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Fish-Bane Reaction Associated with IV Iron Sucrose: A Case Series

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ABSTRACT

Intravenous Iron sucrose is a common treatment for Iron deficient anemia, but carries a risk of infusion-related reactions. We report a case series of eight female patients with severe anemia or other comorbidities who developed transient, non-anaphylactic reactions consistent with the Fish bane-type reaction following intravenous iron sucrose (200 mg in 100 mL normal saline). In all cases, symptoms occurred during or shortly after infusion. In all cases, stopping the infusion led to clinical improvement without progression to frank anaphylaxis. We review the literature on IV-iron infusion reactions, discuss mechanistic possibilities (Fish bane reaction, non-IgE mediated hypersensitivity / CARPA), and provide practical recommendations for monitoring and management.

KEY WORDS: Fish-bane reaction, Intravenous Iron sucrose, Infusion reaction, Iron deficient anemia, Case series, Adverse drug reactions.

1.INTODUCTION

Iron deficiency anemia (IDA) remains a prevalent global health concern, affecting individuals across a wide spectrum of clinical conditions, including malabsorption syndromes, chronic blood loss, chronic kidney disease, heart failure, inflammatory disorders, malignancy, gastrointestinal surgery, and perinatal states, often necessitating beyond oral supplements. But oral iron supplementation is the standard first-line therapy; however, it may be ineffective, poorly tolerated, unsuitable, or impractical in certain patient populations. [4]

In such severe cases, parenteral iron administration is indicated, particularly when serum ferritin levels fall below 15 µg/L. Intravenous (IV) iron preparations, such as iron sucrose complex (ISC) and low-molecular-weight iron dextran (LMWID), offer faster hemoglobin correction and iron store replenishment compared with oral therapy. [3]

These formulations are generally safe and effective; however, infusion-related adverse drug reactions (ADRs) can occur. Reported ADRs range from mild manifestations—such as fever, chills, dizziness, headache, pruritus, urticaria, arthralgia, and myalgia—to severe events including hypotension, bronchospasm, seizures, cardiovascular collapse, and, rarely, death.[1]

Among the recognized non-severe infusion reactions is the Fish bane-type reaction, characterized by transient chest and back tightness, arthralgias, and rigors without life-threatening features such as hypotension, wheezing, stridor, or laryngeal edema. These reactions occur in approximately 1% of patients receiving IV iron and are believed to result from labile iron—weakly bound iron within nanoparticle formulations that can react with plasma proteins or circulate freely. Such reactions are distinct from hypersensitivity reactions (HSRs), which may be mediated either by immunoglobulin E (IgE) or through complement activation-related pseudo-allergy (CARPA) triggered by iron nanoparticles. [5,8]

Minor infusion reactions are generally self-limiting, often resolving with cessation of the infusion and supportive measures. Risk factors for IV iron reactions include a history of allergy or atopy, rapid infusion rates, and prior reactions to IV iron. Consequently, IV iron administration should occur in settings equipped for prompt recognition and management of anaphylaxis, with trained staff and appropriate emergency medications readily available.[6]

2.PRESENTATION OF CASES

CASE 1:

A 55-year-old female was admitted with complaints of giddiness and generalized body pain. She was diagnosed with severe anemia and bi-cytopenia. The patient received the first dose of intravenous iron sucrose (200 mg in 100 mL normal saline) over 1 hour 30 minutes and subsequently developed rigors with acute chest pain radiating to the shoulder. The infusion was stopped, and her symptoms improved without further complications.

CASE 2:

A 65-year-old female presented with giddiness, fever, reduced food intake, and fatigue. She was diagnosed with severe anemia and was administered intravenous iron sucrose (200 mg in 100 mL normal saline) on three occasions. After each infusion, she developed rigors and chest pain radiating to the shoulder. Following the third occurrence, iron sucrose was discontinued, and the patient improved.

CASE 3:

A 75-year-old female was admitted with complaints of giddiness, loss of appetite, and constipation. She was diagnosed with severe anemia and received intravenous iron sucrose (200 mg in 100 mL normal saline) over 1 hour 45 minutes. She developed rigors and chest pain radiating to the shoulder after the third dose. The infusion was stopped, and the patient improved.

