Brief Report

Intravenous Iron Replacement with Sodium Ferric Gluconate Complex in Sucrose for Iron Deficiency Anemia in Adults

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ABSTRACT

Background: When oral iron replacement therapy is ineffective, IV or IM iron dextran products have been used successfully in many patients. However, adverse events, including urticaria, anaphylaxis, and death, sometimes are associated with the use of these products.

Objective: The aim of this study was to assess the efficacy and tolerability of sodium ferric gluconate complex (SFGC) in sucrose in the treatment of adults with iron deficiency anemia.

Methods: This was a single-center, open-label, uncontrolled study. Consecutive adults in need of IV iron replacement who experienced severe reactions to generic IV iron dextran and who had previously failed to respond to oral iron products were treated with a single dose of IV SFGC (312, 375, or 500 mg) infused over 2 hours. A second dose of SFGC could be administered 6 to 8 weeks later, if needed.

Results: Six patients (3 men, 3 women; mean [SD] age, 77.0 [10.4] years) were enrolled. All patients received a single-dose infusion of SFGC, and 2 patients received a second dose. No adverse events were observed at the lower doses (312 and 375 mg); however, both patients given the 500-mg dose reported transient nausea, and 1 had pruritus and the other had transient hypertension.

Conclusion: The results of this study show that SFGC is a satisfactory alternative when IV iron replacement is needed by adults with iron deficiency anemia. (*Curr Ther Res Clin Exp.* 2003;64:263–268) Copyright © 2003 Excerpta Medica, Inc.

Key words: sodium ferric gluconate, iron deficiency anemia, iron dextran.

INTRODUCTION

When iron replacement therapy is necessary, oral iron formulations usually are effective and preferred. Some patients, however, cannot attain or maintain iron repletion by the oral route. Chronic blood loss may exceed the gastrointestinal (GI) absorptive capacity for iron; other disease processes or the use of proton pump inhibitors also may impair iron absorption. When parenteral iron is required, therapy with IV or IM iron dextran products has been successful for many patients; however, some patients may experience adverse events, including urticaria, chills, back pain, anaphylaxis, and death. These events appear to be related to the dextran component, the total dose infused, and underlying patient conditions. Serious hypersensitivity or anaphylactic reactions are not dose related and may occur after the first dose or after repeated infusions in 0.5% to 2% of patients.^{1,2} More common temporary or delayed reactions, such as arthralgia, myalgia, or fever, within 24 hours were reported in 43% of patients receiving higher single doses of iron dextran and in 26% of a group receiving lower doses.^{1,2} In a meta-analysis,³ 2.5% of hemodialysis patients receiving lower-dose infusions had reactions precluding further dosing. In a voluntary safety survey,⁴ 31 fatalities associated with iron dextran therapy were reported in the United States between 1976 and 1996.

The US Food and Drug Administration has given approval to market an alternative IV iron product, sodium ferric gluconate complex (SFGC) in sucrose.* Hemodialysis patients who routinely require parenteral iron supplements have achieved iron replenishment and correction of anemia with weekly short IV infusions of SFGC 100 to 250 mg (iron equivalent/dose); this regimen has been better tolerated and is more convenient than iron dextran for these patients.^{5,6} In the United States, most of the experience with this product has been in patients receiving hemodialysis for renal failure. This situation is considered a first-line indication for the use of SFGC in preference to iron dextran by the US Department of Health and Human Services.⁷ A postmarketing study⁸ of this schedule of SFGC among 1097 hemodialysis patients reported only 1 serious anaphylactic reaction, and this patient also had had anaphylaxis after receiving iron dextran. Among the 71 other patients with prior iron dextran sensitivity, 2.8% had suspected hypersensitivity or drug intolerance with SFGC and the other 97.2% received SFGC without adverse reactions. In the same study, overall adverse events were reported in 9.4% of placebo-treated patients versus 11.0% of SFGC-treated patients.

Although this weekly schedule is suitable for hemodialysis patients and individuals having frequent venous access for other reasons (eg, chemotherapy or antibiotic therapy), a larger-dose infusion providing all or most of the needed iron replacement would be more suitable for others. In Europe, where SFGC has been available for >20 years, additional reported uses for SFGC therapy have

*Trademark: Ferrlecit® (Watson Pharmaceuticals, Inc., Corona, California).

included iron deficiency associated with pregnancy and inflammatory bowel disease. This brief report describes the efficacy and tolerability of SFGC in a consecutive series of adults with iron deficiency anemia who need parenteral iron replacement after failing to respond to oral iron products.

PATIENTS AND METHODS

Consecutive adults in need of IV iron replacement and who had experienced severe immediate reactions to a generic IV iron dextran product were offered treatment with SFGC. Patients provided verbal informed consent to participate in this single-center, open-label, uncontrolled study.

