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Efficacy of ferric carboxymaltose versus iron sucrose in non-dialysis dependent chronic kidney disease

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Abstract

Objective: To determine the efficacy of ferric carboxymaltose versus iron sucrose in non-dialysis-dependent chronic kidney disease patients.

Method: The randomised controlled trial was conducted at the Nephrology Outpatient Department of the Sindh Institute of Urology and Transplantation, Karachi, from April to September 2025, and comprised patients with non-dialysis-dependent chronic kidney disease stages 3-5a and iron deficiency anaemia. The patients were randomised into ferric carboxymaltose group A and iron sucrose group B. Baseline assessments were compared with those taken at four and eight weeks. Data was analysed using SPSS 22.

Results: Of the 128 patients, 64(50%) were in group A; 37(57.8%) males and 27(42.2%) females with mean age 55.1±12.6 years. The remaining 64(50%) patients were in group B; 35(54.7%) males and 29(45.3%) females with mean age 54.2±13.1 years ($p>0.05$). Baseline haemoglobin did not differ between the groups ($p=0.81$). Transferrin saturation and serum ferritin improved significantly more in group A compared to group B ($p<0·001$). Patients in both the groups tolerated the treatment well, with no significant difference in adverse events ($p=0.24$).

Conclusion: Ferric carboxymaltose showed greater effectiveness compared to iron sucrose in the treatment of anaemia and iron stores in non-dialysis-dependent chronic kidney disease patients with comparable safety.

Key Words: Chronic kidney disease, Ferric carboxymaltose, Iron deficiency anaemia, Iron sucrose, Intravenous iron therapy.

Introduction

Anaemia is a prevalent and clinically relevant complication of chronic kidney disease (CKD), especially in patients with non-dialysis-dependent chronic kidney disease (ND-CKD). Fatigue has been associated with inferior quality of life, greater cardiovascular risk and accelerated disease progression. [1] Anaemia in this population primarily results from absolute and functional iron deficiency due to low dietary intake, impaired gastrointestinal absorption, chronic inflammation and high-hepcidin levels that impair the utilisation of iron.[2] As such, iron repletion continues to be a foundation of therapy for anaemia in ND-CKD.

Traditional first-line therapy with oral iron, however, is frequently suboptimal in ND-CKD due to limited gastrointestinal (GI) absorption, intolerance and poor haematological response. [3] These limitations have prompted growing use of intravenous (IV) iron formulations, which avoid GI absorption and deliver iron more reliably and predictably. A randomised controlled trial (RCT) has indicated that IV ferric carboxymaltose (FCM), one of the newer IV iron formulations, significantly improves haemoglobin (Hb) levels as well as serum ferritin and transferrin saturation (TSAT) in patients with renal insufficiency. [3] In addition, a trial indicated that IV FCM can delay or reduce the need for erythropoiesis-stimulating agents by improving iron parameters. [4] Subsequent studies have consistently demonstrated that IV iron is superior to oral iron for a more rapid and sustained correction of anaemia in this population. [5]

FCM is a newer version of IV iron that allows large single doses to be administered with an acceptable safety profile. The pharmacokinetic properties allow controlled release of iron which promote the prompt restoration of iron stores and effective erythropoiesis.

Its efficacy and safety in iron deficiency anaemia of CKD has been confirmed in literature. [6,7]

Another type of IV iron preparation, iron sucrose, is an older and widely used agent that has also proven effective for treating CKD-related anaemia. However, several smaller infusions are required to reach target iron levels, potentially increasing treatment burden and influencing patient adherence. [8] Iron sucrose has a well-established safety profile, but concerns exist regarding cumulative dosing and logistical difficulties in comparison with newer high-dose formulations. Comparative data indicate that FCM provides dosing ease of use, quicker treatment of iron deficiency and lower healthcare resource utilisation. [9,10]

Since the burden of CKD has increased and effective, safe and patient-centred anaemia management strategies are required, it is pertinent to critically compare the relative efficacy of FCM and iron sucrose in ND-CKD patients. The current study was planned to compare these two IV iron treatments in terms of efficiency in anaemia and enhancement of iron parameters in ND-CKD patients.

