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Research Article

Ferric Carboxymaltose Use Evaluation in Heart Failure Patients: Real World Data from Tertiary Care Hospital in the United Arab Emirates

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Abstract

Background: Heart Failure (HF) is a prevalent cardiovascular condition associated with high morbidity and mortality. Anemia, a common comorbidity in HF patients, often worsens outcomes. Intravenous Ferric Carboxymaltose (IV-FCM) has emerged as a treatment for iron deficiency and anemia in this population.

Objectives: This study aimed to evaluate the utilization and clinical impact of IV-FCM in HF patients and suggest a comprehensive protocol for standardizing IV-FCM dosing and blood biomarker monitoring for medical teams.

Methods: We conducted a retrospective review of HF patients prescribed IV-FCM between January 1, 2022, and April 31, 2023, at Tawam Hospital, UAE. Data on patient demographics, laboratory measures, IV-FCM dosing, and compliance with guidelines were collected and analyzed.

Results: A total of 50 HF patients were included, with a mean age of 65, and 66% male. Most patients had NYHA Class II-III HF. Proper initial dosing of IV-FCM was administered in 78% of cases, but compliance with follow-up dosing (28%) and lab measures (38%) was low. In improved patients, TSAT and Ferritin levels increased significantly by 122% and 622%, respectively, after IV-FCM administration. Hemoglobin levels increased by 15.8% on average in improved patients. Poor improvement in lab measures was most common in patients with suboptimal or missed follow-up dosing.

Conclusion: This study highlights the effective use of IV-FCM in managing iron deficiency and improving clinical outcomes in HF patients. Significant increases in TSAT, Ferritin, and hemoglobin levels were observed, along with improved quality of life. These findings support IV-FCM as a valuable therapeutic option in HF care and underscore the importance of guideline compliance for monitoring and follow-up dosing.

Keywords: *Heart Failure; Iron Deficiency; Ferric Carboxymaltose; Monitoring; Algorithm*

Introduction

Heart failure (HF) is one of the most common cardiovascular diseases that has increased in incidence in recent decades and is expected to increase in the future [1]. HF is a clinical syndrome with multiple etiologies, all leading to a decrease in heart pumping capacity. There are two main types of heart failure: heart failure with reduced ejection fraction (HFrEF), also referred to as systolic HF and heart failure with preserved ejection fraction (HFpEF) or diastolic HF. Iron deficiency is common among patients with heart failure, occurring in 40 to

50% of patients with chronic heart failure and up to 80% of patients with acute heart failure. Features intrinsically related to heart failure, such as inflammation, neurohormonal activation, and congestion, are associated with the development of iron deficiency in HF [2]. Anemia is a common comorbidity in HF patients and is often associated with worse outcomes and it correlates with prognosis (higher mortality, low exercise capacity, tissue remodeling, and hospitalization). The more the patient is anemic the worse the outcomes of HF. IV iron replacement for anemia and iron correction show improvement in patients' prognosis (EF, TSAT, Ferritin, QoL, Hgb) for both types of HF [3]. Numerous mechanisms unrelated to hemodynamic dysfunction may underlie impaired exercise tolerance in patients with chronic heart failure. Among them, inadequate oxygen supply and impaired oxygen use by skeletal muscle during exercise contribute to poor clinical status. These findings highlight the substantial burden of anemia and iron deficiency in patients with heart failure and underscore the need for comprehensive early detection, assessment, and treatment strategies to mitigate associated risks and improve patient outcomes.

Background

In heart failure, causes of iron deficiency (ID) include a range of factors leading to absolute or functional iron deficiency. Iron deficiency may have several causes, such as gastrointestinal blood loss, especially in patients receiving aspirin or anti-coagulants, and conditions such as anorexia, malnutrition, or malabsorption. Anemia may be further aggravated by the use of antagonists of the renin-angiotensin-aldosterone system, including angiotensin-converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARB). Blood dilution caused by fluid retention in patients with heart failure can also cause lower hemoglobin levels. Understanding the multiple causes of anemia in heart failure is critical to implementing targeted interventions to treat iron deficiency and anemia. Iron plays a key role in oxygen uptake, transport, and storage, as well as oxidative metabolism in the skeletal muscle. Traditionally, iron deficiency has been considered to have clinical consequences only in the presence of anemia. Alternatively, a reduced hemoglobin level can be viewed as the result of a process beginning with the gradual depletion of iron stores. In HF patients, iron deficiency with or without anemia attenuates aerobic performance and is accompanied by reports of fatigue and exercise intolerance. The repletion of iron in patients who have iron deficiency with heart failure improves cognitive, symptomatic, and exercise performance [4]. Recently, it has been recognized that patients with heart failure may be prone to developing iron deficiency due to a depletion of iron stores or defective iron absorption and the reduced availability of iron recycled in the reticuloendothelial system [5].

