EFFECT OF FERRIC CITRATE HYDRATE ON FIBROBLAST GROWTH FACTOR 23 IN HEMODIALYSIS PATIENTS

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BACKGROUND

Elevated fibroblast growth factor 23 (FGF23) level in hemodialysis patients is associated with mortality. Ferric citrate hydrate decreases FGF23 levels in non-hemodialysis patients. In previous studies, administration of intravenous saccharated ferric oxide increased serum FGF23 levels in hemodialysis patients.

OBJECTIVE

The aim of this study was to investigate the effect of ferric citrate hydrate on FGF23, and reduction of the dosage of erythropoiesis stimulating agents (ESA) and intravenous saccharated ferric oxide.

METHODS

This study was a prospective, open-label, single-arm, single-center trial. Patients who took lanthanum carbonate hydrate received ferric citrate hydrate 750 mg daily instead. The dose was adjusted every two weeks as usual, up to a maximum of 6,000 mg daily, until serum phosphate level was within 3.5 – 6.0 mg/dL. Patients were withdrawn from the study if any adverse events occurred. The dosages of calcium carbonate, vitamin D receptor activators, and cinacalcet were not changed during the study. Patients were monitored for 24 weeks. We evaluated changes in the levels of hemoglobin (Hb), serum phosphate, FGF23, iron, and ferritin, as well as in transferrin saturation (TSAT), dosage of intravenous saccharated ferric oxide and ESA (recombinant human erythropoietin: rHuEPO), and erythropoietin responsiveness index (ERI = weekly ESA dose (units)/dry weight (kg)/hemoglobin (g/dL)).

RESULTS

A total of 38 patients were included. Nine patients were withdrawn from the study and 29 patients were analyzed (**Fig. 1**). Baseline patient characteristics and medications are shown in **Table. 1** and **2**. The final mean dose of ferric citrate hydrate was 1,319 mg daily. Serum phosphate was well controlled (5.7 mg/dL at baseline and 5.1 mg/dL at the end of the study, $P < 0.05$) (**Table. 3**). Mean FGF23 level decreased significantly from 14,020 pg/mL at baseline to 7,101 pg/mL at the end of the study ($P= 0.001$) (**Fig. 2**). Levels of Hb and serum iron, TSAT, and ferritin markedly increased ($P < 0.05$, $P < 0.01$, $P < 0.001$, and $P < 0.001$ respectively), and the dosage of ESA and ERI also significantly decreased compared to baseline ($P < 0.01$ and $P < 0.01$, respectively) (**Table. 4**). The dose of intravenous saccharated ferric oxide was not significantly reduced. Eight patients were withdrawn because of diarrhea (n = 7) and pruritus (n = 1). One patient was admitted to hospital owing to chronic obstructive pulmonary disease which seemed to be unrelated to the administration of ferric citrate hydrate. No serious adverse drug reactions were recorded.

Fig. 1 Study flow chart

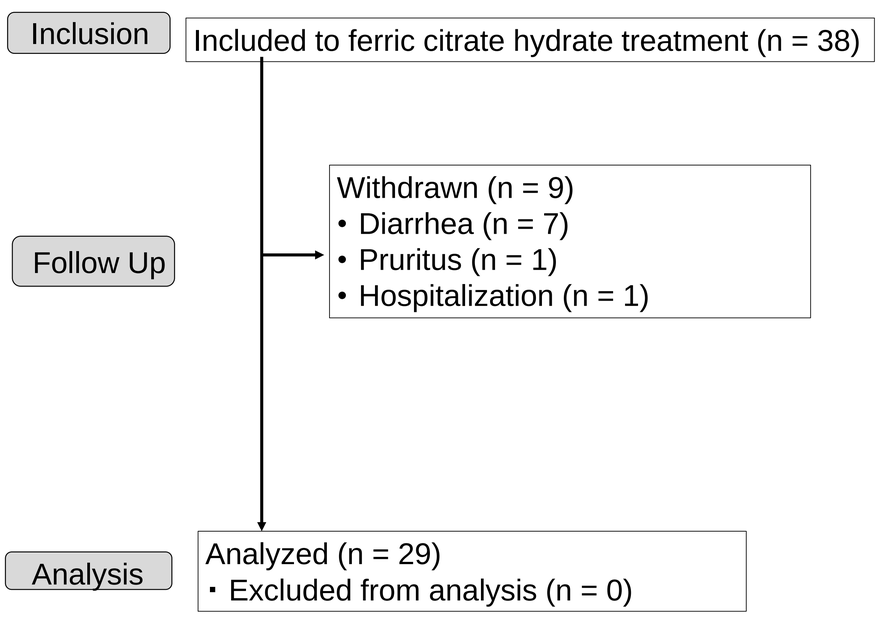

Table.1 Patient characteristics at baseline

n (men/women)	29 (20/9)
Age (years)	62.1 ± 12.9
Cause of ESKD (n)	
Diabetic nephropathy	8
Glomerulonephritis	6
Other	2
Unknown	13
Duration of dialysis (years)	4.8 ± 3.5
Dialysis mode (n)	
HD	27
HDF	1
OHDF	1

Values are shown as numbers or mean ± standard deviation.