Patients and Methods

The RCT was conducted at the Nephrology Outpatient Department of the Sindh Institute of Urology and Transplantation (SIUT), Karachi, from April to September 2025 after approval from the research evaluation unit (REU) of the College of Physicians and Surgeons Pakistan (CPSP), Karachi, and the SIUT ethics review committee. The trial was prospectively registered at ClinicalTrials.gov (Identifier: NCT06994065).

The sample size was calculated using OpenEpi version 3.01 using an expected between-group difference in Hb response of 0.5g/dL, pooled standard deviation of 1.13g/dL, study power of 80%, and two-sided significance level of 5%. [11] The sample was raised using non-probability consecutive sampling technique. Those included were patients aged 18-85 years of either gender, with a diagnosis of ND-CKD stage 3-5a, and iron deficiency anaemia. Patients excluded from the study were those on maintenance haemodialysis, having deficiency of vitamin B12 or folate, being under the effect of

erythropoiesis-stimulating agents, had a known haematological problem, had experienced GI blood loss, or had chronic inflammatory diseases. Informed written consent was obtained for all the participants Baseline demographic and clinical data was noted. Random allocation was performed using a computer-generated random sequence. Allocation concealment was ensured through sequentially numbered, opaque, sealed envelopes prepared and maintained by the Pharmacy Department independent of the investigators. The envelopes were opened only after participant enrolment. Participant and treating physician blinding was not possible because of variations in infusion schedules and/or dosing regimens. Objective laboratory assessment of outcome was used, but outcome assessors were not explicitly blinded to treatment allocation. The investigator wrote the number of the study, medical record number, and date of the patient before opening up the envelope.

Group A was given IV FCM and Group B was given IV iron sucrose. The total iron dose for each patient was calculated using the Ganzoni formula: iron deficit (mg) = body weight (kg) × (target Hb − actual Hb) × 2.4 + iron stores, where iron stores were calculated as 15mg/kg for body weight <35kg and 500mg for body weight ≥35kg. [12]. The medications were given at the nephrology day-care unit as per the grouping. FCM was administered to group A patients as a 1,000mg (maximum) single dose (250mL normal saline infused over an approximately 15–30-minute infusion). Group B patients were given an infusion of iron sucrose (200mg diluted in 100mL normal saline) over a period of about 30 minutes. The amount of infusion was calculated based on iron deficiency. The total dose of iron given to each patient was recorded, and therapy was continued until the desired amount of iron was reached. The adverse effects of the infusion on patients were observed both immediately after and during the infusion process, and documented on a predesigned proforma. All patients completed baseline, 4-week and 8-week follow-up assessments.

Data was analysed using SPSS 22. The normality of continuous data was determined by Shapiro-Wilk test and inspection of histograms. Data for normally distributed variables was presented as mean ± standard deviation (SD), while non-normally distributed

variables were expressed as median with interquartile range (IQR). Frequencies and percentages were used to present categorical variables. Independent sample t-test or Mann Whitney U test was used to compare the groups in case of continuous variables, and chi-square or Fisher's exact test was used to compare the groups in case of categorical variables. P<0.05 was taken to be statistically significant. Absolute changes from baseline to week 8 with respect to Hb, ferritin and TSAT were calculated for each participant. Intergroup differences in mean change were reported with 95% confidence interval (CI).

Results

Of the 128 patients, 64(50%) were in group A; 37(57.8%) males and 27(42.2%) females with mean age 55.1±12.6 years. The remaining 64(50%) patients were in group B; 35(54.7%) males and 29(45.3%) females with mean age 54.2±13.1 years. The groups were comparable at baseline with no significant differences in demographic, clinical, or laboratory parameters (Table 1).

Both the groups demonstrated progressive improvement in Hb and iron parameters at 4 and 8 weeks compared to baseline, but group A patients exhibited a more rapid and greater increase at both follow-up points (p<0.05) (Table 2). The mean Hb rise at 4 weeks was significantly higher in group A compared to group B (p=0.004), and this difference remained significant at 8 weeks (p < 0.001). Similarly, serum ferritin and TSAT levels increased more markedly in group A at both follow-ups (p<0.05). The mean change in Hb from baseline to week 8 (ΔHb) was greater in the carboxymaltose group A compared to group A. Likewise, greater change in serum ferritin (ΔFerritin) and TSAT (ΔTSAT) were observed in group A. (Table 2).

