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Original Article

Comparison of calcium and phosphorus homeostasis between hemodialysis and peritoneal dialysis in patients with end-stage renal disease

Vahideh Sadra[1], Mehran Rahimi[2], Farzad Najafipour[1*], Reza Habibi[1]

[1]Endocrine Research Center, Tabriz University of Medical Sciences, Tabriz, Iran
[2]Cardiovascular Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

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Abstract

Introduction: Chronic kidney disease (CKD) and subsequent end-stage renal disease (ESRD) are public health problems worldwide, and their prevalence is increasing worldwide. Abnormalities in calcium and phosphorus are common problems that need to be considered alongside other important factors when choosing a dialysis method. Hence, the present study aimed to assess and compare the calcium and phosphorus homeostasis in ESRD patients on hemodialysis and peritoneal dialysis (PD).

Methods: In this descriptive cross-sectional study, 150 patients with ESRD on hemodialysis and 150 patients with ESRD on PD in the dialysis department of Imam Reza hospital of Tabriz University were selected randomly. The serum levels of calcium, phosphorus, and intact parathyroid hormone (iPTH) before the initiation of dialysis and one year afterward were considered for comparison.

Results: In the hemodialysis group, 33.1% of patients were female and 66.9% were male but in the PD group, sex distribution was 47% males and 53% females. Following one year of dialysis, mean calcium (Ca), phosphorus (P), and iPTH levels were significantly higher in the hemodialysis group compared to PD patients ($P<0.05$). Also, the mean Ca × P product was significantly higher in patients undergoing PD ($P=0.05$).

Conclusion: Our findings suggested that calcium, phosphorus and iPTH levels increase with prolonged hemodialysis rather than PD, and the rate of Ca × P in patients is significantly higher in PD patients after one year.

Introduction

Chronic kidney disease (CKD) is the presence of kidney damage or function for three or more months regardless of the cause. End-stage renal disease (ESRD) is defined as a glomerular filtration rate (GFR) < 15 mL/min/1.73 m^2 or treatment by dialysis and is the final stage of CKD. It is estimated that over 2 million people are suffering from ESRD worldwide.[1,2] There is an inclining trend for the use of maintenance hemodialysis or peritoneal dialysis (PD) as renal replacement therapy.[3] In the course of CKD, abnormalities in calcium and phosphorus metabolism occur. Several studies report that inadequate phosphorus control is a risk factor for vascular and soft tissue calcification and is associated with the increased morbidity and mortality.[4-6]

Renal osteodystrophy is one of the most important bone disorders in ESRD patients, which is characterized by biochemical abnormalities in calcium, phosphorus, parathyroid hormone and vitamin D and bone turnover abnormalities, and extraskeletal calcifications.[7] Secondary hyperparathyroidism (SHPT), the major feature of CKD mineral bone disease, begins early in the course of CKD and occurs in response to phosphate retention and decreased calcium and 1.25 OH vitamin D (calcitriol).[8,9]

There are two methods used for dialysis; hemodialysis and PD. Each of these methods has risks and benefits. Phosphorus serum levels are both reported to be higher[10] or lower[11] in patients undergoing PD compared to those receiving hemodialysis. Phosphorus serum levels reduce after hemodialysis.[11]

As earlier mentioned, abnormalities in calcium and phosphorus are common problems that need to be considered alongside other important factors when choosing a dialysis method. Hence, the present study aimed to assess and compare the calcium and phosphorus homeostasis in ESRD patients on hemodialysis and PD.

Methods

This descriptive cross-sectional study was conducted in Imam Reza hospital, Tabriz, Iran. 150 ESRD patients who were under hemodialysis and 150 ESRD patients receiving PD, randomly selected, were included in this study. The

***Corresponding Author:** Farzad Najafipour, Email: farzadnajafipour@gmail.com

sample size was determined according to similar studies. Data were collected from the medical documents of the patients.

Inclusion and exclusion criteria

Inclusion criteria for this study were as follows: (1) individuals over 18 who were under dialysis (hemodialysis or PD) at least for a year, (2) the main treatment method was dialysis and they did not have another therapeutic option (kidney transplant), (3) availability of blood tests (calcium, phosphorus, intact parathyroid hormone (iPTH) and albumin) before initiation of dialysis and one year afterward, (4) patients who have not changed their dialysis method (e.g. substituting hemodialysis with PD).

