International Journal of Pharmacy and Pharmaceutical Research (IJPPR)
Volume 31, Issue 6, June 2025 ijppr.humanjournals.com ISSN: 2349-7203

Rapid Intravenous Iron Sucrose Injection: Safety in Non-CKD Patients

Nicolas Medawar, Teddy Lattouf, Yara Samhat, Maria Freifer, Romy Lteif, Jacques Choucair

Saint Joseph University, Faculty of Medicine, Hotel Dieu de France, Beirut the Lebanon

Received: 2025-04-29 Revised: 2025-05-15 Accepted: 2025-05-25

ABSTRACT

Background: Iron deficiency anemia is one of the most common causes of anemia worldwide. While oral iron supplementation remains the first line treatment for this kind of anemia, a lot of patients report unpleasant side effects, in which case intravenous (IV) iron sucrose injections can be used as an alternative to the oral treatment. However, no protocol currently exists for infusions outside of chronic kidney disease (CKD). The goal of this study is to prove the efficacy and safety of a rapid 7-10 minute infusion protocol. **Methods:** A series of 12 patients have received a total of 149 undiluted IV iron sucrose injections (Venofer®) infused over a period of 7 to 10 minutes. All patients were asked about drug-related allergic reactions, especially to iron or vitamin containing drugs. **Results:** No allergic reactions to the iron infusion were observed in the 12-patient sample. 6.7% of the infusions caused a bitter metallic taste and 4.7% required IV relocation due to extravasation associated with pain. Only one patient suffered from chills without a fever that resolved without intervention. **Conclusion:** This fast infusion protocol of IV iron sucrose seems to be well tolerated among non-CKD anemic patients. A larger scale study should be designed to further assess the safety and efficacy of this protocol.

Keywords: Rapid Intravenous, Iron Sucrose Injection, Non-CKD Patients

INTRODUCTION

Anemia is defined as a decrease in the number of circulating erythrocytes below the standard population values. It is acknowledged as a highly prevalent condition, affecting 24.8% of the human population according to epidemiological data from the WHO, with iron deficiency (ID) being its foremost contributor (1). This means that microcytic hypochromic anemia is the most encountered type of anemia (2). A person is considered anemic when their hemoglobin (Hb) concentration falls below 13 g/dl in men or 12 g/dl in women (3). The diagnosis of anemia is straightforward with symptoms such as fatigue, dizziness, drowsiness, cold intolerance and tachycardia (4) and through simple blood tests including complete blood count (CBC), serum iron, ferritin and total iron-binding capacity (5). Oral iron supplementation is indicated for patients suffering from ID anemia or nutritional ID and for pregnant women due to its simple administration and availability (6). However, many patients experience poor absorption, intolerance and adverse effects (7) such as epigastric pain, nausea, constipation, diarrhea, metallic taste and black or tarry stools (8), in which case opting for the intravenous (IV) treatment is a better alternative. Until now, there are no guidelines for the use of this type of IV iron supplementation except for patients with chronic kidney disease (CKD), for which the protocol sets the infusion time to a minimum of 15 or 30 minutes depending on the dose (9).

The goal of this study is to prove the feasibility and safety of IV iron sucrose administration with a minimal infusion time of 7-10 minutes on non-CKD patients that have not previously been mentioned in the literature.

MATERIALS AND METHODS

A series of 12 patients (11females and 1male), with a median age of 45.7 years (26-68) for females and one 72 years old man, were seen in an outpatient clinic for anemia symptoms such as dizziness, drowsiness and fatigue and fulfill the biological definition for ID anemia. They all received direct IV iron sucrose infusions over a period of 7 to 10 minutes. In total, these patients received 149 infusions. The operator used a 5cc syringe to infuse 100mg of IV iron sucrose injection Venofer® without any dilution through a 24-gauge needle into a peripheral vein of the forearm or elbow pit over 7-10 minutes monitored by a chronometer. The physician has always beside him one ampoule of 1mg of epinephrine in case of anaphylaxis. The patients were all in supine position with the physician sitting beside them the entire time of the infusion. The physician squeezes on the syringe very slowly while checking the chronometer. Since this method is very operator dependent, the time of infusion is not fixed for all the patients and varies between 7 and 10 minutes. All patients were asked about drug allergies, especially iron or vitamin allergies since many polyvitamin supplements contain iron. If any patient reported an allergic reaction, the IV infusion is cancelled. The maximal IV iron sucrose dose given was 300mg= 15cc per session.