Adverse events occurred in 9(14.1%) group A patients compared to 14(21.9%) in group B (p=0.24) (Table 3). No severe infusion-related reactions, anaphylaxis, shock, or respiratory compromise occurred in either group.

Discussion

The current RCT shows the superiority of IV FCM compared to iron sucrose in enhancing Hb levels and iron indices in ND-CKD patients with iron-deficiency anaemia. Despite the fact that both treatment regimens led to a dramatic haematological improvement during the 8-week follow-up period, FCM led to a faster and larger increase in Hb, serum ferritin and TSAT, and had an equivalent safety profile.

The increased efficacy of FCM confirmed in this study is biologically plausible and in line with its pharmacological characteristics. [11] FCM is a carbohydrate complex containing stable ferric which enables higher single doses to be administered with a slow release of iron, resulting in a rapid iron store refill and an efficient process of erythropoiesis.[13] Conversely, iron sucrose necessitates several smaller infusions, which can delay optimal iron replacement and lead to slower haematological reactions. These differences in mechanism have been characterised well by recent pharmacological and clinical studies of IV iron preparations. [14]

The current results are in line with studies that have shown better iron parameters using FCM. Hofman et al. showed that FCM versus iron sucrose showed better control of iron status in CKD patients, which supports sustained iron repletion with FCM, although the study population comprised haemodialysis patients. [15] Megha et al. supported the usefulness of IV iron treatment in CKD-associated anaemia, with positive effect of parenteral iron compared to oral therapy in this group. [16]

The identified Hb response can also be attributed to disturbed iron regulation through hepcidin that is commonly increased in CKD. The elevated levels of hepcidin prevent the absorption of iron into the intestines, as well as mobilisation of iron, thus favouring IV iron therapy. Recent data indicates that patients with high levels of hepcidin respond more to IV iron preparations that have the capacity to deliver bioavailable iron effectively. [17] This could be a contributing factor to the faster and more pronounced increase in Hb with FCM observed in the current study.

The existing global practice guidelines focus on personalised iron treatment in CKD, with the balancing of efficacy and safety. Recent guidelines and up-to-date reviews

support IV iron use in patients who cannot or do not respond to oral supplementation, with newer formulations like FCM, having fewer infusions and predictable responses, appearing to be effective but controlled iron repletion. [18,19] At the same time, iron overload and oxidative stress require close attention to ferritin and transferrin.

Safety is another important aspect when using IV iron therapy. In the current study, both FCM and iron sucrose were well-tolerated, and there were no serious adverse events. Even though the number of the mild adverse effects in the iron sucrose group was greater, the difference between the groups was not statistically significant. These findings are consistent with large trials and meta-analyses, including a study which demonstrated low rates of severe hypersensitivity reactions and good overall tolerability with FCM. [20] Furthermore, recent meta-analyses indicate that IV iron therapy does not significantly increase the risk of major adverse events.[21]

The safety profile of modern IV iron preparations, such as FCM, is significantly better than that of older preparations, and appropriate use of IV iron does not have any negative impact on the long-term cardiovascular outcomes as it is used within the recommended limits.

The current results indicate that FCM would be a better choice compared to iron sucrose in the treatment of patients with ND-CKD and iron deficiency anaemia because of its higher efficacy in terms of Hb and iron stores, and comparable safety. Nevertheless, more long-term follow-up studies are required to evaluate the sustainability of these benefits, and their influence on long-term clinical outcomes.

The current study has certain limitations. It was a single-centre study with a comparatively short follow-up period, thus the findings cannot be generalised. Also, observer or performance bias could not be ruled out owing to the absence of blinding.

Conclusion

FCM offered better and faster improvement in Hb levels and iron parameters than iron sucrose in ND-CKD stage 3-5a and iron deficiency anaemia, with no additional adverse

events. Its good efficacy and safety profile justified its use in IV iron replacement in such patients.

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Table 1: Baseline demographic and clinical characteristics of the patients (n=128).

