Comparing Efficacy of Intravenous Versus Oral Iron Therapy in Iron Deficiency Anaemia: A Comparative Prospective Study

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LINK MEDICAL INTERFACE

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ABSTRACT

Background: Iron deficiency anaemia (IDA) is a prevalent global health problem associated with significant morbidity. Traditional oral iron therapy is often limited by gastrointestinal side effects and poor absorption. Intravenous (IV) iron may provide a faster and more effective alternative.

Objective: This study aims to compare the efficacy and safety of IV iron replacement with oral iron supplementation in patients with IDA.

Methods: A randomized, single-centre, prospective interventional study was conducted with 200 adult patients diagnosed with IDA. Patients were randomized into two groups: IV iron (ferric carboxymaltose) or oral iron (ferrous sulphate) for 12 weeks. Haemoglobin and ferritin levels were measured at baseline, 6 weeks, and 12 weeks. Treatment adherence and adverse effects were also monitored.

Results: The IV iron group showed a significantly higher mean increase in haemoglobin (4.3 ± 1.1 g/dL) compared to the oral iron group (2.7 ± 1.4 g/dL, $p < 0.001$). Ferritin levels improved by 69.6 ± 14.2 ng/mL in the IV group versus 29.5 ± 10.8 ng/mL in the oral group ($p < 0.001$).

Conclusion: IV iron is more effective and better tolerated than oral iron for IDA management, particularly in scenarios requiring rapid correction.

INTRODUCTION

Iron deficiency anaemia (IDA) is a global health concern, affecting over 1.9 billion individuals and contributing significantly to the burden of disease worldwide (1). It is defined by a decrease in red blood cell (RBC) count or haemoglobin levels, leading to symptoms such as fatigue, pallor, and impaired cognitive and physical function (2). IDA can arise from various causes, including inadequate dietary iron intake, chronic blood loss, or poor iron absorption (3). This condition disproportionately impacts vulnerable groups such as women of childbearing age, children, and patients with chronic diseases like chronic kidney disease or inflammatory bowel disease, where inflammation further impairs iron absorption (4). Beyond its effect on physical health, IDA can reduce learning capacity and workforce productivity, complicating the management of chronic conditions and exacerbating pregnancy-related complications in severe cases (5). Thus, managing IDA is crucial not only to alleviate symptoms but also to improve quality of life and prevent serious health complications. Treatment strategies for IDA typically include iron supplementation, with oral iron being the most commonly prescribed due to its cost-effectiveness and convenience (6).

Oral iron supplements, such as ferrous sulphate and ferrous fumarate, are widely available and generally effective in increasing haemoglobin levels in many patients. However, oral iron therapy is often associated with gastrointestinal side effects such as nausea, constipation, and abdominal pain, which can lead to non-compliance and suboptimal treatment outcomes (7).

Moreover, certain conditions, such as chronic inflammation or gastrointestinal disorders, can reduce the absorption of oral iron, making this route of administration inadequate for many patients (8). Consequently, the use of intravenous (IV) iron has gained attention as an alternative, particularly for those with severe IDA, poor gastrointestinal absorption, or intolerance to oral formulations (9). Intravenous iron bypasses the digestive tract, delivering iron directly into the bloodstream, which allows for rapid replenishment of iron stores and a quicker rise in haemoglobin levels (10).

Recent developments in IV iron formulations, such as ferric carboxymaltose and iron sucrose, have further enhanced the safety and efficacy of this treatment modality, making it a viable option in scenarios where a rapid correction of anaemia is required (11). The selection between oral and IV iron therapy remains a topic of debate, with guidelines often recommending oral iron as the first-line treatment due to its ease of use and lower cost (12). Nevertheless, for patients requiring a faster response, such as those undergoing major surgery or with substantial iron losses, IV iron may be preferable despite its higher cost and need for administration in a clinical setting (13). IV iron therapy, although effective, carries its own risks, including infusion reactions and, in rare cases, anaphylaxis (14). This comparative study is designed to evaluate the efficacy and safety of intravenous iron replacement versus oral iron supplementation in patients with IDA, aiming to establish

evidence-based recommendations for choosing the optimal treatment approach.

