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SCIENTIFIC INVESTIGATIONS

Intravenous iron therapy in the pediatric sleep clinic: a single institution experience

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Study Objectives: Initial reports of intravenous (IV) iron administration have been promising for children with restless legs syndrome, periodic limb movement disorder, and restless sleep disorder. The aim of the current study was to evaluate further the clinical response to IV iron supplementation in children seen in a pediatric sleep clinic.

Methods: We performed a retrospective chart review of children cared for in a single pediatric sleep clinic who also underwent IV iron infusion. Pre and post IV data regarding their sleep symptoms and ferritin levels were abstracted.

Results: Overall, 63 pediatric sleep patients underwent IV iron infusion, mostly with ferric carboxymaltose (n = 60), for restless legs syndrome (n = 30), periodic limb movement disorder (n = 22), and restless sleep disorder (n = 17). Of the 59 patients with clinical follow-up, 39 (73%) noted improvement in at least 1 symptom, and 14 (26%) did not notice improvement or noticed worsening symptoms. Of the 59 patients with preinfusion and postinfusion labs, the average ferritin level increased from 21.7 (13.3) to 147.9 (120.9) $\mu\text{g/L}$, $P < .001$. Comparing patients who experienced clinical improvement vs those who did not, there were no statistically significant differences in change in ferritin levels ($P = .278$), sex ($P = .452$), or age ($P = .391$). Ferritin change with infusion according to diagnostic subgroups (restless legs syndrome/periodic limb movement disorder/restless sleep disorder) was examined, and no significant differences were noted ($F(2,56) = 0.852$, $P = .432$). In terms of immediate adverse reactions to the IV infusion, 7 (11%) experienced at least 1 side effect, with the most common being behavior change (n = 6) or gastrointestinal discomfort (n = 4); no episodes of anaphylaxis or extravasation were noted.

Conclusions: These data provide additional support for the efficacy and safety of IV iron for pediatric restless legs syndrome, periodic limb movement disorder, and restless sleep disorder recalcitrant to oral iron.

Keywords: pediatric, restless leg syndrome, IV iron

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BRIEF SUMMARY

Current Knowledge/Study Rationale: Initial reports of intravenous iron therapy for children with restless leg syndrome, periodic limb movement disorder, and restless sleep disorder have been promising but limited to small, selected samples. We performed a chart review of children who had undergone intravenous iron infusion for restless leg syndrome/periodic limb movement disorder/restless sleep disorder seen in a single pediatric sleep clinic.

Study Impact: Most children who underwent intravenous iron infusion experienced clinical improvement in sleep-related symptoms, robust increase in ferritin level, and few side effects. These data provide additional evidence for the safety and efficacy of intravenous iron in a diverse sample representative of that seen in pediatric sleep clinics.

INTRODUCTION

Restless sleep is a common presenting concern in the pediatric sleep clinic. While there are many possible contributors to restless sleep (such as sleep-disordered breathing, respiratory disorders, gastroesophageal reflux disease, and otitis media), sleep-related movement disorders (SRMD) are typically a primary consideration.¹ Children with restless legs syndrome (RLS), periodic limb movement disorder (PLMD), or suspected restless sleep disorder (RSD) may experience impaired sleep quality, sleep onset insomnia, or sleep maintenance insomnia and may present with daytime dysfunction such as hyperactivity, inattention, or poor school performance.

