Section: Pharmacology

Original Research Article

AN OPEN-LABEL RANDOMIZED STUDY COMPARING COST, SAFETY, AND EFFECTIVENESS OF FERRIC CARBOXYMALTOSE VS IRON SUCROSE IN TREATING IRON DEFICIENCY ANEMIA IN CHRONIC KIDNEY DISEASE

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Abstract

Background: Iron deficiency anaemia (IDA) is a common complication in chronic kidney disease (CKD), often managed with erythropoiesis-stimulating agents (ESA), oral iron, or intravenous (IV) iron therapy. Current guidelines recommend IV iron in patients with transferrin saturation (TSAT) ≤30% and serum ferritin ≤500 ng/mL. Ferric carboxymaltose (FCM) and Iron Sucrose (IS) are commonly used among available IV formulations. This study compared the safety, efficacy, and pharmacoeconomic profiles of FCM and IS in CKD patients with IDA. **Materials and Methods**: 120 CKD patients with IDA were randomized into two groups to receive either IS (200 mg weekly for 5 weeks) or FCM (500 mg weekly for 2 weeks). All patients were followed for 8 weeks. Efficacy was assessed by changes in haemoglobin (Hb), TSAT, and serum ferritin. Safety was evaluated based on adverse drug reactions (ADRs), and a pharmacoeconomic analysis was conducted. **Results:** ADRs were more frequently reported in the IS group and included itching, fatigue, back pain, and nausea. A rise of ≥1 g/dL in Hb was observed in 88.3% of patients in the FCM group, compared to 80% in the IS group. The cost to achieve a 1 g/dL rise in Hb was significantly lower with FCM (₹2005.99 ± 1877.21) than IS (₹2618 ± 1360.63). Both groups showed statistically significant improvements in Hb, TSAT, and ferritin from baseline to 8 weeks, with FCM showing superior TSAT improvement. **Conclusion:** FCM demonstrated better efficacy, fewer adverse effects, and more cost-effectiveness than IS, making it a preferred option for managing IDA in CKD patients.

INTRODUCTION

Anaemia is a global public health issue with a multifactorial origin, including nutritional deficiencies, chronic infections, inflammatory and chronic diseases, gynecologic and obstetric conditions, and genetic red blood cell disorders.[1] In 2021, approximately 1.9 billion people were affected, accounting for 52 million years lived with disability (YLD).[2]Anaemia is defined by reduced haemoglobin (Hb) concentration and red blood cell count, leading to decreased oxygen-carrying capacity.[3] Its causes are classified into blood loss, increased red cell destruction, and impaired production.[4] In chronic kidney disease (CKD), Anemia is diagnosed when Hb is <13 g/dL in males and <12 g/dL in females.[5] Due to its significant impact on quality of life and survival, timely diagnosis and treatment of Anemia in CKD are essential. The underlying mechanism involves impaired erythropoiesis, requiring treatment with erythropoiesis-stimulating agents (ESAs) and iron supplementation.[6]

Iron balance in CKD patients is often negative due to reduced absorption, chronic loss, increased hepcidin levels, and low bioavailability.[7–8] Diagnosis of iron deficiency anaemia (IDA) in CKD relies on Hb, transferrin saturation (TSAT), and serum ferritin levels. IV iron therapy is recommended for patients with TSAT ≤30% and ferritin ≤500 ng/mL.[5] Oral iron is often poorly absorbed in CKD, making IV iron the preferred option. Though earlier IV iron therapies had safety concerns, newer formulations are effective and safer.[7] Despite improvements, infusion-related adverse reactions remain a concern, emphasizing the need to assess safety profiles. IV iron is generally more effective than oral iron in CKD patients, producing a faster and more robust Hbresponse.[9] Commonly used IV iron preparations include Iron

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Sucrose, Ferric carboxymaltose, Low Molecular Weight Iron Dextran, Ferric Derisomaltose, and Ferumoxytol.[10]

