



LETTER TO THE EDITOR

The Need to Establish an Evidence-Based Limit Value for Serum Ferritin in the Use of Intravenous Iron for Restless Legs Syndrome

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I am writing to highlight to the community involved in the research and management of Restless Legs Syndrome (RLS), the need for some clarity and an evidence-based rationale for the selection of a “cut off” value of serum ferritin concentrations in the decision regarding the use of intravenous (IV) iron infusion in the treatment of RLS.

In the excellent recent article by Allen, et al. [1], much useful information on clinical practice guidelines for RLS was provided. This included the need to ensure that transferrin saturation remained below 45% as a requirement for recommending iron infusion therapy, with which I fully concur. It has also been noted that this therapy may be beneficial for people with RLS without low iron (as long as there is no iron overload) [2].

However, there appears to be considerable uncertainty and potentially confusion as to what should be considered a reasonable and safe level of serum ferritin below which iron infusion therapy can be recommended.

Allen and colleagues [1] conclude: “Nonetheless, given the lack of significant experience with higher serum ferritin levels the expert-based recommendations are to limit the initial IV iron treatment to patients with serum ferritin levels $\leq 100 \mu\text{g/l}$ ”. On the basis of this publication, this cut off value has been taken up in the recommendations and algorithm published in the Mayo Clinic Proceedings [3]: “According to a consensus of RLS experts, the base requirement for any use of

intravenous iron therapy in RLS is that the serum ferritin concentration should be less than $100 \mu\text{g/L}$ ”.

It is not clear, however, what factors have led to this cut-off value of $\leq 100 \mu\text{g/l}$ and whether it might be considered too conservative.

Allen, et al. [1] recognise the following:

“Ferric carboxymaltose 1000 mg is considered effective for the treatment of moderate to severe RLS in patients with a serum ferritin $< 300 \mu\text{g/l}$ and transferrin saturation $< 45\%$ ”.

“IV iron treatment should not be given to patients with serum ferritin $> 300 \mu\text{g/l}$ or transferrin saturation $> 45\%$ ”

Serum ferritin from $300\text{-}1000 \mu\text{g/l}$ is generally used as an alert because this can be indicative of underlying disease. In the case of deliberate IV iron, the elevation of ferritin is intentional. The risk of hepatic iron overload has been reported as being low with serum ferritin concentrations below $1000 \mu\text{g/l}$ [4-6]. There is a risk of fibrosis and cirrhosis above this threshold of $1000 \mu\text{g/l}$ [7]. All haemochromatosis subjects with either hepatic fibrosis or cirrhosis had ferritin concentrations greater than 700 micrograms/L [8].

A recommended serum ferritin cut-off value for initial and subsequent iron infusions should be evidence-based and reconsidered taking the above considerations into account with enhanced collaboration between neurologists and haematologists.

References

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