

Original Article

Use of Iron Sucrose in Dialysis Patients Sensitive to Iron Dextran

Ayham Haddad¹, Rabe'a Abbadi², Ann Marji³

¹Nephrology Division, ²Clinical Pharmacy Department, King Hussein Medical Center,
³Princess Muna College of Nursing, Muta'a University, Amman, Jordan

ABSTRACT. This study aimed to assess the safety and efficacy of iron sucrose in hemodialysis (HD) patients with documented hypersensitivity reactions to iron dextran. Of 205 HD patients who received low molecular weight iron dextran, 15 (7.3%) patients developed documented hypersensitivity reactions. The patients were treated with iron sucrose (100 mg administered as an intravenous push over 5-10 minutes once a week) for 8 weeks. Complete blood count, serum iron, serum ferritin, and parathyroid hormone were measured at the beginning and at the end of the study (except parathyroid hormone). All patients received subcutaneous erythropoietin at a constant dose of 5000 IU twice weekly unless a change was required. All the patients completed the study period and none of them developed hypersensitivity reactions to iron sucrose. The mean hematocrit increased from 23.8% to 32.27% ($p < 0.0001$), the mean serum ferritin from 185 ng/mL to 599 ng/mL ($p < 0.0001$), and the mean serum iron from 29.3 ng/dL to 76.8 ng/dL ($p = 0.01$). We conclude that iron sucrose is safe and effective in HD patients with documented hypersensitivity reactions to low molecular weight iron dextran.

Keywords: Chronic kidney disease, Hemodialysis, Anemia, Iron sucrose, Low molecular weight iron dextran

Introduction

Patients with stage 5 chronic kidney disease (CKD) receiving hemodialysis (HD) are prone to iron deficiency for several reasons including

reduced iron intake due to a low protein diet,^{1,2} interference with gastrointestinal iron absorption from phosphate binders,³ and possibly reduced intestinal iron absorption due to uremia.⁴ HD may worsen iron deficiency because of bleeding from the access site, blood left in the tubes and dialyzer, and frequent blood tests.⁵

The introduction of recombinant human erythropoietin as a therapy for CKD-associated anemia has changed the management of this disorder, but erythropoietin increases the requirements for the substrates of erythropoiesis

Correspondence to:

Dr. Ayham Haddad
Nephrology Division
King Hussein Medical Center
P.O. Box 3808, Amman 1953, Jordan
E-mail: ayhamhaddad@hotmail.com

Table 1. Patient characteristics

| | | |
|---|--------|---------------|
| Gender | Male | 5 |
| | Female | 10 |
| Mean age (years) (range) | | 47.2 (22–70) |
| Mean duration of HD (months) (range) | | 50.4 (12–180) |

mainly iron in order to be efficacious in most of the cases of anemia in HD.

The administration of oral iron preparations has proven to be inadequate to replenish or maintain iron stores necessary for hematopoiesis during erythropoietin therapy.⁶ Parenteral iron therapy in combination with erythropoietin has been shown to be successful and economic method to treat iron deficiency anemia in patients with CKD.⁷ This has resulted in an increased use of iron dextran,⁸ however, it carries the risk of variable adverse reactions ranging from mild forms of skin reactions or gastrointestinal disturbances to hypotension, severe bronchospasm, and death.⁹

Another form of parenteral iron is ferric gluconate, sodium ferric gluconate complex in sucrose. It shares many similarities with iron dextran, most importantly anaphylactic reactions, but there have been no reported deaths.¹⁰⁻¹² To minimize reactions to ferric gluconate, the maximum dose is limited to 125 mg infused slowly over one hour.^{13,14}

A third iron preparation is iron sucrose, iron saccharate. Its use in HD patients has been reported as safe, well tolerated and effective.^{6,10,15} It may be administered in 100 mg doses as an intravenous push over as little as 1 minute and in doses up to 500 mg as a slow intravenous infusion.¹⁶

We conducted our study in HD patients with proven hypersensitivity reactions to a newly introduced low molecular weight iron dextran by treating them with intravenous iron sucrose to evaluate their response to the latter iron preparation.