This study compares the safety, efficacy, and cost-effectiveness of Ferric carboxymaltose (FCM) and Iron Sucrose (IS)—two widely used IV iron preparations—in treating IDA in CKD patients. FCM, a complex of iron(III) hydroxide and carboxymaltose, ensures controlled iron release with minimal serum toxicity and is approved for IDA due to CKD, inflammatory bowel disease, and heavy uterine bleeding.[11-13] A single 750 mg dose has proven safe and effective.[14] IS is a polynuclear iron(III) hydroxide complex in sucrose, indicated for IDA in CKD, cancer, inflammatory bowel disease, pregnancy, and heavy menstrual bleeding.[15] The present study aims to evaluate and compare both drugs in terms of adverse events, cost, and clinical efficacy in CKD-related Anemia.

MATERIALS AND METHODS

Study Design and Setting

This randomized, controlled, open-label, parallel-group comparative study was conducted jointly by the Departments of Pharmacology and Nephrology at Government Medical College, Kozhikode, Kerala, India. After obtaining approval from the Institutional Ethics Committee, the study was carried out over 12 months from 1 February 2012 to 30 January 2013. Written informed consent was obtained from all participants prior to recruitment.

Inclusion and Exclusion Criteria

Patients aged 18 years or older with Stage 3, 4, or 5 Chronic Kidney Disease (CKD) and with haemoglobin levels ≤11.5 g/dL for females and ≤13.5 g/dL for males were included in the study. Additional eligibility criteria included transferrin saturation (TSAT) ≤25% and serum ferritin ≤300 µg/mL. Exclusion criteria included patients with a history of smoking or chronic alcohol use, those who had received intravenous iron within the last four weeks, patients with chronic liver disease, known hypersensitivity to iron preparations, active infections, overt bleeding, and those with a body weight less than 35 kg.

Study Procedure

Patients underwent initial screening, including a detailed medical history, physical examination, and laboratory investigations, including complete blood count (CBC), random blood sugar, renal function tests, serum ferritin, and TSAT. Out of 200 screened patients, 120 eligible patients were enrolled and randomized in a 1:1 ratio using a computer-generated randomization list. Patients were allocated to receive either Ferric Carboxymaltose (FCM group) or Iron Sucrose (IS group), regardless of baseline haemoglobin, body weight, or dialysis status.

In the FCM group, patients received two doses of 500 mg FCM, administered once-weekly infusions over 15 minutes in 250 mL of normal saline. The IS group received 200 mg of Iron Sucrose diluted in 250 mL of normal saline, administered over one hour weekly for five consecutive weeks. Thus, both groups received a total of 1 gram of iron supplementation. Patients receiving erythropoietin therapy were maintained on a stable dose throughout the study. Laboratory parameters—haemoglobin, TSAT, and serum ferritin—were measured at baseline and again at 8 weeks (day 56).

Outcome Measures

The primary outcome was clinical effectiveness, assessed by the change in haemoglobin, TSAT, and serum ferritin levels from baseline to 8 weeks. The secondary outcomes included cost-effectiveness and safety. Cost-effectiveness was evaluated based on direct treatment costs, including drug acquisition (cost of 1 g IV iron therapy), administration-related expenses (hospital time, nursing, consumables), and calculated as the cost per 1 g increase in haemoglobin at week 8. Indirect costs such as transportation, food, and income loss were not included.

Adverse drug reactions (ADRs) were assessed through patient interviews, clinical observation, and physical examination during drug infusion, and follow-up visits at week 4 and week 8. Treatment-emergent ADRs were defined as those occurring within 24 hours of infusion.

Statistical Analysis

Data entry was performed using Microsoft Excel, and statistical analysis was conducted using SPSS version 22. Quantitative variables were expressed as mean ± standard deviation (SD). Between-group comparisons were analyzed using the independent t-test, while within-group changes from baseline to week 8 were assessed using the paired t-test. A p-value of <0.05 was considered statistically significant. Descriptive statistics were used to analyze the frequency and nature of adverse drug reactions.

RESULTS

120 CKD patients were enrolled and randomized equally into two groups: Ferric carboxymaltose (FCM) and Iron Sucrose (IS). The mean age of patients was 49.68 ± 14 years in the IS group and 52.90 ± 11.8 years in the FCM group, with a higher proportion of males in both groups.

