

The Efficacy of Ferumoxytol in Peritoneal Dialysis Patients: A Short Scientific Report

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Abstract

One of the major elements contributing to anemia in Chronic Kidney Disease (CKD) patients is iron deficiency. Iron supplementation in oral form is often not tolerated and ineffectively absorbed. Intravenous (IV) infusion is time consuming and is inconvenient in Peritoneal Dialysis (PD) patients self-treating at home. A new preparation of iron, ferumoxytol, is a carbohydrate-coated, paramagnetic iron oxide nanoparticle, which can be administered as a bolus intravenous injection, allowing the PD patient to more easily comply with current IV iron dosing regimens. Few studies have been done to evaluate the efficacy of ferumoxytol in PD population. We retrospectively reviewed the medical records of peritoneal dialysis patients who received at least one dose of ferumoxytol between January 2010 and August 2010 and observed that 17 patients showed an improvement in hemoglobin (Hb) to 1 gm/dl within a month of treatment along with a decrease in epoetin dosage in subsequent weeks.

Keywords

Anemia, Ferumoxytol, Peritoneal Dialysis

1. Introduction

Anemia is a common finding in chronic kidney disease patients and is attributed to lack of iron deficiency along with decreased production of erythropoietin by the kidneys. Erythropoiesis-stimulating agents (e.g., epoetin alfa,

darbepoetin alfa), lead to iron deficiency from hemoglobin synthesis [1].

In peritoneal dialysis patients there is impaired release of iron from its stores such as macrophages of the reticuloendothelial system in the liver, spleen, and bone marrow. Commonly referred to as reticuloendothelial blockade, it causes a functional iron deficiency in which iron is present but not usable for hemoglobin synthesis. As a result to overcome this blockade and iron deficit from erythropoiesis stimulating agents and blood loss, use of intravenous iron has been successful in treating anemia [2]. United States Food and Drug Administration on June 30, 2009 approved ferumoxytol for the treatment of iron deficiency anemia in adults with chronic kidney disease. The approved dosage regimen is an intravenous dose of 510 mg, followed by a second dose 3 - 8 days later. The drug is given undiluted at a rate of up to 1 ml/second (30 mg/sec). If response in monitoring parameters is not seen (hemoglobin level, ferritin level, transferrin saturation, blood pressure) then regimen can be repeated again [3].

Ferumoxytol is a super-paramagnetic iron oxide nanoparticle that has a polyglucose carboxy-methylether coating. It has a molecular weight of 731 kD. *In vitro* studies have demonstrated that ferumoxytol contains or releases less free (labile) iron than its counterparts. As a result, ferumoxytol can be safely and rapidly administered intravenously in relatively high doses without acute adverse reactions [4].

To our knowledge, very few studies have been done to assess the efficacy of ferumoxytol on peritoneal dialysis patients. Retrospectively, we reviewed the medical records of peritoneal dialysis patients aged 18 years, who received at least one dose of ferumoxytol and analyzed the hematologic changes over a period of 4 months. The primary objective of this study was to analyze improvement in hemoglobin after the administration of ferumoxytol.

2. Method

Study design: A retrospective analysis was conducted on 9 males and 8 females aged 53.5 ± 16.6 years with average weight of 83.94 ± 22.8 kg peritoneal dialysis patients being treated with ferumoxytol for anemia at New Hospital Queens/Cornell University clinic between January 2010 and August 2010. Approval for retrospective analysis was approved by our local research review committee.

The primary objective was to evaluate the effect of ferumoxytol on hemoglobin, hematocrit, ferritin and iron saturation and compare the results of the iron profile pre and post Feraheme dosing.

The study population consisted of end stage renal disease patients on peritoneal dialysis with lab data meeting the iron deficient criteria per our institute, iron transferrin saturation of <20% or serum ferritin of <500 ug/dl. With the exception of 2 patients all others received two doses of the drug. Time elapsed between two consecutive ferumoxytol doses were on an average 10 days. Epoetin dosing interval was not altered and changes in the amount of the erythropoietin stimulating agent was made according to hematologic parameters as per institute guidelines. After initial ferumoxytol dosage, subsequent administration was done based on the response of the iron profile. Data on hemoglobin, ferritin and TSAT were collected at baseline and then on a monthly basis for 4 months. We did not exclude iron depleted patients or with co-morbidities that would effect ferumoxytol and ESA response.

3. Result

The analysis of Hb (**Table 1**) revealed an overall effect ($p = 0.05$), and an increase in Hb value from baseline and 12 weeks post ferumoxytol Hb levels increased from 10.4 gm/dl to 11.3 gm/dl, $p < 0.05$. A similar decline in was observed in the use of epoetin to less than 10,000 Units/week and remain constant till the end of the 4 month period. Comparison of Hb between baseline and week 16 were not significant.

The primary objective of the study was to determine an improvement in Hb range following ferumoxytol administration. At the end point all of the patients showed increase in Hb by 1 gm/dl. Changes in TSAT and ferritin were significant from baseline and increased by three fold.

4. Discussion

Ferumoxytol has the expected efficacy of an intravenous iron compound, with improvements in anemia and iron being evident as early as 4 weeks post ferumoxytol. Additionally, significant decrease in monthly epoetin dose

Table 1. Trends of hemoglobin and iron parameters during ferumoxytol therapy.

Lab	Baseline	4 Wk Post Feraheme	8 Wk Post Feraheme	12 Wk Post Feraheme	16 Wk Post Feraheme
Hemoglobin (g/dL)	10.4 ± 1.0	11.0 ± 0.9*	11.3 ± 0.9*	11.3 ± 1.0*	10.9 ± 1.2
Hematocrit (%)	32.3 ± 3.9	33.8 ± 3.5*	34.6 ± 3.2*	34.6 ± 3.4*	33.6 ± 3.
Ferritin (µg/dL)	279 ± 152	625 ± 248*	743 ± 259*	N/A	640 ± 367*
TSAT (%)	18.1 ± 6.3	37.4 ± 14.7*	36.9 ± 23.7	N/A	32.9 ± 12.9*
Epoetin (U)/week	39,573	29,764	27,058	27,329*	26,585

was noted at 12 weeks post ferumoxytol dosing. Ferumoxytol is a desirable therapeutic option in peritoneal dialysis patients, who typically visit the clinic at monthly intervals.

Alternative iron therapies would require lengthy infusions, or frequent visits to achieve comparable iron delivery. No direct comparisons of ferumoxytol with other parenteral iron preparations have been done in PD to the best of our knowledge; Ferumoxytol may be safely administered intravenously at a much more rapid rate (30 mg/sec) than currently available iron products. Our study has the limitation because of its observation nature and sample size. Ferumoxytol was not directly compared with other formulations (sodium ferric gluconate, iron sucrose, iron dextran)

5. Conclusion

In this short-term study (4 months), ferumoxytol therapy was demonstrated to be effective and safe in patients with PD and anemia. It is equally effective when compared to other intravenous iron formulations (iron sucrose) in increasing hemoglobin levels [5]. With a greater proportion of patients achieving increases of 1 g/dl, the ability to administer intravenous ferumoxytol 510 mg in less than 30 seconds makes it a convenient treatment option for outpatient treatment.

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