The Phosphate Binder Ferric Citrate and Mineral Metabolism and Inflammatory Markers in Maintenance Dialysis Patients: Results From Prespecified Analyses of a Randomized Clinical Trial

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Abstract

Background

Phosphate binders are the cornerstone of hyperphosphatemia management in dialysis patients. Ferric citrate is an iron-based oral phosphate binder that effectively lowers serum phosphorus levels.

Study Design

52-week, open-label, phase 3, randomized, controlled trial for safety-profile assessment.

Setting & Participants

Maintenance dialysis patients with serum phosphorus levels ≥6.0 mg/dL after washout of prior phosphate binders.

Intervention

2:1 randomization to ferric citrate or active control (sevelamer carbonate and/or calcium acetate).

Outcomes

Changes in mineral bone disease, protein-energy wasting/inflammation, and occurrence of adverse events after 1 year.

Measurements

Serum calcium, intact parathyroid hormone, phosphorus, aluminum, white blood cell count, percentage of lymphocytes, serum urea nitrogen, and bicarbonate.

Am J Kidney Dis. **2015 Sep;66(3):479-88. Doi: 10.1053/j.ajkd.2015.03.013**

Results

There were 292 participants randomly assigned to ferric citrate, and 149, to active control. Groups were well matched. For mean changes from baseline, phosphorus levels decreased similarly in the ferric citrate and active control groups (−2.04 ± 1.99 [SD] vs −2.18 ± 2.25 mg/dL, respectively; $P = 0.9$); serum calcium levels increased similarly in the ferric citrate and active control groups (0.22 ± 0.90 vs 0.31 ± 0.95 mg/dL; $P = 0.2$). Hypercalcemia occurred in 4 participants receiving calcium acetate. Parathyroid hormone levels decreased similarly in the ferric citrate and active control groups (−167.1 ± 399.8 vs −152.7 ± 392.1 pg/mL; $P = 0.8$). Serum albumin, bicarbonate, serum urea nitrogen, white blood cell count and percentage of lymphocytes, and aluminum values were similar between ferric citrate and active control. Total and low-density lipoprotein cholesterol levels were lower in participants receiving sevelamer than those receiving ferric citrate and calcium acetate. Fewer participants randomly assigned to ferric citrate had serious adverse events compared with active control.

Limitations

Open-label study, few peritoneal dialysis patients.

Conclusions

Ferric citrate was associated with similar phosphorus control compared to active control, with similar effects on markers of bone and mineral metabolism in dialysis patients. There was no evidence of protein-energy wasting/inflammation or aluminum toxicity, and fewer participants randomly assigned to ferric citrate had serious adverse events. Ferric citrate is an effective phosphate binder with a safety profile comparable to sevelamer and calcium acetate.

Keywords

Ferric citrate was associated with similar phosphorus control compared to active control, with similar effects on markers of bone and mineral metabolism in dialysis patients. There was no evidence of protein-energy wasting/inflammation or aluminum toxicity, and fewer participants randomly assigned to ferric citrate had serious adverse events. Ferric citrate is an effective phosphate binder with a safety profile comparable to sevelamer and calcium acetate.