LATE BREAKING CLINICAL TRIALS

2 in 1: Ferric Citrate for Anemia Management and Phosphate Control in CKD Patients?

Patients with chronic kidney disease (CKD) frequently suffer from anemia because the kidneys no longer synthesize sufficient erythropoietin. This situation is often compounded by iron deficiency, which aggravates the anemia. The causes of iron deficiency are inadequate dietary intake of iron (e.g. low-protein diet), concomitant impairment of absorption in the gut, and blockade of the release of storage iron in the body in the advanced stages of CKD. In addition, dialysis patients experience regular blood and iron loss during treatment. More than 60% of CKD patients have an iron deficiency [1]. According to the new KDIGO guidelines for anemia [2], treatment should commence with intravenous iron. In persistent anemia, an ESA may then be used. Treatment with ESAs should only be initiated if ferritin is 200-500 ng/ml and TSAT 20-30% because ESA therapy has hardly any effect in severe iron deficiency.

Another common complication in CKD is the inadequate increase of the serum phosphate. On average the daily intake of phosphate in the Western European diet is approximately 800-2000 mg. A large proportion of this dietary phosphate is absorbed in the small intestine. Where renal function is impaired the “phosphate balance” can no longer be maintained because the kidneys no longer excrete excess phosphate – the result is hyperphosphatemia. Because elevated serum phosphorus levels correlate with increased mortality [3], control of phosphate levels (dietary phosphate restriction and/or therapy with oral phosphate binders) is necessary.

With the use of ferric citrate as a phosphate binder, both problems – hyperphosphataemia and iron deficiency – can be solved at once. As the new study of Block et al. has shown, the ferric citrate treatment repletes iron stores, increases hemoglobin levels and reduces serum phosphate. This “double effect” has advantages: It could save costs and lower the pill burden. The latter is of importance, too – because the higher the pill burden, the lower the patients’ adherence [4].

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A Double-Blind Placebo Controlled Randomized Trial Of Ferric Citrate Coordination Complex For The Treatment Of Iron-Deficiency Anemia And Reduction Of Serum Phosphate In Patients With Non-Dialysis Dependent Chronic Kidney Disease

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INTRODUCTION AND AIMS: Iron deficiency anemia is common in patients with non-dialysis dependent chronic kidney disease and often remains untreated. In this same population, serum phosphate above 4.0 mg/dl is associated with progressive loss of kidney function, cardiovascular events and mortality.

METHODS: We performed a double-blind, placebo-controlled randomized trial in patients with non-dialysis dependent chronic kidney disease. One-hundred forty nine patients were randomized 1:1 to ferric citrate coordination complex or matching placebo for 12 weeks. Study drug was titrated to achieve a serum phosphate 3.0-3.5 mg/dl. Inclusion criteria included eGFR < 60 ml/min/1.73m², transferrin saturation (TSAT) <30%, serum ferritin <300 ng/ml and serum phosphate ≥4.0-6.0 mg/dl. Use of intravenous iron or erythropoiesis stimulating agents was prohibited. Primary endpoints were change in TSAT and serum phosphate from baseline to end of study.

RESULTS: Ferric citrate treatment significantly increased TSAT from 22 ± 7% to 32 ± 14% and reduced serum phosphate from 4.5 ± 0.6 mg/dL to 3.9 ± 0.6 mg/dL, each p<0.001 versus placebo in whom transferrin saturation remained stable at 21 ± 8% and serum phosphate declined by 0.3 mg/dl. Ferric citrate increased hemoglobin from 10.5 ± 0.8 g/l to 11.0 ± 1.0 (p<0.001 versus placebo), reduced urinary phosphate 39% (p<0.001 versus placebo) and reduced intact FGF23 from 319 ± 577 to 200 ± 386 RU/ml (p=0.017 versus placebo). The incidence and severity of adverse effects were similar between treatment arms. No subject developed sustained hypophosphatemia.

CONCLUSIONS: Ferric citrate safely and effectively repletes iron stores, increases hemoglobin without the need for intravenous iron or ESAs and reduces serum phosphate and urinary phosphate excretion in patients with non-dialysis dependent chronic kidney disease.