Sleep Medicine 14 (2013) 1100–1104

Contents lists available at SciVerse ScienceDirect

Sleep Medicine

journal homepage: www.elsevier.com/locate/sleep

Original Article

Treatment of childhood-onset restless legs syndrome and periodic limb movement disorder using intravenous iron sucrose

Kendra Grim, Bernard Lee, Alan Y. Sung, Suresh Kotagal *

Mayo Clinic, Rochester, MN, United States

ARTICLE INFO

Article history:
Received 26 February 2013
Received in revised form 14 May 2013
Accepted 15 June 2013
Available online 28 August 2013

Keywords:
Iron sucrose
Restless legs syndrome
Periodic limb movement disorder
Childhood
Serum ferritin

ABSTRACT

Objective: An alternative treatment approach is needed for children who cannot tolerate oral iron preparations or when there is a need for rapid replenishment of iron stores. We report on the safety, adverse effects, and efficacy of intravenous iron sucrose in a retrospective sample of children with restless legs syndrome (RLS) or periodic limb movement disorder (PLMD).

Methods: Sixteen children with RLS/PLMD who received intravenous iron sucrose at our institution between 2005 and 2011 were identified. The diagnosis of RLS/PLMD was established after formal sleep consultation and nocturnal polysomnography (PSG). Serum ferritin was assayed in all 16 subjects prior to iron sucrose infusion and in 14 subjects after infusion. The medical records were reviewed for treatment-related details.

Results: The mean age of subjects was 6.6 years (range, 2–16 y; 5/16 girls). The mean periodic limb movement index (PLMI) was 18.2 ± 12.8. Fifteen of the 16 subjects (93.7%) had systemic or neurologic comorbidities. Fourteen of 16 (87.5%) subjects had received prior oral iron supplementation for sleep-related concerns, with the majority of the subjects either having gastrointestinal (GI) side effects or insufficient benefits. Intravenous iron sucrose therefore was provided to these 16 subjects through our outpatient pediatric infusion therapy center. The average dose of intravenous iron sucrose of 3.6 mg/kg was infused over 2 h. The baseline mean serum ferritin was 16.4 ± 6.6 ng/mL. After infusion with intravenous iron sucrose, the mean serum ferritin rose to 45.7 ± 22.4 ng/mL ($n = 14$; [95% confidence interval, 17.2–41.3]; $P < .0001$). Parental assessment of response to iron sucrose therapy was conducted on follow-up clinic visits or via telephone calls. There was improved sleep in 62.5% ($n = 10$) of subjects and no improvement in 12.5% ($n = 2$) of subjects. No follow-up information was available for 25% ($n = 4$) of subjects. Minor adverse events occurred in 25% ($n = 4$) of subjects—two subjects experienced difficulty with peripheral intravenous catheter placement, while two had transient GI symptoms, such as anorexia, nausea, and vomiting. None of the subjects had anaphylaxis.

Conclusions: Intravenous iron sucrose appears to be a relatively effective therapy for patients with childhood-onset RLS/PLMD and iron deficiency who do not tolerate or respond to oral iron supplements. Side effects were transient. The most common adverse events were difficulty with intravenous line placement and GI disturbance. There is a need for systematic prospective studies on the safety and efficacy of intravenous iron sucrose in RLS/PLMD in children.

© 2013 Elsevier B.V. All rights reserved.

1. Introduction

Childhood-onset restless leg syndrome (RLS) occurs in approximately 1.9% of children and in 2% of adolescents [1]. In specialized groups such as children and adolescents seen in sleep centers, the prevalence of RLS can be as high as 5.9% [2]. Patients with RLS develop fragmentation of sleep, with consequent impairment of attention span [3,4], cognition [5], and quality of life [6]. A definitive diagnosis of RLS generally can be made in typically developing children by the age of 5 to 6 years, as they are able to accurately describe their symptoms [1]. When restless and fragmented sleep is encountered in preschool-aged children or in those who are developmentally delayed, the diagnosis of RLS is more difficult. In such instances, the presence of an elevated periodic limb movement index (PLMI) of five or more when associated with a sleep complaint may suggest a periodic limb movement disorder (PLMD) [7]. Periodic limb movements likely are an endophenotype for RLS [8], and they present in approximately 80% of patients with RLS. There appears to be a close relation between RLS and PLMD conditions in children based on family history and long-term follow-up [9,10].