Adverse Drug Reactions (ADRs)

Adverse reactions were observed in 6.66% of the total study population. The IS group reported a higher incidence of ADRs (10%) than the FCM group (3.34%). Reactions included tiredness, nausea, back pain, and itching, with no severe ADRs reported. Most reactions occurred during infusion; one delayed reaction (itching) was noted 10 hours post-infusion in the IS group.

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Cost-Effectiveness

The mean total cost for IV iron therapy was significantly higher in the IS group (₹3398.32 ± 129.56) than in the FCM group (₹2875 ± 78.69) ($p < 0.01$). At 8 weeks, 88.33% of FCM group patients and 80% of IS group patients achieved a haemoglobin (Hb) rise ≥1 g/dL; however, this difference was not statistically significant ($p = 0.311$). The mean cost to achieve a 1 g/dLHb increase was significantly lower in the FCM group (₹2005.99 ± 1877.21) compared to the IS group (₹2618 ± 1360.63) ($p = 0.043$), confirming FCM as the more cost-effective option.

Efficacy Comparison

Baseline parameters (Hb, TSAT, and serum ferritin) were comparable between the two groups with no significant differences ($p > 0.05$). At 8 weeks, mean Hb levels increased to 9.46 ± 1.43 g/dL in the FCM group and 9.37 ± 1.05 g/dL in the IS group. The mean Hb increase was more significant in the FCM group (1.95 ± 0.88) than in the IS group (1.61 ± 0.70), with a statistically significant difference ($p = 0.020$). Both groups significantly improved from baseline Hb levels ($p < 0.000$).

The TSAT increase was significantly higher in the FCM group (14.11 ± 8.60) than in the IS group (10.31 ± 5.73) ($p = 0.005$). Mean TSAT values at week 8 were 33.62 ± 9.74 (FCM) and 29.14 ± 6.31 (IS), also showing statistical significance ($p = 0.003$).

Serum ferritin levels increased in both groups, with FCM showing a more extraordinary mean rise (244.89 ± 79.02) compared to IS (224.16 ± 86.88), although the difference was not statistically significant ($p = 0.174$). At week 8, mean ferritin levels were 445.15 ± 111.58 (FCM) and 433.27 ± 95.63 (IS).

FCM and IS significantly improved Hb, TSAT, and serum ferritin levels over the 8 weeks. However, FCM demonstrated superior cost-effectiveness, better TSAT improvement, fewer adverse events, and a more extraordinary mean Hb rise.

Table 1: Age and gender distribution

	IS (%)	FCM (%)
Mean age in years	49.68	52.90
Gender distribution		
Male	39(65%)	35(58.33%)
Female	21(35%)	25(41.87%)

Table 2: The Adverse drug reaction profile of FCM and IS groups

ADR	IS		FCM		Total	
	N=60	%	N=60	%	N=120	%
Itching	1	1.67	0	0	1	0.83
Tiredness	2	3.33	1	1.67	3	2.5
Backpain	1	1.67	0	0	1	0.83
Nausea	2	3.33	1	1.67	3	2.5
Total	6	10	2	3.34	8	6.66

FCM= Ferric carboxymaltose, IS=Iron sucrose, ADR=Adverse drug reaction

Table 3: Mean value of Hb, TSAT, Serum Ferritin at day 1 before IV Iron administration

Parameters	Group	Mean value at day 1	SD	t	P value
Hb(g/dl)	IS	7.76	1.26	1.001	0.319
	FCM	7.52	1.45		
TSAT(%)	IS	18.83	4.20	0.998	0.320
	FCM	19.51	3.26		
Serum ferritin(µg/ml)	IS	209.09	69.23	0.666	0.51
	FCM	200.26	75.98		

FCM= Ferric carboxymaltose, IS=Iron sucrose, ADR=Adverse drug reaction, Hb=Hemoglobin, TSAT= Transferrin saturation

