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SYSTEMATIC REVIEW

A Systematic Review Investigates the Safety and Efficacy of Intravenous Iron Dosing in Peritoneal Dialysis

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Abstract

Aims/Background Anaemia is a common complication in chronic kidney disease, particularly in people with advanced kidney failure, contributing to increased morbidity and mortality. Iron repletion and erythropoietin-stimulating agents are widely used to manage anaemia, reducing the need for blood transfusions. However, these treatments carry risks, including thrombosis and cardiovascular issues. While intravenous iron is an established therapy for people receiving haemodialysis, its safety and efficacy in people undergoing peritoneal dialysis remain uncertain, partly due to limited data. This review assesses the current evidence on intravenous iron for managing anaemia in peritoneal dialysis, focusing on its impact on iron status, safety, and clinical outcomes.

Methods Systematic searches of MEDLINE, Embase, Cochrane Library, HMIC, AMED and CINAHL were conducted. All eligible studies investigating intravenous iron therapy in adults with end-stage kidney failure undergoing peritoneal dialysis were included. The risk of bias was assessed using the Joanna Briggs Institute checklists for randomised, quasi-randomised and cohort studies. Sensitivity analysis was performed by comparing fixed and random effects models, removing outliers and performing a leave-one-out analysis. Studies had considerable heterogeneity when tested with Cochran's Q Test and the I^2 statistic. Where meta-analyses were not possible, narrative syntheses were conducted due to expected variations in iron dosing and monitoring practices, allowing for a more contextualised analysis of the data across heterogeneous study designs.

Results 9 studies were included (3 studies compared intravenous to oral iron). The mean ferritin increase was 153.07 ng/mL (95% confidence interval (CI): 107.30–198.84; $p < 0.0001$) after sensitivity analysis. The mean transferrin saturation increase was 9.29% (95% CI: 2.98–15.61; $p = 0.0039$).

Conclusion Despite the variability, the included studies consistently show that intravenous (IV) iron improves ferritin, transferrin saturation, haemoglobin, and haematocrit levels, while reporting few adverse events. Future research should focus on optimal dosing, safety, and outcomes beyond anaemia, such as cardiovascular health and quality of life, to maximise patient benefits.

Systematic Review Registration PROSPERO (CRD42022363043).

Key words: renal insufficiency; peritoneal dialysis; anemia; iron deficiencies

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Introduction

Anaemia is a common and significant complication in people with chronic kidney disease (CKD) and end-stage kidney failure (ESKF), contributing to higher

morbidity and mortality rates. The prevalence of anaemia in CKD varies considerably, with rates ranging from 8.4% in stage 1 to 53.4% in stage 5, underscoring the critical need for effective management strategies (Inker et al, 2019; Perlman et al, 2019; Stauffer and Fan, 2014). Treatment strategies often include iron repletion and erythropoietin stimulating agents (ESAs) to reduce dependence on blood transfusions and mitigate associated infectious and immunologic risks. Although these treatments have improved outcomes for people with CKD-related anaemia, ESA use is associated with serious adverse effects, including increased risks of thrombosis and cardiovascular complications at higher haemoglobin targets, as shown by large, randomised trials (Besarab et al, 1998; Drüeke et al, 2006; Singh et al, 2006a).

Erythropoietin (EPO) functions as the controlling factor in erythropoiesis, while iron as the essential building block for haemoglobin synthesis. A decrease in iron or EPO levels, or both, results in the inhibition of erythropoiesis and the development of anaemia (Goodnough, 2012; Kalantar-Zadeh et al, 2009). There are several factors that can also inhibit erythropoiesis, leading to anaemia, including uraemic toxins, inflammatory cytokines (interleukins) and secondary hyperparathyroidism. However, the most common is iron deficiency.

It is important to recognise the definition of iron deficiency and anaemia in people with CKD, which is historically based on 3 parameters: haemoglobin (Hb); serum ferritin (SF), an indicator of stored iron and transferrin saturation (TSAT), an indicator of circulating iron. In CKD, absolute iron deficiency has been defined as TSAT $<$20% and ferritin $<$100 ng/mL in people not on haemodialysis therapy or $<$200 ng/mL in people receiving haemodialysis. Functional iron deficiency has been defined as TSAT $<$20% and ferritin $>$100 ng/mL in people not on dialysis therapy or $>$200 ng/mL in people receiving haemodialysis (Macdougall et al, 2019).

The standard treatment for people undergoing maintenance haemodialysis (HD) involves iron repletion using intravenous (IV) iron preparations, particularly following the findings of the PIVOTAL trial, which demonstrated that proactive "high-dose" IV iron reduced the need for ESAs and blood transfusions without increasing the incidence of infection or hospitalisation and led to a 15% reduction in hospitalisations for heart failure and all-cause mortality (Drüeke and Parfrey, 2012).

However, the safety and efficacy of IV iron in patients undergoing peritoneal dialysis (PD) remain uncertain due to the limited number of randomised controlled trials (RCTs) and concerns about potential iron overload, cardiovascular complications, and increased infection risks. Major guidelines, including those from the National Institute for Health and Care Excellence (NICE) (2021), Kidney Disease Improving Global Outcomes (Drüeke and Parfrey, 2012), National Kidney Foundation Kidney Disease Outcomes Quality Initiative (KDOQI, 2006), and UK Kidney Association (UKKA) (2024) do not provide specific recommendations for IV iron use in the PD population. This uncertainty is further reflected in studies such as the Peritoneal Dialysis Outcomes and Practice Patterns Study (PDOPPS), which found significant variability in the use of ESA and iron therapy among PD patients across different countries (Perl et al, 2016).

The NIMO-CKD (Kalra et al, 2020) study demonstrated that higher doses of IV iron isomaltoside significantly reduced the likelihood of needing retreatment at 1 year and resulted in greater haemoglobin increases in non-dialysis-dependent CKD patients with anaemia, compared to lower doses. Similarly, the FIND-CKD trial (Macdougall et al, 2014) found that targeting higher ferritin with IV ferric carboxymaltose led to reduced need for additional anaemia treatments and greater haemoglobin improvements when compared to oral iron or lower ferritin targets, without increasing adverse events. The IRONMAN (Kalra et al, 2022) trial extended these findings to patients with heart failure, where IV ferric derisomaltose reduced serious cardiac events and hospitalisations, particularly during the coronavirus disease 2019 (COVID-19) period, highlighting the broader benefits of IV iron in anaemia and cardiovascular management.

Due to gaps in current data and the absence of clear guidelines for managing iron supplementation in individuals receiving peritoneal dialysis (PD), recent large studies, such as PIVOTAL, NIMO-CKD, FIND-CKD, and IRONMAN, are often referred to in order to provide insights into the optimal use of IV iron in similar populations. Despite these promising findings, guidelines lack specific recommendations for managing iron deficiency in people receiving PD because the varying efficacy and safety of IV iron administration across different patient populations necessitate further investigation. A Cochrane review conducted in 2019 did not find sufficient evidence to determine if the method of administration of iron has an effect on all-cause mortality, cardiovascular death or quality of life (O'Lone et al, 2019). This is because most of the studies available are small and have short follow-up periods. They also concluded that there is a low certainty of evidence that IV iron increases Hb, SF or TSAT when compared with oral administration in people with CKD. However, the authors did conclude that IV iron reduces the necessary dose of ESAs to maintain a target Hb as compared with oral iron use.

This systematic review aimed to evaluate the current evidence on the efficacy of IV iron in treating anaemia in people receiving PD, with secondary objectives exploring infection rates, hospital admissions, additional anaemia management needs, mortality rates, and the impact on patients' quality of life. By synthesising these findings, this review will contribute to a clearer understanding of the role of IV iron in managing anaemia among people receiving PD, ultimately aiming to improve clinical outcomes for this vulnerable population.

Methods

This study was conducted in accordance with the Cochrane Handbook for Systematic Reviews of Interventions and adhered to the guidelines established by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Page et al, 2021). The PRISMA checklist is available in **Supplementary Material 1**. The study protocol is registered on the PROSPERO database under registration number CRD42022363043: https://www.crd.york.ac.uk/PROSPERO/view/CRD42022363043.

Literature Search

To obtain usable research data, six databases were searched (Medline, Embase, Cochrane Library, HMIC, AMED and CINAHL) from their inception to 1 October 2024. The search was restricted to English-language studies. The search algorithm was tailored to meet the specific requirements of each database, and the detailed search strategy is provided in **Supplementary Material 2**.

