



ORIGINAL ARTICLE

Comparison of intravenous low molecular weight iron dextran and intravenous iron sucrose for the correction of anaemia in pre-dialysis chronic kidney disease patients: a randomized single-centre study in Nigeria

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Abstract

Background: Intravenous low molecular weight iron dextran and iron sucrose have been used for correction of iron deficiency for many years and have been shown to improve anaemia in chronic kidney disease (CKD). However, there is a paucity of head to head comparisons of these parenteral iron preparations. Such comparative efficacy data would be of particular interest in resource-limited African countries, where the majority of CKD patients are unable to afford erythropoiesis-stimulating agents. Therefore, the aim of this study was to compare the effects of these two intravenous iron preparations in pre-dialysis CKD patients.

Methods: Sixty-seven anaemic pre-dialysis CKD patients were randomized to one of two treatment groups. The low molecular weight iron dextran group ($n = 33$) received 1000 mg of low molecular weight iron dextran intravenously in four divided doses of 250 mg. The iron sucrose group ($n = 34$) received 1000 mg of iron sucrose intravenously in five divided doses of 200 mg. Complete blood count, serum creatinine, serum iron, unsaturated iron binding capacity, serum ferritin and transferrin saturation were assessed at baseline. The baseline parameters were repeated in all patients on Day 24. The primary outcome was the proportion of patients achieving a rise in haemoglobin (Hb) concentration of ≥ 1.0 g/dL after iron therapy.

Results: There was no significant difference in the proportion of patients achieving the primary end point between both arms of the study: [7 (21.9%) low molecular weight iron dextran versus 11 (32.4%) iron sucrose; relative risk 0.68, 95% confidence interval (CI): 0.19–1.70; $P = 0.23$]. At Day 24, the mean increase in Hb concentration from baseline was comparable between the two groups: low molecular weight iron dextran 0.4 ± 0.7 g/dL versus iron sucrose 0.6 ± 0.9 g/dL, mean difference 0.2 g/dL (95% CI: -0.26 – 0.61 ; $P = 0.28$). The proportion of patients that experienced at least one or more adverse events was 27.3% in the iron dextran group versus 14.7% in the iron sucrose arm ($P = 0.21$).

Conclusion: Both intravenous low molecular weight iron dextran and intravenous iron sucrose are effective in correcting iron deficiency and anaemia in pre-dialysis CKD patients.

Key words: anaemia, CKD, ferritin, iron, pre-dialysis

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Introduction

Anaemia is a well-recognized complication in patients with chronic kidney disease (CKD), leading to adverse clinical outcomes such as left-ventricular hypertrophy, congestive heart failure, stroke and death [1–3]. In such patients, early identification and prompt treatment of anaemia improves quality of life, and is associated with improvements in cardiovascular morbidity [2]. In the pre-erythropoietin (EPO) era, anaemic CKD patients were largely treated with repeated blood transfusion and anabolic steroids. Both modalities of treatment were associated with undesired effects such as increased risk of infection, iron overload and tendency to develop sensitivity to major histocompatibility antigens with repeated blood transfusion [4, 5], and hirsutism, hepatotoxicity and virilization with anabolic steroids [6]. Subsequently, the advent of recombinant EPO (rHuEPO) in 1987 revolutionized the management of anaemia in CKD patients with aggressive use of erythropoiesis-stimulating agents (ESA) [7].

However, haemoglobin (Hb) synthesis is suboptimal in the presence of iron deficiency [8]. Hence, despite adequate ESA dosing, effective erythropoiesis will not be achieved as long as iron stores are deficient. Therefore, both ESAs and iron are required for optimal correction of anaemia in CKD patients. Furthermore, several studies have shown that administration of intravenous iron alone is capable of correcting renal anaemia [9–11]. This should be of particular interest in resource-limited countries where patients pay out of pocket for care and find it difficult to afford expensive ESA. In addition, large randomized control trials have demonstrated increased cardiovascular events attributed to ESA in an attempt to normalize Hb levels [12–14]. Consequent to this, the aggressive use of ESA has reduced and the use of iron in CKD has increased significantly [15]. Thus, the aim of this study is to compare the efficacy of two main parenteral iron preparations available in most African countries.