Table 4: Hb, TSAT and Serum Ferritin at week 8 after IV Iron administration

	Group	Mean value at week 8	SD	t	P value
Hb(g/dl)	IS	9.37	1.05	0.407	0.685
	FCM	9.46	1.43		
TSAT(%)	IS	29.14	6.31	2.993	0.003
	FCM	33.62	9.74		
Serum ferritin(µg/ml)	IS	433.27	95.63	0.627	0.532
	FCM	445.15	111.58		

FCM= Ferric carboxymaltose, IS=Iron sucrose, ADR=Adverse drug reaction, Hb=Hemoglobin, TSAT= Transferrin saturation

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Table 5: Efficacy of Ferric carboxymaltose (FCM) and Iron sucrose(IS)

	Group	N	Mean value at day 1 before IV Iron administration	SD	Mean value at week 8	SD	Paired Differences mean	SD	t	P value
Hb(g/dl)	IS	60	7.76	1.26	9.37	1.05	1.61	0.70	17.72	<0.000
	FCM	60	7.51	1.46	9.46	1.43	1.95	0.88	17.13	<0.000
TSAT (%)	IS	60	18.83	4.20	29.14	6.31	10.31	5.73	13.93	<0.000
	FCM	60	19.51	3.26	33.62	9.74	14.11	8.60	12.71	<0.000
Serum ferritin(µg/ml)	IS	60	209.09	69.23	433.27	95.63	224.17	86.88	19.99	<0.000
	FCM	60	200.26	75.98	445.15	111.58	244.89	79.02	24	<0.000

FCM= Ferric carboxymaltose, IS=Iron sucrose, ADR=Adverse drug reaction, Hb=Hemoglobin, TSAT= Transferrin saturation

Table 6: Comparison of Hb,TSAT and Serum Ferritin rise after 8 weeks

	Group	Difference in Hb, TSAT and serum Ferritin from base line to 8 weeks	SD	t	P value
Hb (g/dl)	IS	1.61	0.70	3.353	0.020
	FCM	1.95	0.88		
TSAT (%)	IS	10.31	5.73	2.848	0.005
	FCM	14.11	8.60		
Serum ferritin(µg/ml)	IS	224.16	86.88	1.367	0.174
	FCM	244.89	79.02		

FCM= Ferric carboxymaltose, IS=Iron sucrose, ADR=Adverse drug reaction, Hb=Hemoglobin, TSAT= Transferrin saturation

DISCUSSION

Anaemia of chronic kidney disease (CKD) is a common complication associated with increased morbidity and mortality. Management includes erythropoietin supplementation, iron replacement, and optimization of renal function. Due to poor gastrointestinal absorption of iron and persistent blood loss, CKD patients are particularly vulnerable to iron deficiency, making intravenous (IV) iron the preferred method of correction due to its superior efficacy over oral formulations.[16]

This study evaluated the safety, efficacy, and cost-effectiveness of two IV iron preparations—Ferric carboxymaltose (FCM) and Iron Sucrose (IS). A fixed 1 g dose of iron was administered via different regimens: FCM in two 500 mg infusions over two weeks and IS in five 200 mg infusions over five weeks. The simplified administration schedule and shorter infusion duration of FCM are significant advantages, reducing outpatient visits and minimizing the burden on patients requiring repeated IV access.

Our findings support the superior profile of FCM. Both FCM and IS were well tolerated, with a total adverse drug reaction (ADR) incidence of 6.7%, but the incidence was lower in the FCM group (3.34%) than in the IS group (10%). ADRs were mild and self-limiting, with no severe reactions reported. These findings align with previous studies: Rognoni et al. confirmed the excellent safety and efficacy of FCM in CKD-related Anemia,[17] while Charmila A et al., Vikrant S et al., and Charytan C et al. also reported good tolerability and effectiveness of FCM.[18-20]

