Cochrane Commentaries

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Title of review: Parenteral versus oral iron therapy for adults and children with chronic kidney disease

What is this review about?

The use of intravenous compared with oral iron supplements in patients with chronic kidney disease (CKD).

What are the findings?

Ferritin (Figure 1: mean difference 243 µg/L) and transferrin saturation levels (mean difference 10%) were significantly increased by intravenous (IV) iron compared with oral iron, while haemoglobin levels were slightly increased (mean difference 0.9g/dl). The required dose of erythropoiesis stimulating agents (ESA) was significantly reduced in dialysis patients receiving IV iron compared with oral iron (Figure 2). Any change in ESA dose could not be assessed in non-dialysis patients due to lack of trial data. All-cause mortality, cardiovascular mortality, quality of life and patients' adherence to oral iron did not differ significantly but were reported in few studies. Gastrointestinal adverse effects were significantly more common with oral iron while hypotensive and allergic reactions were significantly more common with IV iron.

What are the findings based on?

Twenty eight trials (2098 patients) compared IV with oral iron therapy. Seventeen trials included only patients on haemodialysis or peritoneal dialysis. Nine trials included only non-dialysis patients, one trial included both dialysis and non-dialysis patients and one trial included only patients immediately post- transplant. Only one study enrolled children. The duration of follow up varied from 35 days to 26 months. The most common agents used were IV iron sucrose and oral ferrous sulphate. Nineteen trials included patients on ESAs. There was considerable heterogeneity in all analyses. Heterogeneity remained largely unexplained despite extensive investigation using multiple subgroup analyses, but was likely to be related to the large variation in the relative doses of IV and oral iron used across the studies.

Risk of bias assessment showed that randomization sequence generation and allocation concealment were adequately reported in 12 and six trials respectively. Although no trials reported blinding, all studies were considered at low risk of performance and reporting bias as the primary outcome was laboratory based and unlikely to be influenced by lack of blinding. Reporting of outcome data was complete in 12 studies and 12 studies reported all relevant outcomes. In particular only 50% trials reported on adverse effects. Twelve trials reported receiving support from pharmacological sponsors.

Implications for practice

- Compared with oral iron, IV iron results in higher levels of ferritin and transferrin saturation with a small increase in haemoglobin
- IV iron results in lower doses of ESA compared with oral iron therapy in dialysis patients. Data are not available for non-dialysis patients.
- IV iron is associated with a lower risk of gastrointestinal adverse effects but a higher risk of allergic and hypotensive reactions.
- Study data are inadequate to determine whether mortality and quality of life differ with IV compared with oral iron supplements.

Clinical perspective

This review supports the current use of IV iron in-centre haemodialysis patients to increase iron stores and probably reduce ESA dose and associated cost although there are limited data on all-cause mortality, cardiovascular mortality and morbidity, adverse effects and quality of life. However the trials do not provide sufficient evidence to determine if the benefits exceed the harms in patients with CKD who are receiving peritoneal dialysis or who are not yet requiring dialysis. Further large trials comparing IV with oral iron in these patient groups are required to assess patient-centred outcomes, ESA dose as well as laboratory outcomes to determine if the benefits of IV therapy outweigh the disadvantages including additional clinic visits for treatment.

Citation

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Figure 1: End of treatment or change in ferritin levels in patients with CKD treated with IV or oral iron

