Intravenous iron dextran for severe refractory restless legs syndrome

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ABSTRACT

Reduced brain iron is strongly associated with restless legs syndrome (RLS). Oral iron supplements are commonly recommended for RLS but are largely ineffective secondary to poor absorption and poor tolerability at required doses. Intravenous iron has been shown to increase brain iron content. Surprisingly only a few reports have ever presented data on the clinical effect of high dose intravenous iron for RLS. We identified 25 subjects (age 53.2± 11.9, 7 male) who received at least one infusion of intravenous iron dextran. Demographics are summarized in Table 1. The age of RLS onset was 32.6±13.0 years and 15 had a positive family history of RLS. Overall, this was a very severe and medically refractory group. Baseline ferritins ranged from 5 to 248 (mean 43.5±58.0) and 20/25 had ferritins less than 50. Two subjects did not complete their entire infusion due to anaphylactic type symptoms. Two subjects reported complete their entire infusion due to anaphylactic type symptoms but are included. Overall, 2 subjects reported complete amelioration of all RLS symptoms, 11 reported marked improvement, 2 moderate improvement, 3 mild improvement, and 6 reported no improvement. For those with improvement, the duration of effect was highly variable, mean 15.8±17.7 weeks, range 1-60 weeks. Twelve subjects have had multiple infusions. Adverse events included two subjects with hypotension that required a rush in a within a week of infusion and one reported a headache. Iron dextran can dramatically improve RLS but results are inconsistent and not predicted by patient demographics. In the absence of further rate of anaephilic reactions, iron dextran may be superior to other IV iron preparations.

METHODS

All patients were seen in the Baylor College of Medicine Parkinson’s Disease Center and Movement Disorders Clinic over the past 10 years. Patients were retrospectively identified from our patient database that is maintained by the Baylor Infusion Center. Subjects were excluded if they had a known cause of RLS or were not an inclusion requirement. All subjects underwent a standardized infusion totalling one gm of iron dextran over five hours using a standard protocol. Patients that responded robustly to IV iron (n=13) tended to have a family history of RLS tended to respond better. High molecular weight iron dextran has higher rates of anaephilic reactions compared to oral iron sucrose or sodium ferric gluconate. All preparations are able to increase serum iron; however iron dextran is retained longer and absorbed by macrophages better than the other preparations. This may be important, as iron therapy in theory for RLS requires CNS iron accumulation, which might require days, weeks, or months. We report mixed, but generally favorable open label results from 1 gm of intravenous iron dextran in a group of highly refractory RLS patients. Importantly, we showed good clinical tolerability to subsequent infusions of a long period of time in some cases. We were unable to predict who would respond based on patient demographics, serum iron, or previous response to medications, although those with a positive family history of RLS tended to respond better.

DISCUSSION

We report mixed, but generally favorable open label results from 1 gm of intravenous iron dextran in a group of highly refractory restless legs syndrome (RLS) patients. Importantly, we showed good clinical tolerability to subsequent infusions of a long period of time in some cases. We were unable to predict who would respond based on patient demographics, serum iron, or previous response to medications, although those with a positive family history of RLS tended to respond better.

High molecular weight iron dextran has higher rates of anaephilic reactions compared to oral iron sucrose or sodium ferric gluconate. All preparations are able to increase serum iron; however iron dextran is retained longer and absorbed by macrophages better than the other preparations. This may be important, as iron therapy in theory for RLS requires CNS iron accumulation, which might require days, rather than the shorter time allowed by other iron preparations. Patients usually report a delay of at least three days before achieving any benefit, which would also suggest that the iron requires extended transport into the brain. Iron dextran is proven to increase brain iron based on imaging studies. It is also known to be toxic, and one day intervention, is suggestive of a biological response. Although we have not observed any clinical symptoms after creating abnormally high serum iron stores, free iron is known to be toxic, and potentially facilitates several maladaptive biochemical pathways. We have not evaluated any of these subjects for evidence of oxidative stress, or any other metabolic assessment other than serum ferritin. Therefore our report can not adequately assess long term safety.

REFERENCES