Materials and methods

Study design and participants

The study was a prospective, open label, randomized trial involving 67 pre-dialysis stages 3–5 CKD patients, aged ≥ 18 years, ESA and intravenous iron naïve and with Hb ≤ 11.0 g/dL, ferritin < 200 ng/mL and transferrin saturation (TSAT) $< 25\%$. Exclusion criteria included patients with known haemoglobinopathies, pregnancy, history of atopy, history of significant bleeding, blood transfusion or iron medications in the 3 months preceding recruitment, and active malignancy. The study was conducted over a period of 9 months (March to November 2011) at the Lagos University Teaching Hospital. The research protocol was approved by the Health Research and Ethics committee (HREC) of the Hospital. The aims of the study, intended benefits and possible side effects of the interventions were explained to the participants in a language that they understood. Subsequently, written informed consent was obtained from each patient before enrolment into the study. The study was conducted in accordance with the International Conference on Harmonization – Good Clinical Practice (ICH-GCP) guidelines.

Interventions

The study participants were randomly assigned in a 1:1 ratio to one of two treatment groups. The low molecular weight iron dextran (LMWID) group ($n = 33$) received 1000 mg of low molecular weight iron dextran intravenously in four divided doses of 250 mg. Each 250 mg dose was administered in 250 mL of 0.9%

normal saline over a 3-h period. The iron sucrose group ($n = 34$) received 1000 mg of iron sucrose intravenously in five divided doses of 200 mg. Each 200 mg dose was administered in 250 mL of 0.9% normal saline over a 2-h period. The total dose was given over a period of 10 days, with first dose given on Day 0. Study outcomes were measured 2 weeks after administration of the last dose (Day 24).

Prior to the administration of the full dose of intravenous iron on each occasion, all patients had a test dose of 25 mg of the iron preparation and were observed for 10 min to rule out sensitization to iron. All patients were observed for a period of at least 30 min after administration of each dose of iron before being discharged home. The patients' vital signs were recorded prior to the administration of each dose of iron, every 15 min during the period of the infusion, and prior to being discharged home. Patients were informed of the need to volunteer any unusual symptoms they experienced during the therapy and in addition, specific questions were asked as to the presence of any unusual symptoms at the end of each dose. Patients were provided with a contact number that could be called to report any unusual symptoms occurring in the 24-h period subsequent to the infusion. Adverse events were documented by the investigators/renal nurses.

Patients were instructed not to take any form of oral iron during the period of the study.

Outcome measures

In line with previous studies [16, 17], the primary end point was the proportion of patients that achieved an increase in Hb of ≥ 1.0 g/dL after iron therapy. The pre-defined secondary efficacy outcomes were: (i) the proportion of patients attaining increase in Hb > 11 g/dL after treatment at Day 24, (ii) the proportion of patients achieving a rise in TSAT of $\geq 5\%$ after treatment, (iii) a rise in ferritin of ≥ 160 ng/mL at Day 24 and (iv) a mean increase in Hb concentration from baseline to the end of study.

Determination of sample size

The sample size estimation was based on the proportion of patients expected to achieve a rise in Hb concentration of ≥ 1 g/dL, (44.3%) in the iron sucrose arm derived from a previous study [18] and assuming 21.2% in the LMWID arm will achieve this endpoint. A minimum of 30 patients were required in each treatment group to detect such a difference in response with a two-sided significance level of 5% and a power of 80%. A 10% increase was added to take into account attrition due to loss to follow-up. Thus, the sample size was estimated to be 67.

Method of randomization

To maintain good balance and equal allocation between the two treatment groups, permuted block randomization was used to assign patients into one of the two treatment groups. A block of four with six different arrangements was adopted and odd and even numbers were taken to indicate iron sucrose and low molecular weight iron dextran, respectively. The screening and allocation of the patients were performed by the investigators.

Laboratory measurements

Complete blood count, serum creatinine, serum iron, unsaturated iron binding capacity (UIBC), serum ferritin and transferrin saturation were assessed at baseline. The parameters measured at baseline were repeated in all the patients on Day 24. Estimation of haematocrit, Hb concentration, red blood cell indices, reticulocyte

count and white blood cell count were carried out using automated coulter analyser by Swelab, Stockholm, Sweden. Serum iron and UIBC were determined photometrically with ferrozin as a chromogen, using Cobas C Roche diagnostic kit and run with Roche /Hitachi Cobas C auto analyser (Mannheim, Germany). Total iron binding capacity (TIBC) was calculated as a sum of serum iron and UIBC. TSAT was calculated as the percentage of serum iron from TIBC using the formula: $TSAT = (\text{serum iron} \div \text{TIBC} \times 100) \%$. Serum ferritin was assayed using the Diagnostics Human ferritin enzyme immunoassay test kits (specificity 98.7% and sensitivity 5.0 ng/mL) an enzyme-linked immunosorbent method.

