STRONG CHILDREN'S RESEARCH CENTER

Summer Research Scholar

Name: Toluwani Adelaja

School: University of Michigan

Mentors: Emily K. Cromwell, PhD, DBSM and Heidi V. Connolly, MD

ABSTRACT

Title: Evaluating the efficacy of different iron dosing regimens in pediatric patients with RLS/PLMD

Background: Sleep is a critical determinant of well-being and alongside nutrition and physical activity, is considered one of the main pillars of health[1]. Restless legs syndrome (RLS) and Periodic Limb Movement Disorder (PLMD) are sleep related movement disorders that can significantly impact overall sleep quality and quantity. RLS is characterized by the overwhelming urge to move the legs, usually accompanied uncomfortable sensations that typically occur at rest and are usually worse at night [2]. PLMD is characterized by repetitive, rhythmic limb movements during sleep. Current treatment guidelines by the American Academy of Sleep Medicine (AASM) recommend treating with supplemental iron for serum ferritin levels below 50 ng/ml [3]. Treating pediatric RLS/PLMD with supplemental oral iron can cause gastrointestinal side effects which can affect adherence [4, 5] leading to undertreatment. Compared to daily dosing, alternate-day iron supplementation may enhance iron absorption and reduce gastrointestinal side effects [6]. In July of 2023, our pediatric sleep center changed the iron dosing protocol for patients with RLS/PLMD with the goals of improving iron absorption and side effects. Prior to July of 2023, our dosing guideline was 6mg/kg of elemental iron daily and after July 2023 we modified this to 2 mg/kg of elemental iron on alternate days.

Objective: To assess the efficacy of iron dosing based on 1) ferritin level change and 2) spontaneously reported side effects.

Methods: The current study is a retrospective chart review of patients ages 1-17 years who received care for RLS/PLMD at the University of Rochester Pediatric Sleep Medicine Center between July 2022 and June 2024. Eligible patients (N=454) included 264 patients who received daily iron and 190 patients who received alternate daily dosing. The primary outcome measure was the difference in ferritin level between the initial and three-month lab follow-up. To examine the occurrence of side effects, 60 patients were randomly selected from each of the dosing groups for an in-depth chart review.

Results: An independent samples t-test revealed that the patients who received daily iron had significantly greater increase in ferritin levels at the follow up lab draw ($M = 27.69$, $SD = 43.96$) compared to those treated with alternate day dosing ($M = 16.18$, $SD = 25.91$), $t(436.63) = 3.49$, $p = <0.001$. Patients receiving daily dosing reported over three times as many side effects (18%) compared to the patients in the alternate day dosing group (5%). The most reported side effects included stomach pain (50%) and constipation (43%).

Conclusion: We found that daily iron dosing was more effective at raising blood serum ferritin levels; however, alternate daily dosing leads to fewer reported side effects. These findings have important clinical implications for treating pediatric patients experiencing PLMD/RLS.

References:

1. Schotland, H. and M. Marianna Sockrider, *Healthy sleep in children.* American journal of respiratory and critical care medicine, 2017. **195**(6): p. 11.
2. Picchietti, M.A. and D.L. Picchietti, *Advances in pediatric restless legs syndrome: Iron, genetics, diagnosis and treatment.* Sleep medicine, 2010. **11**(7): p. 643–651.
3. Allen, R.P., et al., *Evidence-based and consensus clinical practice guidelines for the iron treatment of restless legs syndrome/Willis-Ekbom disease in adults and children: an IRLSSG task force report.* Sleep medicine, 2018. **41**: p. 27–44.
4. Pasupathy, E., et al., *Alternate day versus daily oral iron for treatment of iron deficiency anemia: a randomized controlled trial.* Scientific Reports, 2023. **13**(1): p. 1818.
5. Picchietti, D.L., *Should oral iron be first-line therapy for pediatric restless legs syndrome and periodic limb movement disorder?* 2017. p. 220–221.
6. von Siebenthal, H.K., et al., *Alternate day versus consecutive day oral iron supplementation in iron-depleted women: a randomized double-blind placebo-controlled study.* EClinicalMedicine, 2023. **65**.