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Comparison of Oral Liposomal vs Intravenous Iron in Iron Deficiency Anemia Patients with Non-Dialysis- Dependent Chronic Kidney Disease.

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Abstract

Background: Patients with chronic kidney disease (CKD) can receive oral or intravenous iron supplements. Liposomal iron has recently become known as a highly bioavailable alternative with little negative effects.

Objectives: The goal was to assess and compare the efficacy of liposomal oral iron and intravenous iron in treating iron deficient anemia in CKD patients were not yet on dialysis.

Method: CKD patients age between 18-70 years of age, not on dialysis with Hb≤10.5 and iron deficiency were enrolled. Group A received liposomal oral iron while Group B was administered 1000mg of iron sucrose intravenously over a period of 14 days. Subjects of Group A received 1.5g sachet of liposomal oral iron (containing 14mg of iron pyrophosphate) twice a day from day 0 to day 36.

Results: Total 88 patients 44 in each group were included. The study revealed a significant improvement in hemoglobin level (11.07g/dL±0.41 for oral iron and 11.88g/dL±0.41 for IV iron, with a p-value of less than 0.001), ferritin level (173.20ng/ml ±13 for oral iron and 278.36ng/ml ±16.25 for IV iron, with a p-value of less than 0.001), and T-SAT level (29.15%±2.05 for oral iron and 47.66%±3.26 for IV iron, with a p-value of less than 0.001).

Conclusion: According to the results of this study both iron therapies are valuable in improving Hemoglobin, and iron indices, however, IV iron therapy resulted in greater increases in hematological parameters compared to liposomal oral iron therapy. The study observed no GI, allergic or other side effects associated with liposomal oral iron and IV iron sucrose.

Key Words: Efficacy, Liposomal Oral iron, iron sucrose, Iron Deficiency anemia, dialysis, chronic kidney disease.

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Introduction

Individuals suffering from chronic kidney diseases (CKD) often have iron deficiency anemia, which can occur at any stage of the disease. Depending on the severity of CKD, between 20-70% of patients have decreased concentrations of transferrin saturation (TSAT) and serum ferritin.[1-4] Iron deficiency is the primary reason for a poor response to Erythropoietin stimulating agents (ESA), and thus iron supplementation is necessary to enhance iron indices and hemoglobin (Hb) levels, and lower the amount of required ESA. Therefore, treating anemia in CKD patients involves balancing ESA and iron therapy and occasionally blood transfusion.[5]

The National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI) currently recommends either oral or intravenous (IV) iron supplementation for anemic CKD patients with iron deficiency who are not on dialysis.[6]

Iron deficiency anemia can lead to severe outcomes in patients of CKD, like generalized tiredness, lethargy, breathlessness, heart failure, and higher morbidity and mortality rates.[7,8] Iron replacement via oral administration is easy, but it may cause gastric upset and poor compliance. On the other hand, the intravenous route is preferred due to its shorter duration and ability to provide adequate replacement, but it may cause allergic reactions and require hospitalization.[9-11]

Recently, liposomal form of iron, a kind of ferric pyrophosphate, has been made available in Pakistan. It has fewer adverse effects and good gastrointestinal absorption and bioavailability. The study's goal was to assess and compare the ability of liposomal oral iron and intravenous iron in treating iron deficient anemia in patients with CKD who were not on dialysis.

Methods:

This was prospective study with comparison of oral iron and IV iron groups with purposive convenient sampling technique. The study was approved by the IRB vide letter No.690/REG/KEMU/2021 dated: 19/01/2021. The study was conducted at Nephrology department, Mayo Hospital, Lahore from Jan 2022 – June 2022.

Sample Size: Using a significance level of 5% and a power of 90%, an estimated sample size of 88 patients (with 44 patients in each group) was calculated based on a mean value of 17.0 for oral iron and 19.3 for intravenous iron.

Inclusion Criteria

- Age 18-70
- Both genders
- (Hb ≤10.5 g/dL)
- CKD stage 3 to 5.
- Transferrin saturation ≤20%
- Ferritin ≤100 ng/mL
- Not on dialysis
- No ESA use within 8 weeks.

Exclusion criteria

- IV iron administered within 12weeks prior to the study
- There has been a significant loss of blood or a blood transfusion within the last 12 weeks.
- Conditions affecting the liver or cardiovascular system concomitantly.
- Currently undergoing dialysis or awaiting a kidney transplant.
- History of chronic drug and alcohol abuse over past 6 months.
- Active sepsis due to any cause like respiratory tract infection or urinary tract infection, diagnosed by clinical examination and history.
- Allergic reaction to i/v iron.
- Known case of hemoglobinopathies like thalassemia and sickle cell disease.