Statistical analysis

The proportion of patients who achieved the primary end point was compared between the two groups using Fisher's exact test and the corresponding relative risk was estimated using the same crosstabs procedure. A paired t-test was used to evaluate the change in mean Hb, ferritin and TSAT from baseline within a treatment group. The mean change in Hb between both groups was compared using an independent t-test. The proportion of patients that achieved secondary end points was compared between treatment groups by Fisher's exact test. Continuous demographics and baseline characteristics were presented as means and standard deviations while categorical data are presented as proportions or percentages. A logistic regression model was used to evaluate the effect of potential covariates on the odds of achieving a Hb increase of ≥ 1.0 g/dL. A P-value of < 0.05 was considered statistically significant at 95% confidence interval (CI). All analyses were performed using the statistical package for social science (SPSS Inc., Chicago, IL, USA) for windows software version 20.

Results

One hundred and thirty consecutively presenting pre-dialysis CKD patients attending a renal outpatient clinic were screened and 102 were found to be anaemic. On further evaluation of their iron status, 67 had inadequate iron status (iron deplete). Subsequently, these 67 patients were randomized to receive iron sucrose (34 patients) or iron dextran (33 patients). Of these, 63 completed the study. Two patients in each arm were discontinued from the study. The two patients who withdrew from the iron sucrose arm were due to initiation of haemodialysis. One of the two patients in the iron dextran arm experienced a hypersensitivity reaction following the test dose of iron dextran necessitating discontinuation, while the other was lost to follow-up (Figure 1).

Efficacy analyses were on the a modified intent-to-treat population, which included all patients who were randomized and received at least one dose of the study medication and had post-treatment results ($n = 66$), one patient in the LMWID arm did not receive a complete dose of study medication due to a sensitivity reaction to a test dose and also to lacking post-baseline result. The safety analysis was on an intent-to-treat population that comprised all randomized patients ($n = 67$). The demographics and baseline characteristics of both groups upon entry to the study are summarized in Table 1. The demographics and clinical parameters of the study participants were comparable between the two treatment groups.

Efficacy

The proportion of the study participants who achieved the primary end point (defined as increase in Hb ≥ 1 g/dL at any time during the study) was not significantly different between the

two treatment arms [7 (21.9%) low molecular weight iron dextran versus 11 (32.4%) iron sucrose; relative risk 0.68, 95% CI: 0.19–1.70; $P = 0.23$]. The mean increase in Hb concentration was comparable between the groups: 0.4 ± 0.7 g/dL versus 0.6 ± 0.9 g/dL; mean difference 0.2 g/dL (95% CI: -0.26 – 0.61 ; $P = 0.28$) (Table 2). The proportion of patients that achieved an Hb level > 11 g/dL in the iron sucrose group was 8.8% while 12.5% in the iron dextran group achieved this endpoint ($P = 0.48$). A similar proportion of patients in the iron sucrose group and the iron dextran achieved a $\geq 5\%$ rise in TSAT, 79.4% versus 75.0% ($P = 0.56$). There was also no statistically significant difference in the proportion of patients who achieved a rise in ferritin of ≥ 160 ng/mL between both treatment arms (41.2 versus 50.0%; $P = 0.36$) (Table 2). The mean Hb concentration, serum ferritin and TSAT rose significantly from baseline values in both treatment groups (Table 3).

Determinants of likelihood of achieving Hb rise ≥ 1.0 g/dL

A logistic regression model was used to evaluate the effect of potential covariates on the odds of achieving a ≥ 1.0 g/dL Hb response. These covariates were chosen *a priori* based on existing literature suggesting their association with likelihood of Hb ≥ 1.0 g/dL [17, 18]. The covariates were age ≥ 65 years versus < 65 years, baseline serum ferritin < 100 ng/mL versus ≥ 100 ng/mL, male sex versus female sex, baseline Hb < 10 g/dL versus ≥ 10 g/dL, and estimated glomerular filtration rate < 30 mL/min/1.73 m² versus ≥ 30 mL/min/1.73 m². A baseline serum ferritin < 100 ng/mL was the only factor that predicted the odds of achieving a rise in Hb ≥ 1.0 g/dL and was associated with a 6-fold likelihood of achieving a > 1.0 g/dL rise in Hb concentration (Table 4).

