

COMMENTARY

Intravenous iron therapy alleviates symptoms of sleep-related movement disorders in children with minimal side effects

Commentary on Ingram DG, Al-Shawwa B, DelRosso LM, Sharma M. Intravenous iron therapy in the pediatric sleep clinic: a single institution experience. *J Clin Sleep Med*. 2022;18(11):2545–2551. doi: [10.5664/jcsm.10152](https://doi.org/10.5664/jcsm.10152)

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Restless sleep can be defined as a series of persistent or recurrent body movements, arousals, and brief awakenings that occur in the course of sleep.¹ The high prevalence in the pediatric population and potential negative consequences such as insomnia or poor school performance make restless sleep an important research field in order to develop timely and effective treatment for the affected children.² Today, restless sleep is recognized as a separate sleep disorder and many conditions that can lead to restless sleep in children have been identified.

Sleep-related movement disorders (SRMDs) are one of the most common causes of restless sleep. One interesting finding in patients with SRMDs is that they tend to have lower serum ferritin levels, which could be a potential component in the pathophysiological sequence of SRMDs.³ Recent studies suggested that improving low serum ferritin levels by an oral iron supplementation could be modestly beneficial for children with SRMDs, although substantial and significant improvement in the condition with this therapy is yet to be fully proven.⁴ Instead of oral supplementation, some studies used intravenous (IV) iron supplementation, which is currently considered a first-line treatment option in adults with restless legs syndrome (RLS)—a type of SRMD. Results show both greater response and a lower number of side effects in IV iron supplementation compared with oral, although this was done in a small sample of children.⁵

In this issue of the *Journal of Clinical Sleep Medicine*, to expand on this research in children, Ingram et al⁶ conducted a study to assess the efficacy and safety of 15 mg/kg IV ferric carboxymaltose in a sample of 63 children with an average age of 7.2 years. The primary indications for IV ferric carboxymaltose supplementation were RLS (n=30), periodic limb movement disorder (n=16), and restless sleep disorder (n=17). Pre-infusion, most children had restless sleep (85%), while around half of them had sleep-onset difficulty (46%), RLS/urge to move (41%), sleep maintenance difficulty (54%), and daytime behavioral challenges (49%). The fewest number of children experienced unrefreshing sleep (20%).

A benefit of IV iron supplementation therapy compared with giving oral iron supplements are the considerable differences in

terms of side effects. Ingram et al show that only a small percentage of patients experienced side effects with the IV approach: behavior changes (9%), gastrointestinal discomfort (6%), headache (4%), and rash (3%). No serious adverse effects were observed and the authors reported that none of the side effects were outside of the expected and reported range of side effects when iron supplements are used. It seems that the benefit of the IV vs the oral approach stems from bypassing the gastrointestinal tract and therefore largely reducing other potential side effects.

Fifty-three patients had available data after the follow-up, which was, on average, 16.6 weeks after ferric carboxymaltose infusion. Most importantly, the majority of the patients (73%) noted that at least 1 of their symptoms improved, which clearly shows that a large proportion of children with restless sleep symptoms caused by SRMDs and accompanied by iron deficiency could benefit from IV supplementation therapy. Ferritin levels were also significantly higher after follow-up, with an almost 7-fold increase from the initial value of 21.7 µg/L to 147.9 µg/L. This was an important result since other studies showed that improvement in ferritin levels is associated with the improvement of RLS symptoms in 78% of children.⁴ On the other hand, 13 (24%) did not notice improvement and only 1 patient had worsening symptoms.

When looking at specific clinical responses elicited by this therapy, improved restless sleep was the most important one in more than half of the patients. Around one-third of patients showed improvement in sleep onset (26%), sleep maintenance (34%), and RLS symptoms (30%). Fewer said they had more refreshing sleep (15%) and improved daytime symptoms (22%), with one-quarter reporting no substantial change. There were no significant differences between patients who experienced clinical improvement with infusion compared with those that did not in terms of age, sex, ethnicity, past medical history, medication use, and across all other confounders, which indicates the applicability of this method in a wide range of populations. Importantly, one of the main strengths of the study is that the majority of patients experienced clinical and laboratory improvements regardless of medication or medical comorbidities. However, the

authors also emphasized that 84% of children with RLS, 66% of children with suspected restless sleep disorder, and only 58% of children with periodic limb movement disorder improved. They argue that comorbidities may have contributed to the symptoms of sleep disruption but also highlight that the current results support the use of IV iron even in children with significant comorbidities and those taking medications that potentially influence the severity of SRMDs.

Although this is not a placebo-controlled study and future randomized controlled trials are needed, it adds to previous research in this area and demonstrates good evidence in favor of using IV iron supplementation in children for treating SRMDs accompanied with iron deficiency.

CITATION

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