mg of ferrous fumarate with 120 mg ascorbic acid; the other supplement contained 2 mg heme iron plus 16 mg ferrous fumarate. There was a statistically significant difference in serum ferritin and hemoglobin increases among donors versus non-donors (2). As discussed above, this evidence supports the assumption that female blood donors have more efficient iron absorption than do non-donors, due to an increased setpoint for iron storage. Both non-donors and blood donors benefited from iron supplementation. Baynes et al. argues against this finding and supports the claim that "the efficacy of iron supplementation has not been clearly established (1)." There appears to be some benefit from iron supplementation in the female subjects studied although some researchers have questioned this benefit.

The use of ascorbic acid to increase iron absorption is also a topic of disagreement. Research from Hunt et al. questions whether ascorbic acid has significant effects on iron absorption in females consuming self-selected meals (8). Yip et al. claim that "by keeping iron in its reduced form, ascorbate enhances intestinal iron absorption (10)." A molecular mechanism is given to support the later claim while the lack of supplementation in the previous study leaves relevant questions unanswered. Because there is minimal, if any, toxic effects from ascorbic acid supplementation and possible benefit it is still recommended by most organizations that ascorbic acid supplementation accompany iron supplementation.

In a study of sixteen women, non-supplemented women showed a significantly greater decline in iron stores than did supplemented women, 13.09 ± 2.46 and $10.60 \pm$ mg/kg, respectively (5). Supplemented women had mean iron stores 2.49 mg/kg higher than women who did not take oral supplements (5). Iron supplementation appears to have a protective feature, which prevents substantial decreases in serum ferritin compared with non-supplemented women. As stated above this study shows that there is not a significant difference in the setpoint of women donors with respect to supplementation. Supplementation does, however, appear to benefit women in preserving present iron stores (5). Because of this effect women who took supplements reached their setpoint maximum sooner than did non-donors who continued to deplete present stores to replace iron lost by donation.

Conclusion

Female blood donors present a particularly interesting clinical case. Women of childbearing age have increased demands for iron due to menstrual bleeding and increased demand during pregnancy. Many women are iron deficient because of these factors and may require or elect to take supplements. Many women who also donate blood on a regular basis are therefore at risk for iron deficiency anemia. Because hemoglobin remains the standard method for assessing iron stores in donors these women may have iron deficiency anemia as a result of blood donation and the other confounding variables. It seems reasonable that serum ferritin should be regularly tested in those donors to detect and prevent more severe depletion of iron stores.

Female blood donors also have an increased need for iron above the recommended daily allowance to support erythropoiesis and maintain their higher setpoint level. These women may benefit from some form of iron supplementation. Although this benefit has not been clearly defined in all studies, some evidence exists that shows that female blood donors, particularly, can benefit from iron supplementation. Further studies may assess the benefit of absorption enhancing agents, such as ascorbic acid and other factors, that must be optimized to maximize iron absorption.

REFERENCES

1. Baynes RD, Cook JD, Current issues in iron deficiency. *Current Opinion in Hematology*. 1996;3:145-149
2. Borch-Iohnsen B, Halvorse R, Stenberg V, Flesland O, Mowinckel P. The effect of daily low-dose iron supplements in female blood donors with depleted iron stores: comparasis with female non-donors. *Scandinavian Journal of Clinical Laboratory Investigation*. 1993;53:789-791.
3. Ekman M, Reizenstein P. Comparative absorption of ferrous and heme iron with meals in normal and iron-deficient subjects. *Ernyhrungswiss*. 1993;32:67-70.

4. Fryman E, Bystrom M, Jansson U, Edberg A, Hansen T. Side effects of iron supplements in blood donors: superior tolerance of heme iron. *Journal of Laboratory Clinical Medicine*. 1994;123:561-564.
5. Garry PJ, Koehler KM, Simon TL. Iron stores and iron absorption: effects of repeated blood donations. *American Journal of Clinical Nutrition*. 1995;62:611-620.
6. Gavin MW, McCarthy DM, Garry PJ. Evidence that iron stores regulate iron absorption - a setpoint theory. *American Journal of Clinical Nutrition*. 1994;59:1376-1380.
7. *Human Biochemistry and Nutrition: The Laboratory Manual*. 1998;III1-III7.
8. Hunt JR, Gallagher SK, Johnson LK. Effects of ascorbic acid on apparent iron absorption by women with low iron store. *American Journal of Clinical Nutrition*. 1994;59:1381-1385.
9. Lynch SR, Baynes RD. Deliberations and evaluation of the approaches, endpoints and paradigms for iron dietary recommendations. *The Journal of Nutrition*. 1996;126(suppl 9):2404S-2409S.
10. Yip R, Dallman PR. Iron. In: Ziegler EE, Filer LJ, eds. *Present Knowledge in Nutrition*, 7th ed. Washington, DC: ILSI; 1996:149, 277-289s.