Exclusion criteria were (1) patients under 18 receiving hemodialysis, (2) patients under dialysis for less than one year, (3) ESRD patients receiving treatments other than dialysis, (4) patients who have changed their dialysis method in less than one year, (5) pre-existing bone metabolic disease, (6) presence of any kind of active hepatic disease (e.g. hepatitis), (7) presence of any acute disease such as sepsis.

Baseline data for both groups included serum levels of calcium, phosphorus, and iPTH and were checked before initiation of dialysis and one year afterwards. Patients in each group received activated vitamin D and calcium. Based on nephrology guidelines and serum levels of calcium, phosphorus, and iPTH changes like the initiation of chelating agents or altering vitamin D and calcium doses were made by nephrologists.

Statistical analysis

We used the Kolmogorov-Smirnov test to check the normal distribution of the data and decide to use parametric or non-parametric tests. Paired *t* test and Wilcoxon's tests were employed to analyze parametric and non-parametric data, respectively. Linear regression analysis was used to control for confounding factors.

Pretest and posttest were compared to discover changes after treatment. The Statistical Package for the Social Sciences (SPSS) version 22 was utilized to perform statistical analysis. Under the generally accepted definition, if the data resulted in a *P* value less than 0.05, this would suggest that our results are significant (statistically). The quantitative results were reported in mean ± standard deviation (SD) and frequency (percentage) was the method for reporting qualitative results.

Results

In the hemodialysis group, 33.1% of patients were female and 66.9% were male but in the PD group, sex distribution was 47% males and 53% females. Patients' age and body mass index (BMI) are manifested in Table 1.

All of the data in the Kolmogorov-Smirnov test had a *P* value less than 0.05; therefore, data did not have a normal distribution. As a result, we employed non-parametric analyses. In this study, we first checked serum levels of iPTH, calcium, and phosphorus and then therapeutic intervention was initiated. In post-test, the aforementioned variables were rechecked. Due to non-normal distribution, Wilcoxon's test was employed and pre- and post-tests were compared to determine any change in variables after treatment. Based on linear regression analysis, no confounding factor had an impact on the results.

Mean pre-dialysis serum levels of variables and mean serum levels after one year of dialysis for hemodialysis and PD patients are shown in Table 2. Only serum levels of calcium and iPTH had a statistically significant difference (*P* value = 0.001 and 0.008, respectively).

Following one year of dialysis, mean calcium, phosphorus, and iPTH levels were significantly higher in the hemodialysis group compared to PD patients. Also, the mean Ca × P product was significantly higher in patients undergoing PD (Table 3).

Discussion

The classical triad of SHPT pathogenesis in renal

Table 1. Age and body mass index of the patients

Dialysis	Variable	Mean ± SD	Minimum	Maximum
Hemodialysis	Age	55.62±1.33	18	86
	BMI	24.23±0.3	17	34
PD	Age	57.49±1.39	18	96
	BMI	24.01±0.36	14	42

SD: standard deviation, BMI: body mass index; PD, peritoneal dialysis; Ca, calcium.

Table 2. Lab data for patients undergoing hemodialysis and peritoneal dialysis

Dialysis	Variable	Mean ± SD*	Mean ± SD**	*P* value
Hemodialysis	iPTH	338.19±31.71	371.7±26.1	0.008
	Ca	8.64±0.65	8.92±1.5	0.001
	P	5.64±0.12	5.45±0.11	0.370
	Ca×P	40.48±3.31	41.48±8.05	0.345
PD	iPTH	295.86±23.48	283.73±24.18	0.271
	Ca	8.79±0.66	8.7±0.1	0.215
	P	4.91±0.11	4.92±0.12	0.916
	Ca×P	42.83±4.47	42.47±1.06	0.549

SD, standard deviation; iPTH, intact parathyroid hormone; P: phosphorus
*Base line lab data.
**Lab data after one year of dialysis treatment.