* Corresponding author. Address: Mayo Clinic, 200 First Street SW, Rochester, MN 55905, United States. Tel.: +1 507 284 3372; fax: +1 507 284 0727.
E-mail address: kotagal.suresh@mayo.edu (S. Kotagal).

1389-9457/$ - see front matter © 2013 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.sleep.2013.06.006

The efficacy of oral iron therapy has been established in adults with RLS using a randomized, double-blind, placebo-controlled design [11]. Iron therapy in childhood RLS has been critically reviewed [7]. An improvement in symptoms of RLS and correction of insomnia following oral iron therapy was initially reported in adolescents by Kryger et al. [12] in 2002 and also more recently by Mohri et al. [13] in 2012. With regard to PLMD, Simakjornboon et al. [14] treated 25 out of 28 children with this condition using oral iron for 3 months. They noticed a significant reduction in the PLMI in 76% ($n = 19$) of treated subjects. In the subjects who improved, the PLMI dropped from an average baseline value of 27.6 ± 14.9 to 12.6 ± 5.3, with a corresponding rise in the serum ferritin from a pretreatment average of 40.8 ± 27.4 ng/mL to 74.1 ± 13.0 ng/mL. However, oral iron therapy may not be tolerated by some children secondary to intolerable gastrointestinal (GI) side effects, such as nausea, vomiting, and constipation [15]. Additionally the growth spurts of children; the menstrual blood loss in young adolescent women; and the coexisting malabsorptive medical disorders, such as gastroesophageal reflux, *Helicobacter pylori*–related gastritis, chronic diarrhea, and celiac disease, may impair iron absorption, thus hindering optimum treatment of RLS and PLMD [6,15]. An alternative approach to correcting iron deficiency therefore is needed in children and adolescents with RLS/PLMD who experience significant side effects from oral iron or who are unable to sufficiently absorb it. In this regard, studies in adults with RLS who have been treated with intravenous formulations of iron dextran [16], low molecular weight iron dextran [17], and ferric carboxymaltose [18] provide useful guidance about management. Helpful suggestions about the procedure intravenous iron infusion have been provided by Auerbach [19].

There also have been trials of intravenous iron sucrose in adults in RLS [20,21]. In a randomized, double-blind, placebo-controlled trial of intravenous sucrose by Earley et al. [20], there was a small but significant increase in the cerebrospinal fluid ferritin level and a decrease in RLS severity as measured by a global rating scale two weeks after infusion; however, there was no change in PLMs or a brain iron index measured on magnetic resonance imaging. The baseline preinfusion mean serum ferritin in RLS subjects was reasonably high at 78.3 ± 41.7 ng/mL. The authors concluded that high dose intravenous iron sucrose failed to produce a robust change in RLS symptoms. In another randomized, double-blind, multicenter trial on adults with RLS by Grote et al. [21], intravenous iron sucrose infusion also was not associated with a decrease in RLS severity at 11 weeks postinfusion when compared to the placebo group. However, the RLS group did notably improve over the placebo arm in RLS severity during the acute phase (at 7 weeks' postinfusion) and somewhat variably on long-term follow-up. The slightly disparate response to intravenous iron sucrose in these two well-designed studies may be related to the possibility that patients with low levels of serum ferritin (i.e., <50 ng/mL) as seen in the study by Grote et al. [21] may be more likely to benefit from intravenous iron infusion. A high proportion of children with RLS/PLMD actually resemble the latter study [21] with levels of ferritin below 50 ng/mL, and therefore rendering them more likely to benefit from intravenous iron supplementation. For example, 75% (24/32) of subjects had a serum ferritin below 50 ng/mL in one study on childhood RLS [2].

