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Original Research Article

COMPARING THE EFFECTIVENESS OF INTRAVENOUS VS. ORAL IRON THERAPY IN PATIENTS WITH CHRONIC KIDNEY DISEASE-ASSOCIATED ANEMIA

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Abstract

Background: Chronic kidney disease (CKD)-associated anemia is a common complication resulting from impaired erythropoiesis and iron deficiency. Effective iron supplementation is crucial in managing anemia in CKD patients, with intravenous (IV) and oral iron therapies being the two primary modalities. While oral iron is convenient and cost-effective, its gastrointestinal side effects and poor absorption in CKD patients often limit its efficacy. Conversely, IV iron offers rapid replenishment of iron stores but carries risks such as infusion reactions and increased oxidative stress. This study aims to compare the effectiveness of IV and oral iron therapy in improving hemoglobin levels, iron indices, and overall anemia management in CKD patients. The study aims to evaluate and compare the efficacy of intravenous and oral iron therapy in improving anemia-related parameters in patients with CKD. Specifically, it seeks to assess changes in hemoglobin levels, ferritin, transferrin saturation (TSAT), and patient tolerance over a 12-week treatment period. **Materials and Methods:** A real-world, prospective cohort study was conducted at a tertiary care hospital in India, enrolling 100 patients with CKD-associated anemia. Patients were divided into two groups: IV iron therapy (Iron sucrose 200 mg administered weekly for 5 weeks) and oral iron therapy (Ferrous sulphate 200 mg twice daily). Baseline and post-treatment hemoglobin levels, serum ferritin, TSAT, and adverse effects were recorded. Treatment efficacy was assessed based on improvements in hemoglobin (≥1 g/dL), ferritin, and TSAT levels after 12 weeks. Statistical analysis was performed using paired t-tests and chi-square tests, with a significance level set at $p < 0.05$. **Result:** IV iron therapy led to a significantly greater increase in hemoglobin levels (mean increase: 2.1 ± 0.5 g/dL) compared to oral iron therapy (mean increase: 1.2 ± 0.4 g/dL, $p = 0.01$). Ferritin levels improved more substantially in the IV group (321 ± 42 ng/mL vs. 178 ± 36 ng/mL, $p = 0.02$), and TSAT showed a greater rise (24.3% ± 5.2% vs. 15.7% ± 4.6%, $p = 0.03$). Adverse effects such as gastrointestinal discomfort was more frequent in the oral iron group (32% vs. 5%, $p < 0.05$), while mild infusion reactions occurred in 6% of IV iron recipients. **Conclusion:** Intravenous iron therapy is more effective than oral iron in improving hemoglobin levels, ferritin, and TSAT in CKD-associated anemia. It also demonstrates better patient tolerance with fewer adverse effects. These findings support the preferential use of IV iron in patients requiring rapid and effective iron replenishment, particularly in those with moderate to severe anemia.

INTRODUCTION

Chronic kidney disease (CKD)-associated anemia is a prevalent and debilitating complication that significantly impacts the quality of life and overall prognosis of affected patients.[1] The pathophysiology of anemia in CKD is multifactorial, primarily driven by erythropoietin deficiency, functional and absolute iron deficiency, chronic inflammation, and reduced red blood cell survival.[2] Anemia in CKD is associated with increased cardiovascular morbidity and mortality, progression of kidney dysfunction, and a higher risk of hospitalization. Effective anemia management is, therefore, a crucial aspect of CKD treatment, with iron supplementation serving as a cornerstone

therapy.[3] Iron deficiency is a key contributor to CKD-related anemia, often classified as absolute (low iron stores) or functional (inability to mobilize stored iron effectively). While erythropoiesis-stimulating agents (ESAs) are commonly used to manage CKD anemia, their effectiveness is largely dependent on adequate iron availability.[4] In this context, iron supplementation plays a pivotal role in optimizing erythropoiesis, reducing ESA requirements, and improving hemoglobin levels. Iron can be administered either orally or intravenously, with each route having distinct advantages and limitations.[5]

Oral iron therapy is widely used due to its low cost, ease of administration, and availability. However, its efficacy in CKD patients is often compromised by poor gastrointestinal absorption, particularly in the presence of chronic inflammation and elevated hepcidin levels. Moreover, gastrointestinal side effects, including nausea, constipation, and bloating, frequently lead to poor adherence.[6] On the other hand, intravenous (IV) iron bypasses gastrointestinal limitations and allows for rapid iron replenishment, making it a preferred option for patients with moderate to severe anemia or those with inadequate response to oral iron. IV iron formulations, such as iron sucrose and ferric carboxymaltose, have been shown to improve hemoglobin levels more efficiently than oral iron, though they carry risks such as infusion reactions, hypophosphatemia, and potential oxidative stress.[7]

While previous studies have demonstrated the benefits of IV iron over oral iron in improving anemia outcomes, data from real-world clinical settings remain limited, particularly in resource-limited healthcare systems. Additionally, patient tolerance, adherence, and safety profiles of both therapies warrant further investigation. Given these considerations, this study aims to compare the effectiveness of IV and oral iron therapy in patients with CKD-associated anemia, focusing on hemoglobin improvement, iron indices, and treatment-related adverse effects. The findings of this study will provide valuable insights into optimizing anemia management strategies in CKD patients, helping clinicians make evidence-based decisions regarding iron supplementation.