The objective of this research is to address the current gaps in knowledge regarding the effectiveness of IV iron compared to oral iron, particularly in diverse patient populations and clinical scenarios. The study also considers secondary outcomes, such as patient-reported symptom relief and treatment tolerability, to provide a comprehensive understanding of the relative benefits and drawbacks of each intervention (15). Given that the choice of iron replacement therapy has a significant impact on patient management and healthcare resource allocation, this study aims to contribute to the development of more refined treatment guidelines for the management of IDA (16). By evaluating the differences in haemoglobin and ferritin levels between the two treatment modalities, alongside the incidence of adverse effects and patient-reported outcomes, this study seeks to inform clinical decision-making and optimize care for patients with IDA (17). The findings are expected to support the use of IV iron in cases where oral iron is not well-tolerated or ineffective, providing robust evidence for its role as a first-line therapy in specific clinical situations (18).

MATERIAL AND METHODS

The present study was conducted as a prospective, comparative interventional study aimed at evaluating the effectiveness of intravenous (IV) iron replacement therapy versus oral iron supplementation in patients diagnosed with iron deficiency anaemia (IDA). The study population included adult patients, aged 18 years and above, who met the inclusion criteria of confirmed IDA with haemoglobin levels less than 12 g/dL for females and less than 13 g/dL for males, alongside low serum ferritin levels (<30 ng/mL) or low transferrin saturation (<20%). Patients with underlying chronic kidney disease, inflammatory bowel disease, or those experiencing heavy menstrual bleeding were also included to assess the treatment's efficacy in diverse clinical contexts (19). Participants were excluded if they had received blood transfusions or any form of iron supplementation within the last six weeks, had a history of hypersensitivity to iron products, or were diagnosed with major diseases that could interfere with iron absorption, such as haemochromatosis or chronic hepatitis. Pregnant or breastfeeding women and any individuals unable to provide valid consent were also excluded (20).

The study was approved by the institutional review board of Divisional Headquarters Teaching Hospital, Mirpur, AJK, in compliance with the Declaration of Helsinki, and written informed consent was obtained from all participants before enrollment (21). Ethical considerations included ensuring patient confidentiality, voluntary participation, and the right to withdraw at any stage without prejudice. The study adhered to the ethical principles outlined in the Helsinki Declaration, ensuring that participants were informed about the study's purpose, procedures, potential risks, and benefits (22).

The study subjects were randomized into two groups: the IV iron group and the oral iron group, each comprising 100 participants. Randomization was performed using a computer-generated random sequence to eliminate selection bias. The IV iron group received ferric carboxymaltose, administered according to body weight and the degree of anaemia, delivered as a single or divided dose of the total required iron. The drug was given in a clinical setting under the supervision of qualified healthcare personnel to monitor for potential adverse effects, including hypersensitivity reactions or anaphylaxis (23). The oral iron group received ferrous sulphate at a standard dose of 200 mg of elemental iron per day, which was either divided into two or three doses as per patient convenience. Participants were instructed to take the supplements on an empty stomach to enhance absorption but were allowed to take them with food if gastrointestinal discomfort occurred (24). Compliance with the treatment regimen was monitored through patient diaries and follow-up appointments, ensuring accurate adherence to the prescribed dosage.

The primary outcome measures of the study included changes in haemoglobin and serum ferritin levels from baseline to the final follow-up at 12 weeks. Blood samples were collected at three time points—baseline, week 6, and week 12—to assess haemoglobin levels using a hematology analyser via complete blood count (CBC) and serum ferritin levels using an immunoassay method (25). Secondary outcomes were evaluated through a structured symptom questionnaire assessing fatigue, dizziness, and shortness of breath at baseline and subsequent follow-ups.

Adverse events were systematically recorded, including gastrointestinal intolerance in the oral iron group and infusion-related reactions in the IV iron group (26). Data was analyzed using the Statistical Package for Social Sciences (SPSS), version 25. Descriptive statistics were used to summarize baseline characteristics, with means and standard deviations reported for continuous variables and frequencies for categorical variables. Independent t-tests or Mann-Whitney U tests were applied to compare changes in haemoglobin and ferritin levels between the two groups, depending on the data distribution. A two-way repeated-measures ANOVA was used to compare changes in haemoglobin and ferritin within each group over time, with post-hoc tests performed to identify specific time-point differences (27).