Data Collection Procedure

Patients meeting the inclusion criteria were informed about the study details and written consent was taken. A lottery method was used to randomly allocate these patients into two groups. Group A received liposomal oral iron, while Group B received 1000mg of iron sucrose intravenously in divided doses. Group B patients within day 0 to day 14, received infusions containing 200mg of iron sucrose administered in a 100ml solution of 0.9% NaCl over 30 minutes to 1 hour. Liposomal oral iron 1.5g sachets containing 14mg of iron pyrophosphate were administered to patients from day 0 to day 36. The study endpoint was an increase in Hb levels of at least 1g/dL at the end of the study.

Following the completion of oral treatment and one week after the final IV infusion, we assessed Hb levels, as well as iron-related indices i.e., serum iron content, ferritin levels, and transferrin saturation.

Statistical Analysis Procedure

The statistical analysis was conducted using SPSS (version 26, IBM Corp. Armonk, NY). Mean and standard deviation were reported for quantitative variables such as age, Hb levels, and serum ferritin levels. Additionally, qualitative variables such as gender, iron deficiency anemia, and allergic reactions were considered. A t-test was utilized to compare the oral iron and intravenous iron groups, with a significance level of< 0.05 for p-values.

Results

Baseline characteristics including baseline iron indices are shown in table 1.

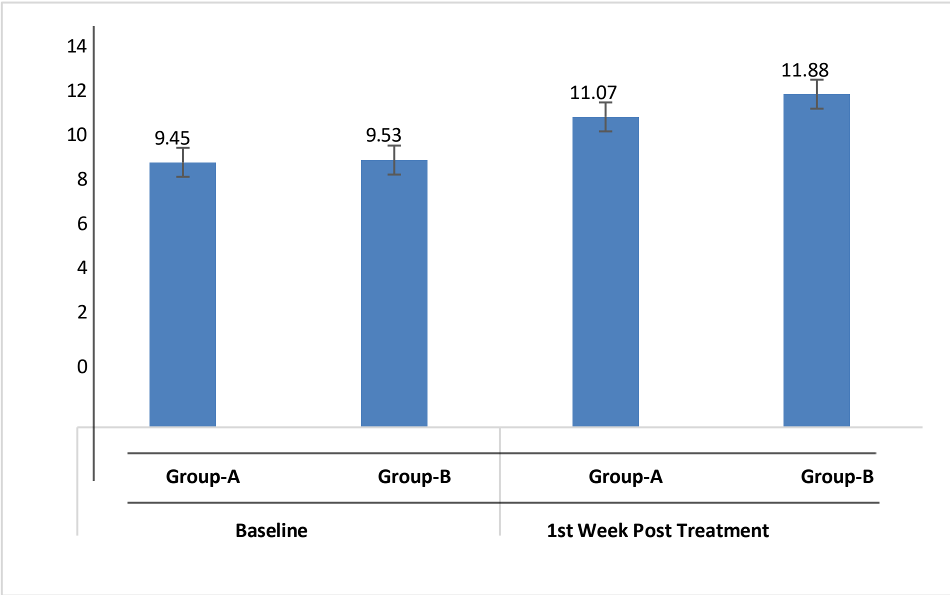
Table-1: Base line characteristics of. 88 CKD stage 3-5 non dialysis patients.

	Group A (n=44)	Group B (n=44)
Age	45.48±13.7	41.05±15.28
Male	21(47.73%)	19(43.18%)
Female	23(52.27%)	25(56.82%)
CKD Stage-3	11(25%)	10(22.73%)
CKD Stage-4	20(45.45%)	11(25%)
CKD Stage-5	13(29.55%)	23(52.27%)
Hb level	9.45±0.22	9.53±0.23
Ferritin	65.09±14.24	62.77±13.58
TSAT	16.67±1.27	16.88±1.16

There was a significant increase in hemoglobin, ferritin and TSAT post iron supplementation in both groups, Figure 1,2,3 p<0.05.

After one week of treatment, the Hb levels of Group-B patients were significantly higher than those of Group-A patients, with values of 11.07g/dL±0.41 and 11.88g/dL±0.41, respectively (p-value<0.001. Similarly Group-B patients had a significantly higher average ferritin levels compared to Group-A, with levels of 173.20ng/mL±13 and 278.36ng/mL±16.25, respectively (p- value<0.001), and a significantly higher average T-SAT level compared to Group-A, with levels of 29.15%±2.05 and 47.66%±3.26, respectively (p-value<0.001).

