Understanding Iron and Restless Legs Syndrome

Iron is essential for all living cells in the body. Its major function in the cell is to interact with oxygen to produce energy for the cell in the form of ATP (an energy molecule). It is because of this association between iron and oxygen, as well as the potential for oxidative damage, that iron is highly regulated inside and outside of the cell. It is also because of the concern about oxidative damage that much of the research on iron has focused on iron overload effects. This is also why many doctors are reluctant to give iron for extended periods. Unfortunately, iron deficiency, not iron overload, has had the most profound effects on world health; and research on the long term effects of brain iron deficiency is limited.

Iron and your body

When iron enters the bloodstream, about 80-85% will go to your bone marrow where it will be used to make red blood cells. The next largest proportion of iron is distributed to your liver. A small percentage, probably less than 5%, is redistributed to other organs, including the muscles, kidneys, heart and brain. The brain gets less than 0.1% of the newly absorbed iron. Since the largest volume of iron is actually in your red blood cells, when those red blood cells die, they are broken down by special cells which are found in the spleen called macrophages. The macrophage operates to collect, store, and redistribute iron back to the different organs.

Although most iron will go back to the bone marrow and liver, a greater percentage of iron will go to other organs like the brain. Your brain may depend more on the spleen/macrophage stores of iron than on what is absorbed immediately from your diet.

Understanding low iron levels

With low iron stores, the percentage of iron going to bone marrow increases. Under severe iron deficient conditions, as much as 99% of the body's iron will go to the bone marrow. This permits the body to continue to make red blood cells and prevents the person from becoming anemic, but it essentially starves other organs (including the brain) of iron.

Under low or deficient iron conditions, the brain is not equally affected. The areas most affected appear to be those associated with the dopamine system.

Iron deficiency without anemia has been associated with increased fatigue, depression, cognitive impairment, decreased work capacity, and also RLS.

The usual approach to the determination of body iron stores is the use of specific blood tests. The hemoglobin/hematocrit tests are the most commonly requested measures, primarily because of the physician's concern as to whether your iron is low enough to cause anemia. However, even in those RLS patients with severe iron deficiency, anemia is uncommon. Therefore, the hemoglobin/hematocrit are of minimal value.

Currently, the best guide to body iron stores is the serum ferritin (a protein found inside cells that stores iron for later use). The single limitation of the serum ferritin is that any mild infection or inflammation may falsely elevate the ferritin level and this may last up to six weeks after inflammation or infection has resolved. Therefore, the ferritin level may only reflect this inflammatory process and not the true state of the body iron stores.

The other indices like serum iron level, total iron binding capacity, and percent iron saturation may be of value in concert with the serum ferritin, as these factors are sometimes less affected by the inflammation or infection. Your serum iron level will increase significantly within 15 minutes of taking iron-containing food and will vary by nearly 50% from the morning to the nighttime level. Therefore a fasting, early-morning blood test is recommended in order to improve the interpretation of the results.

Raising low iron levels

Meat, fish, and liver provide the most absorbable form of iron. The iron contained in leafy green vegetables is not always broken down adequately by the human GI tract, therefore, the same amount of iron that may be contained in the vegetable may not deliver the same amount of iron found in meat or liver.

Iron pills can also be used to increase iron stores but should not be taken with food or milk as this will markedly reduce iron absorption. One can further enhance iron absorption by taking iron pills combined with either vitamin C or orange juice.

An alternative approach to getting iron into the body is intravenous infusions. Currently, there are four different formulations of intravenous iron available for use. They include iron dextran, iron glucose, iron gluconate, and ferumoxytol. With intravenous infusion, one can deliver (over a course of either a single injection or several injections) the maximum amount of iron needed to replace iron deficient stores. However intravenous iron presents a low risk of serious

allergic reaction. Therefore, it is typically considered only if oral iron fails to improve iron stores. When taking oral iron, it may take as little as three months to as much as six or nine months before adequate stores can be obtained in some individuals.

Based on current research, it is recommended to treat patients with iron supplements whose ferritin levels are less than 75 ug/l, with the goal of getting the ferritin above 100 ug/l. The serum ferritin, iron, TIBC (total iron binding capacity) and percent iron saturation should be checked every three months until the goals are reached.

Once you have reached your ferritin goals, whether you should remain on iron at a lower dose than initially used, will vary from individual to individual.

If there are continued problems with blood loss because of GI bleeding or menstrual issues, then some level of iron supplementation should probably be continued. The best guide is to stop the iron and then check a serum ferritin level in three and six months to see if there is any indication that the ferritin level is dropping again. If the ferritin level is dropping after discontinuing the iron supplements, then some level of daily supplementation may be required in order to maintain those iron levels in a clinically optimal range.

A randomized, double-blind, placebo-control study of 1000 mg of iron given intravenously showed significant improvements in RLS symptoms in patients who had normal hemoglobin levels and whose ferritin levels ranged between 5 and 113 ug/l. Therefore treating RLS patients whose ferritin level is 100 ug/l or less with intravenous iron may provide an alternative option to oral iron supplementation.

Conclusion

Keeping the body's iron stores at an optimal level is a complex process involving periodic blood tests and intervention as needed. For individuals with RLS, it is important to work with a healthcare provider who understands the delicate balance of RLS symptoms and iron supplementation.

This publication has been reviewed and approved by the RLS Foundation Scientific and Medical Advisory Board. Literature distributed by the RLS Foundation, including this publication, is offered for information purposes only and should not be considered a substitute for the advice of a healthcare provider. The RLS Foundation does not endorse or sponsor any products or services.

Please become an RLS Foundation member and receive our quarterly newsletter, *NightWalkers*, as well as access to our library of handouts and brochures with the most current information available about RLS. Go to www.rls.org/join to help us Find a Cure!

RLS
RESTLESS LEGS SYNDROME FOUNDATION

The RLS Foundation is dedicated to improving the lives of the men, women, and children who live with this often devastating disease. Our mission is to increase awareness, improve treatments and, through research, find a cure for restless legs syndrome.