Functional and absolute iron deficiency

Functional iron deficiency is where the function of absorption is disturbed, this happens when Hepcidin (overproduced when a hyper-inflammatory disease such as HF is present) binds to Ferroprotein and destroys it (making it non-functional) which leads to low oral iron absorption and movement from cells. So, the iron stores in this case are normal inside the cells but cannot be transferred to blood or Hg so it is "non-functional" which is a decrease in iron bioavailability but not a deficiency. On the other hand, reduction of Iron stores due to reduced intake and/or increased hemorrhage is considered an absolute iron deficiency.

Anemia is detected similarly to the general populace by hemoglobin (Hb) level below an established threshold. Specifically, anemia is characterized by Hb levels below 13 g/dl in men and below 12 g/dl in women. Iron deficiency in heart failure is recognized by a serum ferritin level below 100 µg/L or a serum ferritin level between 100 and 299 µg/L with a transferrin saturation value (TSAT) below 20% [6].

Ferric carboxymaltose in HF

The latest American and European guidelines for acute and chronic HF management recommend IV iron supplementation, including ferric carboxymaltose, for the treatment of iron deficiency in patients with HF. The standard dose is 1000 mg once or 750 mg weekly for 2 weeks at baseline and 500 mg follow-up dosing depending on iron studies [7,8].

Clinical evidence has demonstrated the benefits of FCM in HF patients. Studies like the IRON-HF and FAIR-HF trials have shown significant improvement in NYHA functional class, exercise capacity, and quality of life in patients treated with FCM compared to those receiving

a placebo. FCM administration results in substantial increases in serum ferritin and transferrin saturation (TSAT), indicating effective replenishment of iron stores. Improved hemoglobin levels alleviate anemia symptoms such as fatigue and weakness, and better management of HF symptoms can potentially reduce HF-related hospitalizations and associated healthcare costs.

In clinical practice, the dosing and administration of FCM should be tailored to the severity of iron deficiency and the patient's weight, with maintenance doses adjusted based on follow-up lab results. A comprehensive protocol for FCM administration involves an initial evaluation to confirm iron deficiency, appropriate initial dosing, and regular monitoring of iron parameters and hemoglobin levels. This includes baseline assessments and post-administration monitoring at regular intervals. Overall, FCM is a valuable therapeutic option for managing iron deficiency in HF patients, leading to significant improvements in iron parameters, hemoglobin levels, functional status, and quality of life. A structured protocol for FCM administration and monitoring is essential for ensuring effective management and optimal patient outcomes.

	CONFIRM-HF (2015)	EFFECT-HF (2017)	AFFIRM-HF (2020)	IRON-CRT (2021)
FCM Dosing (mg)	500 - 2000 mg	500 - 2000 mg	Ganzoni formula	500 - 1500 mg
Interval (Weeks)	0, 6, 12*, 24*, 36*	0, 6, 12*	0, 6, 12*, 24*	0, 6, 12*

Table 1: *IV ferric carboxymaltose dosing in clinical trials [9-12].*

**If ID Persists.*

Aim of the Study

To emphasize the effectiveness of Intravenous Ferric Carboxymaltose (IV-FCM) in the management of iron deficiency in patients with heart failure, this study aimed to evaluate its use and clinical effects. By monitoring usage patterns and clinical outcomes associated with IV FCM administration, we aimed to gain insights into its effectiveness in treating iron deficiency in patients with heart failure. Through a comprehensive assessment, including analysis of guideline compliance, changes in hemoglobin, TSAT, and Ferritin levels, and other relevant clinical parameters, we aimed to elucidate the real-world impact of IV-FCM treatment in this patient group. The results of this study have the potential to inform clinical practice and provide a decision aid for the use of IV-FCM as a therapeutic intervention for iron deficiency in patients with heart failure through a suggested utilization protocol for standardizing IV-FCM dosing and blood biomarker monitoring for medical teams.

Methods

An extensive literature search was conducted to extract the most recently published guidelines for managing anemia in HF. We conducted a retrospective review chart of HF patients who were prescribed IV Ferric Carboxymaltose (IV-FCM) between January 1, 2022, and April 31, 2023, at a tertiary healthcare facility (Tawam Hospital) in the United Arab Emirates.