Safety

Table 5 summarizes the frequency of adverse events in iron sucrose and LMWID groups. A total of 14 participants (5 iron sucrose, 9 LMWID) experienced adverse events during the study. The most common side effect observed during this study was hypotension, accounting for 38.4% of all adverse events experienced, and the majority of the adverse events were self-limiting. The proportion of patients who experienced at least one or more adverse events was higher in the iron dextran arm compared with the iron sucrose arm 9/33 (27.3%) versus 5/34 (14.7%); however, this did not reach statistical significance ($P = 0.21$).

Discussion

Studies involving a direct comparison of the efficacy of intravenous iron sucrose and low molecular weight iron dextran are sparse in the literature. In this head to head comparative trial, we have demonstrated that both intravenous iron sucrose and low molecular weight iron dextran were similarly effective in the management of iron deficiency anaemia as demonstrated by improved parameters associated with iron deficiency anaemia, notably Hb concentration, ferritin and TSAT. In agreement with our findings, several studies have demonstrated a rise in Hb and iron parameters following intravenous iron in pre-dialysis CKD patients and that this may delay or avoid the need for ESA therapy (9–11). This finding is particularly important in resource-poor countries where patients find it difficult to cope with the cost of ESA. In Nigeria, 4000 IU of epoetin-beta (Roche Recormon) is estimated at 9000 ₦, which is equivalent to 45 USD, and this is mainly borne by the patients and their caregivers. In addition, the use of intravenous iron in our patients is likely to reduce treatment of anaemia with repeated blood transfusion, which is associated