A mainstay of evaluation and treatment of the child with SRMD is assessment of iron body stores. Suboptimal iron

stores within the context of pediatric sleep medicine are typically defined as a ferritin level of $< 50 \mu\text{g/mL}$ for the child with restless sleep.² Children with SRMD often clinically benefit from iron supplementation in the setting of suboptimal ferritin level.^{2–5} Although oral iron supplementation is typically pursued, it comes with the challenges of constipation, difficulty with adherence, and failure to achieve goal ferritin levels.⁶ These challenges were recently examined in detail in a study by DelRosso and colleagues,⁶ who found that 35/77 children who were placed on oral supplemental iron were nonresponders (increase in ferritin of at least $10 \mu\text{g/mL}$ from baseline); within that group of nonresponders, constipation was a frequent (45%) side effect and no change in symptoms was noted in the majority (71%) of children. As a result, intravenous delivery of iron has been pursued as an alternative route of delivery, with superior

results recently observed in both clinical and laboratory parameters as compared to oral supplementation.^{7,8} In fact, intravenous (IV) iron and ferric carboxymaltose (FCM) are recommended as first-line treatment for adults with RLS.⁹ However, the evidence is scarce for pediatric RLS/PLMD, and the most current guidelines only mention iron sucrose.⁹

While the initial reports of IV iron were promising and performed in very well-defined samples, they were limited by relatively small patient numbers and the exclusion of children with moderate to severe neurodevelopmental disorders.^{7,8} In this study we sought to assess the efficacy and safety of IV FCM infusion in a diverse pediatric sleep medicine referred population with sleep complaints secondary to sleep-related movement disorders. A secondary aim was to assess for possible correlates of response to IV FCM. We hypothesized that children with SRMD would benefit from iron supplementation even in the presence of significant comorbidities.

METHODS

Children were identified for inclusion if they had been seen and evaluated in the Children's Mercy sleep clinic as well as underwent IV iron infusion through our hematology service between January 2020 through October 2021. Indications for IV iron infusion included RLS, PLMD, and probable RSD in the context of iron deficiency, with diagnosis rendered by the treating pediatric sleep medicine physician. Specifically, the diagnoses of RLS as well as PLMD were determined by a board-certified pediatric sleep medicine physician in all cases presented in the series. Children who fulfilled symptomatic criteria for RLS according to the *International Classification of Sleep Disorders*, third edition were assigned that diagnosis. PLMD was diagnosed when a sleep study demonstrated a periodic leg movement index of at least 5/h in conjunction with supportive clinical symptoms. In cases where a child had a clinical diagnosis of RLS as well as documented PLMD on polysomnography, a primary diagnosis of RLS was recorded. In cases where no clinical diagnosis of RLS was rendered but the child had PLMD, a diagnosis of PLMD was recorded. Those children without a diagnosis of RLS or PLMD but with a high clinical suspicion of RSD (restless, disrupted sleep in conjunction with daytime impairment) and fit all other criteria but body movement count by polysomnography (at the time of the study the criteria for scoring large muscle movements were not available) were recorded as probable RSD.¹⁰ Ferritin levels were generally performed in conjunction with clinical visits and therefore were not consistently in the fasting state. Given that a minimal number of children had data available for transferrin saturation and/or C-reactive protein, meaningful analysis of these parameters was not possible.

Children received IV FCM as a single dose at 15 mg/kg (maximum dose 750 mg) in outpatient setting. FCM was prepared by hospital pharmacy diluting with 0.9% sodium chloride to a concentration of 2 to 4 mg/mL. Intravenous access was obtained and FCM was administered as a slow infusion over 5–15 minutes. Vital signs including heart rate and blood pressure were monitored at baseline, end of infusion, and at discharge at 30 minutes postinfusion. Families were instructed to

get complete blood count and ferritin level checked at 6-week and 12-week intervals after first dose. Patients were given IV iron sucrose per manufacturer label dosing as an alternative if their insurance did not cover FCM or due to ordering provider preference. Children with continued suboptimal iron stores (ferritin < 50 µg/L) after the initial infusion were offered a second infusion. Families were instructed to have labs checked every 6–8 weeks. The decision to give a second infusion considered several factors, including change in ferritin level, interim clinical response, and shared decision making with the family. A second IV iron infusion would be given if there were continued symptoms and suboptimal ferritin levels < 50–75 µg/L. In general, the children who failed oral iron and subsequently were referred for IV infusion did not continue their oral iron following infusion.