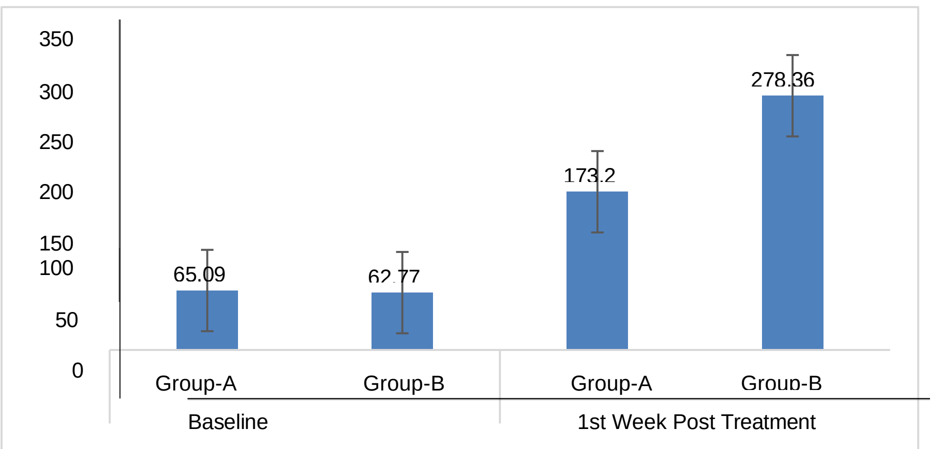
Figure 1: Baseline characteristics and iron indices in 88 patients with CKD 3-5 not yet on dialysis at the time of inclusion into the study.



Discussion

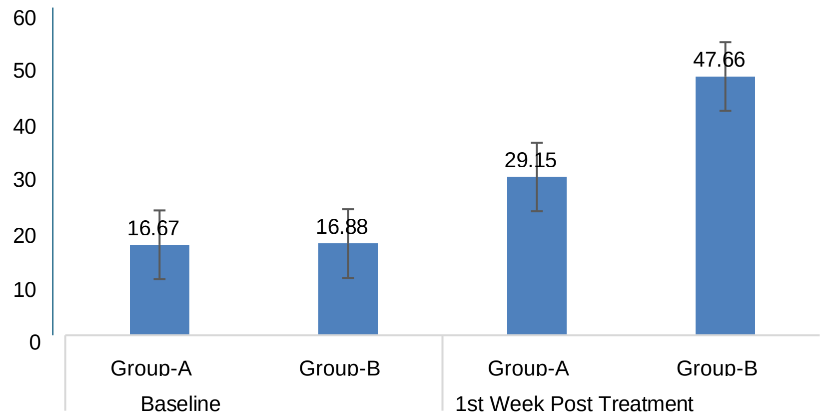
Our study of CKD stage 3-5 patients who were not yet on dialysis revealed that both routes of iron supplementation was effective in increasing the iron indices as well as Hb levels. Although Hb, ferritin, and T-SAT levels improved in both treatment groups, patients receiving intravenous iron therapy had higher iron levels than patients receiving oral iron therapy. The mean rise in ferritin levels indicated that intravenous iron replaced body iron more quickly than oral iron. Additionally, IV iron considerably boosted TSAT levels, another marker of iron supply for erythropoiesis, more than oral iron.

Figure-2: Serum Ferritin level in 88 patients with CKD 3-5 not yet on dialysis before and one week after completing iron supplementation.



In a study by Marrahi et al., liposomal iron was examined for use in stage 3 CKD patients who were GI intolerant to traditional oral iron therapy.[12] Increases in Hb levels after six and twelve months were the main outcome indicators. According to this study, Hb levels considerably increased after using FeSO4 for six months compared to the baseline (0.49±0.19 g/dL and 0.36±0.19 g/dL, respectively, p-value <0.05), adherence to treatment medication and no adverse responses were noticed that would have necessitated stopping the treatment. The follow-up duration for our study was substantially shorter than the study by Marrahi.

Figure-3: T-SAT level in 88 patients with CKD 3-5 not yet on dialysis before and one week after completing iron supplementation.



Pisani et al. carried out a study with a shorter follow-up time and had findings similar to our study.[13] Utility of liposomal iron was supported by the study by Arenas et al. showing good adherence and tolerance.[14] Another study by that adding subcutaneous erythropoietin to liposomal iron for 12 weeks improved hematological indices and quality of life in elderly anemics without end-stage kidney disease, with no adverse effects noted and excellent tolerance.[15]

Longer-term follow-up studies have shown that liposomal oral therapy is as effective as IV iron therapy in increasing hematological parameters, has fewer side effects, and is better tolerated by patients with ND-CKD.[13,14]

A phospholipid envelope is incorporated into the pharmacological design of liposomal or sucrose iron, a novel oral iron product that is more accessible than other oral iron compounds. In addition, compared to other oral medicines, it is linked to much fewer gastrointestinal adverse effects.[14,16]

Conclusion

The results of the study show that individuals with non-dialysis chronic renal disease can improve their Hb, ferritin, and T-SAT levels with both oral liposomal and IV iron therapy. However, compared to liposomal oral iron therapy, intravenous iron therapy led to greater increases in hematological markers. In this study, CKD 3-5 patients receiving liposomal oral iron therapy and IV iron did not develop any significant adverse reactions.

Conflict of interest: None declared

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