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Comparison of serum fibroblast growth factor 23 (FGF23) levels and Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD) parameters in home hemodialysis and center hemodialysis

Ev hemodiyalizi ve merkez hemodiyalizinde serum fibroblast büyüme faktörü 23 (FGF23) seviyeleri ve Kronik Böbrek Hastalığı-Mineral ve Kemik Bozukluğu (CKD-MBD) parametreleri üzerindeki etkilerinin karşılaştırılması

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Abstract

Purpose: This study aims to compare serum fibroblast growth factor 23 (FGF23) levels and chronic kidney disease-mineral and bone disorder (CKD-MBD) parameters in patients undergoing home hemodialysis (HHD) and center hemodialysis (CHD).

Materials and methods: A total of 42 patients over 18 years old who had been receiving dialysis treatment for at least six months were included in the study. The patients were divided into two groups: HHD (n=17) and CHD (n=25). Demographic data, dialysis duration, biochemical parameters (serum phosphorus, calcium, parathyroid hormone (PTH), albumin, hemoglobin, FGF23, etc.), and medication use were recorded. Serum FGF23 levels were measured using an enzyme-linked immunosorbent assay (ELISA) method from blood samples taken before midweek HD sessions. Frequency distributions were expressed as percentages and compared using the chi-square test.

Results: The Kt/V values were higher in the HHD group (2.4±0.1 vs. 1.6±0.1), while serum phosphorus levels were lower (4.1±1.1 vs. 5.0±1.2 mg/dL). Although FGF23 levels were lower in the HHD group, the difference was not statistically significant (383±423 vs. 441±480 pg/mL, p=0.05). Erythropoietin (Epo) usage was significantly lower in the HHD group (47% vs. 92%, p=0.001).

Conclusion: HHD was associated with better phosphorus control and a reduced requirement for EPO compared to CHD. The lower FGF23 levels in HHD suggest that this modality may offer advantages in CKD-MBD, cardiovascular outcomes, and mortality. However, these findings need to be supported by prospective studies involving larger patient populations.

Keywords: FGF23, home hemodialysis, center hemodialysis, chronic kidney disease, dialysis.

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Öz

Amaç: Bu çalışma, ev hemodiyalizi (HHD) ve merkez hemodiyalizi (CHD) tedavisi altındaki hastalarda serum fibroblast büyüme faktörü 23 (FGF23) seviyelerini ve Kronik Böbrek Hastalığı-Mineral ve Kemik Bozukluğu (CKD-MBD) parametrelerini karşılaştırmayı amaçlamaktadır.

Gereç ve yöntem: Çalışmaya 18 yaş üstü, en az 6 aydır diyaliz tedavisi alan 42 hasta dahil edildi. Hastalar, HHD (n=17) ve CHD (n=25) olmak üzere iki gruba ayrıldı. Demografik veriler, diyaliz süresi, biyokimyasal parametreler (serum fosfor, kalsiyum, parathormon (PTH), albümin, hemoglobin, FGF23 vb.) ve ilaç kullanımı kaydedildi. Serum FGF23 seviyeleri, haftanın ortasında HD seansı öncesi alınan kan örneklerinden ELISA yöntemi ile ölçüldü. Gruplar arasındaki frekans dağılımları yüzdeli olarak ifade edildi ve ki-kare testi ile karşılaştırıldı.

Bulgular: HHD grubunda Kt/V değerleri daha yüksek (2,4±0,1 vs. 1,6±0,1) ve serum fosfor seviyeleri daha düşük (4,1±1,1 vs. 5,0±1,2 mg/dL) bulundu. FGF23 seviyeleri HHD grubunda daha düşük olmasına rağmen, iki grup arasında istatistiksel olarak anlamlı fark tespit edilmedi (383±423 vs. 441±480 pg/ml, p=0,05). EPO kullanımı HHD grubunda belirgin şekilde daha düşük bulundu (%47 vs. %92, p=0,001).

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Sonuç: HHD, CHD'ye kıyasla daha iyi fosfor kontrolü ve daha düşük EPO gereksinimi ile ilişkilendirildi. FGF23 seviyelerinin HHD'de daha düşük olması, bu modalitenin CKD-MBD, kardiyovasküler sonuçlar ve mortalite açısından avantaj sağlayabileceğini düşündürmektedir. Ancak, bu bulguların daha geniş hasta gruplarında prospektif çalışmalar ile desteklenmesi gerekmektedir.

Anahtar kelimeler: FGF23, ev hemodiyalizi, merkez hemodiyalizi, kronik böbrek hastalığı, diyaliz.

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Introduction

Over the past 10-15 years, home hemodialysis (HHD) has emerged as an alternative modality, particularly with nocturnal dialysis or extended dialysis session durations [1]. Various studies have demonstrated that HHD improves serum phosphorus control, reduces phosphate binder requirements, and allows for a more liberalized diet [2-4].

