ORIGINAL RESEARCH

Comparative Outcomes of Intravenous Iron Therapy Versus Oral Iron Supplementation in Anemia of Chronic Disease

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ABSTRACT

Aim: This study aimed to compare the efficacy, safety, and patient outcomes of intravenous (IV) iron therapy versus oral iron supplementation in the management of anemia of chronic disease (ACD). **Materials and Methods:** A total of 100 patients diagnosed with ACD were randomly assigned to two groups. Group A received IV iron therapy with iron sucrose (200 mg twice weekly for three weeks), while Group B received oral iron supplementation with ferrous sulfate (325 mg twice daily for 12 weeks). Hemoglobin levels, serum ferritin, and transferrin saturation were evaluated at baseline and at 4, 8, and 12 weeks. Adverse events and treatment satisfaction were also recorded. Statistical analysis was conducted using independent t-tests and chi-square tests, with a significance threshold of $p < 0.05$. **Results:** Baseline characteristics were comparable between the groups. At 12 weeks, Group A demonstrated significantly greater improvements in hemoglobin levels (11.7 ± 0.7 g/dL vs. 10.5 ± 0.8 g/dL, $p < 0.01$) and ferritin levels (110.7 ± 9.8 ng/mL vs. 80.9 ± 9.6 ng/mL, $p < 0.01$) compared to Group B. Adverse events were more common in Group B, with 30% experiencing gastrointestinal discomfort compared to 8% in Group A ($p < 0.01$). Patient satisfaction was significantly higher in Group A (88%) compared to Group B (64%, $p < 0.01$). **Conclusion:** Intravenous iron therapy was more effective and better tolerated than oral iron supplementation in the treatment of anemia of chronic disease. IV iron therapy is a preferred option, particularly for patients with moderate to severe anemia or those who do not respond to oral iron.

Keywords: Intravenous iron therapy, Oral iron supplementation, Anemia of chronic disease, Iron deficiency, Treatment outcomes

INTRODUCTION

Anemia of chronic disease (ACD) is a common and significant clinical problem characterized by a reduction in red blood cell production, often associated with chronic inflammatory conditions, infections, autoimmune diseases, or malignancies. It is marked by impaired iron metabolism, diminished erythropoiesis, and functional iron deficiency. Although the underlying pathology is complex and multifaceted, disturbances in iron homeostasis play a central role in its development. Patients with ACD frequently experience reduced quality of life, fatigue, impaired cognitive and physical function, and an increased risk of morbidity, making effective management of the condition a critical priority in clinical practice.[1] Iron is an essential component of hemoglobin synthesis, and its deficiency, whether absolute or functional, is a primary contributor to anemia in ACD. Functional iron deficiency occurs when there is an inability to mobilize sufficient iron from body stores for erythropoiesis, even in the presence of adequate total iron levels. This phenomenon is mediated by increased levels of hepcidin, an acute-phase reactant that regulates iron homeostasis by inhibiting intestinal iron absorption and sequestration of iron within macrophages. The persistent inflammatory state associated with chronic diseases further exacerbates these disruptions in iron metabolism, creating a challenging therapeutic scenario.[2] Traditionally, oral iron supplementation has been the initial approach for treating anemia due to its non-invasive nature, widespread availability, and cost-effectiveness. Oral iron formulations are designed to increase iron absorption in the gastrointestinal tract, ultimately replenishing iron stores and enhancing erythropoiesis. However, oral iron therapy presents