Patient charts were reviewed, and variables of interest abstracted to a secure, encrypted REDCap database. Measures assessed included sex, ethnicity, age, primary indication for IV iron, previous oral iron response, past medical history, medications, baseline laboratory data, baseline symptoms, IV iron formulation and dose, side effects experienced during infusion, follow-up labs, and symptom response to infusion. Specifically, sleep medicine or hematology clinic notes or family messages following infusion were examined for documented side effects and clinical symptom changes following infusion. Symptoms of interest recorded from clinical notes before infusion included the presence or absence of restless sleep, urge to move, sleep onset difficulty, sleep maintenance difficulty, unrefreshing sleep, and/or daytime behavioral challenges. Clinical notes following infusion were examined for change noted in any of the following: restless sleep, urge to move, sleep onset, sleep maintenance, restful sleep, daytime behavior, no change, or worsening symptoms. In addition, charts were reviewed for pre/post International Restless Legs Scale (IRLS) scores and polysomnographic data, but due to a very limited number of patients with postinfusion data available for these measures, analysis was not possible. Specifically, only 4 children had both preinfusion and postinfusion polysomnographic data available, and 2 patients had both preinfusion and postinfusion IRLS scores available.

Continuous variables were summarized as means (standard deviation), and categorical variables were summarized with counts and percentages. In addition to descriptive statistics, group comparisons were performed to assess changes over time as well as differences in response between participants' characteristics. Paired *t*-tests were used when assessing changes in continuous variables over time, and unpaired *t*-tests were used when groups were independent; Levine's test was employed to assess for equivalence of variances with appropriate *P* value selected based on result. Group differences in categorical variables were assessed via chi-square tests, with Fisher's exact test used in instances when cells contained insufficient expected counts. All *P* values are 2-sided, and *P* < .05 was taken as statistically significant. This study obtained an exempt determination from the Children's Mercy Institutional Review Board (STUDY00002054).

RESULTS

Overall, 63 children who received care in the pediatric sleep clinic subsequently underwent intravenous iron infusion. Child

ages range from 0 to 19 years, with an average of 7.2 (5.1) years, and the primary indication for infusion was RLS (n = 30), PLMD (n = 16), or RSD (n = 17). There were more males (n = 39, 61%) than females (n = 24, 38%) represented in the sample. Most patients were Caucasian (n = 55, 87%), followed by Latino (n = 3, 5%), Black (n = 2, 3%), Asian or Pacific Islander (n = 2, 3%), and American Indian or Alaskan native (n = 1, 1%). Reflective of a tertiary care children's hospital, medical and behavioral comorbidities were common in our sample, as follows: neurodevelopmental disorder besides autism/attention deficit-hyperactivity disorder (n = 21, 33%), attention deficit-hyperactivity disorder (n = 12, 19%), behavioral problems (n = 16, 25%), autism (n = 10, 15%), gastroesophageal reflux (n = 11, 17%), anxiety/mood disorder (n = 9, 14%), epilepsy (n = 5, 7%), learning difficulties (n = 4, 6%), hypothyroidism (n = 3, 4%), kidney disease (n = 3, 4%), heart disease (n = 1, 1%), and other (n = 24, 38%). Similarly, most children were on at least 1 medication, including: asthma inhalers (n = 22, 34%), nasal steroids (n = 21, 33%), antihistamine (n = 19, 30%), antidepressant (n = 18, 28%), melatonin (n = 12, 19%), stimulant (14%), antacid (n = 9, 14%), antiepileptic medication (n = 6, 9%), antipsychotic (n = 1, 1%), and other (n = 30, 47%).