Table. 2 Medications at baseline

Phosphate binders (mg)	
lanthanum carbonate hydrate	1,457 ± 627
Precipitated calcium carbonate (n = 23)	2,424 ± 1,137
Vitamin D receptor activator (n)	
Alfacalcidol	17
Calcitriol	3
Cinacalcet (n)	7
Saccharated ferric oxide (mg/4W)	50 ± 69
rHuEPO (U/4W)	21,379 ± 15,520

Values are shown as numbers or mean ± standard deviation.

Table.3 Changes in laboratory data

	Baseline	Week 24	P value
Phosphate (mg/dL)	5.72 ± 1.03	5.08 ± 1.02	0.016
Calcium (mg/dL)	9.19 ± 0.35	9.23 ± 0.34	0.559
Intact PTH (pg/mL)	171 ± 136	149 ± 118	0.337
Hb (g/dL)	11.0 ± 1.0	11.6 ± 1.5	0.046
Iron (μg/dL)	57.4 ± 24.7	77.3 ± 26.4	0.004
TSAT (%)	18.7 ± 8.8	30.2 ± 11.8	<0.001
Ferritin (ng/mL)	40.7 ± 27.6	99.7 ± 59.1	<0.001

Values are shown as mean ± standard deviation.

Fig. 2 Change in Intact FGF23

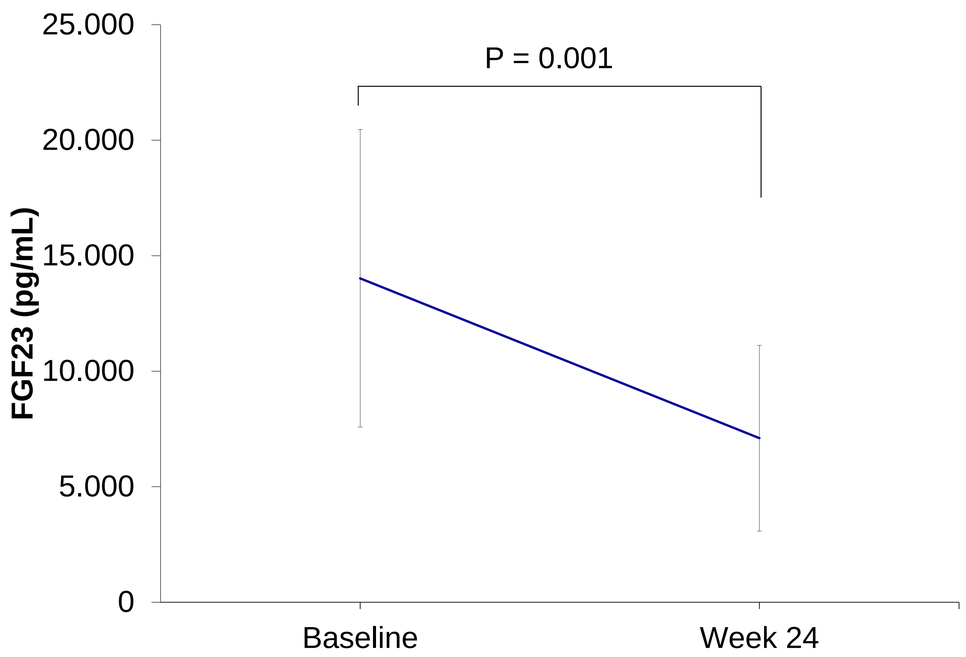

Table.4 Changes in dosage of medications

	Baseline	Week 24	P value
Ferric citrate hydrate (mg)	750	1,319 ± 741	
Saccharated ferric oxide (mg/4W)	50 ± 69	25 ± 57	0.017
rHuEPO (U/4W)	21,379 ± 15,520	12,586 ± 13,260	0.009
ERI	9.1 ± 7.3	5.4 ± 6.4	0.006

Values are shown as mean ± standard deviation.

CONCLUSIONS

Treatment of hyperphosphatemia with ferric citrate hydrate was effective, resulting in decreased serum FGF23 levels in hemodialysis patients, as well as the dosage of ESA and ERI.

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