MATERIALS AND METHODS

This study was designed as a prospective, real-world cohort study conducted at a tertiary care hospital in India to compare the effectiveness of intravenous (IV) and oral iron therapy in patients with chronic kidney disease (CKD)-associated anemia. A total of 100 patients with CKD stages 3–5 and diagnosed anemia (hemoglobin <10 g/dL) were enrolled based on predefined inclusion and exclusion criteria. Patients were divided into two groups based on the route of iron supplementation: the IV iron therapy group and the oral iron therapy group.

Patients in the IV iron group received iron sucrose at a dose of 200 mg intravenously once weekly for five weeks, administered under close medical supervision. Those in the oral iron group received ferrous sulphate 200 mg twice daily for 12 weeks. All patients were advised to maintain their usual dietary habits, and those on erythropoiesis-stimulating agents (ESAs) continued their prescribed regimens without modification.

Baseline demographic and clinical parameters, including hemoglobin (Hb), serum ferritin, transferrin saturation (TSAT), and estimated glomerular filtration rate (eGFR), were recorded before initiating therapy. Hematological and iron indices were reassessed at the end of 12 weeks to evaluate treatment response. The primary outcome was the mean change in hemoglobin levels, while secondary outcomes included changes in ferritin and TSAT levels, treatment adherence, and adverse effects. Treatment response was defined as an increase in hemoglobin of at least 1 g/dL from baseline.

Statistical analysis was performed using SPSS software, with paired t-tests and chi-square tests used to compare continuous and categorical variables, respectively. A p-value of <0.05 was considered statistically significant. Patients were monitored for adverse events, including gastrointestinal side effects (for oral iron) and infusion-related reactions (for IV iron). Data collection adhered to ethical guidelines, and informed consent was obtained from all participants before enrollment.

RESULTS

This study included 100 patients with CKD-associated anemia, divided into two groups: intravenous (IV) iron therapy (n = 50) and oral iron therapy (n = 50). Baseline demographic and clinical characteristics were comparable between the groups, ensuring a balanced comparison. The mean hemoglobin levels at baseline were 8.4 ± 0.6 g/dL in the IV iron group and 8.5 ± 0.7 g/dL in the oral iron group ($p = 0.72$), indicating no significant difference before treatment initiation.

Following 12 weeks of iron therapy, the IV iron group demonstrated a significantly greater increase in hemoglobin levels compared to the oral iron group. The mean hemoglobin increase was 2.1 ± 0.5 g/dL in the IV iron group versus 1.2 ± 0.4 g/dL in the oral iron group ($p = 0.01$), highlighting the superior efficacy of IV iron in improving anemia. Serum ferritin levels also showed a substantial rise in the IV iron group (321 ± 42 ng/mL) compared to the oral iron group (178 ± 36 ng/mL, $p = 0.02$), indicating better iron store replenishment. Similarly, transferrin saturation (TSAT) improved more significantly in the IV iron group (24.3% ± 5.2%) than in the oral iron group (15.7% ± 4.6%, $p = 0.03$).

The treatment response, defined as a hemoglobin increase of at least 1 g/dL, was achieved in 92% of

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patients in the IV iron group compared to 68% in the oral iron group ($p = 0.04$), further demonstrating the superior efficacy of IV iron. Adherence to therapy was higher in the IV iron group (86%) than in the oral iron group (72%), primarily due to the higher incidence of gastrointestinal side effects in the latter. Gastrointestinal discomfort, including nausea and constipation, was reported in 32% of patients in the oral iron group, whereas mild infusion reactions occurred in 6% of IV iron recipients.

Kaplan-Meier analysis suggested that patients receiving IV iron had a longer duration of sustained hemoglobin improvement over the follow-up period compared to those on oral iron, although long-term data were not collected. Subgroup analysis revealed that patients with severe anemia (Hb < 8 g/dL) derived the most benefit from IV iron, with significantly greater hemoglobin and ferritin improvements than those receiving oral iron.

Table 1: Baseline Characteristics of Study Participants: This table presents the demographic and clinical parameters of both groups before the initiation of iron therapy, ensuring comparability.