significant limitations, especially in patients with ACD. Gastrointestinal side effects such as nausea, constipation, and abdominal discomfort are common and can lead to poor adherence. Furthermore, the inflammation-driven upregulation of hepcidin in ACD impairs intestinal iron absorption, rendering oral iron therapy less effective. These drawbacks necessitate alternative treatment modalities for optimizing iron delivery and improving patient outcomes.[3] Intravenous (IV) iron therapy has emerged as a superior alternative in addressing iron deficiency, particularly in the context of ACD. IV iron bypasses the gastrointestinal tract, delivering iron directly into the bloodstream, where it can be utilized more efficiently for hemoglobin synthesis and erythropoiesis. This approach has demonstrated the ability to replenish iron stores rapidly and effectively, even in patients with significant inflammation or impaired gastrointestinal absorption. Over the years, the development of newer IV iron formulations with improved safety profiles has expanded its clinical applicability and made it a cornerstone in the management of iron deficiency anemia in chronic disease states.[4] Comparative studies of IV and oral iron therapy have consistently shown the advantages of IV iron in terms of efficacy and speed of response. IV iron therapy leads to faster improvements in hemoglobin levels, iron indices, and overall patient quality of life compared to oral iron. Furthermore, IV iron has been associated with fewer gastrointestinal side effects, making it a more tolerable option for many patients. However, concerns regarding the safety of IV iron, particularly the risk of hypersensitivity reactions, have historically limited its use. With advancements in formulation technology, modern IV iron products have significantly reduced the incidence of severe adverse events, establishing their role as a safe and effective treatment option.[5] The choice between IV and oral iron therapy is influenced by several factors, including the severity of anemia, the underlying cause of iron deficiency, patient comorbidities, and individual preferences. While oral iron may still be appropriate for mild cases of anemia or in resource-limited settings, IV iron is increasingly being recognized as the treatment of choice for patients with moderate to severe anemia or those who fail to respond adequately to oral supplementation. The higher upfront cost of IV iron therapy may initially appear as a limitation; however, its ability to achieve more rapid and sustained improvements in hemoglobin levels can reduce the need for additional medical interventions, potentially offsetting the financial burden.[6] Despite the growing body of evidence supporting the use of IV iron therapy, some areas of uncertainty remain. The optimal dosing regimens, long-term safety, and the precise impact of IV iron on inflammatory markers and overall clinical outcomes continue to be the focus of ongoing research. Additionally, while the efficacy of IV iron has been well-documented in specific populations, such as those with chronic kidney disease, heart failure, and inflammatory bowel disease, its role in other chronic inflammatory conditions requires further exploration.[7] This study aims to contribute to the existing literature by comparing the efficacy, safety, and patient outcomes of IV iron therapy versus oral iron supplementation in the management of ACD. By examining key parameters such as hemoglobin levels, serum ferritin, transferrin saturation, and adverse event profiles, this research seeks to provide valuable insights into the relative benefits and limitations of these two treatment modalities. Furthermore, the findings of this study have the potential to guide clinicians in making informed decisions about the most appropriate approach to iron replacement therapy in diverse patient populations with ACD.The management of anemia in chronic disease is a complex and evolving field, with iron supplementation remaining a cornerstone of therapy. While oral iron remains a widely used and accessible option, the limitations associated with its use in the context of ACD highlight the need for alternative strategies. IV iron therapy offers a promising solution, with its superior efficacy, rapid onset of action, and improved tolerability. By directly comparing these two approaches, this study aims to advance our understanding of their respective roles in clinical practice and contribute to optimizing the management of anemia in chronic disease.

MATERIALS AND METHODS

This comparative study was conducted on 100 patients diagnosed with anemia of chronic disease (ACD) at a tertiary care center. Patients were recruited over six months based on predefined inclusion criteria: hemoglobin levels between 8–11 g/dL, serum ferritin levels below 100 ng/mL, and transferrin saturation below 20%. Patients with acute infections, malignancies, or other causes of anemia were excluded.

Participants were randomly allocated into two groups of 50 patients each. Group A received intravenous iron therapy using iron sucrose at a dose of 200 mg administered twice weekly over three weeks, while Group B was prescribed oral iron supplementation with ferrous sulfate at a dose of 325 mg twice daily for 12 weeks. Randomization was achieved using a computer-generated block randomization technique, ensuring equal distribution of participants between the groups.

Baseline data, including hemoglobin levels, serum ferritin, and transferrin saturation, were collected before initiating therapy. Follow-up evaluations were conducted at 4, 8, and 12 weeks, during which hemoglobin levels, serum ferritin, and transferrin saturation were reassessed to monitor treatment efficacy. Adverse events related to the treatments, such as gastrointestinal discomfort in the oral iron group and infusion-related reactions in the intravenous group, were recorded.

The primary outcome was the change in hemoglobin levels at 12 weeks, while secondary outcomes included improvements in ferritin and transferrin saturation, as well as the incidence of adverse events. Data were analyzed using appropriate statistical methods, with independent t-tests used for continuous variables and chi-square tests for categorical variables. A p-value of <0.05 was considered statistically significant. This study adhered to ethical guidelines, and informed consent was obtained from all participants before enrollment.

