Safety of Accelerated IV Iron Administration in Inpatients with Heart Failure and Iron Deficiency: *A Retrospective Single Arm Cohort Study*

Nicole Kremer, PharmD; Shaylee Peterson, BScPharm, ACPR, PharmD

May 2023

Background

- Up to 50% of heart failure (HF) patients meet criteria for iron deficiency, which impacts quality of life (fatigue, exercise intolerance). Iron deficiency and anemia are also independent risk factors for mortality in this population.
- IV iron has been shown to improves symptom of iron deficiency in HF patients, and may reduce the risk of HF hospitalizations. Oral iron is not different from placebo, so IV is the mainstay.
- Iron sucrose is the preferred IV product for inpatients in Interior Health due to cost. However, iron sucrose has a recommended maximum weekly dose of 300 mg. As such, multiple infusions over weeks to months are required to replete iron stores, which poses a barrier to full repletion.
- Frequent hospitalizations in HF patients provide an opportunity to replete iron stores in an accelerated manner while admitted.
- Recent data supports efficacy and safety of accelerated IV iron administration in HF patients. However, data assessing safety of accelerated iron sucrose in hospitalized HF patients are lacking.

Objective

- To describe the incidence of adverse reactions associated with accelerated IV iron sucrose administration in patients with heart failure and iron deficiency admitted to Royal Inland Hospital.

Methods

Design	Retrospective single-arm cohort study using RIH EMR (chart review)
Inclusion	Adults admitted to RIH between July 1/21 and Nov 30/22 with a diagnosis of HF (any LVEF) and iron deficiency (ferritin <100 ng/mL OR TSAT <20%)
Exclusion	eGFR <30 mL/min or dialysis
Intervention	Received >1 dose of IV iron sucrose within 7 d
Comparator	No comparator
Data Extraction	EMR → progress notes, nursing notes, vital signs, admission notes, med orders, etc. Duplicate data extraction for 10% of population
Analysis	Descriptive statistics

Interior Health

UBC

Outcomes

Primary	Incidence of adverse effects: • Hypotension (SBP ≤90 mmHg within 4h) • Fever (≥38 C within 4h) • Myalgia (within 24h) • Death (prior to discharge)
Secondary	• Incidence of any other adverse effects (N/V, HA, SOB, chest tightness, rash, hives, other) (during or within 4h) • Administration of diphenhydramine and/or epinephrine (within 4h)

Results

77 screened → 34 met inclusion criteria → 2 excluded (confidential charts) → 32 included

Data only from July 1, 2021 to October 31, 2022
(due to coding delays)

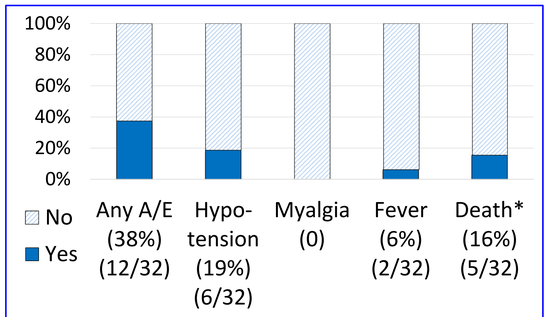
Table 1 – Participants (n=32)

Sex	59% female, 41% male
Age	77 years (mean), range 31-91 years
Reason for Admission	75% HF Others: COPD, GIB, AF, hepatic failure, other. 91% in acute decompensated HF
LVEF	43% (mean), range 10-70% 44% <40 | 12% 40-50 | 44% >50
eGFR	64 mL/min (mean), range 30-120 mL/min
Ferritin	58 ng/mL (mean), range 9-356 ng/mL
TSAT	9% (mean), range 4-24%

Table 2 – Iron Sucrose Dosing

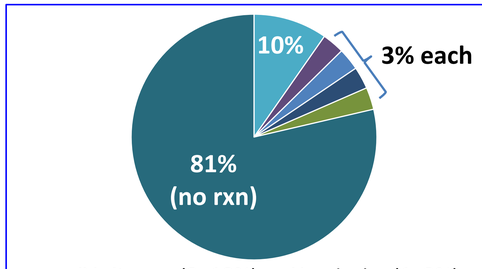
Dose per Infusion	200 mg: 47%	300 mg: 53%
Frequency	Q1d: 31% Q2d: 56%	Q3d: 9% Q5d: 3%
Total # Doses	Two: 25% Three: 56%	Four: 9% Five: 9%
Total Dose	756 mg (mean), range 400-1200 mg	

Figure 1 – Primary Outcome



***Deaths**:
1. Vascular infection
2. Aspiration pneumonia
3. End stage HF
4. MAiD
5. Myocardial infarction

Figure 2 – Secondary Outcomes



No epinephrine/diphenhydramine use reported.

Discussion

Findings:

- 53% of patients experienced any adverse event. The most common were hypotension (19%), death (16%) and IV site reactions (9%). No episodes of hypersensitivity reactions were reported, evidenced by no diphenhydramine or epinephrine use.
- Previously reported adverse event rates in this population are ~40-80%, which is comparable to the present study.
- Hypotension was likely influenced by concurrent acute HF, increased diuretic use, and use of guideline-directed chronic heart failure therapy.
- The mortality rate was higher than expected, but has several factors to consider. Iron deficiency and anemia are independent risk factors for mortality in this population. Most patients were also admitted with acute HF, which has a 6-9% risk of death before discharge. Patients also has advanced age and comorbidities. Therefore, the population studied was at increased risk of death regardless of iron. However, without a control group, it is unclear whether accelerated iron contributed.

Strengths:

- First study assessing safety of accelerated iron sucrose in hospitalized HF patients.
- Important clinical question.
- Duplicate extraction for 10% of data.
- Real world data improves generalizability.

Limitations:

- No comparator group.
- Not all adverse events captured, dependent on documentation in EMR.
- Additional variables not controlled or recorded (eg: diuretic use, baseline blood pressure, etc.
- Heterogeneous iron protocols.

Future Research:

- Study design including a comparator group to identify associations, ideally RCT or prospective controlled observational study.
- Control for confounding factors, such as diuretic dose, baseline blood pressure, etc.
- Consistent intervention dose and frequency.

Conclusions

The overall adverse event rate was 53%, with most common being hypotension, death, and IV site reactions. Adverse event rates in this study were similar to previously reported rates. However, the 16% death rate was higher than expected. Without a comparator group, it is unclear the extent to which accelerated iron administration affects adverse event rates. However, accelerated iron sucrose appears to have standard adverse event rates. Additional research is required to clarify causal associations between accelerated iron sucrose and adverse reactions in heart failure patients.