All patients previously had an oral iron trial. With oral iron supplementation, 61 (96%) could not achieve goal ferritin, 42 (66%) did not experience symptom improvement, and 27 (42%) did not tolerate oral iron due to side effects. In terms of baseline symptoms preinfusion, 54 (85%) had restless sleep, 26 (41%) RLS/urge to move, 29 (46%) sleep onset difficulty, 34 (54%) sleep maintenance difficulty, 13 (20%) unrefreshing sleep, and 31 (49%) daytime behavioral challenges. The primary indications for IV iron infusion in our sample were RLS (n = 30, 47%), PLMD (n = 16, 25%), suspected RSD (n = 17, 27%).

Of the 63 patients who underwent iron infusion, 60 (95%) received FCM and 3 (4%) received iron sucrose. The reasons for iron sucrose instead of FCM were insurance denial of FCM (n = 1) and provider preference (n = 2). One of the three (33%) children who received iron sucrose required more than 1 infusion compared to 10/60 (16%) who received FCM. In total, 7 (11%) patients experienced at least 1 side effect following infusion. Reported side effects experienced immediately proximal to the infusion included: behavior change (n = 4, 9%), gastrointestinal discomfort (n = 3, 6%), headache (n = 3, 4%), and rash (n = 2, 3%). The specific behavioral changes noted included: worsening daytime behavior (n = 1), decreased engagement/activity level (n = 1), crying (n = 1), and aggressive/dysregulated behavior (n = 1) with kicking, punching, removing clothing, and rolling on ground. There were no cases of extravasation, lightheadedness, fever, chest pain, breathing problems, anaphylaxis, or blood pressure problems. There was no significant change in phosphorus levels preinfusion vs postinfusion (4.6 [0.5] mg/dL vs 4.4 [0.1] mg/dL, $P = .302$) for the 18 children with data available; levels at the postinfusion time point ranged from 3.5 to 5.6, indicating no cases of significant hypophosphatemia.

Clinical follow-up data were available for 53 patients. Overall, 39 (73%) noted at least 1 symptom improvement, 13 (24%) did not notice improvement, and 1 (1%) had worsening symptoms (Figure 1). Specific clinical responses noted included:

improved restless sleep (n = 28, 52%), improved RLS/urge to move (n = 16, 30%), improved sleep onset (n = 14, 26%), improved sleep maintenance (n = 18, 34%), more refreshing sleep (n = 8, 15%), improved daytime symptoms (n = 12, 22%), no substantial change (n = 13, 24%), worsening sleep (n = 1, 1%), and other (n = 3, 5%), which included improved headaches and appetite. Overall, 59 patients had preinfusion and postinfusion ferritin levels, which increased from 21.7 (13.3) to 147.9 (120.9) $\mu\text{g/mL}$, $P < .001$. There was a nonsignificant trend for those children who received FCM to have greater increase in ferritin level compared to iron sucrose (27.0 [8.5] vs 131.5 [120.0] $\mu\text{g/mL}$, $P = .140$). A 1-way analysis of variance was performed to compare change in ferritin level with infusion between diagnostic groups (RLS/PLMD/RSD), and there were no significant differences noted ($F(2,56)=0.852$, $P = .432$). Age at infusion did not correlate with ferritin change ($r = .094$, $P = .481$), and the difference in male vs female participants regarding ferritin change did not reach statistical significance (95.4 [56.7] vs 145.9 [143.2] $\mu\text{g/mL}$, $P = .113$).