Patients and Methods

Our center provides HD therapy to a total of 205 patients with kidney failure, and as a standard measure, all our patients receive erythropoietin and intravenous iron for the management

of anemia. Recently, we started to use low molecular weight iron dextran. A total of 15 (7.3%) patients developed various types of hypersensitivity reactions to the test dose of the low molecular weight iron dextran, ranging from urticaria to mild shortness of breath to hypotension. Those 15 patients were switched to intravenous iron sucrose while maintaining the dose of erythropoietin after a period of two weeks from discontinuing the low molecular weight iron dextran. Patient characteristics are shown in table 1.

Iron sucrose was administered in doses of 100 mg via intravenous push over 5-10 minutes during the first hour of the HD session once per week. The erythropoietin dose was continued as subcutaneous injections of 5000 IU twice weekly at the end of the HD session, and the dose was maintained unless required modification.

Patients receiving angiotensin converting enzyme (ACE) inhibitors at the beginning of the study continued to receive them during the 8 week study period, but these was not added to the treatment regimen of the other patients.

Laboratory data collected at the beginning of the study were complete blood count (CBC), serum iron, serum ferritin and parathyroid hormone concentrations. At the end of the study these measurements were repeated except for the parathyroid hormone.

Statistical analysis

Data are presented as the mean. Student's "t" test was used to compare the results and P values less than 0.05 were considered statistically significant.

Results

A total of 15 patients who had documented hypersensitivity reactions to test doses of low

Table 2. Hematologic parameters (mean values)

| | Baseline | End of study | P value |
|------------------------|----------|--------------|----------|
| Hematocrit (%) | 23.8 | 32.3 | < 0.0001 |
| Serum ferritin (ng/mL) | 185 | 599 | < 0.0001 |
| Serum iron (ng/mL) | 29.3 | 76.7 | 0.01 |

molecular weight iron dextran received iron sucrose. None of these patients manifested any form of hypersensitivity reactions to iron sucrose injections, and there were no effects on intradialytic blood pressure.

The initial mean hematocrit was 23.8% and this increased to 32.3% after 8 weeks ($p < 0.0001$). Of note, 73% of patients achieved a hematocrit of more than 33%, while 80% achieved a hematocrit of more than 30% with the same dose of erythropoietin as used before starting iron sucrose therapy. The mean serum ferritin increased from 185 ng/mL to 599 ng/mL ($p < 0.0001$) and the mean serum iron also increased from 29.3 ng/dL to 76.7 ng/dL ($p = 0.01$). Table 2 summarizes these data.

Discussion

Iron dextran has been the only available parenteral iron preparation for a long time. However, its use has been associated with increased risk of allergic reactions, even after reaction-free previous use.^{8,9} Reported reactions to iron dextran include a wide range of symptoms and findings, such as pruritus, palpable purpura, rash, abdominal pain, flank pain, arthralgias, myalgias, fever, hypotension, pulmonary edema, wheezing, stridor, and angioedema.¹⁰ The most severe reactions to iron dextran meet the criteria for anaphylaxis.

The results of our study demonstrate the safety and efficacy of iron sucrose administration in a group of patients all sensitive to low-molecular weight iron dextran. The introduction of iron sucrose for HD patients has been described as safe and effective, even in patients with documented hypersensitivity reactions to other iron preparations.^{10,15,16} The North American study by Van Wyck included a less homogeneous group of 22 patients presenting sensitivity to either low- or high-molecular-weight dextran.¹⁰

The rate of allergic reactions to iron dextran varies in the literature. Among our patients we recorded 7.3% rate of hypersensitivity reactions to low molecular weight iron dextran.