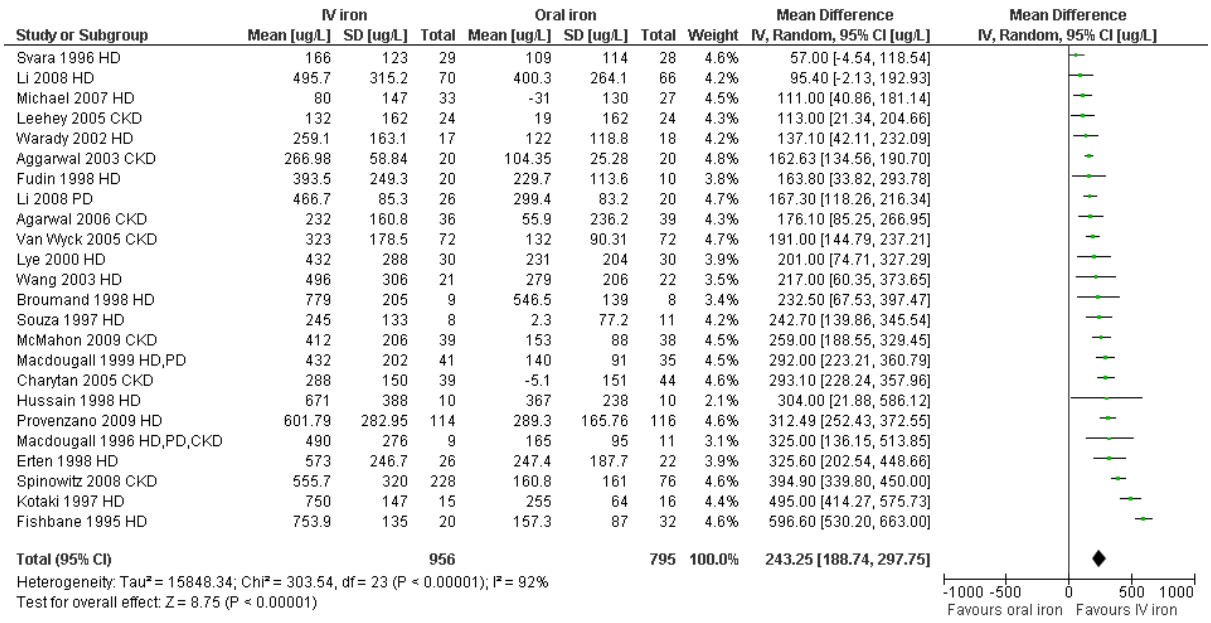
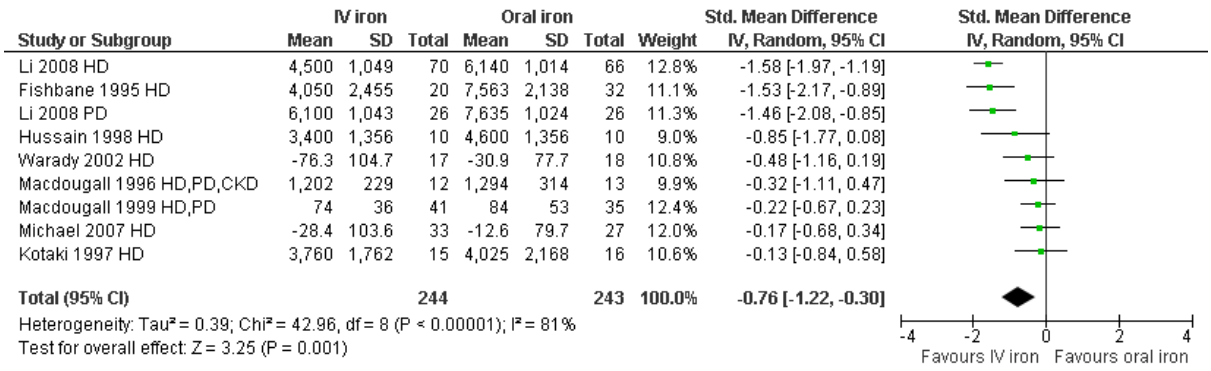


Figure 2: End of treatment or change in ESA dose in dialysis patients treated with IV or oral iron


IV iron
Oral iron
Std. Mean Difference
Std. Mean Difference
Study or Subgroup
Mean SD Total Mean SD Total Weight
IV, Random, 95% CI
IV, Random, 95% CI
Li 2008 HD 4,500 1,049 70 6,140 1,014 66 12.8% -1.58 [-1.97, -1.19]
Fishbane 1995 HD 4,050 2,455 20 7,563 2,138 32 11.1% -1.53 [-2.17, -0.89]
Li 2008 PD 6,100 1,043 26 7,635 1,024 26 11.3% -1.46 [-2.08, -0.85]
Hussain 1998 HD 3,400 1,356 10 4,600 1,356 10 9.0% -0.85 [-1.77, 0.08]
Warady 2002 HD -76.3 104.7 17 -30.9 77.7 18 10.8% -0.48 [-1.16, 0.19]
Macdougall 1996 HD,PD,CKD 1,202 229 12 1,294 314 13 9.9% -0.32 [-1.11, 0.47]
Macdougall 1999 HD,PD 74 36 41 84 53 35 12.4% -0.22 [-0.67, 0.23]
Michael 2007 HD -28.4 103.6 33 -12.6 79.7 27 12.0% -0.17 [-0.68, 0.34]
Kotaki 1997 HD 3,760 1,762 15 4,025 2,168 16 10.6% -0.13 [-0.84, 0.58]
Total (95% CI) 244 243 100.0% -0.76 [-1.22, -0.30]
Heterogeneity: Tau² = 0.39; Chi² = 42.96, df = 8 (P < 0.00001); I² = 81%
Test for overall effect: Z = 3.25 (P = 0.001)
-4 -2 0 2 4
Favours IV iron
Favours oral iron