There are no reports on the efficacy of intravenous iron sucrose for the treatment of RLS/PLMD in children to date. However, there are some childhood studies on intravenous iron sucrose infusion for indications such as iron deficiency anemia and renal disease. In a prospective observational study, Anbu et al. [22] reported on their experience of providing 870 iron sucrose infusions, each over 90 min, to 72 children with chronic renal disorders. The major side effect was transient abdominal pain that developed in 4.1% ($n = 3$) of patients. The authors concluded that intravenous iron sucrose infusion in children was safe. In the prospective observational study of Pinsk et al. [15], intravenous iron sucrose was administered to 45 children between the ages of 11 months and 16 years with anemia who had failed treatment with oral iron. One of 45 subjects (2.2%) developed a severe side effect of temporary and reversible reduced blood pressure. These authors also concluded that intravenous iron sucrose was well-tolerated and had good clinical results with minimal adverse reactions.

With this background and given the limited treatment options for childhood RLS/PLMD, we report on the safety and efficacy of intravenous iron sucrose in this age group.

2. Subjects and methods

Since 2005 intravenous iron sucrose has been administered at our institution to select children with iron deficiency when oral iron therapy has been unsuccessful or associated with considerable side effects. Our subjects were a subset of 60 patients who had received iron sucrose for various indications such as iron deficiency anemia. The patients had been referred to our sleep center for assessment of sleep initiation or maintenance difficulties or nonrestorative sleep. Subsequent to approval by our institutional review board, 19 children with possible RLS/PLMD were initially identified on record review. Three of 19 subjects were excluded—two because the diagnosis of RLS/PLMD was unclear and one because of the presence of significant comorbid obstructive sleep apnea (OSA). The remaining 16 formed the study group. There were 1356 subjects with RLS and 923 subjects with PLMD below the age of 18 years during this time period. Our 16 subjects composed 0.7% of this entire RLS/PLMD group. The diagnosis of RLS/PLMD was based on the 2003 National Institutes of Health Consensus Conference criteria [23]. All patients had undergone a formal sleep medicine consultation. Although nocturnal polysomnography (PSG) is not routinely indicated for the diagnosis of RLS in older children who are able to provide an accurate history, the test was obtained in all of our older subjects due to suspicion of comorbid sleep disorders such as OSA. The complex comorbid health problems of our subjects are shown in Table 1. In younger subjects who were unable to provide an accurate history, PSG was obtained to assess the etiology of sleep fragmentation (i.e., due to PLMs). The polysomnograms were reviewed by a board-certified sleep specialist (SK). Initial serum ferritin levels were obtained at the time of the sleep clinic consultation if RLS was suspected or subsequent to the polysomnogram if the PLMI was five or higher.

Information was gathered about demographics and sleep-related and systemic comorbidities, baseline serum ferritin level, reason for not being able to tolerate oral iron therapy, and dose of iron sucrose which had been intravenously infused. Iron sucrose dose was prescribed by the sleep medicine specialist (SK). All patients had peripheral intravenous catheters inserted by a nurse on the vascular access team or by a pediatric anesthesiologist. An extrapolated dose of 1.21–6.8 mg/kg per dose (maximum 120 mg) of iron sucrose was prescribed. The infusions were performed in our ambulatory Pediatric Infusion Therapy Center, using a syringe pump or an intravenous piggyback infusion kit and were completed over 2 h. The nursing flow sheets were reviewed for serial pulse and blood pressure readings and for complications that might have occurred during the infusion period. The electronic medical records also were reviewed for notations about response to therapy, especially improvement in sleep and follow-up serum ferritin levels.

Summary statistics (mean [standard deviation]) were gathered for the quantitative variables. Two-tailed t tests were used to compare serum ferritin levels at baseline vs during oral iron treatment and at baseline vs after intravenous iron sucrose infusion.

Download English Version:

https://daneshyari.com/en/article/6061141

Download Persian Version:

https://daneshyari.com/article/6061141

Daneshyari.com