RESULTS

No patient reported any history of allergic reaction to iron after taking an accurate and extensive past medical history. No skin or specific allergen tests were done. Additionally, no allergic reaction to Venofer® was observed in our 12-patient sample.4 of the 11 females underwent a bariatric surgery, 4 others had hypermenorrhea with heavy blood loss not fully substituted by maximal oral iron supplementation. The remaining 3 have gastric intolerance to oral iron. The only male had severe Crohn's disease requiring a partial colectomy along with oral treatment. Patients experienced an unpleasant bitter taste in 6.7% (10/149) of our interventions. The operator had to relocate the IV needle to another peripheral site on the forearm due to extravasation in 4.7% (7/149) of our intervention. This complication caused pain on the extravasation site that was rated 4/10 and 6/10 on the numeric pain rating scale 1-10. One young female also reported a cold sensation with chills but without fever, 6 hours after the infusion but got better afterward without needing any medication.

DISCUSSION

Anemia is a serious global public health problem that particularly affects young children and pregnant women. WHO estimates that 42% of children less than 5 years of age and 40% of pregnant women worldwide are anemic (10). There are three main classifications of anemia based on the size of the red blood cells (mean corpuscular volume, MCV): microcytic (MCV < 80 fL), normocytic (MCV 80-100 fL), and macrocytic (MCV > 100 fL). Among our patients, the predominant condition observed is microcytic anemia, which aligns with the criteria of this study (11). Hemoglobin production in bone marrow relies on iron, insufficient iron levels make the production of adequate hemoglobin difficult for red blood cells. Additionally, blood loss, whether from ulcers, cancer, or frequent use of certain pain relievers, can also contribute to this type of anemia (12). However, none of these medical problems were reported among our patients. ID anemia can cause various symptoms ranging from tiredness, weakness, dizziness or light-headedness, to drowsiness, which was particularly notable upon the patients' initial arrival at the clinic. It is mainly associated with pale or yellowish skin and cold hands and feet (10). Venofer® is often administered as part of the treatment regimen to address iron-deficiency anemia seen in all our cases, along with the following complications: gastric intolerance to oral iron, non-dialysis-dependent chronic kidney disease, menorrhagia, chronic inflammatory anemia, Crohn's disease, malabsorption due to bariatric surgery (13) and other acute or chronic inflammatory conditions, along with aplastic anemia (14). Limitations currently exist in the available guideline for the IV administration of Venofer®. The existing protocols primarily focus on differentiation treatments for the dialysis dependent and non-dialysis dependent CKD patients. For adult patients with hemodialysis-dependent CKD (HDD-CKD), Venofer® is given as a 100 mg IV push over 5 minutes. Conversely, for those with non-dialysis-dependent CKD (NDD-CKD), the dosage is increased to 200 mg IV push over the same duration. Moreover, in HDD-CKD patients, Venofer® can also be administered as a 100 mg/100 ml infusion, diluted with 0.9% Sodium Chloride injection, over 15 minutes. For NDD-CKD patients, the infusion dosage is adjusted to 200 mg /100 mL over the same duration. Alternatively, for patients with peritoneal-dialysis-dependent CKD (PDD-CKD), the recommended regimen consists of two doses of 300 mg /250 mL administered over 1.5 hours (15). This distinction, while important, can leave health care providers with limited guidance on managing IV iron therapy for anemic patients with preserved kidney function. While a general protocol exists for administering IV iron to non-CKDpatients, it lacks the specificity to comprehensively address the needs of patients with varying health conditions. The Hinchingbrooke health care NHS trust protocol, used for intravenous iron sucrose Venofer® approved on the 23rd of January 2008, states that the first infusion of Venofer® must include a test dose: 25mg of Venofer® should be infused over a period of 15 minutes and facilities for cardiopulmonary resuscitation should be available. If no adverse events occur during the test dose, the remainder of the dose should be given at an infusion rate of not more than 50ml in 15 minutes. Then subsequent doses may be given over 15 minutes (100mg) or 30 minutes (200mg) (16). Considering the cost of this inhospital protocol especially in non insured patients or lacking third party payers in a low income country and the current logistic limitations of these protocols, our study aimed to prove that intravenous iron sucrose could be administered as a specific treatment for non-CKD patients via peripheral intravenous line over a 7-to-10-minute period without a test dose as outpatients. A series of 12 patients (11 females, 1 male) suffering from anemia symptoms received IV treatment following the previously described protocol, with an infusion time that varied between 7 to 10 minutes.

