FPIN's Clinical Inquiries

Iron Deficiency in Heart Failure

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Clinical Question

Is intravenous iron more effective than oral iron for the treatment of iron deficiency in patients with heart failure?

Evidence-Based Answer

Treatment of iron deficiency in patients with heart failure using intravenous iron improves function, fatigue, and quality of life, and decreases risk of hospitalizations compared with placebo. (Strength of Recommendation [SOR]: B, based on a randomized controlled trial [RCT].) A small RCT suggests that treatment with intravenous and oral iron is equivalent in patients with heart failure. (SOR: C, based on a small RCT with disease-oriented outcomes.) Oral iron can be used to increase hemoglobin and iron levels in patients with heart failure. (SOR: C, based on a retrospective cohort study.)

Evidence Summary

A multicenter RCT of 304 ambulatory patients with symptomatic heart failure (ejection fraction less than 45%; New York Heart Association [NYHA] class II or III) examined the effects of treatment with intravenous iron compared with placebo.[1] All patients had iron deficiency, defined as a ferritin level less than 100 ng per mL (225 pmol per L); if the ferritin level was 100 to 300 ng per mL (225 to 674 pmol per L), a transferrin saturation (Tsat) less than 20% and hemoglobin level less than 15 g per dL (150 g per L) were required. The average hemoglobin level was 12.4 g per dL (124 g per L) in each group. Patients in the treatment group received a 500- to 2,000-mg (based on body weight) bolus of ferric carboxymaltose at baseline and week 6, then 500 mg at weeks 12, 24, and 36. Placebo consisted of a normal saline bolus. Overall, 53 patients did not complete the trial (29 in the treatment group; 24 in the placebo group); 26 died (12 in the treatment group; 14 in the placebo group). Compared with the placebo group, the treatment group had greater improvement in the six-minute walk test from baseline at 24 weeks (+18 m vs. –16 m; mean difference = 33 m; 95% confidence interval [CI], 13 to 53). There was also significant improvement at 36 weeks (mean difference = 42 m; 95% CI, 21 to 62) and 52 weeks (mean difference = 36 m; 95% CI, 16 to 57). Fatigue scores on a 10-point visual analog scale were significantly better in the treatment group at 24, 36, and 52 weeks. Quality-of-life scores (based on the Kansas City Cardiomyopathy Questionnaire) were improved in the treatment group at 36 weeks (mean difference = 5.0 on a 100-point scale; 95% CI, 1.6 to 8.3) and 52 weeks (mean difference = 4.5; 95% CI, 1.1 to 7.9). Hospitalization for worsening heart failure over one year was decreased in the iron treatment group compared with placebo (hazard ratio = 0.39; 95% CI, 0.19 to 0.82), with no statistically significant differences in adverse events.

A small RCT of 23 patients with iron-deficiency anemia and systolic heart failure compared oral iron (200 mg ferrous sulfate three times per day for eight weeks) with intravenous iron (200 mg once per week for five weeks) and placebo over three months.[2] Participants had stable ambulatory heart failure (NYHA class II to IV), ejection fraction less than 40%, and anemia (based on World Health Organization criteria). Of the 23 initial participants, primary endpoint data were available for only 18; three died (two in the intravenous group, one in the oral group). Changes in hemoglobin from baseline to 90 days did not differ between the groups (intravenous = +1.04 mg per dL [104 g per L]; oral = +1.69 mg per dL [169 g ▶

per L]; placebo = +1.1 mg per dL [110 g per L]; analysis of variance $P = .561$). This trial did not evaluate symptomatic improvement.

A retrospective trial examined the effectiveness of oral iron replacement in 105 patients with iron deficiency (ferritin level less than 100 ng per mL, or less than 300 ng per mL with Tsat less than 20%) and systolic heart failure (left ventricular ejection fraction less than 45%).[3] Patients received oral iron (average dosage, 130 mg per day) for a median of 164 days. Treatment with oral iron significantly increased iron levels (34 to 69 mcg per dL [6.1 to 12.4 µmol per L]; $P < .0001$), Tsat (9.9% to 20.8%; $P < .0001$), and hemoglobin levels (10.5 to 11.7 g per dL [105 to 117 g per L]; $P < .0001$). This study did not assess patient symptoms.

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