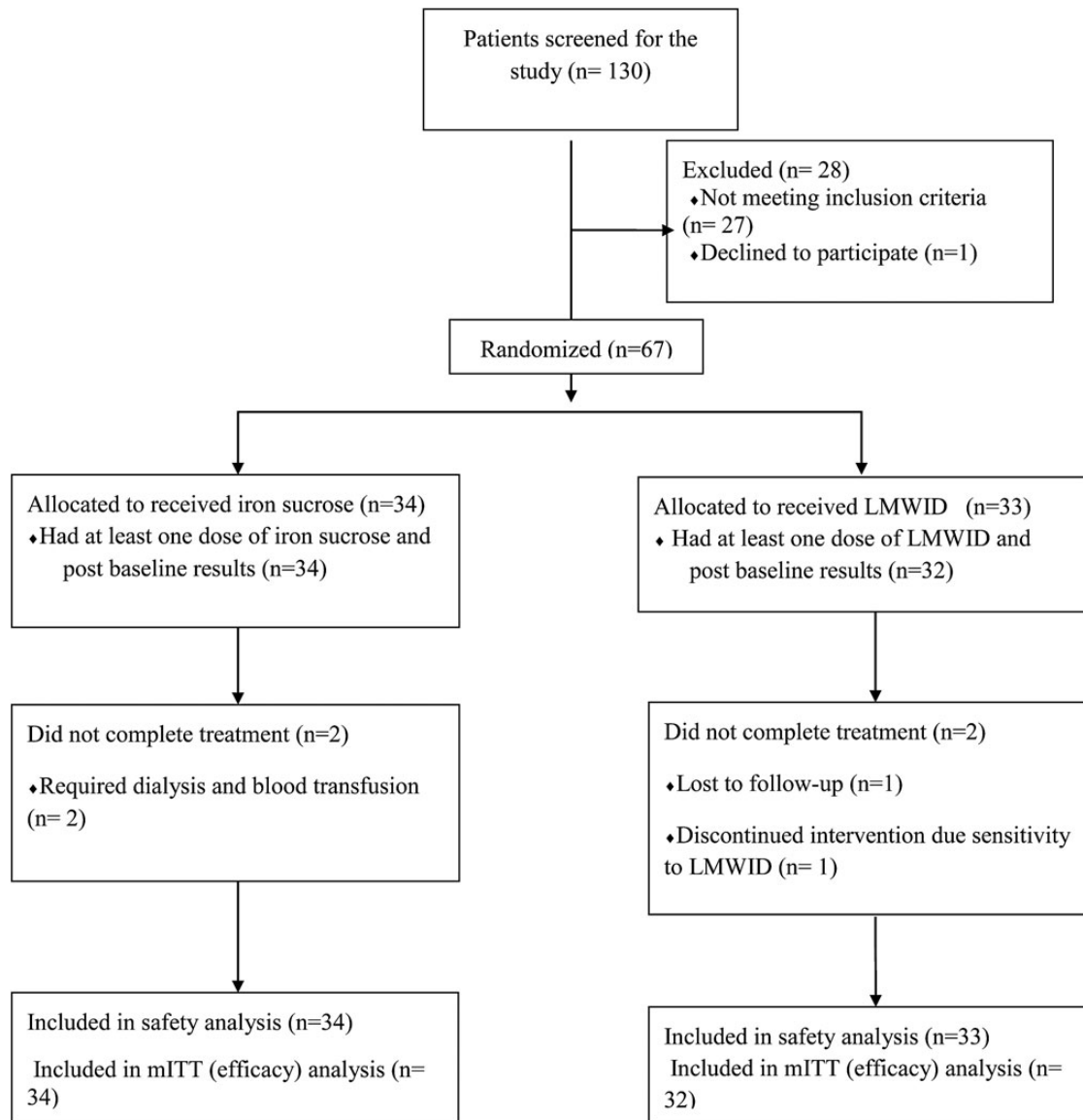


Fig. 1. Participant disposition. mITT, modified intent-to-treat.

with numerous side effects. Our results are in line with previous observational studies in the UK in which no difference was found between intravenous iron sucrose and low molecular weight iron dextran [19, 20]. The mean change in Hb concentration seen in the iron sucrose group (0.6 g/dL) is also similar to that reported by Silverberg et al. (0.6 g/dL) [21] and Tagboto et al. (0.53 g/dL) [22]. Determinants of anaemia response to iron therapy are not well established. However, few studies that have evaluated the relationship between baseline levels of iron status tests and erythropoietic response to an intravenous iron yielded contradictory results. For example, both Van Wyck et al. [18] and Gotloib et al. [23] found no correlation between base line ferritin, TSAT and the erythropoietic response. On the other hand, Stancu et al. [24] found that the combination of low TSAT and ferritin predicted a response to intravenous iron. This finding is consistent with our study in which we found baseline serum ferritin <100 ng/mL as the only factor that predicted a rise in Hb ≥ 1.0 g/dL.

There are safety concerns regarding intravenous iron especially with the life-threatening anaphylactic reactions attributed

to iron dextran. However, some studies have documented that low molecular weight iron dextran has a comparable safety profile to other iron preparations [19, 20, 25]. Adverse effects were reported in 21% of the study population. In the majority of cases, the adverse events were self-limiting requiring no active intervention. However, one patient was excluded from the study on account of hypotension and urticaria following administration of a test dose of iron dextran. This emphasizes the need for a test dose before administering iron dextran preparations. None of the patients had a reaction with a test dose of iron sucrose. This is in agreement with Macdougall and Roche [11]. The overall proportion of patients that experienced at least one or more adverse events was 27.3% in the iron dextran group and 14.7% in the iron sucrose arm. The numerically higher proportion in LMWID was also noted by Anirban et al. [26] who compared intravenous low molecular weight iron dextran, sodium ferric gluconate complex and iron sucrose in patients with advanced CKD on and off dialysis. In our study, contrary to that by Anirban et al. [26], this difference was not significant. The true incidence

Table 1. Demographics and baseline characteristics of both groups

Variables	Iron sucrose N = 34	LMWID N = 33	P-value
Age (years)	51.0 ± 13.0	53.2 ± 12.3	0.48
Gender, n (%)			
Male	15 (44.1%)	17 (51.5%)	0.54
Female	19 (55.9%)	16 (48.5%)	0.54
Weight (kg)	71.2 ± 17.6	75.5 ± 12.9	0.27
Height (m)	1.66 ± 0.08	1.67 ± 0.09	0.71
BMI (kg/m ²)	26.7 ± 4.7	27.3 ± 4.8	0.65
Serum albumin (g/L)	36.1 ± 8.6	37.9 ± 6.9	0.32
SBP (mmHg)	148.5 ± 18.1	146.7 ± 16.5	0.66
DBP (mmHg)	90.0 ± 12.1	90.8 ± 9.9	0.75
eGFR (mL/min/1.73 m ²)	21.3 ± 13.3	24.8 ± 12.6	0.36
Haemoglobin (g/dL)	9.1 ± 1.1	9.3 ± 1.2	0.30
MCV (fL)	80.8 ± 6.1	80.3 ± 8.0	0.75
MCH (Pg)	27.0 ± 4.1	27.8 ± 2.6	0.36
MCHC (g/dL)	34.4 ± 1.4	34.5 ± 1.6	0.77
Serum Iron (µmol/L)	14.4 ± 7.1	12.2 ± 2.6	0.16
TIBC (µmol/L)	61.0 ± 14.3	53.2 ± 19.9	0.07
Serum ferritin (ng/mL)	100.7 ± 83.5	121.6 ± 72.0	0.28
TSAT (%)	23.8 ± 7.8	25.1 ± 6.8	0.48
Reticulocyte count	1.25 ± 0.4	1.29 ± 0.5	0.74
Aetiology of CKD, n (%)			
DM	9 (26.5%)	12 (38.7%)	0.28
Hypertension	17 (53.1%)	11 (35.5%)	0.28
CGN	2 (6.2%)	3 (9.7%)	0.20
ADPKD	1 (3.1%)	2 (6.5%)	0.31
BPH	2 (6.2%)	3 (9.7%)	0.67
Unknown	3 (9.4%)	2 (0.0%)	0.30