Data including patient demographics, baseline and follow-up TSAT, Ferritin, hemoglobin levels, and IV-FCM dosing were collected and analyzed. The primary endpoints were changes from baseline laboratory measures and compliance with guideline and clinical trial dosing protocols of IV-FCM.

Result

Iron deficiency in heart failure

This study evaluated the use of FCM, an intravenous iron replacement product available as Ferinject (50 mg/ml, 10 ml vial) at Tawam Hospital, according to the ACC/AHA/HFSA 2023 HF guidelines and the FDA indication. The study included 50 patients with HF from January 2022 to April 2023. Of these, 88% had HFrEF and 12% had HFpEF. Most patients (90%) had comorbid dyslipidemia and diabetes, and

10% had CKD. Patients with iron deficiency anemia received IV FCM under cardiology service. The study population comprised 33 males (66%) and 17 females (34%), with a mean age of 68 years and a mean weight of 68 kg.

Baseline Characteristics		Total
Gender N (%)	Male	33 (66)
	Female	17 (34)
Age Mean (SD)		68 (± 12)
Wt. Mean (SD)		69 (± 18)
Heart Failure N (%)	HFrEF	44 (88)
	HFpEF	6 (12)
Diabetes N (%)		23 (46)
Dyslipidemia N (%)		45 (90)
Hypertension N (%)		4 (8)
Ischemic Heart Disease N (%)		6 (12)
Afib N (%)		12 (24)
CKD N (%)		4 (8)
Osteoporosis N (%)		6 (12)
Coronary Artery Disease N (%)		3 (6)
BPH N (%)		5 (10)

Table 2: *Baseline characteristics.*

Compliance assessment

The compliance was assessed based on the latest emerging evidence from the American and European guidelines, FDA drug labels, clinical trials protocols, and expert consensus about FCM dosing and lab assessments in ID patients with HF.

FCM Dosing	Labs
Initial FCM dosing	Labs done initially
Follow-up FCM dosing	Labs done at follow-up
Follow-up FCM intervals	Follow-up labs intervals

Table 3: *Compliance criteria.*

In this study we found at baseline, 76% of patients received the ideal FCM dose of 1000 mg or 750 mg twice (7 days apart), and the rest received different doses (4% with 750 mg once, 10% with 500 mg for the CKD patients).

The follow-up recommendation was to recheck iron studies (TSAT, Ferritin, and Hgb) at weeks 12, 24, and 36. There was no documentation at week 6. At week 12, 64% of the patients had Hgb < 15g/dl but only 14% of them received the ideal dose of 500 mg. Also, 22% of the patients had no Hgb level measurement. At week 24, 12 patients had Hgb > 15 g/dl, 6 of them with low TSAT < 20 and 2 with low ferritin < 100 µg/L, but only 6 patients received IV FCM with different doses (10% with 1000 mg and 2% with 750 mg) which is not recommended as in our references. At week 36, 22 patients had Hgb < 15 g/dl, 4 of them with low TSAT < 20 and 2 with low ferritin < 100 µg/L, but only 5 patients received the dose of IV FCM, which did not follow the recommendations (Figure 1 and 2).

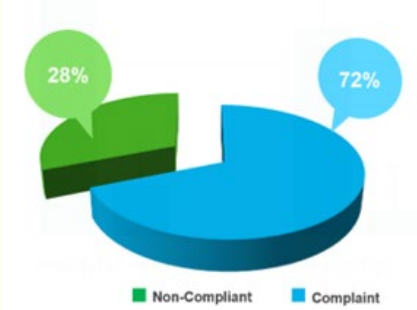

Figure 1: Compliance - Dosing

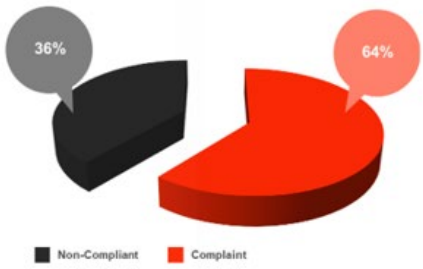

Figure 2: Compliance – Lab follow up

Labs improvement

There was a significant average improvement from baseline till the last received dose in both TSAT and Ferritin levels, 122% and 622%, respectively. Hgb was also improved by on average 15.8% from baseline till the last dose of FCM.