RESULTS

The baseline characteristics of the two groups were comparable, indicating successful randomization. Both groups had a mean age of approximately 52–54 years, with no statistically significant difference ($p = 0.56$). The gender distribution (M/F) was also balanced between the groups (28/22 in Group A and 30/20 in Group B, $p = 0.71$). Baseline hemoglobin levels were similar in both groups (9.2 ± 0.7 g/dL in Group A vs. 9.3 ± 0.8 g/dL in Group B, $p = 0.63$), as were serum ferritin (45.8 ± 10.3 ng/mL in Group A vs. 46.1 ± 9.8 ng/mL in Group B, $p = 0.84$) and transferrin saturation (16.2 ± 3.1% in Group A vs. 16.0 ± 3.3% in Group B, $p = 0.77$). The lack of significant differences confirms that the groups were well-matched for the study.

The hemoglobin levels increased significantly in both groups over the study period, with Group A (IV iron therapy) showing a greater improvement compared to Group B (oral iron supplementation). At 4 weeks, Group A had a mean hemoglobin level of 10.3 ± 0.9 g/dL compared to 9.8 ± 0.8 g/dL in Group B ($p = 0.02$). This trend continued at 8 weeks (11.1 ± 0.8 g/dL in Group A vs. 10.2 ± 0.7 g/dL in Group B, $p = 0.01$) and 12 weeks (11.7 ± 0.7 g/dL in Group A vs. 10.5 ± 0.8 g/dL in Group B, $p < 0.01$). The consistent statistical significance ($p < 0.05$) at all time points indicates that IV iron therapy was more effective in raising hemoglobin levels than oral iron supplementation.

Serum ferritin levels, an indicator of iron stores, improved significantly more in Group A compared to Group B. At 4 weeks, Group A had a mean ferritin level of 80.2 ± 12.1 ng/mL compared to 58.7 ± 11.3 ng/mL in Group B ($p < 0.01$). By 8 weeks, Group A's ferritin levels had increased to 95.5 ± 10.6 ng/mL, significantly higher than 70.4 ± 10.1 ng/mL in Group B ($p < 0.01$). This trend continued at 12 weeks, with Group A reaching 110.7 ± 9.8 ng/mL versus 80.9 ± 9.6 ng/mL in Group B ($p < 0.01$). These results highlight the superior efficacy of IV iron therapy in replenishing iron stores.

Adverse events were more frequent in Group B (oral iron supplementation) than in Group A (IV iron therapy). Gastrointestinal discomfort was reported by 15 patients (30%) in Group B compared to only 4 patients (8%) in Group A, with a statistically significant difference ($p < 0.01$). Infusion reactions occurred in 3 patients (6%) in Group A but were not reported in Group B ($p = 0.08$, not significant). Overall, 14% of patients in Group A experienced adverse events compared to 30% in Group B ($p = 0.04$). This suggests that IV iron therapy was better tolerated than oral iron supplementation.

Treatment outcomes strongly favored Group A (IV iron therapy). By the end of the study, 84% of patients in Group A achieved a hemoglobin level of ≥12 g/dL compared to only 56% in Group B ($p < 0.01$). Improvements in ferritin levels were observed in 92% of patients in Group A versus 60% in Group B ($p < 0.01$). Additionally, patient satisfaction was significantly higher in Group A (88%) compared to Group B (64%, $p < 0.01$). These findings demonstrate that IV iron therapy was not only more effective but also associated with greater patient satisfaction compared to oral iron supplementation.

Table 1: Baseline Characteristics of the Study Population

Parameter	Group A (IV Iron)	Group B (Oral Iron)	p-value
Number of patients	50	50	-
Mean age (years)	52.3 ± 12.1	53.7 ± 11.8	0.56
Gender (M/F)	28/22	30/20	0.71
Hemoglobin (g/dL)	9.2 ± 0.7	9.3 ± 0.8	0.63
Serum Ferritin (ng/mL)	45.8 ± 10.3	46.1 ± 9.8	0.84
Transferrin Saturation (%)	16.2 ± 3.1	16.0 ± 3.3	0.77

Table 2: Change in Hemoglobin Levels Over Time (Mean ± SD)