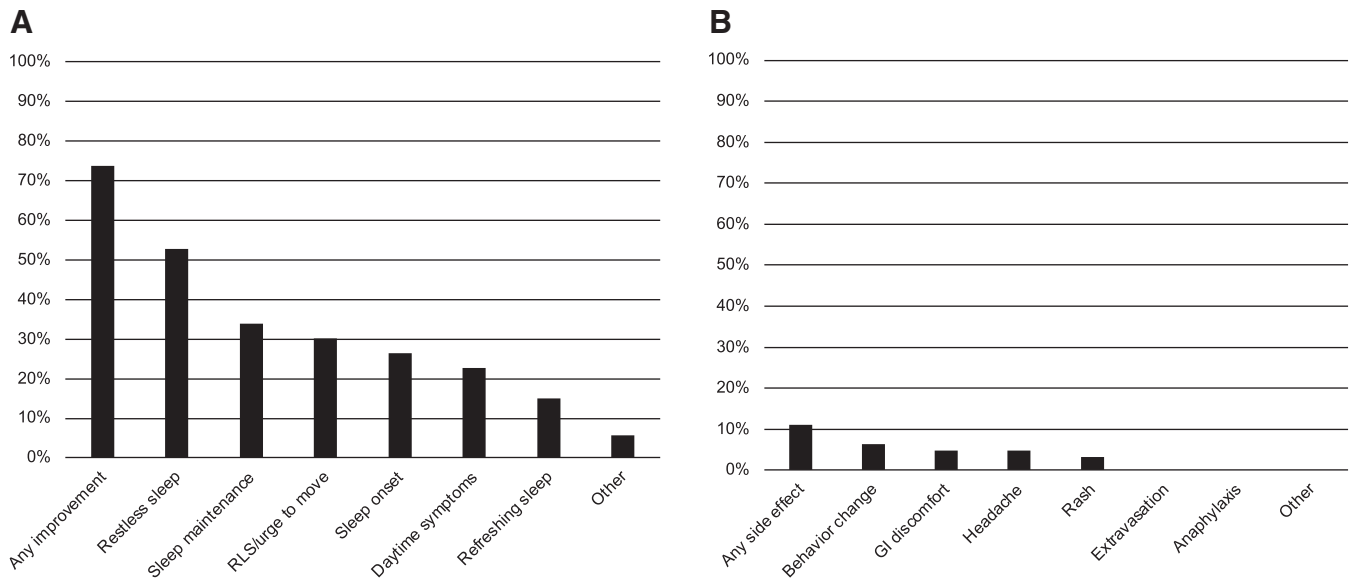
The duration of symptom change was examined. The average time between date of infusion and date of recorded follow-up symptoms for n = 53 was 16.6 (11.1) weeks, and the average time between infusion and follow-up ferritin level for n = 59 was 12.7 (9.1) weeks. To further examine the time course of symptom and ferritin levels following infusion, we examined those participants who underwent 1 infusion. As presented in Figure 2, a 1-way ANOVA was performed among the 48 children who underwent 1 infusion and had follow-up ferritin level available and found a significant effect of time since infusion ($F(3,44)=5.134$, $P = .004$). Post hoc analysis demonstrated that the average follow-up ferritin level 0–4 weeks postinfusion was significantly higher than at all other time points ($P < .05$). Of the 42 children who underwent 1 infusion and had clinical symptom follow-up data available, there was no significant difference found in the proportion of those who experienced clinical improvement by weeks since infusion ($\chi^2(3, n = 42) = 2.139$, $P = .544$), as follows: 77.8% at 0–8 weeks, 65.0% at 8–16 weeks, 80.0% at 16–24 weeks, and 100% at 24 or more weeks.

A variety of baseline participant characteristics were explored as possible predictors of clinical response to iron infusion, with results presented in Table 1. There were no significant differences in between patients who experienced clinical improvement with infusion compared to those that did not in terms of age, sex, ethnicity, past medical history, medication use, primary indication for infusion, baseline symptoms, oral iron response, iron formulation, number of infusions, baseline ferritin, follow-up ferritin, or ferritin change. Patients who were using nasal steroids had a slightly higher incidence of adverse reaction with infusion (23% vs 5%, $P = .036$). Otherwise, there were no significant differences in any characteristics examined between adverse reaction groups.

