

IRON THERAPY FOR RLS

1. The benefits of iron therapy have been known since 1953. (Niles Brage Norlander)¹. Research demonstrates that RLS patients have lower brain iron stores, and that iron therapy can be beneficial even if the patient is not anaemic.²
2. The key measurement for iron is serum ferritin, also known as iron stores, measured in micrograms per litre (µg/L). Ferritin values between 25 - 250 µg/L are considered normal and many doctors regard 300 µg/L serum ferritin as the accepted, safe upper limit. However many RLS patients need levels above 300µg/L and haematologists regard levels of up to 1000µg/L as safe.³
3. A full panel, morning, fasting blood test should be taken to measure serum ferritin, serum iron, total iron-binding capacity and percentage transferrin saturation.
4. Iron absorption from the gut is regulated by the hormone hepcidin which reduces the amount of iron the body will absorb as ferritin levels increase. This limits the effectiveness of oral supplementation and influences iron therapy as below.
5. The Mayo Clinic Algorithm, written by the world's top RLS experts, recommends that all RLS patients with serum ferritin of 75 µg/L or less and transferrin saturation below 45%, should receive a trial of oral iron⁴, e.g. ferrous fumarate or ferrous bisglycinate.
6. Oral supplements are normally taken on an empty stomach as other foods reduce iron absorption. Mornings are recommended as hepcidin levels are normally lowest, and vitamin C taken at the same time can help absorption. Lastly, studies have shown that hepcidin levels rise in the 24 hours after taking an iron supplement and fall thereafter making it more effective if taken as a double dose every 48 hours⁵. If gastric intestinal symptoms develop, supplements can be taken with food.
7. Follow up blood tests should be repeated after 3 to 4 months and then every 3 to 6 months until serum ferritin is greater than 100µg/L. If RLS is unresolved or worsens, supplementation should still continue.
8. Intravenous iron should be first line therapy if the patient has moderate to severe, or refractory RLS and serum ferritin is between 75 and 100 µg/L because oral absorption of iron at these higher ferritin levels is likely to be minimal. It may also be considered if the RLS is severe and oral supplementation would take too long or where the patient has gastrointestinal disorders and oral iron is not tolerated.⁶
9. Most trials of intravenous iron therapy in RLS use ferric carboxymaltose, administered in a single dose of 1000 mg, or 2 doses of 500 mg at 5 to 7 day intervals. Clinical response can take up to 6 weeks or longer. Pre-treatment with sedating anti-histamines containing diphenhydramine should be avoided as it worsens RLS. Cetirizine or loratadine are safer options. If RLS does not improve, repeated infusions can be given in at least 12-week intervals.
10. It is generally accepted that intravenous iron will help alleviate symptoms of RLS in 60% of cases

¹ Nordlander NB. Therapy in restless legs syndrome. Acta. Med Scand 145:453-457

² https://www.cochrane.org/CD007834/MOVEMENT_iron-treatment-restless-legs-syndrome

³ Medical Case Report on Repeat Treatment of Restless Legs Syndrome with Intravenous Infusion of Iron, <https://pubmed.ncbi.nlm.nih.gov/34703445/>

⁴ The Management of Restless Legs Syndrome: An Updated Algorithm, [https://www.mayoclinicproceedings.org/article/S0025-6196\(20\)31489-0/fulltext](https://www.mayoclinicproceedings.org/article/S0025-6196(20)31489-0/fulltext)

⁵ Alternate day versus consecutive day oral iron supplementation in iron-depleted women: a randomized double-blind placebo-controlled study, [https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370\(23\)00463-7/fulltext](https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(23)00463-7/fulltext)

⁶ The Management of Restless Legs Syndrome: An Updated Algorithm, *ibid.*