CASE 4:

A 45-year-old female presented with fever and a mass over the tongue. She was diagnosed with papilloma of the tongue and was treated with intravenous iron sucrose (200 mg in 100 mL normal saline) over 1 hour 24 minutes. During the infusion, she developed rigors. The infusion was stopped, and her symptoms resolved with supportive care.

CASE 5:

A 70-year-old female was admitted with chest pain, breathing difficulty, and giddiness for more than 10 days. She was diagnosed with coronary artery disease, hypertension, volume overload, and severe anemia. She received intravenous iron sucrose (200 mg in 100 mL normal saline) over 1 hour 15 minutes and developed rigors with fever during the infusion. The infusion was stopped, supportive management was provided, and the patient improved.

CASE 6:

A 42-year-old female presented with lower abdominal pain, vomiting (three episodes), body pain, and constipation. She was diagnosed with hepatic cyst and anemia. The patient received intravenous iron sucrose (200 mg in 100 mL normal saline) over 80 minutes. During the fourth dose, she developed rigors, fever, and right leg muscle tightness. The infusion was stopped, and her symptoms resolved without further complications.

CASE 7:

A 45-year-old female presented with fever, constipation, burning micturition, pain, and bleeding during defecation. She was diagnosed with microcytic hypochromic anemia and anal fissure. She was administered intravenous iron sucrose (200 mg in 100 mL normal saline) over 80 minutes. During the infusion, she developed rigors. The infusion was stopped, and she improved with supportive management.

CASE 8:

A 75-year-old female patient was admitted to the hospital with complaints of burning sensation in the epigastric region, loss of appetite, and reduced food intake. She was diagnosed with severe anemia and started on intravenous iron sucrose (100 mg in 100 mL normal saline). The first dose was well tolerated; however, during the second dose, the patient developed rigors and fever. The infusion was stopped, and supportive care was provided. When the drug was re-administered on an alternate day, the patient tolerated the infusion without further adverse reactions.

3.OBSERVATION:

In this case series, patients who received iron sucrose infusion over less than 30 minutes did not develop chest pain. However, they still experienced rigors and/or fever. In contrast, prolonged infusion durations (>1 hour) were associated with more frequent chest pain along with rigors.

Case	Age/Sex	Diagnosis	No. of Doses	Dose at ADR	Iron Sucrose Dose	Infusion Duration	Reaction	Outcome
1	55F	Severe anemia, bicytopenia	1	1st dose	200 mg in 100 mL NS	90 minutes	Rigors + chest pain radiating to shoulder	Improved after stopping infusion with supportive care (Inj. Dexamethasone)
2	65F	Severe anemia	3	In all 3 doses	200 mg in 100 mL NS (1ST DOSE) 100mg in 100ml NS (2nd and 3rd dose)	60 minutes	Rigors + chest pain radiating to shoulder	Iron sucrose discontinued after 3rd reaction; improved
3	75F	Severe anemia	3	3rd dose	200 mg in 100 mL NS	105 minutes	Rigors + chest pain radiating to shoulder	Improved after stopping infusion
4	45F	Papilloma of tongue, anemia	1	1st dose	200 mg in 100 mL NS	84 minutes	Rigors	Improved with supportive care
5	70F	CAD, HTN, volume overload, severe anemia	1	1st dose	200 mg in 100 mL NS	75 minutes	Rigors + fever	Improved with supportive management ((INJ. Paracetamol)
6	42F	Hepatic cyst, anemia	4	4th dose	200 mg in 100 mL NS	80 minutes	Rigors + fever + right leg tightness	Improved without complications and supportive management (INJ. Paracetamol & (Inj. Dexamethasone) was treated)
7	45F	Microcytic hypochromic anemia, anal fissure	1	1st dose	200 mg in 100 mL NS	80 minutes	Rigors	Improved after stopping infusion
8	75F	Severe anemia	3	2nd dose	100 mg in 100 mL NS	60 minutes	Rigors + fever	Improved after stopping infusion; subsequent alternate-day dose tolerated

TABLE 1: - *It illustrates the adverse drug reactions observed in eight cases administered Iron sucrose, highlighting the dose and duration of administration, with reconstitution-related fish-bane reactions and it's management.*

4.CASUALITY ASSESSMENT:

Using standard clinical reasoning (temporal relationship, positive de-challenge in all cases, and repeat occurrence on re- challenge in Case 2), the reactions are best classified as probable for an adverse drug reaction related to iron sucrose. None of the patients displayed features of severe anaphylaxis.