Continuous variables are presented as mean ± standard deviation and categorical data as frequencies (percentages).

SPB, systolic blood pressure; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; BMI, body mass index; MCV, mean corpuscular volume; MCH, mean corpuscular haemoglobin; MCHC, mean corpuscular haemoglobin concentration; TSAT, transferrin saturation; fL, femtolitre; pg, picogram; LMWID, low molecular weight iron dextran; CGN, chronic glomerulonephritis; DM, diabetes mellitus; BPH, benign prostatic hypertrophy; ADPKD, autosomal dominant polycystic kidney disease.

Table 2. Efficacy profile between treatment groups

Variables	Iron sucrose (n = 34)	LMWID (n = 32)	P-value
Absolute rise in Hb ≥ 1 g/dL	11 (32.4%)	7 (21.9%)	0.23
Mean increase in Hb (g/dL)	0.6 ± 0.9	0.4 ± 0.7	0.28
Hb level after treatment > 11 g/dL	3 (8.8%)	4 (12.5%)	0.48
Change in TSAT ≥ 5%	27 (79.4%)	24 (75.0%)	0.56
Ferritin change ≥ 160 ng/mL	14 (41.2%)	16 (50.0%)	0.36

Continuous variables are presented as mean ± standard deviation and categorical data as frequencies (percentages).

Hb, haemoglobin; LMWID, low molecular weight iron dextran; TSAT, transferrin saturation.

of anaphylaxis, a rare but potentially fatal complication of administration of intravenous iron due to pre-formed antibodies, was not ascertained. The hypersensitivity reaction from a test dose that led to one patient's withdrawal would probably have resulted in a fatal complication with the administration of a full dose. However, as a limitation of this study it has to be considered that the number of patients enrolled was small, making it difficult to draw conclusions on the incidence of this rare, but important complication with either of the two study medications.

Table 3. Effect of intravenous irons on anaemia and iron status within treatment group

Treatment groups	Variables	Pre-treatment	Post-treatment	P-value
Iron sucrose	Haematocrit (%)	26.6 ± 3.5	28.1 ± 3.9	<0.01*
	Haemoglobin (g/dL)	9.1 ± 1.1	9.7 ± 1.2	<0.01*
	Ferritin (ng/mL)	100.7 ± 83.5	259.7 ± 122.3	<0.01*
	TSAT (%)	23.8 ± 7.8	32.4 ± 6.6	<0.01*
Iron dextran	Haematocrit (%)	27.2 ± 3.3	28.3 ± 3.6	<0.01*
	Haemoglobin (g/dL)	9.3 ± 1.2	9.7 ± 1.0	0.02*
	Ferritin (ng/mL)	121.6 ± 72.0	283.3 ± 127.6	<0.01*
	TSAT (%)	25.1 ± 6.8	34.4 ± 9.2	<0.01*

Data are presented as mean ± standard deviation.

TSAT, transferrin saturation.

*P < 0.05.

Table 4. Logistic regression analysis of factors associated with achieving Hb ≥ 1.0 g/dL

Variables	OR	95% CI	P-value
Age	0.81	0.17–6.98	0.93
Sex	0.60	0.35–10.92	0.44
Baseline Hb	1.83	0.53–32.93	0.18
Ferritin	6.3	1.13–7.63	0.01*
eGFR	1.37	0.45–23.15	0.24

Covariates were age ≥ 65 years versus < 65 years, baseline serum ferritin < 100 ng/mL versus ≥ 100 ng/mL, male sex versus female sex, baseline Hb < 10 g/dL versus ≥ 10 g/dL and eGFR < 30 mL/min versus ≥ 30 mL/min.