Eligibility Criteria and Literature Screening

The research question and eligibility criteria for this systematic review were formulated using the Population, Intervention, Comparison, Outcome (PICO) method:

- Population: Adults undergoing peritoneal dialysis.
- Intervention: Intravenous iron infusion.
- Comparison: Oral iron, or no comparator.
- Outcomes: Efficacy (haemoglobin, haematocrit, ferritin, transferrin saturation or ESA dose), infection, admissions, mortality, quality of life and acceptability.

Inclusion criteria for the study were: (1) patients undergoing peritoneal dialysis (all forms); (2) intravenous iron infusion; (3) randomised control trials, cohort study or quasi-randomised study. Case reports and reviews were excluded. Studies that did not primarily involve peritoneal dialysis patients or the administration of intravenous iron were excluded.

Titles and abstracts from the search results were screened, and relevant or potentially relevant studies underwent full-text reviews. Two independent authors (SS and RM) applied the inclusion and exclusion criteria, with disagreements resolved through discussion or, if necessary, consultation with a third reviewer (SB). A Preferred Reporting Item for Systematic Reviews and Meta-analyses (PRISMA) diagram (Fig. 1) is shown below.

Data Extraction and Review

Screened studies were uploaded to the Covidence™ systematic review software (Veritas Health Innovation, Melbourne, VIC, Australia). Two researchers (SS and RM) independently extracted data from the articles. Numerical data were obtained from tables, text, or figures. Any discrepancies that arose during the process were discussed and resolved with the supervising author (SB). The included studies are summarised in Table 1.

Quality Evaluation

The Joanna Briggs Institute checklists for risk-of-bias (randomised controlled trials, cohort studies, quasi-randomised studies) were employed to assess the quality of the included studies. Two researchers (SS and RM) independently utilised these tools during the evaluation process. Discrepancies between researchers were resolved by consulting the supervising author (SB).

Data Analysis

R version 4.4.2™ (R Project 2024, Austria, https://cran.r-project.org/bin/windows/base/old/4.4.2/) was used to analyse the data and generate forest plots. Continuous data was assessed using mean difference (MD) or standard mean difference (SMD) with 95% confidence intervals (CI), no dichotomous data was extracted. A difference was considered statistically significant when the *p*-value was <0.05. Statistical heterogeneity was calculated using Cochran's Q Test and I^2 statistic. When $I^2 > 50\%$ (and $Q = p < 0.05$), indicating significant statistical heterogeneity, effect sizes were combined using a random effects model (if $I^2 < 50\%$ and $Q = p > 0.05$, the fixed-effects model was used). When significant heterogeneity was detected ($I^2 > 50\%$), the stability of the results was evaluated through sensitivity analysis. Sensitivity analysis was performed by comparing fixed- and common-effect models and systematically excluding one study at a time to assess the impact of each study on the overall results. Given the expected heterogeneity in iron dosing, monitoring, and prescribing practices, a narrative synthesis has also been performed to summarise the findings.

Results

1862 studies were found via database searches, and 951 duplicates were identified and removed. A further 831 were removed at the title and abstract screening, and 71 were removed at full-text review. 9 studies were included in this systematic review and meta-analysis (Fig. 1). A summary of included studies is listed in Table 1. A detailed description of the baseline haematological characteristics of the participants of each study is listed in Table 2.

Quality Assessment

The risk of bias was evaluated independently by two authors using Joanna Briggs Institute (JBI) checklists for RCTs, Cohort and non-randomised studies (Fig. 2) (JBI, 2024).

Serum Ferritin

Intravenous (IV) iron consistently demonstrated significant increases in serum ferritin levels across studies, outperforming oral iron, which produced more modest improvements. The magnitude of ferritin elevation varied but was consistently greater in the IV iron groups over time (Table 3). Baseline ferritin levels ranged widely across studies, from 46.1 to 323 ng/mL. While Singh et al (2006b) did not report numerical changes in ferritin, they observed a statistically significant increase from baseline in the IV iron group, which was not observed in the oral iron group. A random-effects model (Fig. 3) estimated a mean ferritin increase of 118.62 ng/mL (95% CI: 61.98–175.26; $p < 0.0001$), with high heterogeneity ($I^2 = 97.1\%$; $p < 0.0001$).

Table 1. Summary of studies.

Author, Year, Location	Research design	Duration	Participants	Intervention and comparator	Primary outcome(s)
Prakash et al, 2001 Canada	Retrospective cohort study	1 week	61 (Total) 33 (Iron dextran) 23 (Iron saccharate) 5 (Both)	Iron dextran or iron saccharate 500 mg (25 mg test then 475 mg) (Initially iron dextran, switched to iron saccharate once available)	Hb TSAT Ferritin Hct
Portolés-Pérez et al, 2019 Spain	Retrospective cohort study	12 months	91	Ferric carboxymaltose 500 or 1000 mg	Ferritin TSAT EEI
Johnson et al, 2001 Australia	Prospective cross-over study	12 months	28	Iron polymaltose 200 mg every 2 months Alternating 4 months: oral, IV, oral Comparator: Ferrous sulphate 350 mg BD	Hb TSAT Ferritin ESA
Ahsan, 1998 USA	Non-randomised experimental study	6 months	25	Iron dextran 1000 mg (25 mg test then 975 mg) Single dose Comparator: Ferrous sulphate 325 mg TDS	Hct TSAT
Richardson et al, 2001 UK	Non-randomised experimental study	13 months	81	Iron dextran 300 mg then 200 mg	Hb Ferritin %HRC ESA

Table 1. Continued.

Author, Year, Location	Research design	Duration	Participants	Intervention and comparator	Primary outcome(s)
Dittrich et al, 2002 Austria	Non-randomised experimental study	12 months	45	Iron sucrose 50 mg every other week until serum ferritin >100 µg/L then monthly	ERI Hb ESA Ferritin TSAT Serum iron
Mitsopoulos et al, 2020 Greece	Non-randomised experimental study	9 months	18	Iron sucrose 6 monthly doses, 1st dose 200 mg, with 5 further doses of 100 mg.	Hb Ferritin TSAT
Singh et al, 2006b USA	Randomised controlled trial	12 weeks	96	Iron sucrose 3 divided doses: 300 mg (day 1 & 15), 400 mg (day 29)	Peak Hb increase
Li and Wang, 2008 China	Randomised controlled trial	8 weeks	46	Iron sucrose 200 mg weekly for 4 weeks then alternate weeks for 4 weeks Comparator: Ferrous succinate 200 mg TDS	Response rate (Hb increase >15 g/L or Hct increase >5%) Hct

Hb, haemoglobin; TSAT, transferrin saturation; Hct, haematocrit; EEI, ESA effectiveness index; ESA, erythropoietin stimulating agent; %HRC, percentage of hypochromic red cells; TDS, three times a day; BD, twice a day; IV, intravenous; ERI, erythropoietin resistance index.

Table 2. Baseline haematological characteristics of study participants.

Study	Serum ferritin (ng/mL)	Transferrin saturation (%)	Haemoglobin (g/dL)	ESA dose	Haematocrit (%)
Prakash et al, 2001	104.9 ng/mL	17%	9.8 g/dL	7279 IU/week	29%
Portolés-Pérez et al, 2019	213.4 ± 145.8 ng/mL	18.6 ± 7.8%	10.7 ± 1.2 g/dL	80 (40–160) µg/month	ND
Johnson et al, 2001	323 ± 46 ng/mL	24.2 ± 1.7%	10.7 ± 0.3 g/dL	91.0 ± 10.0 U/kg/week	ND
Ahsan, 1998	IV: 89.9 ± 46.5 ng/mL Oral: 174.1 ± 56.2 ng/mL	IV: 11.3 ± 3.5% Oral: 30.1 ± 3.5%	ND	IV: 7886 ± 1449 U/week Oral: 6370 ± 1553 U/week	IV: 31.0 ± 0.9% Oral: 33.0 ± 1.0%
Richardson et al, 2001	240 ng/mL (107–390)	ND	11.0 g/dL (10.1–12.6)	42 (25–95) IU/kg/week	ND
Dittrich et al, 2002	Deficient: 46.1 (30.8–66.5) ng/mL Functional: 179.0 (124.5–214.3) ng/mL Replete: 199.5 (154.0–340.8) ng/mL	Deficient: 16.30% (10.13–21.98) Functional: 16.62% (10.95–18.13) Replete: 25.33% (22.55–38.99)	Deficient: 11.9 (11.3–12.3) g/dL Functional: 11.5 (10.8–12.0) g/dL Replete: 11.6 (10.9–13.1) g/dL	Deficient: 122.0 (70.4–153.8) IU/kg/week Functional: 96.3 (53.7–134.0) IU/kg/week Replete: 30.8 (0.0–85.4) IU/kg/week	ND
Mitsopoulos et al, 2020	143 ± 111 ng/mL	26.2 ± 7.1%	10.0 ± 0.9 g/dL	72.2 ± 88.8 U/kg/week	ND
Singh et al, 2006b	IV: 167.5 ng/mL Oral: 194.2 ng/mL	IV: 19.80% Oral: 16.80%	IV: 10.6 g/dL Oral: 10.5 g/dL	IV: 11,681 IU/week Oral: 7932 IU/week	ND
Li and Wang, 2008	IV: 110.6 ± 54.1 ng/mL Oral: 111.2 ± 54.8 ng/mL	IV: 19.4 ± 8.8% Oral: 19.3 ± 8.1%	IV: 8.8 ± 0.8 g/dL Oral: 8.8 ± 0.9 g/dL	IV: 114 ± 24 IU/kg/week Oral: 115 ± 25 IU/kg/week	IV: 24.2 ± 2.3% Oral: 24.1 ± 2.8%

Hb, haemoglobin (g/dL); TSAT, transferrin saturation (%); Hct, haematocrit (%); ND, no data.