Hemodialysis is the most commonly used renal replacement therapy that significantly improves the prognosis of end-stage renal disease (ESRD) patients [5]. Conventional in-center hemodialysis (CHD) is performed three times a week, with each session lasting four hours, while HHD is performed at least three times per week with a session duration of at least six hours. Peritoneal dialysis (PD) is also an alternative dialysis modality [6]. Globally, 89% of dialysis patients undergo HD, while 11% receive PD. However, mortality rates among CHD patients remain relatively high, with all-cause mortality being seven times higher and cardiovascular mortality eight times higher than in the general population [7].

In parallel, fibroblast growth factor 23 (FGF23) has been recognized as a key regulator of phosphate and vitamin D metabolism over the past decade. FGF23, a potent calcium and phosphorus regulator, is produced by osteoblasts and osteocytes. It reduces phosphorus levels by promoting phosphate excretion and inhibiting 1.25(OH)2D3 formation [8]. In the early stages of chronic kidney disease (CKD), FGF23 secretion is upregulated to maintain phosphate balance, but this subsequently leads to decreased 1.25(OH)2D3 synthesis and triggers secondary hyperparathyroidism [9]. As kidney function deteriorates, the ability to promote phosphate excretion declines due to a reduction in functional nephrons, and abnormally elevated FGF23 becomes a uremic toxin strongly associated with adverse clinical outcomes [10].

FGF23 levels are extremely high in dialysis patients [11], correlating with serum phosphorus concentrations and increasing with enteral phosphate intake and vitamin D sterol treatment [12]. Although serum phosphorus concentration has long been associated with cardiovascular disease and mortality in dialysis patients, FGF23 has also been identified as an independent predictor of cardiovascular disease and mortality in both the general and dialysis populations [13].

Given that elevated FGF23 is linked to increased cardiovascular and all-cause mortality [4], we hypothesized that HHD could lower serum FGF23 levels by altering CKD-MBD parameters, potentially reducing mortality. However, the impact of different dialysis modalities on circulating FGF23 levels, underlying regulatory mechanisms, and potential clinical benefits remains unclear. This retrospective study aimed to investigate whether FGF23 levels were lower in CHD versus HHD patients and whether this difference could improve patient prognosis by comparing serum FGF23 levels, CKD-MBD-related parameters, hemoglobin, and albumin levels between these two dialysis modalities.

Materials and methods

Study design and population

This retrospective study includes patients aged 18 years or older receiving HHD, who remained on this treatment modality for at least six months between 2015 and July 2024, as well as patients undergoing CHD at the center. Patients with malignancies, severe infections, or advanced cardiac or hepatic failure, as well as those not meeting the inclusion criteria, were excluded. Consequently, a total of 42 patients who met the criteria were included in the study.

CHD Group: Underwent HD three times per week, each session lasting four hours, with a blood flow rate of 200-360 mL/min and a dialysate flow rate of 500 mL/min.

HHD Group: Underwent HD three times per week, with sessions lasting at least six hours, a blood flow rate of 200-300 mL/min, and a dialysate flow rate of 300-500 mL/min.

All HD patients used polysulfone membranes (1.5-2.1 m²), and anticoagulation was maintained using heparin or low-molecular-weight heparin.

Ethics approval was obtained from the Pamukkale University Non-Interventional Clinical Research Ethics Committee (approval date: 21.01.2025/02, file no: E-60116787-020-643233).

Demographic data, dialysis duration, and primary ESRD causes were collected from the Pamukkale University Faculty of Medicine and Electronic medical records (e-Nabız). Biochemical parameters, including calcium (Ca), phosphorus (P), hemoglobin (Hb), albumin (Alb), ferritin, 25-hydroxyvitamin D, intact parathyroid hormone (iPTH), and Kt/V, were recorded. Serum intact FGF23 levels were measured using the enzyme-linked immunosorbent assay (ELISA) kit (E0059Hu, BT Lab, Shanghai, China) on blood samples collected before midweek dialysis sessions (typically before the second treatment session of the week). Samples were obtained according to a standardized schedule to ensure consistency and were drawn from the arteriovenous fistula (or central venous catheter, if applicable) immediately prior to heparin administration. Blood samples were collected in 2 mL biochemical tubes, centrifuged at 3.500 rpm for 20 minutes at room temperature within 15 minutes of collection, and the resulting sera were stored at -80°C until the day of analysis.

Statistical analysis

All continuous data were expressed as mean ± standard deviation (SD). Independent sample t-tests were used to analyze differences between the two groups. Frequency distributions were expressed as percentages and compared using the chi-square test. A $p<0.05$ was considered statistically significant.

Results

A total of 42 dialysis patients were included (HHD: n=17, CHD: n=25). The mean ages were 47.8±12.8 and 53.1±11.9 years for the HHD and CHD groups, respectively. The dialysis duration was significantly longer in the HHD group (106.6±48.7 vs. 48.1±44.5 months) (Table 1).

Regarding erythropoietin (EPO) use, 47% (n=8) of HHD patients and 92% (n=23) of CHD patients used EPO, with a statistically significant difference between the two groups ($p=0.001$). No significant differences were observed in the use of iron supplements, phosphate binders, calcimimetics, or vitamin D (Table 2).