Given the potential for both minor and serious adverse events associated with this treatment, our study closely monitored participants for any side effects. Among our 50 patients' sample, some did experience a bitter metallic taste (6.7% of our interventions), however the observed side effect is not novel, having been previously documented in the prescribing information with an accordance of 7,9% for NDD-CKD patients. One young female participant experienced a sensation of cold with chills approximately six hours following the infusion. Notably, this episode was not accompanied by fever and resolved spontaneously without requiring any medication. Furthermore, repositioning of the needle to an alternative site was necessitated in 4.7% of cases due to extravasation, a slightly higher rate than previously documented (2,2%) for NDD-CKD patients. These extraction events resulted in patient-reported pain scores ranging from 4 to 6 on the numeric pain rating scale. It is well-established that this treatment can cause a range of side effects, some mild and transient that may include diarrhea (7,2%), nausea (8,6%) and vomiting (5,0%) alongside with administration site disorders, including infusion site pain or burning (5,8%), as prescribed by the FDA regarding the administration of Venofer® (Iron Sucrose Injection) for NDD-CKD patients (15). In addition, more common effects like dysgeusia (bitter taste), headaches, rash, and chest discomfort (17,18) are frequently seen in patients. While these adverse reactions are frequently observed in adult patients, it is important to state that in pediatric patients: headache, respiratory tract viral infection, peritonitis, vomiting, pyrexia and many others (15) are more frequently experienced. However, none of these commonly reported side effects were observed in our study participants. In some cases, less common but more serious side effects can be encountered such as hypotension, iron toxicity leading to anaphylactic shocks and hypersensitivity reactions (HSR) (18). In fact, these acute reactions can be life-threatening which is why risk factors that could increase the incidence and severity of the HSR should be well known and monitored, including anyone with previous reaction to IV iron, fast iron infusion rate, history of other drug allergy, severe asthma or eczema, severe respiratory or cardiac disease (19). The absence of reported iron allergies in the patient's medical histories aligns with the favorable safety profile observed in this study. Given the potential severity of these side effects, observation of the patients for 30 minutes after the infusion (20) and proper accessibility of equipment for dealing with anaphylaxis and cardiopulmonary resuscitation (15) are necessary risk minimization measures that were taken. It is important to note that no hypersensitivity incidents occurred among the patients, and no apparent complications due to the infusion time were encountered. This new IV infusion did not trigger or cause any special or additive side effects.

CONCLUSION

This new administration method of Venofer® in a shorter infusion time did not show any significant difference in the frequency of adverse effects in comparison with already established protocols. The absence of hypersensitivity and allergic reactions amongst this patient sample suggests tolerability of this administration method and warrants further investigation into the safety profile of this administration method. The promising results of this pilot study encourage the design of a larger, long-term study to definitively assess the safety and efficacy of the proposed protocol on anemic patients with normal renal function.

REFERENCES:

1.Chaudhry HS, Kasarla MR. Microcytic Hypochromic Anemia. In: StatPearls. StatPearls Publishing; 2024. Accessed March 23, 2024. http://www.ncbi.nlm.nih.gov/books/NBK470252/
2.Massey AC. Microcytic anemia. Differential diagnosis and management of iron deficiency anemia. Med Clin North Am. 1992;76(3):549-566. doi:10.1016/s0025-7125(16)30339-x
3.Iron Deficiency in Chronic Kidney Disease: Updates on Pathop... : Journal of the American Society of Nephrology. Accessed March 23, 2024. https://journals.lww.com/jasn/fulltext/2020/03000/iron_deficiency_in_chronic_kidney_disease__updates.5.aspx
4.Tg D. Iron Deficiency Anemia. The Medical clinics of North America. 2017;101(2). doi:10.1016/j.mcna.2016.09.004
5.Elstrott B, Khan L, Olson S, Raghunathan V, DeLoughery T, Shatzel JJ. The role of iron repletion in adult iron deficiency anemia and other diseases. Eur J Haematol. 2020;104(3):153-161. doi:10.1111/ejh.13345
6.Powers JM, Buchanan GR. Diagnosis and management of iron deficiency anemia. Hematol Oncol Clin North Am. 2014;28(4):729-745, vi-vii. doi:10.1016/j.hoc.2014.04.007
7.Intravenous Versus Oral Iron for the Treatment of Anemia in Inflammatory Bowel Disease: A Systematic Review and Meta-Analysis of Randomized Controlled Trials -PubMed. Accessed March 23, 2024. https://pubmed.ncbi.nlm.nih.gov/26765407/
8.Tolkien Z, Stecher L, Mander AP, Pereira DIA, Powell JJ. Ferrous Sulfate Supplementation Causes Significant Gastrointestinal Side-Effects in Adults: A Systematic Review and Meta-Analysis. PLoS One. 2015;10(2):e0117383. doi:10.1371/journal.pone.0117383
9.DailyMed -VENOFER-iron sucrose injection, solution. Accessed March 23, 2024. https://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=626dc9e5-c6b4-4f9c-9bf4-774fd3ae619a
10.McLean E, Cogswell M, Egli I, Wojdyla D, Benoist B de. Worldwide prevalence of anaemia, WHO Vitamin and Mineral Nutrition Information System, 1993–2005. Public Health Nutrition. 2009;12(4):444-454. doi:10.1017/S1368980008002401
11.Trost LB, Bergfeld WF, Calogeras E. The diagnosis and treatment of iron deficiency and its potential relationship to hair loss. J Am Acad Dermatol. 2006;54(5):824-844. doi:10.1016/j.jaad.2005.11.1104
12.Camaschella Clara. Iron-Deficiency Anemia. New England Journal of Medicine. 2015;372(19):1832-1843. doi:10.1056/NEJMra1401038
13.Anvari S, Samarasinghe Y, Alotaiby N, Tiboni M, Crowther M, Doumouras AG. Iron supplementation following bariatric surgery: A systematic review of current strategies. Obesity Reviews. 2021;22(9):e13268. doi:10.1111/obr.13268
14.Gozzard D. When is high-dose intravenous iron repletion needed? Assessing new treatment options. Drug Des Devel Ther. 2011;5:51-60. doi:10.2147/DDDT.S15817
15.Venofer® Dosing and Administration. Accessed April 14, 2024. https://www.venofer.com/dosing
16.Gravier A, Descargues G, Marpeau L. [How to avoid transfusion in the post-partum period: importance of an intravenous iron supplement]. J Gynecol Obstet Biol Reprod (Paris). 1999;28(1):77-78.

17.Auerbach M, Henry D, Derman RJ, Achebe MM, Thomsen LL, Glaspy J. A prospective, multi-center, randomized comparison of iron isomaltoside 1000 versus iron sucrose in patients with iron deficiency anemia; the FERWON-IDA trial. Am J Hematol. 2019;94(9):1007-1014. doi:10.1002/ajh.25564
18.Macdougall IC, Bircher AJ, Eckardt KU, et al. Iron management in chronic kidney disease: conclusions from a "Kidney Disease: Improving Global Outcomes" (KDIGO) Controversies Conference. Kidney International. 2016;89(1):28-39. doi:10.1016/j.kint.2015.10.002
19.Rampton D, Folkersen J, Fishbane S, et al. Hypersensitivity reactions to intravenous iron: guidance for risk minimization and management. Haematologica. 2014;99(11):1671-1676. doi:10.3324/haematol.2014.111492
20.Schaefer B, Meindl E, Wagner S, Tilg H, Zoller H. Intravenous iron supplementation therapy. Molecular Aspects of Medicine. 2020;75:100862. doi:10.1016/j.mam.2020.100862

How to cite this article: Nicolas Medawar et al. Ijppr.Human, 2025; Vol. 31 (6): 246-249.
Conflict of Interest Statement: All authors have nothing else to disclose.