Variable	Group A (FCM) n=64	Group B (Iron Sucrose) n=64	p-value
Age (years), mean ± SD	55.1 ± 12.6	54.2 ± 13.1	0.71
Male gender, n (%)	37 (57.8%)	35 (54.7%)	0.72
Female gender, n (%)	27 (42.2%)	29 (45.3%)	0.72
Weight (kg), mean ± SD	67.4 ± 11.2	66.1 ± 10.8	0.49
CKD Stage 3, n (%)	19 (29.7%)	21 (32.8%)	0.69
CKD Stage 4, n (%)	31 (48.4%)	29 (45.3%)	
CKD Stage 5a, n (%)	14 (21.9%)	14 (21.9%)	
Diabetes Mellitus, n (%)	34 (53.1%)	36 (56.3%)	0.72
Hypertension, n (%)	48 (75.0%)	46 (71.9%)	0.68
Haemoglobin (g/dL), mean ± SD	9.66 ± 1.14	9.71 ± 1.12	0.81
Serum Ferritin (ng/mL), median (IQR)	78 (54–112)	82 (56–118)	0.64
Transferrin Saturation (%), mean ± SD	18.3 ± 4.6	17.9 ± 4.4	0.62

FCM: Ferric carboxymaltose, CKD: Chronic kidney deiseae, SD: Standard deviation, IQR: Interquartile range.

Table 2: Intergroup comparison of haemoglobin and iron parameters at baseline, 4 weeksand 8 weeks.

Parameter	Time Point	Group A (FCM) (n=64)	Group B (Iron Sucrose) (n=64)	p-value

Haemoglobin (g/dL)	Baseline	9.66 ± 1.14	9.71 ± 1.12	0.81
	4 Weeks	10.82 ± 1.03	10.29 ± 1.01	0.004
	8 Weeks	11.48 ± 1.02	10.92 ± 0.98	<0.001
Serum Ferritin (ng/mL)	Baseline	78 (54–112)	82 (56–118)	0.64
	4 Weeks	246 (198–312)	168 (142–221)	<0.001
	8 Weeks	324 (268–402)	212 (176–289)	<0.001
Transferrin Saturation (%)	Baseline	18.3 ± 4.6	17.9 ± 4.4	0.62
	4 Weeks	28.4 ± 6.1	23.2 ± 5.6	<0.001
	8 Weeks	32.6 ± 6.8	26.9 ± 5.9	<0.001
Absolute Change from Baseline to Week 8				
ΔHaemoglobin (g/dL)	Week 8 – Baseline	+1.82	+1.21	<0.001
ΔSerum Ferritin (ng/mL)	Week 8 – Baseline	+246	+130	<0.001
ΔTransferrin Saturation (%)	Week 8 – Baseline	+14.3	+9.0	<0.001

Data presented as mean ± standard deviation (SD) or median with interquartile range (IQR), as appropriate. Δ denotes change from baseline to week 8.
FCM: Ferric carboxymaltose.

Table 3: Intergroup comparison of adverse events between ferric carboxymaltose (FCM) and iron sucrose groups

Adverse Event	Group A (FCM) n (%)	Group B (Iron Sucrose) n (%)	p-value*
Any adverse event	9 (14.1)	14 (21.9)	0.24
No adverse event	55 (85.9)	50 (78.1)	—
Nausea	3 (4.7)	5 (7.8)	0.47
Dizziness/Light-headedness	2 (3.1)	4 (6.3)	0.40
Itching	2 (3.1)	3 (4.7)	0.65
Urticaria	1 (1.6)	2 (3.1)	0.56
Symptomatic hypotension	1 (1.6)	0 (0.0)	0.31

*Chi-square test or Fisher's exact test, as appropriate.