CI, confidence interval; eGFR, estimated glomerular filtration rate; OR, odds ratio; Hb, haemoglobin. *P < 0.05.

The strength of this study lies in studying patients not previously on ESA as compared with several other trials where patients were concurrently initiated on ESAs and thus confounding the potential effects of iron therapy on changes in Hb. In addition, to our knowledge this is the first comparative study from sub-Saharan Africa that has compared the two most frequently used parenteral iron preparations. The limitations of our study include the following. Firstly, the study duration was relatively short to draw conclusions on long-term efficacy and safety profiles of either preparation. Nevertheless, findings from this trial have contributed to our understanding of the relative efficacy and safety profiles of two of the most commonly used intravenous iron preparations in Africa. Secondly, the relatively small sample size might have precluded detection of important differences between the two treatment groups. Thirdly, the relative cost of intravenous iron sucrose compared with low molecular weight iron dextran was not adequately assessed. A conclusive comparison would entail considerations of the cost of the iron preparations, infusion sets, patient convenience, nursing time and number of hospital visits. However, based on the drug cost per mg iron, intravenous iron sucrose is costlier than low molecular weight iron dextran (prices for 1000 mg of iron: iron sucrose 85.10 USD versus LMWID 55.20 USD). Similarly in the UK, iron sucrose is more expensive than LMWID [for 200 mg iron, GBP £18.70 (+10%) for iron sucrose versus GBP £15.94 for low molecular weight iron dextran] [27]. Additionally, currently available intravenous iron preparations in Nigeria vary in unit price thus making it difficult to generalize our findings to other health

Table 5. Frequency of adverse events in each treatment group

Adverse events	Iron sucrose N = 34	LMWID N = 33	P-value
≥1 event	5 (14.7%)	9 (27.3%)	0.21
Hypotension	1 (2.9%)	4 (12.1%)	0.19
Dizziness	1 (2.9%)	2 (6.1%)	0.61
Elevated blood pressure	1 (2.9%)	1 (3.0%)	0.98
Chest tightness	0 (0.0%)	2 (6.1%)	0.24
Joint pain	1 (2.9%)	2 (6.5%)	0.61
Urticaria	0 (0.0%)	1 (3.0%)	0.49
Vomiting	1 (2.9%)	0 (0.0%)	0.98
Diarrhoea	0 (0.0%)	1 (3.0%)	0.49
Tachycardia	0 (0.0)	1 (3.0%)	0.49
Pain at injection site	1 (2.9%)	0 (0.0%)	0.98

One patient in each treatment group reported two adverse events.

care settings. Since drug cost may also be a consideration in choosing parenteral iron agents in resource-poor countries, there is need for larger multicentre comparative clinical trials to guide treatment choice among the various currently available intravenous iron preparations in Africa.

In conclusion, intravenous low molecular weight iron dextran and iron sucrose are equally effective for increasing Hb level and replenishing iron stores in pre-dialysis CKD patients. In addition, serum ferritin is the preferred predictor for determining response to parenteral iron treatment in iron deficiency anaemia.

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Conflict of interest statement

None declared.