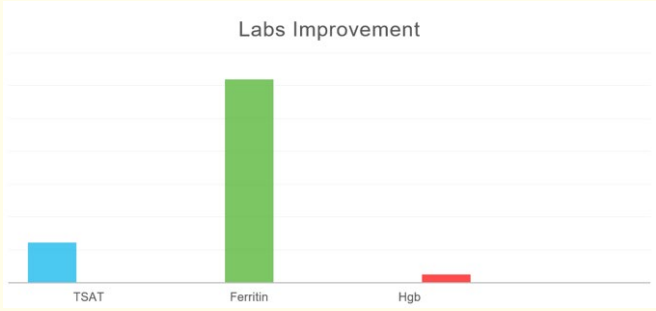

Figure 3: *Lab improvements.*

Discussion

The study demonstrated that correcting iron deficiency with Intravenous Ferric Carboxymaltose (IV-FCM) in patients with chronic heart failure can lead to significant clinical benefits. This finding is particularly important because oral iron supplementation has been reported to be ineffective for iron repletion and does not improve exercise capacity in patients with iron deficiency and heart failure. Despite these benefits, our cohort revealed that compliance with guidelines regarding the dosing of IV-FCM and follow-up laboratory assessments was suboptimal. Ensuring adherence to these guidelines is essential for achieving the best possible outcomes. Managing both anemia and heart failure is critical for optimizing overall health and improving patient prognosis, as evidenced by enhancements in ejection fraction (EF), transferrin saturation (TSAT), ferritin levels, quality of life (QoL), and hemoglobin (Hgb) levels in both types of heart failure.

To improve the implementation of evidence-based therapies and guidelines, multidisciplinary collaborative protocols and pharmacist-led initiatives should be adopted and replicated in various settings. Establishing pharmacist-driven protocols for iron deficiency screening and iron replacement in heart failure patients could standardize care, ensuring more consistent and effective treatment. This approach underscores the importance of a coordinated effort among healthcare professionals to enhance patient outcomes in heart failure management.

In developing our protocol, we drew inspiration from the scientific statement by Beavers., *et al*. (2023) on managing iron deficiency in heart failure, which provided a detailed framework for iron assessment and repletion strategies. While the flowchart presented in our study is uniquely worded and adapted for our specific clinical context, it is influenced by the principles outlined in their work. This acknowledgment not only recognizes the comprehensive nature of their guidelines but also emphasizes the need for adherence to such protocols in routine clinical practice.

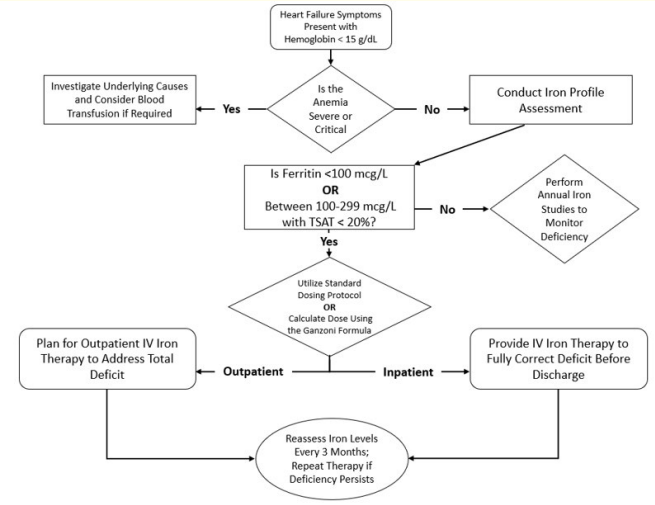

Figure 4: *Suggested protocol for IV-FCM dosing and iron panel monitoring.*

Limitations of the Study

The study has limitations that may impact the interpretation of its findings. Variations in clinical practice can lead to inconsistencies in treatment and outcomes. There is uncertainty regarding the optimal dose of IV-FCM administration and the selection of blood biomarkers for follow-up assessments, which may result from a lack of detailed recommendations outlining therapy doses and a well-defined strategy to track patient improvement. Additionally, patient non-compliance with clinic appointments poses a significant limitation, as failure to attend follow-up appointments can make it difficult to monitor changes in clinical parameters and dosing. Despite these limitations, the study aims to provide insightful information about the use and clinical impact of IV-FCM in heart failure patients.

Conclusion

This study highlights the effective use of IV-FCM in managing iron deficiency and improving clinical outcomes in HF patients. Significant increases in TSAT, Ferritin, and hemoglobin levels were observed, along with improved quality of life. These findings support IV-FCM as a valuable therapeutic option in HF care and underscore the importance of guideline compliance for monitoring and follow-up dosing.

Author/Funding Disclosures

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Declaration of Use of LLM Tools

Chat-gpt was used for grammar check and maintaining professionalism after framing sentences.

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