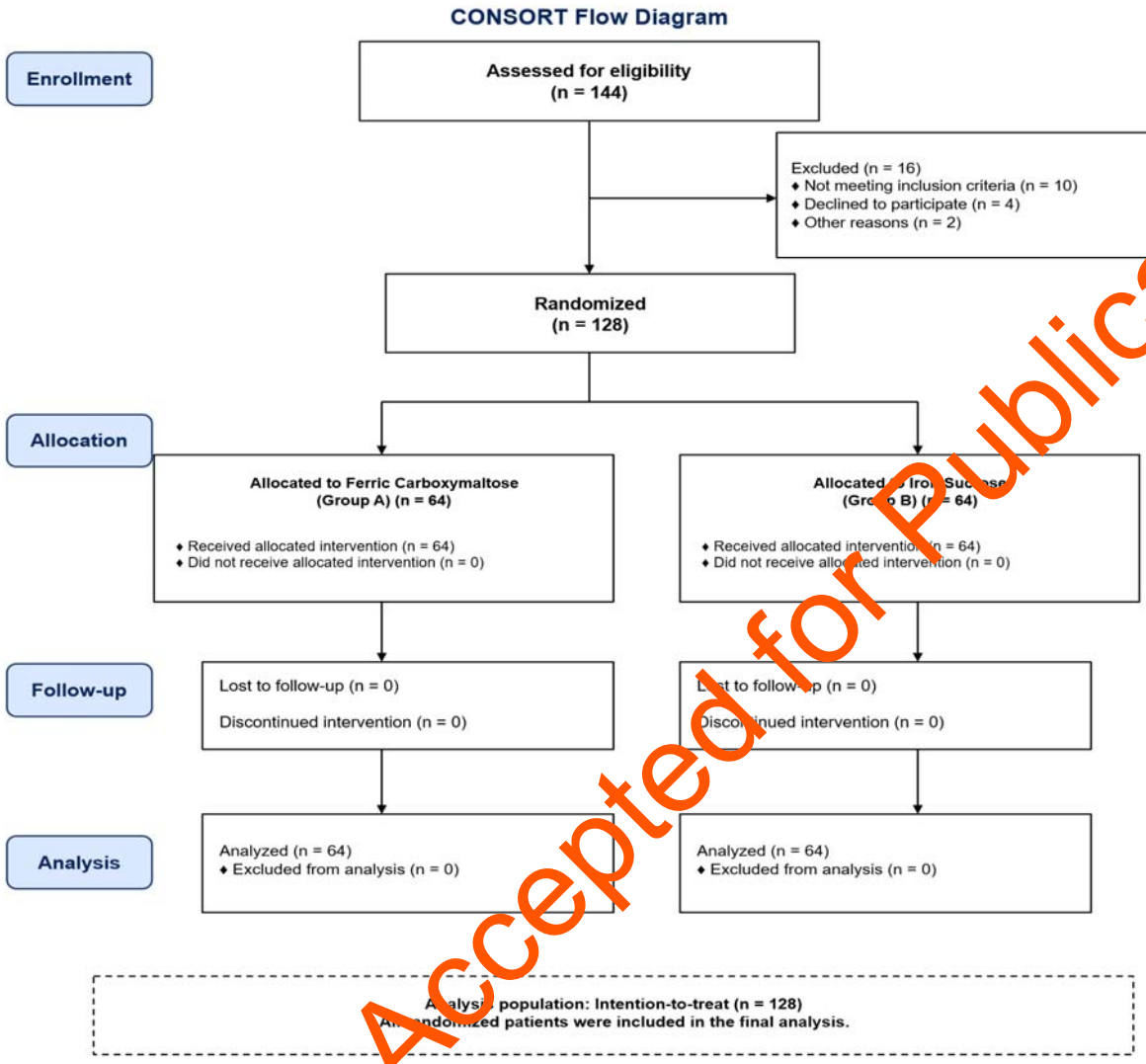

Figure: Consolidated Standards of Reporting Trials (CONSORT) flow diagram.

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AUTHORS' CONTRIBUTIONS:

KK: Concept, design, data collection, analysis, drafting, final approval and agreement to be accountable for all aspects of the work.

SS: Supervision, data interpretation, revision, final approval and agreement to be accountable for all aspects of the work.

RA & NV: Data collection, analysis, revision, final approval and agreement to be accountable for all aspects of the work.

NHJ: Supervision, critical intellectual input, final approval and agreement to be accountable for all aspects of the work.

ZK: Design, data interpretation, review, final approval and agreement to be accountable for all aspects of the work.