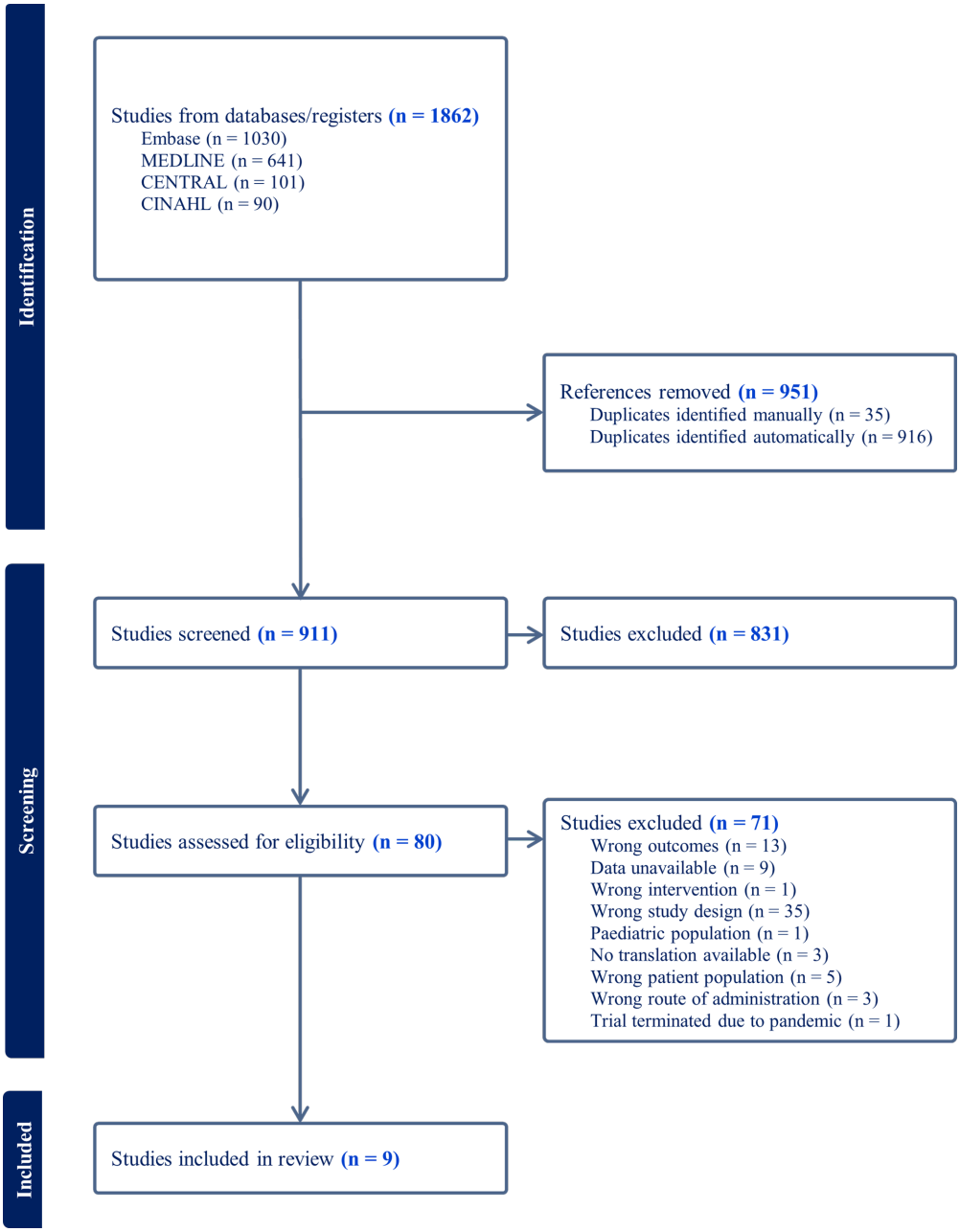

Fig. 1. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) diagram.

Sensitivity analyses were conducted to assess the robustness of our findings by excluding outlier studies (Dittrich et al, 2002; Johnson et al, 2001 excluded) (Fig. 4). This was done to evaluate whether the pooled effect size was influenced by studies with extreme effect estimates. When outliers were excluded, the pooled effect size (random model) increased from 118.62 (95% CI: 61.98–175.26; $p <$ 0.0001) to 153.07 (95% CI: 107.30–198.84; $p < 0.0001$), and heterogeneity (I^2) was reduced from 97.1% to 90.6% ($p < 0.0001$).

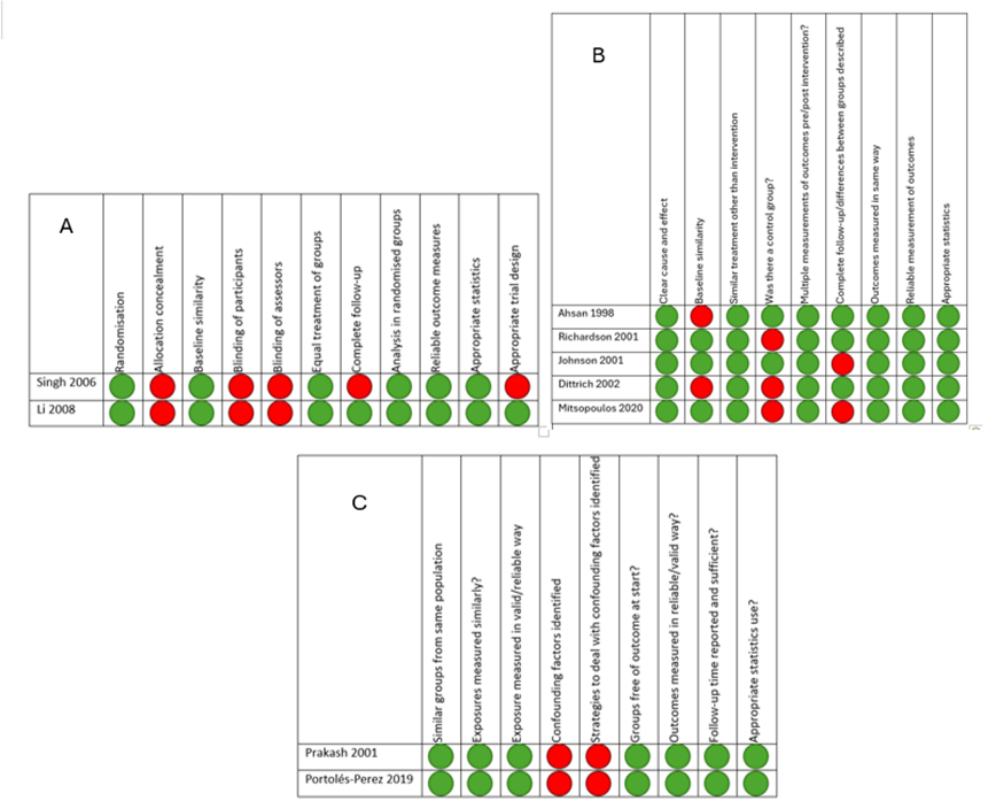

Fig. 2. Joanna Briggs Institute (JBI) Checklists. Green = yes/strong, red = no/weak. (A) Randomised controlled trials. (B) Quasi-randomised and non-randomised studies. (C) Retrospective studies.