Patients were treated in an outpatient ambulatory care clinic unit or in a hospital. After premedication with hydrocortisone 100 mg IV, chlorpheniramine 25 g IV, and a 1-mL test dose of SFGC infused over 10 minutes, SFGC (312, 375, or 500 mg) in 100 to 200 mL of isotonic saline was infused by registered nurses over 2 hours. The dose of SFGC was escalated using an arbitrary arithmetic progression to explore the efficacy and tolerability of the infusion. Vital signs and symptoms were closely monitored by registered nurses during the infusion and for 30 minutes after completion. Patients could receive a second infusion 6 to 8 weeks later, if their hemoglobin values had not increased above 10 g/dL by that time.

RESULTS

A total of 6 patients (3 men, 3 women; mean [SD] age, 77.0 [10.4] years) received the SFGC infusions. All 6 patients had symptomatic iron deficiency anemia and had not responded to oral iron supplementation because of GI disorders and hemorrhage (Table). Four patients were requiring repeated transfusions of packed red blood cells. All 6 patients had comorbid illnesses. Surgery for GI neoplasia was planned for 3 patients.

All patients received a single dose of SFGC, and 2 patients (numbers 2 and 5) received a second dose 6 to 8 weeks later. The first 2 patients received 312-mg doses of SFGC with satisfactory results. Subsequently, 3 patients received 375-mg doses (1 of these received 2 doses at this level) and 2 patients (1 of whom had received 312 mg previously) received 500 mg, all as single-dose infusions (Table). All patients were followed up ≥ 5 weeks after infusion.

No adverse events were observed at the lower (312 and 375 mg) doses. The 2 patients who received a 500-mg dose reported transient nausea; of these, 1 also had pruritus responsive to additional chlorpheniramine, and the other had transient hypertension (180/100 mm Hg) lasting 15 minutes. No episodes of hypotension, back pain, or anaphylaxis were reported. Patient 5 required additional transfusions of packed red blood cells because of continued GI bleeding after the first iron infusion. He was given a second infusion at the same 375-mg dose 6 weeks after the first infusion. After multiple endoscopic examinations

Table. Baseline and clinical characteristics of study patients.

Patient No.	Age/Sex	Clinical Data	Pre-Rx Levels				Post-Rx Levels		
			Hb, g/dL	Iron/TIBC, mg/dL	Ferritin, ng/mL	SFGC Dose, mg iron eq.	Hb, g/dL (weeks post-Rx)	Iron/TIBC, mg/dL	
1	72/F	GI bleeding; jejunal carcinoid resected	10.4	33/335	13	Absent iron	11.5 (8)	52/264	
2	60/F	Esophagitis/reflux; chronic PPI Rx	8.6	50/525	11	Absent iron	10.0 (8)	61/580	
Second dose 3	–	–	10.0	61/580	Not done	–	12.1 (3)	74/514	
	80/F	Gastric ulcer and diverticular bleeding on NSAID and PPI Rx	8.6	14/357	3	Not done	11.5 (8)	Not done	
4	77/M	GI bleeding; carcinoma of colon	7.6	16/383	11	Not done	11.0 (7)	Not done	
5	84/M	Chronic GI bleeding; vascular ectasias of colon	8.3	40/364	22	Absent iron	11.6 (10)	Not done	
Second dose 6	–	–	9.7	–	–	–	12.3 (18)	Not done	
	90/M	GI bleeding; chronic PPI Rx; carcinoma of colon	9.9	9/274	Not done	Absent iron	10.6 (2)	Not done	

Rx = treatment; Hb = hemoglobin; TIBC = total iron binding capacity; SFGC = sodium ferric gluconate complex; iron eq. = iron equivalent dose; GI = gastrointestinal; PPI = proton pump inhibitor treatment; NSAID = nonsteroidal anti-inflammatory drug; F = female; M = male.

Normal ranges: iron: 49–191 µg/mL; TIBC: 250–450 µg/mL; ferritin: 22–322 ng/mL.

to obliterate angiodysplasias, his hemoglobin concentration stabilized at 12.3 g/dL. Patient 2 received a 312-mg infusion, and 8 weeks later her hemoglobin concentration was 10.0 g/dL, reflecting continuing iron deficiency. She then received a 500-mg infusion, which increased the hemoglobin concentration to 12.1 g/dL but did not replenish iron stores (the original iron deficit was calculated to be >2500 mg). After controlling the GI hemorrhaging, clinically significant hemoglobin responses occurred in each patient (Table), despite the fact that these doses would not be expected to provide full-dose iron replacement. The posttreatment hemoglobin concentration 3 to 24 weeks after the infusions reflected the achievement of stable patient conditions.

DISCUSSION

Correction of iron deficiency anemia in adults with multiple medical conditions can be problematic, especially in patients with continuing blood loss or impaired GI iron absorption. Such patients also may have other metabolic impairments as a result of iron deficiency. Furthermore, they may deplete blood bank reserves. In patients with substantial blood loss, erythropoiesis may be limited by iron availability for hemoglobin synthesis, even in the presence of marrow iron stores.⁹ Iron dextran infusions have been useful but have an inferior safety record compared with SFGC.

CONCLUSIONS

SFGC is a satisfactory alternative when rapid IV iron replacement is needed. Repeated doses can be given. Infusions ≥ 500 mg over 2 hours in patients similar to those described here should be assessed further, because both patients who received SFGC 500 mg in this study experienced adverse events.

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