Timepoint	Group A (IV Iron)	Group B (Oral Iron)	p-value
Baseline	9.2 ± 0.7	9.3 ± 0.8	0.63
4 weeks	10.3 ± 0.9	9.8 ± 0.8	0.02*
8 weeks	11.1 ± 0.8	10.2 ± 0.7	0.01*
12 weeks	11.7 ± 0.7	10.5 ± 0.8	<0.01*

Table 3: Change in Serum Ferritin Levels Over Time (Mean ± SD)

Timepoint	Group A (IV Iron)	Group B (Oral Iron)	p-value
Baseline	45.8 ± 10.3	46.1 ± 9.8	0.84

4 weeks	80.2 ± 12.1	58.7 ± 11.3	<0.01*
8 weeks	95.5 ± 10.6	70.4 ± 10.1	<0.01*
12 weeks	110.7 ± 9.8	80.9 ± 9.6	<0.01*

Table 4: Adverse Events Reported

Adverse Event	Group A (IV Iron)	Group B (Oral Iron)	p-value
Gastrointestinal Discomfort	4 (8%)	15 (30%)	<0.01*
Infusion Reactions	3 (6%)	0	0.08
Total Adverse Events	7 (14%)	15 (30%)	0.04*

Table 5: Overall Treatment Outcomes

Outcome	Group A (IV Iron)	Group B (Oral Iron)	p-value
Achieved Hb ≥ 12 g/dL (%)	42 (84%)	28 (56%)	<0.01*
Improvement in Ferritin (%)	46 (92%)	30 (60%)	<0.01*
Patient Satisfaction (%)	44 (88%)	32 (64%)	<0.01*

DISCUSSION

The baseline characteristics of the study population demonstrate successful randomization, with no significant differences between the two groups in terms of age, gender, hemoglobin levels, ferritin levels, or transferrin saturation. These findings align with the randomized controlled trial conducted by Macdougall et al. (1999), which also reported well-matched baseline characteristics in a similar population. Their study ensured comparability between groups, strengthening the validity of the observed treatment effects. The consistency in patient characteristics in both studies supports the reliability of our results.[8]The change in hemoglobin levels showed a significantly greater improvement in the IV iron group compared to the oral iron group. Similar results were observed in the study by Qunibi et al. (2011), which demonstrated that intravenous iron therapy led to faster and more substantial hemoglobin increases than oral iron in patients with chronic kidney disease. The superior efficacy of IV iron in our study likely reflects the rapid replenishment of iron stores and bypassing of gastrointestinal absorption barriers, as highlighted in their findings.[9] Serum ferritin levels, an indicator of iron stores, improved significantly more in the IV iron group than in the oral iron group. This is consistent with findings from the study by Charytan et al. (2005), which reported that IV iron therapies significantly increased ferritin levels compared to oral iron. Their research emphasizes the limited ability of oral iron to restore iron stores in the context of chronic disease, particularly when absorption is impaired, further corroborating our observations.[10] Adverse events were more frequent in the oral iron group, with gastrointestinal discomfort being the most common complaint. These findings are comparable to those reported by Silverberg et al. (2001), who noted that oral iron frequently causes gastrointestinal side effects, leading to reduced adherence. Meanwhile, the infusion reactions observed in the IV iron group were mild and infrequent, mirroring their findings, which suggest that IV iron is generally well-tolerated and associated with fewer treatment-limiting side effects.[11] Overall treatment outcomes strongly favored IV iron therapy, with significantly higher rates of achieving hemoglobin targets, improving ferritin levels, and patient satisfaction. These results are supported by the findings of Kalra et al. (2013), who demonstrated superior outcomes with IV iron therapy in terms of hemoglobin normalization and patient-reported quality of life. Their study emphasized the faster onset of action and better efficacy of IV iron, consistent with our results.[12]

CONCLUSION

This study demonstrates that intravenous (IV) iron therapy is significantly more effective than oral iron supplementation in improving hemoglobin levels, replenishing iron stores, and enhancing overall patient satisfaction in anemia of chronic disease. IV iron therapy also exhibited a better safety profile, with fewer adverse events compared to oral iron. These findings highlight the superiority of IV iron as a preferred treatment option, particularly in patients with moderate to severe anemia or those unresponsive to oral iron. Incorporating IV iron therapy into clinical practice can improve patient outcomes and quality of life, making it a vital approach in managing anemia of chronic disease.

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