DISCUSSION

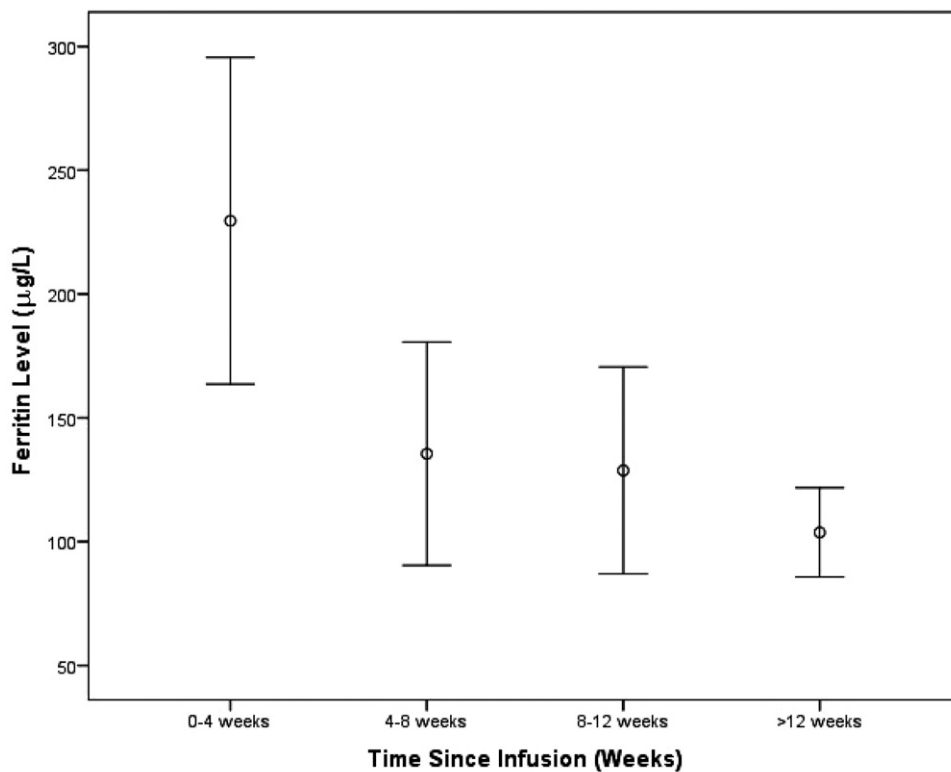
In support of our hypothesis, these data demonstrate that a large number of children benefited from receiving IV iron for sleep complaints secondary to SRMD and iron deficiency. In fact, 73% of children experienced improvement in at least 1

Figure 1—Overall improvement in response to IV iron therapy.



Overall improvement in clinical symptoms (A) and side effects (B) in response to IV iron therapy. IV = intravenous.

Figure 2—Follow-up ferritin levels in weeks among children who had a single IV iron infusion during the study period.



One-way analysis of variance identified an overall difference between groups ($F(3,44) = 5.134, P = .004$). Post hoc analysis demonstrated that the average follow-up ferritin level 0–4 weeks postinfusion was significantly higher than at all other time points ($P < .05$). Data are means \pm 95% confidence intervals.

Table 1—Clinical response and side effects related to intravenous iron infusion according to patient characteristics.