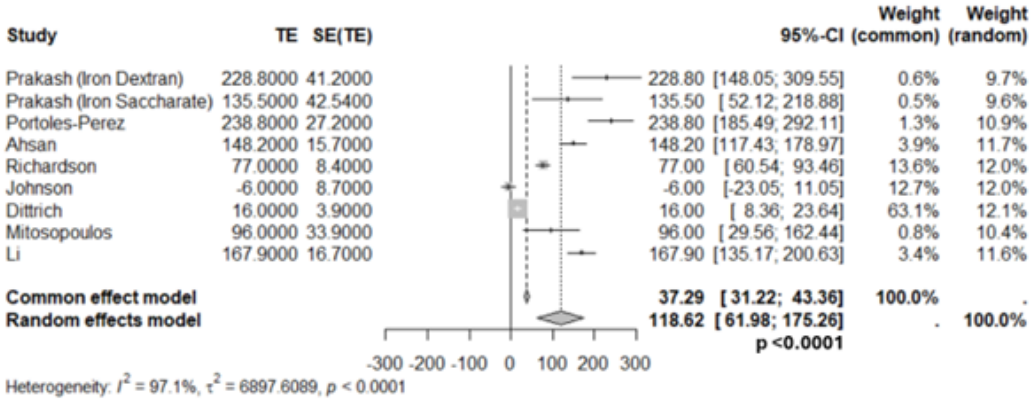

Fig. 3. Forest plot (serum ferritin), random effects model. TE, treatment effect; SE, standard error.

Transferrin Saturation (TSAT)

Intravenous iron generally led to significant and sustained increases in TSAT across studies, often surpassing oral iron in improving iron availability (Table 4).

Table 3. Serum ferritin.

Study ID	Baseline SF IV iron	Baseline SF comparator	ΔSF IV	ΔSF comparator
Prakash et al, 2001	104.9 ng/mL	ND	All: 293.1 at 6 months +188.2 ng/mL Iron Dextran: 310.4 ± 236.7 at 6 months +228.8 ng/mL Iron Saccharate: 279.1 ± 204.0 at 6 months +135.5 ng/mL	ND
Portolés-Pérez et al, 2019	213.4 ± 145.8 ng/mL	ND	452.2 ± 259.6 at 12 months +238.8 ng/mL	ND
Johnson et al, 2001	323 ± 46 ng/mL	ND	Completed: 317 ± 46 ng/mL at 12 months –6 ng/mL Withdrawn: 338 ± 128 ng/mL +15 ng/mL	ND
Ahsan, 1998	89.9 ± 46.5 ng/mL	174.1 ± 56.2 ng/mL	278.9 ± 56.5 at 6 months +189.0 ng/mL	214.9 ± 66.9 at 6 months +40.8 ng/mL
Richardson et al, 2001	240 (107–390) ng/mL	ND	317 (193–497) at 13 months +77 ng/mL	ND

Table 3. Continued.

Study ID	Baseline SF IV iron	Baseline SF comparator	ΔSF IV	ΔSF comparator
Dittrich et al, 2002	Deficient: 46.1 (30.8–66.5) ng/mL Functional: 179.0 (124.5–214.3) ng/mL Replete: 199.5 (154.0–340.8) ng/mL	ND	Deficient: 111.0 (92.0–130.0) at 12 months +64.9 ng/mL Functional: 122.5 (109.3–214.0) at 12 months +56.5 ng/mL Replete: 216.5 (184.3–282.3) at 12 months +17 ng/mL Combined: 124.0 (102.0–206.0) at 12 months +16.0 ng/mL	ND
Mitsopoulos et al, 2020	143 ng/mL ± 111	ND	1 month post-infusion: 260 ± 159 +117 ng/mL 3 months post-infusion: 239 ± 144 +96 ng/mL (–21)	ND
Singh et al, 2006b	167.5 ng/mL	194.2 ng/mL	Significant increase from baseline ($p = 0.0004$)	No significant increase from baseline
Li and Wang, 2008	110.6 ± 54.1 ng/mL	111.2 ± 54.8 ng/mL	466.7 ± 85.3 at 8 weeks +356.1 ng/mL	299.4 ± 83.2 at 8 weeks +188.2 ng/mL

ng/mL, nanograms per milliliter; ND, no data; SF, serum ferritin (ng/mL).

Table 4. Transferrin saturation.

Study ID	Baseline TSAT IV iron	Baseline TSAT comparator	ΔTSAT IV	ΔTSAT comparator
Prakash et al, 2001	17%	ND	All: 24% at 6 months +7% Iron Dextran: 24% ± 9 at 6 months +6% Iron Saccharate: 23% ± 1 at 6 months +7%	ND
Portolés-Pérez et al, 2019	18.6% ± 7.8	ND	27.6% ± 11.1 at 12 months +9.0%	ND
Johnson et al, 2001	24.2% ± 1.7	ND	Completed: 24.8% ± 2.1 at 12 months +0.6% Withdrawn: 22.7% ± 3.0 –1.5%	ND
Ahsan, 1998	11.3% ± 3.5	30.1% ± 3.5	33.7% ± 3.7 at 6 months +22.4%	22.6% ± 4.0 at 6 months –7.5%

Table 4. Continued.

Study ID	Baseline TSAT IV iron	Baseline TSAT comparator	ΔTSAT IV	ΔTSAT comparator
Dittrich et al, 2002	Deficient: 16.30% (10.13–21.98) Functional: 16.62% (10.95–18.13) Replete: 25.33% (22.55–38.99) Combined: 19.21% (12.95–23.98)	ND	Deficient: 20.15% (16.32–30.51) at 12 months +3.85% Functional: 15.23% (11.17–23.72) at 12 months –1.39% Replete: 29.68% (22.22–35.22) at 12 months +4.35% Combined: 23.20% (16.32–31.78) at 12 months +3.99%	ND
Mitsopoulos et al, 2020	26.2% ± 7.1	ND	1 month post-infusion: 33.1% ± 11.4 +6.9% 3 months post-infusion: 32.3% ± 9.5 +6.1% (–0.8%)	ND
Singh et al, 2006b	19.8%	16.8%	No significant difference in increase between groups. Peak TSAT significantly higher than control group ($p = 0.0098$).	No significant difference in increase between groups.
Li and Wang, 2008	19.4% ± 8.8	19.3% ± 8.1	37.8% ± 16.1 at 8 weeks +18.4%	25.7% ± 17.5 at 8 weeks +6.4%

ND, no data.

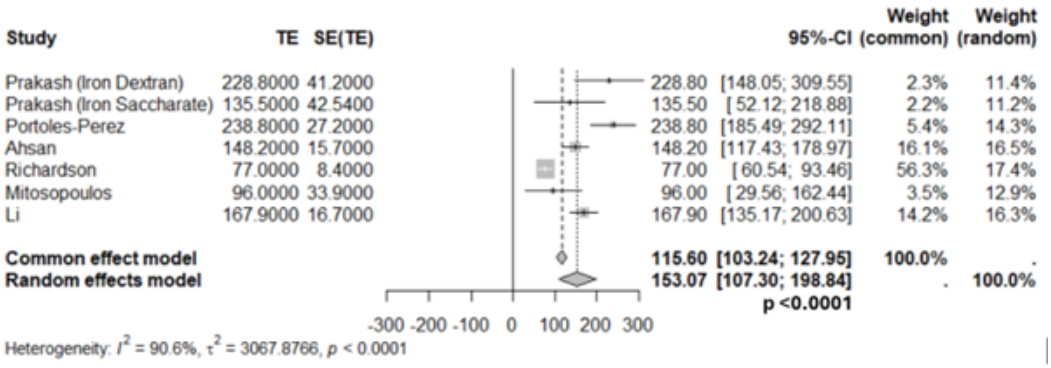

Fig. 4. Forest plot (serum ferritin), random effects model.

Singh et al (2006b) did not provide numerical TSAT values but reported no significant overall difference between groups; however, the peak TSAT was significantly higher in the intravenous iron group compared to the oral group ($p = 0.0098$). Notably, Dittrich et al (2002) observed a reduction in TSAT within the functional group treated with intravenous iron, while increases were reported in the iron-deficient, iron-replete, and combined groups. A random-effects model (Fig. 5) estimated a mean TSAT increase of 9.29% (95% CI: 2.98–15.61; $p = 0.0039$), with high heterogeneity ($I^2 = 99.1\%$; $p < 0.0001$).

Sensitivity analyses by comparing fixed and common effect models, excluding outlier studies and the leave-one-out method did not significantly affect the pooled result or heterogeneity.