Table 3. Comparison of lab data of HD patients and that of PD patients

Variable	Mean ± SD of the variables in HD patients	Mean ± SD of the variables in PD patients	P value
iPTH (pg/mL)	371.7±26.1	283.73±24.18	0.000
Calcium (mg/dL)	8.92±1.5	8.7±0.1	0.003
Phosphorus (mg/dL)	5.45±0.11	4.92±0.12	0.001
Ca × P (mg^2/dL^2)	41.48±8.05	42.47±1.06	0.000

HD, hemodialysis; PD, peritoneal dialysis; iPTH, intact parathyroid hormone; P, phosphorus.

insufficiency consists of higher levels of phosphorus, lower levels of calcium, and vitamin D deficiency.[12] Recently molecular mechanisms of phosphorus homeostasis and SHPT pathogenesis have been linked to FGF-23. Increased serum FGF-23 levels induce low blood levels of phosphorus, suppression of calcitriol, and hyperparathyroidism.[13] In another theory, deduced from the severely elevated FGF-23 levels in CKD patients, CKD-associated hyperphosphatemia triggers FGF-23 production to promote renal phosphorus excretion.[14]

This study reports statistically significant differences in calcium, phosphorus, iPTH, and Ca × P product between patients on HD and patients receiving PD. Our results showed higher levels of phosphorus, calcium, and iPTH in HD patients, but lower Ca × P product. In the prospective study conducted by Noordzij et al, they included 586 PD and 1043 HD patients. The main difference between this study and Noordzij and colleagues' study was that they followed patients for three months after the start of dialysis, but our reported serum levels were checked one year after initiation of the dialysis. They reported significantly higher levels of phosphorus and Ca × P product in HD patients, but unlike our study, serum levels of calcium were higher in patients receiving PD (P<0.05). The interesting point is that serum levels of iPTH did not differ significantly between the two groups in their study.[15]

In our study, calcium and phosphorus levels were higher in the HD group. Time-averaged serum phosphorus concentrations in Evenepoel and colleagues' study in the HD patients were significantly lower compared to the PD patients and iPTH levels were higher in PD group. However, only iPTH concentrations of pre-dialysis for HD group and mid-morning for PD differed significantly.[10] In two other studies the P values for two groups regarding the serum levels of calcium and phosphorus were more than 0.05. Patients included in Kim and colleagues' study were on dialysis for at least three months and this should be noted that Xu and colleagues' results should be interpreted in the light of a specific study population (end-stage diabetic nephropathy patients).[16,17] Lu et al studied dialysis methods in China and Italy and reported a significant difference only in serum levels of phosphorus between the two groups in China. It was also reported that iPTH and phosphorus levels between HD and PD patients were significantly different in the two countries.[18] So, these conflicting results between studies can somehow be justified by the institutes where dialysis takes place, as little differences in management and guidelines may exist between institutes.

We found that serum levels of iPTH and calcium in HD patients increase significantly one year after the start of dialysis. In one study serum levels of calcium, phosphorus, and Ca × P product increased significantly 6 months after initiation of dialysis. Also, they reported a significant decrease in iPTH levels for one year.[11] Dias et al studied the effect of urgent-start dialysis on phosphorus and iPTH. They reported significant reduction in serum levels of phosphorus in PD patients after 6 months of dialysis and no significant change in iPTH levels in both groups.[19]

Five-year follow-up has shown significant differences in phosphorus levels between the two groups, but not in calcium or iPTH levels.[18]

Study Highlights

What is current knowledge?

- Abnormalities in calcium and phosphorus are common problems that need to be considered alongside other important factors when choosing a dialysis method.

What is new here?

- This study showed higher levels of phosphorus, calcium, and iPTH in HD patients, but lower Ca × P product.

Limitations of this study

This study was limited by its retrospective nature: there is a need for prospective randomized controlled studies to be performed in the future. We could not follow the patients for a longer period. Authors believe studies on the mortality and morbidity in patients who are on dialysis need to have an acceptable long follow-up.

Conclusion

There are conflicting results regarding calcium, phosphorus, and iPTH in the literature. We found a significant difference between PD and HD groups regarding calcium, phosphorus, iPTH, and Ca × P product. All of the aforementioned markers were higher in patients on hemodialysis except Ca × P product. Large-scale studies with clear addressing of confounding factors conducted with the most accurate guidelines will help to solve this controversy.

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Author Contributions

VS and FN conceived of the presented idea. FN and RH developed the theory and performed the computations. MR and VS verified the analytical methods. RH and MR supervised the findings of this work. All authors discussed the results and contributed to the final manuscript.

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Ethical Issues

This study was approved by the Ethics Committee of Tabriz University of Medical Sciences, Tabriz, Iran (Ethics No. IR.TBZMED.REC.1397.267). Consent was explained and obtained from the subjects.

Conflict of Interests

The authors declare no conflicts of interest concerning the authorship and/or publication of this article.

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