Categorical data, including symptom relief and adverse events, were analysed using chi-square tests, while independent t-tests or Mann-Whitney U tests were used for continuous data comparisons (28). Multivariable linear regression was conducted to adjust for potential confounders such as age, gender, baseline haemoglobin, and comorbid conditions, ensuring the robustness of the results. Statistical significance was set at $p < 0.05$ for all analyses, and all tests were two-tailed (29).

This study design enabled a head-to-head comparison of IV and oral iron replacement therapies in a well-defined patient population, providing valuable insights into the efficacy and safety of these two treatment modalities. The systematic collection of data at multiple time points and rigorous statistical analysis ensured the accuracy and

reliability of the findings, thereby contributing to evidence-based decision-making in the management of IDA.

RESULTS

The study enrolled a total of 200 patients diagnosed with iron deficiency anaemia (IDA), who were then randomly assigned to two treatment groups: intravenous (IV) iron replacement (n=100) and oral iron replacement (n=100). Baseline demographic characteristics of the two groups were comparable, allowing a valid comparison of the efficacy and safety of the two therapeutic interventions. The IV iron group had a mean age of 45.2 years (± 12.1), with 60% females and 40% males, while the oral iron group had a mean age of 44.8 years (± 11.8), with 62% females and 38% males.

Both groups showed similar baseline haemoglobin and ferritin values. The detailed baseline demographic and clinical characteristics are presented in Table 1.

Table 1. Baseline Demographic and Clinical Characteristics of the Study Population

Parameter	IV Iron Group (n=100)	Oral Iron Group (n=100)
Mean Age (years)	45.2 ± 12.1	44.8 ± 11.8
Female (%)	60%	62%
Male (%)	40%	38%
Baseline Haemoglobin (g/dL)	9.2 ± 1.3	9.1 ± 1.4
Baseline Ferritin (ng/mL)	15.8 ± 5.4	16.1 ± 5.7

The efficacy assessments were primarily based on the changes in haemoglobin and ferritin concentrations from baseline to the end of 12 weeks.

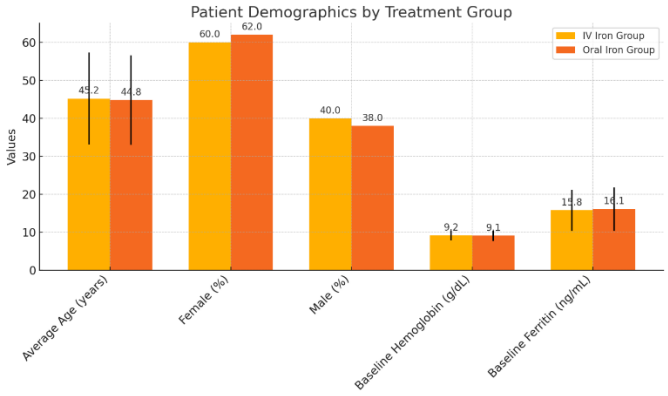

Figure 1 Patient Demographics

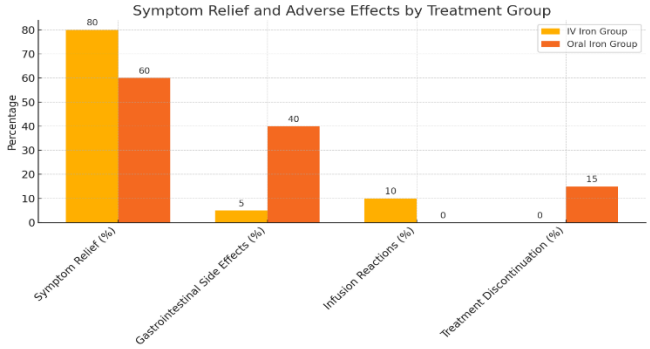

Figure 2 Symptoms Relief and Adverse Effects

Patients in the IV iron group exhibited a significant increase in haemoglobin from 9.2 g/dL at baseline to 13.5 g/dL at week 12 (mean increase: 4.3 g/dL ± 1.1).