This study further demonstrated the cost-effectiveness of FCM. The mean total cost of therapy and the cost required to raise 1 g/dL of haemoglobin were significantly lower in the FCM group. These results echo those of Minutolo R et al., who reported substantial cost savings with FCM in CKD patients.[21] Moreover, Qunibi WY et al. and Jane E. Onken et al. established that FCM not only offers a cost advantage but also provides a safe and effective alternative to multiple IS infusions, particularly in non-dialysis dependent CKD patients.[22-23]

Regarding efficacy, both groups showed significant increases in haemoglobin (Hb), transferrin saturation (TSAT), and serum ferritin levels from baseline to 8 weeks. Although the mean rise in Hb and serum ferritin was not significantly different between groups, the mean TSAT at 8 weeks was significantly higher in the FCM group ($p = 0.003$). Furthermore, the rise in Hb and TSAT from baseline was significantly more significant in the FCM group ($p = 0.020$ and 0.005, respectively), supporting its superior therapeutic response. While 88.33% of FCM-treated patients and 80% of IS-treated patients achieved at least a 1 g/dLHb increase, this difference was not statistically significant.

Both formulations effectively treated iron deficiency anaemia (IDA) in CKD, as demonstrated by statistically significant intra-group improvements in all efficacy parameters. However, based on this study, FCM is a better option considering its higher efficacy, lower ADR incidence, and greater cost-effectiveness.

CONCLUSION

This study concludes that Ferric carboxymaltose (FCM) is a more effective and patient-friendly option than Iron Sucrose (IS) for the treatment of

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iron deficiency anaemia (IDA) in patients with chronic kidney disease (CKD). FCM demonstrated superior cost-effectiveness, a more convenient dosing schedule, and a shorter infusion time while maintaining a favourable safety profile. Both IV iron preparations significantly improved haemoglobin, transferrin saturation, and serum ferritin levels; however, FCM showed a more significant overall rise in key efficacy parameters with fewer adverse effects. Given its rapid administration, reduced infusions, and enhanced pharmacoeconomic profile, FCM is a practical and efficient choice for managing IDA in CKD patients.