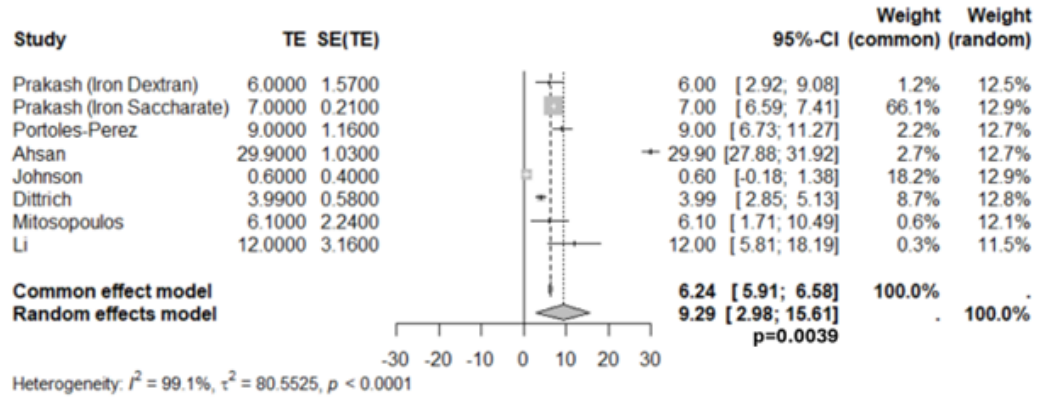

Fig. 5. Forest plot (transferrin saturation), random effects model.

Erythropoietin Stimulating Agent (ESA) Dose and Effectiveness Indexes

There was a variety of units used to report ESA doses, as well as ESA effectiveness index (EEI) and erythropoietin resistance index (ERI), both quotients of ESA dose and haemoglobin. Intravenous (IV) iron therapy consistently reduced ESA requirements across most studies, with greater reductions compared to oral iron or ESA alone. Despite variability in reduction, IV iron effectively lowered the ESA dose required to maintain or improve haemoglobin (Table 5). In Richardson et al

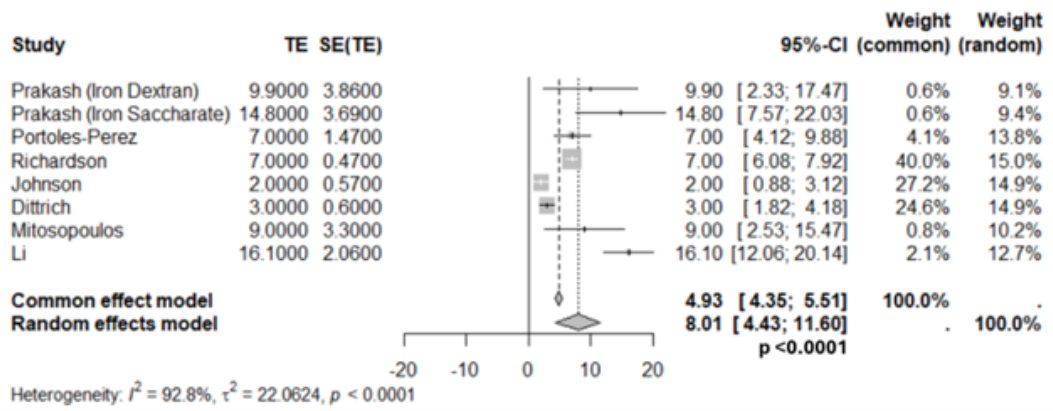

Fig. 6. Forest plot (haemoglobin), random effects model.

(2001), a small increase in ESA dose was reported, however, escalating patient's doses was designed in the study methods. Due to methodological variability in the data reported, no meta-analysis was performed on erythropoietin doses.

Haemoglobin (Hb)

Intravenous (IV) iron consistently led to increases in Hb levels across studies, with the extent of improvement influenced by the iron regimen and baseline Hb levels (Table 6). In the two studies comparing IV and oral iron, Hb improvements were observed in both groups, though IV iron consistently demonstrated a greater effect. Notably, Ahsan (1998) did not report Hb outcomes. Among the remaining eight studies, baseline Hb levels varied significantly, ranging from 88.3 g/L in Li and Wang (2008) to 119 g/L in the iron-deficient subgroup of Dittrich et al (2002) A random-effects model (Fig. 6) estimated a mean Hb increase of 8.01 g/L (95% CI: 4.43–11.60; $p < 0.0001$) with high heterogeneity ($I^2 = 92.8\%$; $p < 0.0001$).

Haematocrit

The available data suggest that IV iron improves haematocrit levels more effectively than oral iron. Among studies reporting haematocrit outcomes, IV iron groups exhibited greater increases, ranging from 1% to 11%. In studies comparing IV and oral iron, oral iron either led to a decrease in haematocrit (–1.6%) or achieved a smaller increase compared to IV iron (6.4% vs. 11.1%) (Table 7). A random-effects model (Fig. 7) estimated a mean haematocrit increase of 5.69% (95% CI: 3.83–7.55; $p < 0.0001$), with high heterogeneity ($I^2 = 91.2\%$; $p = 0.0008$).

Adverse Events

The safety profiles of IV iron administration indicate a generally low incidence of adverse effects across multiple studies. Notably, several investigations reported no significant adverse reactions associated with IV iron treatments. Overall, the findings from these studies suggest that IV iron administration is safe, with serious adverse events being rare and the incidence of infections comparable to alternative treatments (Table 8).

Table 5. Erythropoiesis-stimulating agent dose.

	Baseline ESA dose IV iron	Baseline ESA dose comparator	ΔESA dose IV	ΔESA dose comparator
Prakash et al, 2001	7279 IU/week	ND	Combined: 5900 IU/week at 6 months –1379 IU/week Iron Dextran: 6482.8 ± 3978.7 IU/week at 6 months –1850.5 IU/week Iron Saccharate: 7058.8 ± 6814.2 IU/week at 6 months –1885.6 IU/week	ND
Portolés-Pérez et al, 2019	80 (40–160) µg/month	ND	Mean: 55.7 ± 81 µg/month at 12 months –20.8 µg/month Median: 60 (40–120) µg/month at 12 months –20 µg/month EEI: 1.4 (0–6.1) µg/month per g/dL at 12 months –2.9 µg/month per g/dL	ND
Johnson et al, 2001	91.0 ± 10.0 IU/kg/week	ND	Completed: 82.4 ± 14.5 IU/kg/week at 12 months –8.6 IU/kg/week Withdrawn: 102 ± 13 IU/kg/week +11 IU/kg/week	ND
Ahsan, 1998	7886 ± 1449 IU/week	6370 ± 1553 IU/week	4779 ± 981 IU/week at 6 months –3107 IU/week	9998 ± 1027 IU/week +3628 IU/week

Table 5. Continued.

	Baseline ESA dose IV iron	Baseline ESA dose comparator	ΔESA dose IV	ΔESA dose comparator
Richardson et al, 2001	42 (25–95) IU/kg/week	ND	45 (27–101) IU/kg/week at 13 months +3 IU/kg/week	ND
Dittrich et al, 2002	Deficient: 122.0 (70.4–153.8) IU/kg/week Functional: 96.3 (53.7–134.0) IU/kg/week Replete: 30.8 (0.0–85.4) IU/kg/week Combined: 78.7 (39.8–147.1) IU/kg/week	ND	Deficient: 61.9 (33.6–113.8) IU/kg/week at 12 months –60.1 IU/kg/week Functional: 109.5 (67.9–129.9) IU/kg/week at 12 months +13.2 IU/kg/week Replete: 42.8 (27.1–77.6) IU/kg/week at 12 months +12.0 IU/kg/week Combined: 61.5 (29.9–116.7) IU/kg/week at 12 months –17.2 IU/kg/week	ND
Mitsopoulos et al, 2020	72.2 ± 88.8 IU/kg/week	ND	At 1 month post final infusion: 69.1 ± 76.5 IU/kg/week –3.1 IU/kg/week At 3 months post final infusion: 82.2 ± 104.4 IU/kg/week +10 IU/kg/week (+13.1)	ND
Singh et al, 2006b	11,681 IU/week	7932 IU/week	ND	ND
Li and Wang, 2008	114 ± 24 IU/kg/week	115 ± 25 IU/kg/week	6100 ± 1043 IU/week at 8 weeks –1476 IU/week	7635 ± 1024 IU/week at 8 weeks +0 IU/week

µg/month, micrograms per month; IU/kg/week, international units per kilogram per week; EEI, ESA effectiveness index (micrograms per month per gram per decilitre [µg/month per g/dL]); ND, no data.