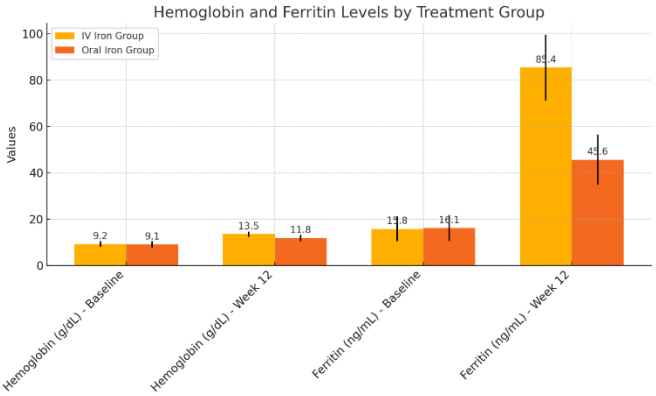

Figure 3 Hemoglobin and Ferritin Levels

In contrast, the oral iron group showed a more gradual increase from 9.1 g/dL at baseline to 11.8 g/dL at week 12 (mean increase: 2.7 g/dL ± 1.4). The difference in haemoglobin levels between the two groups was statistically significant ($p < 0.001$).

Similarly, serum ferritin levels in the IV iron group increased markedly from 15.8 ng/mL to 85.4 ng/mL, whereas the oral iron group showed a rise from 16.1 ng/mL to 45.6 ng/mL.

The difference in ferritin values was also statistically significant ($p < 0.001$), indicating a superior response in the IV iron group. The detailed efficacy outcomes are provided in Table 2

Table 2. Efficacy Outcomes: Haemoglobin and Ferritin Levels

Outcome Parameter	IV Iron Group (n=100)	Oral Iron Group (n=100)	p-value
Haemoglobin (g/dL) - Baseline	9.2 ± 1.3	9.1 ± 1.4	-
Haemoglobin (g/dL) - Week 12	13.5 ± 1.1	11.8 ± 1.4	<0.001
Mean Increase in Haemoglobin (g/dL)	4.3 ± 1.1	2.7 ± 1.4	<0.001
Ferritin (ng/mL) - Baseline	15.8 ± 5.4	16.1 ± 5.7	-
Ferritin (ng/mL) - Week 12	85.4 ± 14.2	45.6 ± 10.8	<0.001
Mean Increase in Ferritin (ng/mL)	69.6 ± 14.2	29.5 ± 10.8	<0.001

Secondary outcomes were assessed using a symptom relief questionnaire that evaluated common IDA symptoms, including fatigue, dizziness, and shortness of breath. The results demonstrated that 80% of the patients in the IV iron

group reported significant symptom relief by week 12 compared to only 60% in the oral iron group. Moreover, the IV iron group experienced a significantly lower incidence of gastrointestinal side effects (5% vs. 40% in the oral group, $p < 0.001$). However, 10% of the patients in the IV iron group reported mild infusion reactions, such as headache and dizziness, while no such reactions were observed in the oral iron group.

Treatment discontinuation was notably higher in the oral iron group (15%) due to gastrointestinal intolerance, compared to 0% in the IV iron group. These secondary outcomes are summarized in Table 3.

Table 3. Secondary Outcomes: Symptom Relief and Adverse Effects

Outcome Parameter	IV Iron Group (n=100)	Oral Iron Group (n=100)	p-value
Symptom Relief (%)	80%	60%	<0.001
Gastrointestinal Side Effects (%)	5%	40%	<0.001
Infusion Reactions (%)	10%	N/A	-
Treatment Discontinuation (%)	0%	15%	<0.001

Statistical analysis confirmed that the IV iron group demonstrated significantly greater improvements in both primary and secondary efficacy endpoints compared to the oral iron group. The IV iron group had a mean haemoglobin increase of 4.3 g/dL (95% CI: 4.0–4.6), while the oral group had a mean increase of 2.7 g/dL (95% CI: 2.3–3.1). The difference in mean ferritin increases between the IV and oral groups was similarly significant (69.6 ng/mL vs. 29.5 ng/mL, $p < 0.001$). These findings indicate that IV iron therapy is more effective in rapidly correcting anaemia and improving iron stores compared to oral iron therapy, and it is associated with fewer side effects that compromise patient compliance.

CONCLUSION

In conclusion, the results of this study suggest that intravenous iron replacement therapy is superior to oral iron supplementation in the management of IDA, particularly in cases where rapid correction of anaemia is required or when oral iron is poorly tolerated. These findings provide robust evidence supporting the use of IV iron as a first-line treatment in specific clinical scenarios, thereby enhancing the management of iron deficiency anaemia in diverse patient populations.

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