REFERENCES

1. World Health Organization. Anaemia [Internet]. Geneva: World Health Organization; 2023 [cited 2025 Apr 13]. Available from: https://www.who.int/news-room/fact-sheets/detail/anaemia
2. Gardner WM, Razo C, McHugh TA, Hagins H, Vilchis-Tella VM, Hennessy C, Taylor HJ, Perumal N, Fuller K, Cercy KM, Zoeckler LZ. Prevalence, years lived with disability, and trends in anaemia burden by severity and cause, 1990–2021: findings from the Global Burden of Disease Study 2021. The Lancet Haematology. 2023 Sep 1;10(9):e713-34.
3. Turner J, Parsi M, Badireddy M. Anemia.[Updated 2023 Aug 8]. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. 2024.
4. Kumar V, Abbas AK, Aster JC. Robbins &Cotran Pathologic Basis of Disease-General Pathology, Vol 1: First Bangladesh Edition-E-Book. Elsevier Health Sciences; 2017 May 12.
5. McMurray J, Parfrey P, Adamson JW, Aljama P, Berns JS, Bohlius J, Drüeke TB, Finkelstein FO, Fishbane S, Ganz T, MacDougall IC. Kidney disease: Improving global outcomes (KDIGO) anemia work group. KDIGO clinical practice guideline for anemia in chronic kidney disease. Kidney International Supplements. 2012:279-335.
6. Del Vecchio L, Longhi S, Locatelli F. Safety concerns about intravenous iron therapy in patients with chronic kidney disease. Clinical Kidney Journal. 2016 Apr 1;9(2):260-7.
7. Auerbach M, Deloughery T. Single-dose intravenous iron for iron deficiency: a new paradigm. Hematology 2014, the American Society of Hematology Education Program Book. 2016 Dec 2;2016(1):57-66.
8. Skorecki K, Chertow GM, Marsden PA, Taal MW, Yu ASL. Brenner and Rector's The Kidney. 10th ed. Vol. 2, Hematologic aspects of kidney disease. In: Skorecki K, Chertow GM, Marsden PA, Taal MW, Yu ASL, editors. Philadelphia: Elsevier; 2016. p. 1875-1899.
9. Schaefer B, Meindl E, Wagner S, Tilg H, Zoller H. Intravenous iron supplementation therapy. Molecular aspects of medicine. 2020 Oct 1; 75:100862.
10. Van Doren L, Auerbach M. IV iron formulations and use in adults. Hematology. 2023 Dec 8;2023(1):622-9.
11. Silverstein SB, Rodgers GM. Parenteral iron therapy options. American journal of hematology. 2004 May;76(1):74-8.
12. Seid MH, Mangione A, Valaoras TG, Anthony LB, Barish CF. Safety Profile of Iron Carboxymaltose, a New High Dose Intravenous Iron in Patients with Iron Deficiency Anemia. Blood. 2006 Nov 16;108(11):3739.
13. Keating GM. Ferric carboxymaltose: a guide to its use in iron deficiency. Drugs & Therapy Perspectives. 2015 May; 31:143-9.
14. Barish CF, Koch T, Butcher A, Morris D, Bregman DB. Safety and efficacy of intravenous ferric carboxymaltose (750 mg) in the treatment of iron deficiency anemia: two randomized, controlled trials. Anemia. 2012;2012(1):172104.
15. Beguin Y, Jaspers A. Iron sucrose–characteristics, efficacy and regulatory aspects of an established treatment of iron deficiency and iron-deficiency anemia in a broad range of therapeutic areas. Expert Opinion on Pharmacotherapy. 2014 Oct 1;15(14):2087-103.
16. Hashmi MF, Aeddula NR, Shaikh H, Rout P. Anemia of chronic kidney disease. StatPearls [Internet]; StatPearls Publishing: Treasure Island, FL, USA. 2024.
17. Rognoni C, Venturini S, Meregaglia M, Marmifero M, Tarricone R. Efficacy and safety of ferric carboxymaltose and other formulations in iron-deficient patients: a systematic review and network meta-analysis of randomised controlled trials. Clinical drug investigation. 2016 Mar; 36:177-94.
18. Charmila A, Natarajan S, Chitra TV, Pawar N, Kinjawadekar S, Firke Y, Murugesan U, Yadav P, Ohri N, Modgil V, Rodge A. Efficacy and safety of ferric carboxymaltose in the management of iron deficiency anemia: a multi-center real-world study from India. Journal of Blood Medicine. 2022 Jun 8:303-13.
19. Vikrant S, Parashar A. The safety and efficacy of high dose ferric carboxymaltose in patients with chronic kidney disease: A single center study. Indian Journal of Nephrology. 2015 Jul 1;25(4):213-21.
20. Charytan C, Bernardo MV, Koch TA, Butcher A, Morris D, Bregman DB. Intravenous ferric carboxymaltose versus standard medical care in the treatment of iron deficiency anemia in patients with chronic kidney disease: a randomized, active-controlled, multi-center study. Nephrology Dialysis Transplantation. 2013 Apr 1;28(4):953-64.
21. Minutolo R, Berto P, Liberti ME, Peruzzu N, Borrelli S, Netti A, Garofalo C, Conte G, De Nicola L, Del Vecchio L, Locatelli F. Ferric carboxymatose in non-hemodialysis CKD patients: A longitudinal cohort study. Journal of Clinical Medicine. 2021 Mar 23;10(6):1322.
22. Qunibi WY, Martinez C, Smith M, Benjamin J, Mangione A, Roger SD. A randomized controlled trial comparing intravenous ferric carboxymaltose with oral iron for treatment of iron deficiency anaemia of non-dialysis-dependent chronic kidney disease patients. Nephrology Dialysis Transplantation. 2011 May 1;26(5):1599-607.
23. Onken JE, Bregman DB, Harrington RA, Morris D, Buerkert J, Hamerski D, Iftikhar H, Mangoo-Karim R, Martin ER, Martinez CO, Newman GE. Ferric carboxymaltose in patients with iron-deficiency anemia and impaired renal function: the REPAIR-IDA trial. Nephrology Dialysis Transplantation. 2014 Apr 1;29(4):833-42.

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