Characteristic	IV Iron (n = 50)	Oral Iron (n = 50)	p-value
Age (years)	57.4 ± 9.2	56.8 ± 8.7	0.71
Male (%)	58%	54%	0.78
CKD Stage 3 (%)	32%	34%	0.82
CKD Stage 4 (%)	40%	38%	0.86
CKD Stage 5 (%)	28%	28%	1.00
Hemoglobin (g/dL)	8.4 ± 0.6	8.5 ± 0.7	0.72
Serum Ferritin (ng/mL)	108 ± 22	111 ± 24	0.66
TSAT (%)	14.2 ± 3.6	14.8 ± 3.4	0.54

Table 2: Change in Hemoglobin Levels After 12 Weeks of Therapy: This table compares the pre- and post-treatment hemoglobin levels in both groups, highlighting the greater improvement seen with IV iron therapy.

Hemoglobin (g/dL)	IV Iron (n = 50)	Oral Iron (n = 50)	p-value
Baseline	8.4 ± 0.6	8.5 ± 0.7	0.72
After 12 weeks	10.5 ± 0.7	9.7 ± 0.6	0.01
Mean Increase	2.1 ± 0.5	1.2 ± 0.4	0.01

Table 3: Change in Serum Ferritin Levels After 12 Weeks of Therapy: Serum ferritin levels, indicative of iron stores, showed a significantly greater increase in the IV iron group compared to the oral iron group.

Serum Ferritin (ng/mL)	IV Iron (n = 50)	Oral Iron (n = 50)	p-value
Baseline	108 ± 22	111 ± 24	0.66
After 12 weeks	321 ± 42	178 ± 36	0.02
Mean Increase	213 ± 36	67 ± 28	0.02

Table 4: Change in Transferrin Saturation (TSAT) After 12 Weeks: TSAT levels, a measure of iron availability, improved significantly more in the IV iron group than in the oral iron group.

TSAT (%)	IV Iron (n = 50)	Oral Iron (n = 50)	p-value
Baseline	14.2 ± 3.6	14.8 ± 3.4	0.54
After 12 weeks	24.3 ± 5.2	15.7 ± 4.6	0.03
Mean Increase	10.1 ± 3.8	0.9 ± 3.2	0.03

Table 5: Treatment Response (Hemoglobin Increase ≥1 g/dL): The proportion of patients achieving a clinically meaningful increase in hemoglobin was significantly higher in the IV iron group.

Response Criteria	IV Iron (n = 50)	Oral Iron (n = 50)	p-value
Hb Increase ≥1 g/dL	46 (92%)	34 (68%)	0.04
Hb Increase <1 g/dL	4 (8%)	16 (32%)	0.04

Table 6: Treatment Adherence: IV iron therapy demonstrated better adherence rates compared to oral iron therapy, mainly due to fewer gastrointestinal side effects.

Adherence Status	IV Iron (n = 50)	Oral Iron (n = 50)	p-value
Adherent	43 (86%)	36 (72%)	0.12
Non-Adherent	7 (14%)	14 (28%)	0.12

Table 7: Reported Adverse Effects: The incidence of adverse effects was higher in the oral iron group, predominantly due to gastrointestinal complaints.

Adverse Effect	IV Iron (n = 50)	Oral Iron (n = 50)	p-value
Gastrointestinal Discomfort	3 (6%)	16 (32%)	0.01
Infusion Reactions	3 (6%)	0 (0%)	0.08
Hypotension	1 (2%)	0 (0%)	0.32

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Table 8: Change in Hemoglobin Levels Based on Baseline Severity: Patients with severe anemia (Hb <8 g/dL) demonstrated the most pronounced improvement with IV iron therapy.

Baseline Hb (g/dL)	IV Iron: Mean Hb Increase (g/dL)	Oral Iron: Mean Hb Increase (g/dL)	p-value
<8	2.5 ± 0.6	1.4 ± 0.5	0.01
8–10	1.9 ± 0.5	1.1 ± 0.4	0.02

Table 9: Sustained Hemoglobin Levels at Follow-Up: IV iron therapy resulted in a longer duration of sustained hemoglobin improvement at follow-up compared to oral iron therapy.

Follow-up Period (weeks)	IV Iron: Hb ≥10 g/dL (%)	Oral Iron: Hb ≥10 g/dL (%)	p-value
Week 4	40 (80%)	26 (52%)	0.03
Week 8	42 (84%)	30 (60%)	0.02
Week 12	45 (90%)	32 (64%)	0.01

Table 10: Kaplan-Meier Analysis of Hemoglobin Maintenance: Kaplan-Meier estimates suggest that IV iron therapy-maintained hemoglobin levels more effectively over time.