Patient Characteristic	Improvement in at Least 1 Symptom following Infusion (n = 53)			Experience at Least 1 Side Effect Related to Infusion (n = 63)		
	Yes (n = 39)	No (n = 14)	P	Yes (n = 7)	No (n = 56)	P
Age	7.8 (5.3)	7.7 (5.4)	.950	8.8 (5.9)	7.0 (5.1)	.391
Sex						
Male	24	7	.452	3	36	.412
Female	15	7		4	20	
Ethnicity						
Caucasian	36	11	.322	5	50	.214
Other	3	3		2	6	
Past medical history						
Autism	6	2	1.000	1	9	1.000
ADHD	7	4	.453	2	10	.609
Anxiety/mood disorder	6	3	.684	2	7	.260
Behavioral problems	12	3	.732	2	14	1.000
Learning problems	2	1	1.000	2	2	.058
Headaches	5	0	.309	1	5	.522
Hypothyroidism	3	0	.557	0	3	1.000
Kidney disease	2	1	1.000	1	2	.302
Epilepsy	3	1	1.000	1	4	.457
Heart disease	1	0	1.000	0	1	1.000
GERD	7	2	1.000	3	8	.095
Other developmental dz	9	6	.182	4	17	.209
Medications						
Antidepressant	13	4	1.000	4	14	.095
Antihistamine	10	5	.504	3	16	.422
Stimulant	8	1	.416	1	8	1.000
Antipsychotic	1	0	1.000	0	1	1.000
Antiepileptic	4	0	.563	1	5	.522
Antacid	6	2	1.000	3	6	.054
Melatonin	6	5	.134	3	9	.120
Asthma inhalers	11	6	.336	2	20	1.000
Nasal steroids	9	7	.090	5	16	.036
Indication for IV iron						
RLS	22	4	.180	3	27	.963
PLMD	7	5		2	14	
Suspected RSD	10	5		2	15	
Oral iron trial						
GI side effects	16	5	.727	2	25	.689
No sx improvement	25	10	.748	7	35	.085
Poor ferritin response	37	14	1.000	7	54	1.000
Baseline symptoms						
Restless sleep	31	13	.416	6	48	1.000
RLS/urge	19	4	.192	3	23	1.000
Sleep onset	19	7	.934	4	25	.694
Sleep maintenance	21	7	.805	6	28	.112
Unrefreshing sleep	8	2	1.000	1	12	1.000
Daytime behavior	23	4	.051	6	25	.053

(continued on following page)

Table 1—Clinical response and side effects related to intravenous iron infusion according to patient characteristics. (Continued)

Patient Characteristic	Improvement in at Least 1 Symptom following Infusion (n = 53)			Experience at Least 1 Side Effect Related to Infusion (n = 63)		
	Yes (n = 39)	No (n = 14)	P	Yes (n = 7)	No (n = 56)	P
Iron formulation						
Ferric carboxymaltose	37	13	1.000	7	53	1.000
Iron sucrose	2	1	1.000	0	3	1.000
# IV infusions						
1	31	11	1.000	4	48	.095
>1	8	3		3	8	
Baseline ferritin	21.1 (14.0)	22.1 (13.0)	.819	21.8 (19.2)	22.0 (12.7)	.974
Follow-up ferritin	163.1 (137.9)	127.5 (84.2)	.387	194.5 (135.0)	142.6 (119.5)	.324
Ferritin change from baseline	141.9 (137.2)	104.3 (76.6)	.353	176.6 (127.7)	120.5 (118.1)	.278

ADHD = attention deficit-hyperactivity disease, dz = disorder, GERD = gastroesophageal reflux disease, GI = gastrointestinal disease, IV = intravenous, PLMD = periodic limb movement disorder, RLS = restless legs syndrome, sx = symptom.

sleep-related symptom. Our results are important because they provide information on response to IV iron in a diverse, medically complex group of patients with SRMD. Children with RLS, PLMD, and suspected RSD are frequently encountered in the pediatric sleep clinic and rarely present with a single symptom. As evidenced by our patient cohort, many of our patients had neurodevelopmental disorders, other comorbidities, and/or used medications reflecting an actual sleep center population. This augments findings from previous studies using FCM in children with RSD or RLS in which other comorbidities or medications were part of the exclusion criteria^{7,8}; the strict inclusion and exclusion criteria may explain the higher percent of improvement (94%) in those studies. Like prior studies, ours also demonstrated a robust improvement in ferritin levels with IV FCM.