Table 6. Haemoglobin.

	Baseline Hb IV iron	Baseline Hb comparator	ΔHb IV	ΔHb comparator
Prakash et al, 2001	98.3 g/L	ND	All: 110.5 g/L at 6 months +12.2 g/L Iron Dextran: 106.7 ± 22.2 g/L at 6 months +9.9 g/L Iron Saccharate: 113.1 ± 17.7 g/L at 6 months +14.8 g/L	ND
Portolés-Pérez et al, 2019	107 ± 12 g/L	ND	114 ± 14 g/L at 12 months +7 g/L	ND
Johnson et al, 2001	107 ± 3 g/L	ND	Completed: 109 ± 3 g/L at 12 months +2 g/L Withdrawn: 101 ± 5 g/L –6 g/L	ND
Richardson et al, 2001	110 g/L (101–126)	ND	117 g/L (110–127) at 13 months +7 g/dL	ND

Table 6. Continued.

	Baseline Hb IV iron	Baseline Hb comparator	ΔHb IV	ΔHb comparator
Dittrich et al, 2002	Deficient: 119 g/L (113–123) Functional: 115 g/L (108–120) Replete: 116 g/L (109–131) Combined: 118 g/L (110–124)	ND	Deficient: 120 (110–128) g/L at 12 months +1 g/L Functional: 120 (109–124) g/L at 12 months +5 g/L Replete: 123 (120–132) g/L at 12 months +7 g/dL Combined: 121 (112–128) g/L at 12 months +3 g/dL	ND
Mitsopoulos et al, 2020	100 ± 9 g/L	ND	At 1 month post final infusion: 109 g/L ± 1.2 +9 g/L At 3 months post final infusion: 109 g/L ± 14 +9 g/L (+0 g/L)	ND
Singh et al, 2006b	106 g/L	105 g/L	Significant increase from baseline at each 2-week interval 59.1% had >10 g/L increase Median time to increase 48.3 d Peak Hb increase 13 g/L	No significant increase from baseline at any 2-week interval 33.3% had >10 g/L increase Median time to increase 51.4 d Peak Hb increase 6 g/L
Li and Wang, 2008	88.3 ± 8.3 g/L	88.6 ± 8.8 g/L	122.1 ± 10.5 at 8 weeks +33.8 g/L	106.3 ± 10.4 at 8 weeks +17.7 g/L

g/L, grams per litre; ND, no data.

Table 7. Haematocrit.

	Baseline Hct IV iron	Baseline Hct comparator	ΔHct IV	ΔHct comparator
Prakash et al, 2001	29%	ND	30% at 6 months +1%	ND
Ahsan, 1998	31.0 ± 0.9%	33.0 ± 1.0%	36.0 ± 1.0% at 6 months +5.0%	31.4 ± 1.1% at 6 months –1.6%
Li and Wang, 2008	24.2 ± 2.3%	24.1 ± 2.8%	35.3 ± 2.5% at 8 weeks +11.1%	30.5 ± 2.4% at 8 weeks +6.4%

ND, no data.

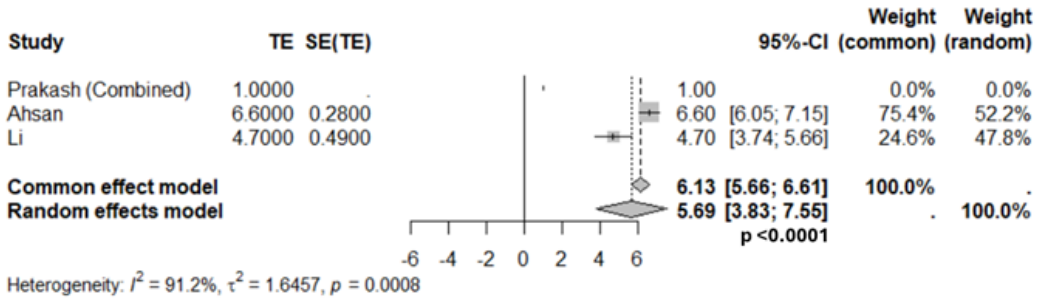

Fig. 7. Forest plot (haemoglobin), random effects model.

Patient Reported Outcome Measures

No data was reported on quality of life, symptom burden or other patient reported outcome measures. Similarly, there was no data on mortality.

Discussion

This review identified several key patterns and themes regarding the use of IV iron in people receiving PD, with substantial heterogeneity observed across studies. Understanding the sources and implications of this heterogeneity is crucial for interpreting the findings, informing future research, and optimising clinical practice to maximise patient outcomes.

Exploring Differences and Reasons for High Heterogeneity

The included studies demonstrated considerable heterogeneity in population characteristics, interventions, outcome measures, and study design, which challenges direct comparisons and limits the feasibility of a meta-analysis. While most studies included patients receiving PD and categorised them by iron status—deficient (ferritin <100 ng/mL), functional (ferritin >100 ng/mL and TSAT <20%), or replete (TSAT >20%)—there were notable differences in how these categories were defined.

Interventions varied widely, with studies employing different IV iron preparations, doses, and dosing intervals, or combining multiple interventions over time. A

Table 8. Adverse events.

Prakash et al, 2001	Iron Dextran: 1 patient experienced anaphylaxis (2.9%), side effects reported in 14.7% of participants. There was no significant difference in the incidence of peritonitis between groups.
Portolés-Pérez et al, 2019	Ferric Carboxymaltose: no hypersensitivity reactions, treatment discontinuations, or dose adjustments due to serious adverse events were reported. Two deaths and seven episodes of peritonitis occurred following ferric carboxymaltose administration, none were attributed to the treatment. Common non-serious adverse events noted included headache and mild hypotension.
Johnson et al, 2001	Increased frequency of gastrointestinal disturbances in the oral group.
Ahsan, 1998	No adverse reactions or abnormalities in liver function tests were documented.
Richardson et al, 2001	No adverse reactions.
Dittrich et al, 2002	Iron Sucrose - systemic side effects reported in 0.5% of applications, with instances of hypotension and nausea occurring after a single administration. Localised pain at the injection site was observed in 0.3% of applications.
Mitsopoulos et al, 2020	Iron Sucrose 3 patients withdrew from the study due to unrelated complications. No significant adverse events were attributed to the IV iron treatment.
Singh et al, 2006b	Iron Sucrose - no serious adverse drug events were recorded. 1 patient discontinued treatment after developing moderate swelling and pruritus, which resolved within two hours. Three episodes of hypotension were reported, though two were likely unrelated to the treatment.
Li and Wang, 2008	Iron Sucrose - no adverse events were noted. 40% of patients in the oral iron group reported gastrointestinal side effects.

total of five IV iron preparations were used, including iron sucrose (n = 4; Dittrich et al, 2002; Mitsopoulos et al, 2020; Singh et al, 2006b; Li and Wang, 2008), iron dextran (n = 3; Prakash et al, 2001; Ahsan, 1998; Richardson et al, 2001), saccharate (n = 1; Prakash et al, 2001), polymaltose (n = 1; Johnson et al, 2001), and ferric carboxymaltose (n = 1; Portolés-Pérez et al, 2019). Follow-up periods ranged from one week (Prakash et al, 2001) to 13 months (Richardson et al, 2001), and no two studies used the same dosing regimen.

Outcome measures also differed across studies. While all studies reported erythropoietin-stimulating agent (ESA) doses and serum ferritin levels, most included TSAT (Richardson et al (2001) did not, Singh et al (2006b) provided numerical baseline data but not for outcome data) and haemoglobin (Hb) (Ahsan (1998) did not) as outcomes, but only three reported haematocrit (Hct) (Prakash et al, 2001; Ahsan, 1998; Li and Wang, 2008). Primary outcomes varied, with Dittrich et al (2002) focusing on the erythropoietin resistance index (ERI), Singh et al (2006b)

on peak Hb increases, and Li and Wang (2008) on response rates in Hb or Hct. Furthermore, 3 studies did not report confidence intervals or standard deviations (Richardson et al, 2001; Dittrich et al, 2002; Singh et al, 2006b), which limits the precision and reliability of reported outcomes.

Methodological differences exacerbated the variability. Approaches to measuring ESA dose changes were inconsistent, employing different units or resistance indices. Additionally, the lack of blinding and control groups in most studies introduced potential bias, undermining the reliability of the findings (only Singh et al (2006b) and Li and Wang (2008) were blinded). Study designs were also diverse, including two retrospective cohorts (Prakash et al, 2001; Portolés-Pérez et al, 2019), one cross-over trial (Johnson et al, 2001), four quasi-randomised studies (Ahsan, 1998; Richardson et al, 2001; Dittrich et al, 2002; Mitsopoulos et al, 2020), and two randomised controlled trials (Singh et al, 2006b; Li and Wang, 2008).

