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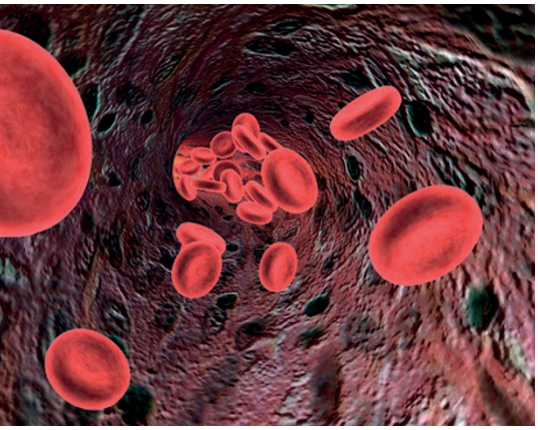
CHRONIC KIDNEY DISEASE

Serious adverse effects associated with IV iron in CKD

Iron-deficiency anaemia is very common in patients with chronic kidney disease (CKD). Primary findings from the REVOKE study now show that among nondialyzed patients with CKD and iron-deficiency anaemia, intravenous (IV) iron therapy is associated with an increased risk of serious adverse events, including infections and cardiovascular complications. "A larger randomized trial to establish the safety of IV iron should now be mandated by the FDA," states researcher Rajiv Agarwal. "For now, oral iron seems to be a safer approach when confronted with iron-deficiency anaemia in patients with CKD."



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Agarwal and colleagues initiated the REVOKE trial to assess whether IV iron would accelerate the progression of loss of kidney function compared to oral iron therapy in patients with iron-deficient anaemia and CKD. "Animal studies have consistently shown that iron administration worsens kidney disease," explains Agarwal. "Among animals receiving endotoxin, iron increases inflammation and mortality. Pilot studies have also suggested that patients with CKD experience an increase in proteinuria following administration of a single dose of IV iron sucrose."

The researchers randomly allocated 136 patients with iron-deficiency anaemia and nondialysis CKD to receive either oral iron sulfate or IV iron sucrose to evaluate the between-group difference in the change in slope of measured glomerular filtration rate (GFR) over 2 years. The trial was terminated early on the basis of an increase in the rate of serious adverse effects in the IV iron group and little chance of finding a between-group difference in GFR. Over a median follow up of 24 months (interquartile range 11.0–24.3 months), GFR declined similarly in both treatment groups (oral iron –3.6 ml/min/1.73 m^2 per year versus IV iron –4.0 ml/min/1.73 m^2 per year). The adjusted incidence rate ratio in the IV iron group was 2.12 (95% CI 1.24–3.64, P <0.006) for infections requiring hospitalization and 2.51 (95% CI 1.56–4.04, P <0.001) for cardiovascular events. "These findings are consistent with the biology of the drug, and show that long-term safety should be established before using IV iron liberally in patients with nondialysis CKD," says Agarwal.

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