Studies with successful oral iron supplementation have shown that when ferritin levels improve, symptoms or RLS improve in 78% of children.¹¹ While a mainstay of treatment is typically optimization of body iron stores, inability to achieve goal ferritin levels and bothersome side effects associated with oral supplementation are commonplace and a barrier to effective therapy.⁷ The benefit of our approach is that IV iron bypasses the gastrointestinal tract, avoiding unwanted side effects of constipation, teeth staining, and bad taste. While we only had 3 patients receiving iron sucrose, they also achieved clinical improvement at a similar rate compared to FCM, although there was a nonsignificant trend for less ferritin level improvement. Given the small number of children receiving iron sucrose in our sample, our study is likely underpowered to detect differences. A single report on 16 children receiving IV iron sucrose, showed improvement in 62.5% of children.¹² Comparable to previous studies, we found that 11% of our children reported side effects to IV iron infusion. None of our side effects were outside of the expected and reported for the iron preparations used.

An interesting point worth discussing is the fact that 84% of children with RLS, 66% of children with suspected RSD, and only 58% of children with PLMD improved. We speculate that comorbidities may have contributed to the symptoms of sleep disruption. For instance, a systematic review of the literature demonstrated that 67.8% of children with a psychiatric disorder presented with restless sleep.¹ Furthermore, a recent study has reported that antidepressants, particularly selective serotonin reuptake inhibitors, are associated with increased periodic leg movements in children.¹³ These factors can contribute to sleep symptoms not associated with decreased iron stores. While our analysis of primary indications, comorbidities, and medications did not reveal any differences in clinical response that met statistical significance, our sample size may have been underpowered to detect such differential responses. The current results support the use of IV iron even in children with significant comorbidities and taking medications that potentially influence severity of sleep-related movement disorders. Our finding of an association between increased use of intranasal steroids in children who had side effects was unexpected, and we speculate may represent those children with a higher propensity for atopy; in contrast, it may be spurious related to the large number of comparisons performed.

Limitations to our study include single-center experience, open label design, no control group, no inclusion of validated symptom assessment scale, lack of follow-up laboratory data, and lack of follow-up PSG data. These limitations are largely related to the retrospective nature of our study. As the current study is not placebo controlled, we cannot rule out placebo effect. However, we feel this is unlikely given multiple positive results in placebo-controlled trials of IV iron for RLS in adults.^{14,15} That said, future placebo-controlled trials in children are warranted. Another limitation is regarding time course. The data presented can only inform the bounded time period of the current study, and long-term, multiyear studies would be

needed to adequately address more prolonged durability of symptom and laboratory response. In addition, because publication of RSD polysomnographic criteria occurred after the study period, we were unable to use formal sleep study movement criteria for our patients with probable RSD. Although a major limitation of the current study was the lack of structured sleep symptom questionnaire data, we feel that the changes in symptoms presented are likely clinically meaningful in degree given that they were significant enough to be recorded in clinic notes based on family report. While validated symptom scales would be helpful for ensuring measurement precision, ultimately the most important outcomes of interest are those experienced in real world clinical settings. Despite these limitations, our study had several significant strengths. Specifically, our sample size was relatively large compared to prior published experience with IV iron in children with sleep problems, and the fact that our sample was inclusive of children with significant comorbidities and concomitant medications allows our results to be more robust and generalizable to a typical pediatric sleep clinic population. Overall, the current study presents novel and clinically relevant data based on real life implementation of IV iron in a pediatric sleep clinic that builds on previously published smaller, highly controlled studies.⁸ Importantly, the majority of patients in our study experienced clinical and laboratory improvements regardless of medication or medical comorbidities.

In conclusion, our study has demonstrated the feasibility of IV iron supplementation in a large, complex pediatric patient population, showing a sustained and clinically important improvements in symptoms and a mild side effect profile with improved ferritin levels 12 weeks or more. Future areas of research include randomized controlled studies, studies using objective pre and post infusion polysomnography, and markers of brain iron stores that can identify children that will respond to IV iron.

ABBREVIATIONS

FCM, ferric carboxymaltose
 IV, intravenous
 PLMD, periodic limb movement disorder
 RLS, restless legs syndrome
 RSD, restless sleep disorder
 SRMD, sleep-related movement disorders

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DISCLOSURE STATEMENT

All authors have seen and approved this manuscript. The authors report no conflicts of interest.