References

- Jurkovic CT, Abramson JL, Vaccarino LV et al. Association of high serum creatinine and anemia increases the risk of coronary events: results from the prospective community-based atherosclerosis risk in communities (ARIC) study. *J Am Soc Nephrol* 2003; 14: 2919–2925
- Dowling TC. Prevalence, etiology, and consequences of anemia and clinical and economic benefits of anemia correction in patients with chronic kidney disease: an overview. *Am J Health Syst Pharm* 2007; 64 (13 Suppl 8): S23–S25
- Fishbane S. Anemia and cardiovascular risk in the patient with kidney disease. *Heart Fail Clin* 2008; 4: 401–410
- Besarab A, Frinak S, Yee J. An indistinct balance: the safety and efficacy of parenteral iron therapy. *J Am Soc Nephrol* 1999; 10: 2029–2043
- Ward HJ. Implications of recombinant erythropoietin therapy for renal transplantation. *Am J Nephrol* 1990; 2: 44–47
- KDOQI Clinical Practice Guidelines and Clinical Practice Recommendations for Anemia in Chronic Kidney Disease. *Am J Kidney Dis* 2006; 47 (5 Suppl 3): S11–S145
- Eschbach JW, Egrie JC, Downing MR et al. Correction of the anemia of end-stage renal disease with recombinant human erythropoietin. Results of a combined phase I and II clinical trial. *N Engl J Med* 1987; 316: 73–78
- Drueke T. Hyporesponsiveness to recombinant human erythropoietin. *Nephrol Dial Transplant* 2001; 7: 25–28
- Mircescu G, Garneata L, Capusa C et al. Intravenous iron supplementation for the treatment of anaemia in pre-dialyzed chronic renal failure patients. *Nephrol Dial Transplant* 2006; 21: 120–124
- Silverberg DS, Blum M, Agbaria Z et al. The effect of i.v. iron alone or in combination with low-dose erythropoietin in the rapid correction of anemia of chronic renal failure in the pre-dialysis period. *Clin Nephrol* 2001; 55: 212–219
- Macdougall IC, Roche A. Administration of intravenous iron sucrose as a 2-minute push to CKD patients: a prospective evaluation of 2,297 injections. *Am J Kidney Dis* 2005; 46: 283–289
- Singh AK, Szczech L, Tang KL et al. Correction of anemia with epoetin alfa in chronic kidney disease. *N Engl J Med* 2006; 355: 2085–2098
- Szczech LA, Barnhart HX, Inrig JK et al. Secondary analysis of the CHOIR trial epoetin-alpha dose and achieved hemoglobin outcomes. *Kidney Int* 2008; 74: 791–798
- Solomon SD, Uno H, Lewis EF et al. Erythropoietic response and outcomes in kidney disease and type 2 diabetes. *N Engl J Med* 2010; 363: 1146–1155
- Freburger JK, Ng LJ, Bradbury BD et al. Changing patterns of anemia management in US hemodialysis patients. *Am J Med* 2012; 125: 906–914
- Qunibi WY, Martinez C, Smith M et al. 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. *Nephrol Dial Transplant* 2011; 26: 1599–1607
- Charytan C, Qunibi W, Bailie GR. Comparison of intravenous iron sucrose to oral iron in the treatment of anemic patients with chronic kidney disease not on dialysis. *Nephron Clin Pract* 2005; 100: 11
- Van Wyck DB, Roppolo M, Martinez CO et al. A randomized, controlled trial comparing IV iron sucrose to oral iron in anemic patients with nondialysis-dependent CKD. *Kidney Int* 2005; 68: 2846–2856
- Sinha S, Chiu DY, Peebles G et al. Comparison of intravenous iron sucrose versus low-molecular-weight iron dextran in chronic kidney disease. *J Ren Care* 2009; 35: 67–73
- Moniem KA, Bhandari S. Tolerability and efficacy of parenteral iron therapy in hemodialysis patients, a comparison of preparations. *Transfus Altern Transfus Med* 2007; 9: 37–42
- Silverberg DS, Iaina A, Peer G et al. Intravenous iron supplementation for the treatment of the anemia of moderate to severe chronic renal failure patients not receiving dialysis. *Am J Kidney Dis* 1996; 27: 234–238
- Tagboto S, Cropper L, Mostafa S et al. Intravenous iron in chronic kidney disease: haemoglobin change shortly after treatment of patients neither on dialysis nor on erythropoietin. *J Ren Care* 2008; 34: 112–115
- Gotloib L, Silverberg D, Fudin R et al. Iron deficiency is a common cause of anemia in chronic kidney disease and can often be corrected with intravenous iron. *J Nephrol* 2006; 19: 161–167
- Stancu S, Barsan L, Stanciu A et al. Can the response to iron therapy be predicted in anemic nondialysis patients with chronic kidney disease? *Clin J Am Soc Nephrol* 2010; 5: 409–416
- Sav T, Tokgoz B, Sipahioglu MH et al. Is there a difference between the allergic potencies of the iron sucrose and low molecular weight iron dextran? *Ren Fail* 2007; 29: 423–426
- Anirban G, Kohli HS, Jha V et al. The comparative safety of various intravenous iron preparations in chronic kidney disease patients. *Ren Fail* 2008; 30: 629–638
- Bhandari S. Update of a comparative analysis of cost minimization following the introduction of newly available intravenous iron therapies in hospital practice. *Ther Clin Risk Manag* 2011; 7: 501–509