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Original Article

Significance of residual renal function for phosphate control in chronic hemodialysis patients

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Abstract

Background: The aim of this study was to compare mineral metabolism between anuric and nonanuric chronic hemodialysis patients, and determine the differences in phosphate control between the two groups.

Methods: A total of 77 chronic hemodialysis patients were enrolled in this cross-sectional study from January 2012 to February 2012. Patient demographics, laboratory findings, medication histories, and vascular calcification scores were collected. We divided the patients into anuric and nonanuric groups according to the residual renal function and then compared their clinical features. Multivariate binary regression analysis was used in each group to determine the independent factors related to phosphate control.

Results: The mean patient age was 59.27 ± 13.95 years, and 57.1% of patients were anuric. In anuric patients, dialysis vintage was significantly longer, but the mean Kt/V was not different between groups. Serum phosphate, fibroblast growth factor (FGF)-23, and Ca/P products were significantly higher, and $1,25(OH)_2D_3$ levels were significantly lower in the anuric patients, although the intact parathyroid hormone and 25(OH)D levels were not different. In anuric patients, LnFGF-23 [hazard ratio (HR) 2.894, 95% confidence interval (CI) 1.294–6.474, $P=0.010$] was an independent factor predictive of phosphate control. However, in the nonanuric patients, glomerular filtration rate (HR 0.409, 95% CI 0.169–0.989, $P=0.047$) and blood urea nitrogen (HR 1.090, 95% CI 1.014–1.172, $P=0.019$) were independent factors predictive of phosphate control.

Conclusion: In chronic hemodialysis patients, preservation of residual renal function is a significant determinant of phosphate control, and the factors associated with phosphate control is different depending on the residual renal function status. In the anuric patients, FGF-23 is most significantly associated with phosphate control; however, glomerular filtration rate and blood urea nitrogen are more important than FGF-23 in the nonanuric HD patients.

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Introduction

Residual renal function (RRF) is an important determinant of mortality and morbidity in chronic dialysis patients. In previous studies, the degree of RRF was found to be inversely associated with the severity of left ventricular hypertrophy and cardiovascular death in peritoneal dialysis patients [1,2]. Preserved RRF was also observed to be associated with better all-cause and cardiac-specific mortality in hemodialysis (HD) patients [3,4]. These associations may be related to the better clearance of mid to large molecular uremic toxin and fluid removal from the residual kidney in nonanuric dialysis patients [5,6].

Phosphate, which is excreted through urine, is the key molecule in chronic kidney disease-mineral and bone disorder (CKD-MBD). Under normal physiologic conditions, phosphate removal is determined mainly by the expression of type II Na–Pi cotransporters at the tubular epithelium [7], which are controlled by dietary phosphate, parathyroid hormone (PTH), vitamin D, and fibroblast growth factor-23 (FGF-23) [8,9]. In chronic dialysis patients with RRF, phosphate can be excreted through the remnant nephron; however, in anuric dialysis patients, serum phosphate cannot be excreted through urine. Therefore, phosphate control may differ depending on the RRF status.

In this study, we aimed to compare mineral metabolism between anuric and nonanuric chronic HD patients and determine the differences in phosphate control between these groups according to RRF.

Methods

Participants

From January 2012 to February 2012, a total of 77 HD patients from our dialysis unit were enrolled in this study. All patients were older than 18 years and undergoing maintenance HD therapy for end-stage renal disease for more than 3 months. The participants were dialyzed thrice weekly for more than 4 hours per session, using low-flux membranes. The standard dialysate calcium concentration was 3.5 mEq/L. Exclusion criteria included severe malnutrition, acute infection, hepatic dysfunction, and malignancy. Approval of the local ethics committee was obtained for this study, and all patients provided written informed consent.

Data collection

Demographics and medical histories were reviewed; dialysis treatment parameters such as dialysis vintage, blood flow rate, and single-pool Kt/V were assessed; and nutritional markers, such as normalized protein nitrogen appearance (nPNA), subjective global assessment (SGA), total protein, albumin, and total cholesterol levels were checked. Biochemical CKD-MBD factors and associated medication histories during the study period were collected. All the predialysis blood samples were obtained for routine laboratory assessment by standard techniques, and a part of these samples was stored at -80°C for performing the enzyme-linked immunosorbent assay (ELISA) study in all patients. Analysis of serum calcium was performed by the ortho-cresolphthalein complexone method using a Roche/Hitachi Modular-DP analyzer (Roche Diagnostics, Basel, Switzerland); calcium levels were corrected for serum albumin. Analysis of serum phosphate was performed by the phosphomolybdate reduction method using a Roche/Hitachi Modular-DP analyzer (Roche Diagnostics). The serum level of intact PTH (iPTH) was assessed by a total iPTH immunoradiometric assay, which quantifies both PTH(1–84) and the N-truncated PTH fragments. Serum 25(OH)D and 1,25 $(OH)_2D_3$ levels were measured using a radio immunoassay. Serum FGF-23 and serum fetuin A levels were measured using an ELISA kit (ELISA, Immutopics, San Clemente, CA, USA—for FGF-23; ELISA, R&D Systems, Minneapolis, MN, USA—for feutin A), according to the manufacturer's protocol.

Calculations and definitions

We defined anuria as a 24-hour urine output of < 100 mL, and the glomerular filtration rate (eGFR) of the anuric patients was estimated to be 0.00 mL/minute/1.73 m^2. For the nonanuric patients, GFR was estimated by the numerical averages of the 24-hour creatinine clearance and urea nitrogen clearance. A 24-hour urine collection was made after the longest interdialysis period. A cardiovascular event was defined as myocardial infarction, stroke, or transient ischemic attack. Single-pool Kt/V (spKt/V) was calculated using the natural logarithm formula [10], and the nPNA was calculated according to the method of Bergström et al [11]. The optimal phosphate level was defined as the phosphate level between 2.5 mg/dL and 4.5 mg/dL, which is considered a normal value in our clinic. All medications were prescribed according to the 2009 Kidney Disease: Improving Global Outcome CKD-MBD treatment guidelines.

Aortic arch calcifications were calculated based on posterior–anterior plain chest X-rays, using Ogawa et al's method [12], by a physician who was independent of this study. The intraobserver variability of this method was 5.3%.

Statistical analysis

Data were analyzed using SPSS for Windows, version 17.0 (SPSS Inc., Chicago, IL, USA). For continuous variables, the mean $\pm$ standard deviation was used for normally distributed data; otherwise, the median was shown. Differences between the two groups were assessed using a Student t test or Chi-square test, as appropriate. Pearson or Spearman correlation coefficients were used to test the correlation between eGFR and other variables. To evaluate the influence of parameters on the control of optimal phosphate levels, nonparametric variables were Ln-transformed to achieve normality; after transformation of the variables, we performed binary logistic regression analysis. A P value of < 0.05 was considered statistically significant.

Table 1. Causes of end-stage renal disease

Diagnosis	%
Diabetes	53.25
Glomerulonephritis	20.78
Hypertension	14.28
ADPKD	6.49
Neurogenic bladder	3.89
Unknown	1.29

Data are presented as %.
ADPKD, autosomal dominant polycystic kidney disease.