Table 1. Biochemical values in patients undergoing treatment with home and center-based hemodialysis

	Home Hemodialysis (n=17)	Central hemodialysis (n=25)	Test value	*p* value
Age	47.8±12.8	53.1±11.9	t=-1.360	*p*=0.182
Dialysis Duration (months)	106.6±48.7	48.1±44.5	t=3982	*p*=0.0001*
KT/V	2.39±0.1	1.6±0.1	t=6.647	*p*=0.0001*
Hemoglobin(gr/dL)	12.1±1.5	11.1±1.5	t=2.001	*p*=0.052
Albumin (g/L)	39.4±5.9	38.5±3.3	t=0.570	*p*=0.572
Calcium (mg/dL)	8.8±0.5	9.0±1.0	t=-0.533	*p*=0.597
Phosphorus (mg/dL)	4.1±1.1	5.0±1.2	t=-2.368	*p*=0.023*
PTH (ng/L)	510±444	340±292	t=1.497	*p*=0.142
Vitamin D (µg/L)	14.7±13.2	12.7±13.8	t=-0.471	*p*=0.640
FGF23 (pg/ml)	383±423	441±480	t=-0.397	*p*=0.694

Kt/V: Dialysis adequacy index, PTH: Parathyroid Hormone, FGF23: fibroblast growth factor 23, t:Independent sample t-tests, *: $p<0.05$

Table 2. Medications used in patients undergoing home hemodialysis and center hemodialysis

Treatment	Home hemodialysis (n=17)	Central hemodialysis (n=25)	Test value	*p* value
Vitamin D use	6 (35%)	16 (64%)	χ^2=3.343	*p*=0.067
Phosphate binder use	11 (65%)	18 (72%)	χ^2=0.252	*p*=0.616
Erythropoietin Use	8 (47%)	23 (92%)	χ^2=10.572	*p*=0.001*
Iron use	6 (35%)	15 (60%)	χ^2=2471	*p*=0.116

χ^2: chi-square test, *: *p*<0.05

Discussion

Consistent with previous studies, urea clearance (Kt/V) was found to be higher in HHD. This higher clearance was associated with significantly lower serum phosphorus levels and reduced requirements for EPO and phosphate binders, suggesting improved mortality outcomes [14]. Furthermore, this study found that serum FGF23 levels were lower in the HHD group, which may serve as a bridge linking CKD-MBD to left ventricular hypertrophy and all-cause mortality. While multiple studies have focused on regulating high FGF23 levels in dialysis patients, their results have been inconsistent. Increased phosphate load is well-known to stimulate FGF23 secretion [15], but the molecular mechanism remains unclear. Although vitamin D plays a positive regulatory role in FGF23 expression, in this study, despite lower vitamin D use in HHD patients, phosphate binder use was lower in the CHD group.

While multiple studies have explored the regulation of elevated FGF23 levels in dialysis patients, their findings remain inconsistent. Increased phosphate load is well known to stimulate FGF23 secretion [15], though the precise molecular mechanisms remain unclear. Vitamin D plays a positive regulatory role in FGF23 levels. Although no statistically significant difference was observed between dialysis modalities, the trend of lower FGF23 levels in HHD may be attributed to reduced phosphate load. Interestingly, despite lower vitamin D usage in the HHD group, phosphate binder use was significantly lower in CHD patients.

PTH is another potential regulator of FGF23 in CKD, as both PTH and FGF23 levels tend to increase in patients with impaired renal function. Lavi Moshayoff et al. [16] suggested that PTH might upregulate FGF23 expression in vitro, though other studies have failed to confirm a direct regulatory effect. In this study, PTH levels were higher in HHD patients, whereas FGF23 levels were lower, a finding that contrasts with the CHD group.

Another significant result of this study was the significantly lower EPO requirement in the HHD group. Similar to findings by Ok et al. [17], we observed a reduced need for EPO in HHD patients. Although iron use was also lower in HHD patients, this difference did not reach statistical significance.

This study has several limitations. Firstly, the retrospective design of the study. Secondly, the relatively small sample size reduces the power to detect differences between the two dialysis modalities, particularly in terms of FGF23 levels. Thirdly, the fact that this study was conducted as a single-center study. Lastly, FGF23 levels were measured only once, and changes over time were not evaluated. Larger, multicenter, and prospective studies are needed to validate these findings.

In conclusion, in this study, although no statistically significant difference in FGF23 levels was observed between HHD and CHD patients, FGF23 levels were lower in the HHD group. This finding suggests that HHD may provide better phosphorus control and reduce phosphate binder medication use. Additionally, the significantly lower EPO requirement in the HHD group indicates potential benefits of this dialysis modality on erythropoiesis. However, given the study's small population and retrospective design, these findings need to be validated by larger, randomized controlled trials.

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Authors contributions: D.A. has constructed the main idea and hypothesis of the study. M.C. and G.G. developed the theory and arranged the material and method section. M.B., E.B. and H.A., have done the evaluation of the data in the Results section. Discussion section of the article. Written by D.A., M.C., M.B., E.B. and H.A. reviewed, corrected, and approved. In addition, all authors discussed the entire study and approved the final version.

Conflict of interest: No conflict of interest was declared by the authors.

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