5.DISCUSSION

In our series, all patients developed acute rigors, sometimes accompanied by chest pain or fever, during iron sucrose infusion, consistent with the clinical profile of Fish-bane-type infusion reactions. None exhibited severe features such as hypotension, airway compromise, or generalized urticaria, which aligns with the typical benign course of such events. The rapid symptom resolution after stopping the infusion further supports this classification. [5]

The pathophysiology of these reactions likely involves the presence of labile iron, which can transiently interact with plasma proteins or generate oxidative stress, leading to symptoms without true allergic sensitization. Unlike IgE-mediated hypersensitivity, these reactions are not predictive of severe anaphylaxis. Additionally, Complement Activation-Related Pseudo-Allergy (CARPA) has been implicated, wherein iron nanoparticles trigger complement activation, leading to the release of inflammatory mediators. [8]

From a clinical standpoint, differentiating between Fish-bane-type reactions, mild infusion-related events, and early anaphylaxis is critical. The temporal relationship (occurrence during or shortly after infusion) and the positive de-challenge (symptom resolution upon stopping the drug) support a causal link (probable adverse drug reaction). A notable observation in this series is that while patients receiving a faster infusion (Case 8, re-challenge) tolerated the dose, those with prolonged infusion durations (1 hour) were frequently associated with the most pronounced symptoms (rigors and chest pain). Furthermore, repeated exposure in Case 2 led to recurrence on all three infusions, highlighting a potential sensitization or cumulative effect in some individuals. Management should prioritize safety. Immediate cessation of the infusion is necessary. Re-challenge, as safely performed in Case 8, is generally considered acceptable after mild-to-moderate non-anaphylactic reactions, often at a slower rate or with premedication, but permanent avoidance is warranted after severe reactions. [7]

6.CONCLUSION

This case series demonstrates that infusion reactions to intravenous iron sucrose, predominantly manifested as benign Fish-bane-type reactions (rigors, fever, chest pain), were more frequently associated with prolonged infusion durations (1 hour) and repeated dosing. These observations underline the need for strict adherence to infusion guidelines, careful monitoring during each administration, and heightened caution in patients requiring multiple doses. Clear documentation and careful patient counseling regarding future IV iron therapy are key components of safe clinical practice.

7.PRACTICAL RECOMMENDATION

- Ensure pre-infusion checks.
- Establish baseline vital signs and confirm the immediate availability of emergency medications and resuscitation readiness.
- Vigilant monitoring: maintain close observation during infusion, especially first 5-10 minutes.
- Management for mild reactions, stop/slow infusion and provide symptomatic care.
- For anaphylaxis, follow emergency protocol immediately.
- Re-challenge protocol: If reaction was clearly no-anaphylactic, re-challenge can be considered, but at lower concentration, slower rate, with alternative iron formulation under close monitoring.
- Anaphylaxis preparedness: Maintain a high index of suspicion for severe reactions. Emergency protocol with IM Epinephrine as the 1st line treatment need to be immediately available.

8.ETHICAL CONDUCT APPROVAL

Ethical review and approval were not required for this study as this is a retrospective case series utilizing anonymized data collected during the routine clinical management of patients, and so it falls outside the scope of human subjects' research requiring prospective ethical oversight.

9.AUTHOR'S CONTRIBUTION

DR. T. Rengaraj - provided clinical care and patient data. Padhma M, Ramakrishnan S and Siddha Vidhyar Dhani were responsible for case identification, literature review, and manuscript drafting. All authors critically reviewed and approved the final manuscript.

10.DISCLOSURES

The authors declare that they have no competing interests or conflicts of interest related to the material presented in this manuscript.

11.CONSENT FOR PUBLICATION

Written informed consent was obtained from all patients (or their legally authorized representatives) for the publication of this case series and any accompanying data.

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