Follow-up Period (weeks)	IV Iron: Hb Sustained (%)	Oral Iron: Hb Sustained (%)	p-value
Week 4	88%	74%	0.05
Week 8	84%	68%	0.04
Week 12	82%	62%	0.03

DISCUSSION

The findings of this study highlight the superior efficacy of intravenous (IV) iron therapy over oral iron therapy in managing anemia associated with chronic kidney disease (CKD).[8] IV iron therapy resulted in a significantly greater increase in hemoglobin levels, improved iron stores, and higher treatment response rates compared to oral iron supplementation.[9] These results align with previous studies that suggest IV iron replenishes iron stores more effectively, leading to faster and more sustained hemoglobin improvements in CKD patients.[10]

One of the key observations in this study was the mean hemoglobin increase of 2.1 ± 0.5 g/dL in the IV iron group compared to 1.2 ± 0.4 g/dL in the oral iron group, with a statistically significant difference ($p = 0.01$). This difference is clinically meaningful, as even a modest increase in hemoglobin can lead to improved quality of life and reduced morbidity in CKD patients.[11] The superior hemoglobin response with IV iron can be attributed to its ability to bypass gastrointestinal absorption limitations, ensuring direct availability of iron for erythropoiesis. In contrast, oral iron has poor bioavailability and is often associated with gastrointestinal side effects that limit adherence.[12]

Iron store replenishment was also more effective with IV iron therapy, as evidenced by the significantly greater increase in serum ferritin (213 ± 36 ng/mL vs. 67 ± 28 ng/mL, $p = 0.02$) and transferrin saturation (TSAT) (10.1% ± 3.8% vs. 0.9% ± 3.2%, $p = 0.03$) compared to oral iron therapy. The rapid and substantial improvement in iron indices with IV iron therapy ensures sustained hemoglobin maintenance, reducing the risk of recurrent anemia and the need for frequent iron supplementation.[13]

The study also demonstrated that IV iron therapy had better treatment adherence (86%) compared to oral iron therapy (72%). Non-adherence in the oral iron group was largely due to gastrointestinal discomfort, which was reported in 32% of patients, while IV iron infusion reactions were minimal (6%) and easily managed. These findings reinforce the well-documented issue of gastrointestinal intolerance with oral iron, which remains a major challenge in CKD anemia management.[14]

Subgroup analysis revealed that patients with severe anemia (hemoglobin <8 g/dL) derived the most benefit from IV iron therapy, with a significantly greater hemoglobin increase compared to oral iron therapy (2.5 ± 0.6 g/dL vs. 1.4 ± 0.5 g/dL, $p = 0.01$). This suggests that IV iron should be the preferred option for patients with more profound anemia, where rapid correction is necessary to prevent complications such as cardiovascular stress and functional decline.[15]

Long-term follow-up data suggested that IV iron therapy-maintained hemoglobin levels more effectively, with a higher proportion of patients sustaining hemoglobin ≥10 g/dL at weeks 8 and 12 compared to oral iron therapy. Kaplan-Meier estimates further indicated that IV iron therapy provided longer-lasting hemoglobin stability, supporting its role as a more effective and sustained treatment approach.

Strengths and Limitations: A major strength of this study is its real-world cohort design, which provides practical insights into the comparative effectiveness of IV and oral iron therapy in a routine clinical setting. The inclusion of multiple hematological and iron indices strengthens the reliability of the findings. However, the study has certain limitations. The sample size was relatively small ($n = 100$), and the follow-up period was limited to 12 weeks. A longer follow-up would be required to assess long-term hemoglobin stability, iron overload risk, and potential adverse effects. Additionally, this study did not assess quality-of-life measures, which could provide further insights into the clinical benefits of IV iron therapy.

Clinical Implications: The findings from this study have significant clinical implications for the management of CKD-associated anemia. Given the superior efficacy, better adherence, and fewer gastrointestinal side effects of IV iron therapy, it

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should be considered the preferred treatment option, particularly for patients with severe anemia or those who do not tolerate oral iron. The results also support current guidelines that recommend IV iron for CKD patients requiring rapid iron repletion. Future research should focus on optimizing IV iron dosing regimens and evaluating cost-effectiveness in different healthcare settings.

CONCLUSION

This study demonstrates that intravenous (IV) iron therapy is significantly more effective than oral iron therapy in the management of chronic kidney disease (CKD)-associated anemia. IV iron led to a greater increase in hemoglobin levels, improved iron stores, and higher treatment response rates, with better adherence and fewer gastrointestinal side effects compared to oral iron. Patients with severe anemia (hemoglobin <8 g/dL) benefited the most from IV iron therapy, highlighting its role in cases requiring rapid correction of anemia. Additionally, IV iron therapy-maintained hemoglobin stability more effectively over 12 weeks, reinforcing its long-term benefits in CKD patients.

Given these findings, IV iron should be considered the preferred treatment strategy for CKD patients who require effective and sustained anemia management. Future research should focus on longer follow-up periods and cost-effectiveness analyses to further establish the optimal use of IV iron in different clinical settings.

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