This variability in populations, interventions, outcomes, and methodological approaches, compounded by incomplete reporting of statistical data, further limits the applicability of a meta-analysis. A narrative synthesis provides a more suitable approach to contextualising and interpreting these findings.

Consistency of Study Conclusions

Despite variations in methodology and procedures, the overall direction of the results across studies was broadly consistent, with no study reporting a negative effect of IV iron. Most studies demonstrated improvements in serum ferritin levels, with those including an oral iron comparator typically showing a more substantial effect for IV iron. Only Johnson et al (2001) demonstrated a reduction in serum ferritin, albeit very small. Nearly all studies reported increases in TSAT; however, findings were mixed in specific subgroups. For instance, Dittrich et al (2002) observed a small decrease in TSAT in the functional subgroup, while Singh et al (2006b) found no statistical difference between intravenous and ESA-only groups but reported a significantly higher peak TSAT in the IV iron group. Studies reporting on ESA dose reduction or stability consistently indicated that IV iron either reduced or maintained the ESA dose, with Dittrich et al (2002) subgroup analysis showing minor increases in replete and functional groups. Additionally, haemoglobin and haematocrit levels consistently improved across all studies, regardless of subgroup, following IV iron administration.

This is consistent with the PIVOTAL trial in people on haemodialysis where they saw the median monthly dose of ESAs significantly reduced in the proactive group (IV iron administered when ferritin $<$700 µg/L and TSAT $<$40%) compared to the reactive group, with improvements in haemoglobin in both arms. It is also consistent with the FIND-CKD trial in people with CKD stage 3–5 (not on dialysis) where the high ferritin arm (IV iron administered when ferritin $<$600 µg/L and TSAT $<$40%) had significantly increased haemoglobin when compared to the oral arm.

Common Findings on Influencing Factors and Study Limitations

Two of the quasi-randomised studies recognised the inherent limitations and biases introduced by open-label designs and highlighted the practical challenges of blinding in IV iron trials (Ahsan, 1998; Mitsopoulos et al, 2020). Developing a placebo for IV iron and achieving participant blinding is complex and costly, making them rare in this context. Ahsan (1998) study, which allocated patients with lower iron stores to the IV group, reflects real-world practice; however, it also introduces confounding due to inadequate controls. These common limitations across studies underscore the need for cautious interpretation of findings and for future studies to address these biases more rigorously.

Comparison of IV Iron to Other Iron Supplementation Modalities

Comparative data on IV versus oral iron were limited, with only two studies directly comparing the two (Ahsan, 1998; Li and Wang, 2008), one study comparing ESA alone to ESA plus IV iron (Singh et al, 2006b) and one study comparing oral and IV iron in a cross-over design (Johnson et al, 2001). In the UK, the standard treatment for PD patients involves oral iron with IV "top-ups" if oral iron proves insufficient or is poorly tolerated. IV iron may offer advantages over oral iron in terms of absorption and fewer side effects, while oral iron remains preferable in terms of cost-effectiveness and avoidance of cannulation. Future studies should explore these trade-offs further, especially in relation to patient tolerability and adherence, alongside efficacy outcomes.

In the FIND-CKD trial, they compared 2 IV arms: high ferritin (400–600 µg/L) and low ferritin (100–200 µg/L); to oral iron only in people with CKD stages 3–5, not on dialysis or ESA. There was a significantly reduced incidence of initiation of anaemia therapy (a composite of ESA, transfusion or other iron therapy) when compared to the oral arm.

Dosing Strategies

The reviewed studies highlighted significant variability in the dosing regimens of IV iron, with no two studies using identical formulations, doses, or dosing frequencies. Recent large randomised controlled trials investigating the use of IV iron in different populations (PIVOTAL, FIND-CKD, NIMO-CKD, and IRONMAN) have suggested potentially optimal dosing strategies, though these were beyond the scope of the studies reviewed here. Further research is needed to determine an effective and safe dosing regimen for people receiving PD, balancing efficacy and safety. Evidence on dosing strategies is crucial to guide clinical practice on IV iron administration in this patient population.

The NIMO-CKD trial, conducted among individuals with CKD not on dialysis and with iron deficiency anaemia, found that participants who received higher doses of IV iron (>1000 mg) were significantly more likely to achieve haemoglobin levels exceeding 110 g/L. Furthermore, they had a markedly reduced likelihood of requiring subsequent IV iron treatment.

Future Research

Future research into IV iron therapy for PD patients must address significant gaps in current knowledge to optimise treatment strategies and improve patient outcomes. One critical area is the comparative effectiveness of oral versus IV iron. Although oral iron remains a commonly used treatment, its efficacy compared to total dose IV iron infusion, particularly in achieving and maintaining adequate Hb levels and managing iron stores, has not been fully explored. Direct comparisons are needed to assess the relative benefits, tolerability, and cost-effectiveness of these approaches.

Another important gap lies in the understanding of optimal iron targets. Evidence is limited regarding the risks and benefits of targeting different ferritin and TSAT levels. For instance, the clinical implications of aiming for high iron targets, such as TSAT up to 40% and SF up to 700 ng/mL, versus low targets, such as TSAT up to 20% and SF up to 100 ng/mL, remain unclear. Research is needed to determine how these targets influence anaemia management, risks of iron overload, and broader clinical outcomes.

The studies reviewed have largely concentrated on haematological outcomes, overlooking broader clinical endpoints and patient-reported measures that significantly impact patient well-being. Given the established link between anaemia in dialysis patients and adverse events such as cardiovascular complications and mortality, future research should prioritise examining the effects of IV iron on cardiovascular outcomes, including heart failure and myocardial infarction. Additionally, investigating patient-reported outcomes, such as fatigue, physical function, and overall well-being, could offer valuable insights into how improvements in anaemia translate into enhanced quality of life.

Future trials should also explore the broader impact of IV iron therapy on mortality, infection rates, hospitalisation rates, and the need for blood transfusions. Cognitive function, physical function, and symptom burden, including breathlessness and fatigue, are critical areas that remain underexplored. Moreover, long-term safety outcomes, such as the risks of iron overload, oxidative stress, and associated complications, require further investigation. By addressing these gaps, future studies can provide a more comprehensive understanding of the benefits and risks associated with IV iron therapy, guiding more patient-centred and effective treatment strategies for individuals receiving peritoneal dialysis.

The underlying mechanisms influencing the response to iron therapy also remain poorly understood. Factors such as erythropoietin resistance and the interplay between iron therapy and inflammation need further exploration to develop more personalised treatment approaches. Research should aim to uncover these mechanisms to enable tailored strategies that optimise efficacy while minimising risks.

To address these gaps, future studies must incorporate rigorous methodologies, including randomised controlled trials with adequate blinding to minimise bias. Uniform outcome measures and robust data collection on both clinical and patient-reported outcomes are essential to improve the comparability and relevance of findings. Holistic and multidisciplinary study designs that integrate long-term follow-up are crucial for generating actionable evidence that can guide clinical decision-

making. By addressing these areas, future research will help refine iron therapy strategies, improving outcomes and quality of care for patients on peritoneal dialysis.

Conclusion

This systematic review of iron supplementation in people receiving PD has shown that intravenous iron is effective at improving haematological factors and reducing ESA requirements. However, due to the relatively small studies and high heterogeneity in study design, there remains a lack of overall certainty. It is unclear whether using intravenous iron corresponds to improvements in hard clinical outcomes such as mortality, infection rates or incidence of transfusions. There is an equipoise on which intravenous iron preparation, at which dose and interval are most effective for PD. A randomised trial is rapidly needed.

Key Points

- Iron deficiency is common in people receiving peritoneal dialysis.
- The most optimal method of repletion remains to be validated in randomised controlled trials.
- The trials to date have yet to demonstrate an improvement in clinical outcomes beyond anaemia.
- Until such trials are carried out iron replenishment with oral or intravenous iron remains the mainstay of therapy to improve haemoglobin levels and potential symptoms.

Availability of Data and Materials

All the data of this study are included in this article.

Author Contributions

SS, SH and SB designed the research study. SS and RM performed the research. SS and RM analysed the data. SS drafted the manuscript. All authors contributed to the important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

SB was a previous trustee for KRUK, and has received honorarium from Vifor CSL, Pharmacosmos, GSK and Astellas for lectures. RM, SH and SS declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://www.magonlinelibrary.com/doi/suppl/10.12968/hmed.2024.0874.