In our study, there were no reactions to iron sucrose, which is compatible with what has been found in previous studies.⁵ The safety of iron sucrose is further confirmed in a large retrospective safety analysis,¹⁷ where this substance is rated with the most advantageous safety profile compared to iron gluconate and iron dextran. However, other studies reported minor hypersensitivity reactions to iron sucrose (Pruritus).¹⁰

Our patients tolerated intravenous iron sucrose with significant improvement in their hematocrit, serum ferritin, and serum iron levels. Moreover, we noticed that the initial levels of serum ferritin did not predict the response to iron sucrose therapy, as all our patients showed significant improvement. Furthermore, we observed no effect related to other medications prescribed to the patients, namely, ACE inhibitors.

We conclude that iron sucrose is safe and effective in HD patients with documented hypersensitivity reactions to low molecular weight iron dextran.

Acknowledgment

We thank Vifor International and their local representative in Jordan (Al-Kudri drug store) for providing material for the study.

References

1. Herbert Herbert V. Recommended dietary intakes (RDI) of iron in humans. *Am J Clin Nutr* 1987;45:679-86.
2. Bezoda WR, Bothwell TH, Charlton RW, et al. The relative dietary importance of haem and non-haem iron. *S Afr Med J* 1983;64:552-6.

3. Cannata JB, Gomez-Alonso C, Fernandez-Menendez MJ, et al. Iron uptake in aluminium overload: In vivo and in vitro studies. *Nephrol Dial Transplant* 1991;6:637-42.
4. Boddy K, Lawson DH, Linton AL, Will G. Iron metabolism in patients with chronic renal failure. *Clin Sci* 1970;39:115-21.
5. Silverberg DS, Blum M, Kaplan E, Iaina A. Intravenous ferric saccharate as an iron supplement in dialysis patients. *Nephron* 1996;72:413-7.
6. Chaytan C, Schwenk MH, Al-Saloum MM, Spnowitz BS. Safety of iron sucrose in HD patients intolerant to other parenteral iron products. *Nephron Clin Pract* 2004;96:c63-6.
7. Maccougall IC, Tucker B, Thompson J, et al. A randomized controlled study of iron supplementation in patients treated with erythropoietin. *Kidney Int* 1966;50:1694-99.
8. Hamstra RD, Block NH, Schocket AL. Intravenous iron dextran in clinical medicine. *JAMA* 1980;243:1726-31.
9. Fishbane S, Ungureanu VD, Maeska JK, et al. The safety of intravenous iron dextran in HD patients. *Am J Kidney Dis* 1996;28:529-34.
10. Wyck DB, Cavallo G, Spinowitz BS, et al. Safety and efficacy of iron sucrose in patients sensitive to iron dextran: North American Clinical Trial. *Am J Kidney Dis* 2000;36:88-97.
11. Fishbane S, Kowalski EA. The comparative safety of intravenous iron dextran, iron saccharate and sodium ferric gluconate. *Semin Dial* 2000;13:381-4.
12. Faich G, Strobos J. Sodium ferric gluconate complex in sucrose: Safer intravenous iron therapy than iron dextran. *Am J Kidney Dis* 1999;33:464-70.
13. Matzke GR. Intravenous iron supplementation in end stage renal disease. *Am J Kidney Dis* 1999;33:595-7.
14. Zanen AL, Adriaansen HJ, Van Bommel EJ, et al. Oversaturation of transferrin after intravenous ferric gluconate in haemodialysis patients. *Nephrol Dial Transplant* 1996;11: 820-4.
15. Yee J, Besarab A. Iron sucrose: The oldest iron therapy becomes new. *Am J Kidney Dis* 2002; 40:1111-21.
16. Chaytan C, Levin N, Al-Saloum M, et al. Efficacy and Safety of iron sucrose for iron deficiency in patients with dialysis-associated anemia: North American Clinical Trial. *Am J Kidney Dis* 2001;37:300-7.
17. Bailie GR, Clark JA, Lane CE, Lane PL. Hypersensitivity reactions and deaths associated with intravenous iron preparations. *Nephrol Dial Transplant* 2005;20:1443-9.