References

Ahsan N. Intravenous infusion of total dose iron is superior to oral iron in treatment of anemia in peritoneal dialysis patients: a single center comparative study. Journal of the American Society of Nephrology. 1998; 9: 664–668. https://doi.org/10.1681/ASN.V94664

Besarab A, Bolton WK, Browne JK, Egrie JC, Nissenson AR, Okamoto DM, et al. The effects of normal as compared with low hematocrit values in patients with cardiac disease who are receiving hemodialysis and epoetin. The New England Journal of Medicine. 1998; 339: 584–590. https://doi.org/10.1056/NEJM199808273390903

Dittrich E, Schillinger M, Sunder-Plassmann G, Hörl WH, Vychytil A. Efficacy of a low-dose intravenous iron sucrose regimen in peritoneal dialysis patients. Peritoneal Dialysis International. 2002; 22: 60–66.

Drüeke TB, Parfrey PS. Summary of the KDIGO guideline on anemia and comment: reading between the (guide)line(s). Kidney International. 2012; 82: 952–960. https://doi.org/10.1038/ki.2012.270

Drüeke TB, Locatelli F, Clyne N, Eckardt KU, Macdougall IC, Tsakiris D, et al. Normalization of hemoglobin level in patients with chronic kidney disease and anemia. The New England Journal of Medicine. 2006; 355: 2071–2084. https://doi.org/10.1056/NEJMoa062276

Goodnough LT. Iron deficiency syndromes and iron-restricted erythropoiesis (CME). Transfusion. 2012; 52: 1584–1592. https://doi.org/10.1111/j.1537-2995.2011.03495.x

Inker LA, Grams ME, Levey AS, Coresh J, Cirillo M, Collins JF, et al. Relationship of Estimated GFR and Albuminuria to Concurrent Laboratory Abnormalities: An Individual Participant Data Meta-analysis in a Global Consortium. American Journal of Kidney Diseases. 2019; 73: 206–217. https://doi.org/10.1053/j.ajkd.2018.08.013

Joanne Briggs Institute (JBI). Critical Appraisal Tools. 2024. Available at: https://jbi.global/critical-appraisal-tools (Accessed: 20 December 2024).

Johnson DW, Herzig KA, Gissane R, Campbell SB, Hawley CM, Isbel NM. A prospective crossover trial comparing intermittent intravenous and continuous oral iron supplements in peritoneal dialysis patients. Nephrology, Dialysis, Transplantation. 2001; 16: 1879–1884. https://doi.org/10.1093/ndt/16.9.1879

Kalantar-Zadeh K, Streja E, Miller JE, Nissenson AR. Intravenous iron versus erythropoiesis-stimulating agents: friends or foes in treating chronic kidney disease anemia? Advances in Chronic Kidney Disease. 2009; 16: 143–151. https://doi.org/10.1053/j.ackd.2008.12.008

Kalra PA, Bhandari S, Spyridon M, Davison R, Lawman S, Mikhail A, et al. NIMO-CKD-UK: a real-world, observational study of iron isomaltoside in patients with iron deficiency anaemia and chronic kidney disease. BMC Nephrology. 2020; 21: 539. https://doi.org/10.1186/s12882-020-02180-2

Kalra PR, Cleland JGF, Petrie MC, Thomson EA, Kalra PA, Squire IB, et al. Intravenous ferric derisomaltose in patients with heart failure and iron deficiency in the UK (IRONMAN): an investigator-initiated, prospective, randomised, open-label, blinded-endpoint trial. Lancet. 2022; 400: 2199–2209. https://doi.org/10.1016/S0140-6736(22)02083-9

KDOQI. KDOQI Clinical Practice Guidelines and Clinical Practice Recommendations for Anemia in Chronic Kidney Disease. 2006. Available at: https://kidneyfoundation.cachefly.net/professionals/KDOQI/guidelines_anemia/cpr32.htm (Accessed:

20 December 2024).

Li H, Wang SX. Intravenous iron sucrose in peritoneal dialysis patients with renal anemia. Peritoneal Dialysis International. 2008; 28: 149–154.

Macdougall IC, Bock AH, Carrera F, Eckardt KU, Gaillard C, Van Wyck D, et al. FIND-CKD: a randomized trial of intravenous ferric carboxymaltose versus oral iron in patients with chronic kidney disease and iron deficiency anaemia. Nephrology, Dialysis, Transplantation. 2014; 29: 2075–2084. https://doi.org/10.1093/ndt/gfu201

Macdougall IC, White C, Anker SD, Bhandari S, Farrington K, Kalra PA, et al. Intravenous Iron in Patients Undergoing Maintenance Hemodialysis. The New England Journal of Medicine. 2019; 380: 447–458. https://doi.org/10.1056/NEJMoa1810742

Mitsopoulos E, Lysitska A, Pateinakis P, Lamprou V, Intzevidou E, Minasidis I, et al. Efficacy and safety of a low monthly dose of intravenous iron sucrose in peritoneal dialysis patients. International Urology and Nephrology. 2020; 52: 387–392. https://doi.org/10.1007/s11255-019-02362-4

National Institute for Health and Care Excellence (NICE). Chronic kidney disease: assessment and management. 2021. Available at: https://www.nice.org.uk/guidance/ng203 (Accessed: 20 December 2024).

O'Lone EL, Hodson EM, Nistor I, Bolignano D, Webster AC, Craig JC. Parenteral versus oral iron therapy for adults and children with chronic kidney disease. The Cochrane Database of Systematic Reviews. 2019; 2: CD007857. https://doi.org/10.1002/14651858.CD007857.pub3

Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ (Clinical Research Ed.). 2021; 372: n71. https://doi.org/10.1136/bmj.n71

Perl J, Davies SJ, Lambie M, Pisoni RL, McCullough K, Johnson DW, et al. The Peritoneal Dialysis Outcomes and Practice Patterns Study (PDOPPS): Unifying Efforts to Inform Practice and Improve Global Outcomes in Peritoneal Dialysis. Peritoneal Dialysis International. 2016; 36: 297–307. https://doi.org/10.3747/pdi.2014.00288

Perlman RL, Zhao J, Fuller DS, Bieber B, Li Y, Pisoni RL, et al. International Anemia Prevalence and Management in Peritoneal Dialysis Patients. Peritoneal Dialysis International. 2019; 39: 539–546. https://doi.org/10.3747/pdi.2018.00249

Portolés-Pérez J, Durá-Gúrpide B, Merino-Rivas JL, Martín-Rodriguez L, Hevia-Ojanguren C, Burguera-Vion V, et al. Effectiveness and safety of ferric carboxymaltose therapy in peritoneal dialysis patients: an observational study. Clinical Kidney Journal. 2019; 14: 174–180. https://doi.org/10.1093/ckj/sfz153

Prakash S, Walele A, Dimkovic N, Bargman J, Vas S, Oreopoulos D. Experience with a large dose (500 mg) of intravenous iron dextran and iron saccharate in peritoneal dialysis patients. Peritoneal Dialysis International. 2001; 21: 290–295.

Richardson D, Bartlett C, Jolly H, Will EJ. Intravenous iron for CAPD populations: proactive or reactive strategies? Nephrology, Dialysis, Transplantation. 2001; 16: 115–119. https://doi.org/10.1093/ndt/16.1.115

Singh AK, Szczech L, Tang KL, Barnhart H, Sapp S, Wolfson M, et al. Correction of anemia with epoetin alfa in chronic kidney disease. The New England Journal of Medicine. 2006a; 355: 2085–2098. https://doi.org/10.1056/NEJMoa065485

Singh H, Reed J, Noble S, Cangiano JL, Van Wyck DB. Effect of intravenous iron sucrose in peritoneal dialysis patients who receive erythropoiesis-stimulating agents for anemia: a randomized, controlled trial. Clinical Journal of the American Society of Nephrology. 2006b; 1: 475–482. https://doi.org/10.2215/CJN.01541005

Stauffer ME, Fan T. Prevalence of anemia in chronic kidney disease in the United States. PLoS ONE. 2014; 9: e84943. https://doi.org/10.1371/journal.pone.0084943

UK Kidney Association (UKKA). Clinical Practice Guideline: Anaemia of Chronic Kidney Disease. 2024. Available at: https://ukkidney.org/sites/renal.org/files/FINAL%20VERSION%20-%20%20UKKA%20ANAEMIA%20OF%20CKD%20GUIDELINE%20-%20Sept%202024.pdf (Accessed: 20 December 2024).