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Original Article

Phosphate Clearance in End Stage Kidney Disease Patients on Hemodialysis

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Abstract

Objective: To assess the effect of dietary phosphate intake, delivered dialysis dose (Kt/V, online clearance monitoring (OCM), urea reduction ratio (URR) and total weekly hemodialysis (HD) duration on phosphate levels and other factors affecting its clearance.

Methods: This study was carried out on 34 ESRD patients on maintenance hemodialysis. Patients' characteristics were all recorded on a pre-designed Questionnaire. Blood samples were collected from the arterial end before connecting the arterial line and rinsing the puncture needle; specimens after HD were collected from the arterial line at the end of dialysis; before collection the blood flow rate was reduced to 50 mL/min.

Results: Out of 34 hemodialysis patients, 41% (14/34) of patients were compliant to thrice weekly hemodialysis. There were 16 (47.1%) females and 18 (52.9%) males, age ranging from 17 to 87 and mean age of 59.6 years. Mean pre- & post-HD phosphate were 6.01mg/dl and 2.59mg/dl, respectively. There was a significant mean difference in pre- and post-dialysis phosphate levels ($p< 0.01$). PRR had no significant association with Kt/V, OCM, URR and blood volume passing through the dialyzer, UF volume, residual urine output, use of phosphate binders or hematocrit. The post-dialysis phosphate was lower in patients with higher Kt/V, URR and OCM ($r = -0.417$ $p = 0.014$, $r = -0.307$ $p = 0.07$, $r = -0.295$ $p = 0.091$ respectively). Patients who had a longer weekly time on dialysis had a lower pre-dialysis phosphate levels ($r = -0.34$, $p = 0.049$).

Conclusion: The pre-dialysis phosphate inversely correlated to total weekly dialysis time rather than Kt/V of a single session, total phosphate intake or dose of phosphate binders. Despite significant removal of phosphate during a single session of adequate dialysis, noncompliance to the prescribed three times a week dialysis and thus, decreased total weekly duration of dialysis may be responsible for hyperphosphatemia.

Keywords: End stage kidney disease, Hemodialysis, Phosphate clearance.

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Introduction

Hyperphosphatemia is a significant issue in the management of mineral and bone disease among dialysis-dependent populations. Consequences of hyperphosphatemia are secondary hyperparathyroidism, extraosseous calcification, vascular and valvular calcification, left ventricular hypertrophy, calciphylaxis and increased mortality.[1-5]

The retention of phosphate can contribute to secondary hyperparathyroidism through several mechanisms.[6,7]:

1. Decline in Serum Calcium: When phosphate levels rise, it can lead to a decrease in serum calcium. This imbalance triggers the parathyroid glands to become overactive, resulting in increased production of parathyroid hormone (PTH).
2. Reduced Calcitriol Production: Elevated phosphate can suppress the production of calcitriol, further exacerbating secondary hyperparathyroidism.
3. Calcitriol Resistance: Even if calcitriol is present, resistance to its actions within the parathyroid gland can occur due to high phosphate levels. This resistance prevents proper feedback regulation of PTH secretion.
4. Direct Effect on PTH Secretion: Phosphate can

directly influence PTH secretion independently of changes in serum calcitriol or calcium levels. This disruption in PTH regulation contributes to the development of secondary hyperparathyroidism.

The KDIGO guidelines emphasize the importance of monitoring phosphate, calcium, and parathyroid hormone (PTH) levels in patients with CKD. In non-dialysis CKD patients (Stages G3a–G5D), regular assessments of serum phosphate, calcium, and PTH levels are crucial.

Abdominal radiographs are recommended to evaluate vascular calcification. Detecting calcification in blood vessels is essential because it is associated with cardiovascular risk. Echocardiography is useful for detecting valvular calcification, which is also linked to cardiovascular complications.[8,9]

Elevated phosphate levels are associated with increased morbidity and mortality in CKD patients.[10,13] To address this, we consider Dietary Restrictions, Phosphate Binders, Adequate Dialysis.[14,15,16] Factors affecting phosphate clearance during dialysis have been reported in few analysis.[18] These include duration of dialysis, exercise, creatinine reduction ratio, flux of dialyzer, membrane surface area, plasma phosphate level, vascular access.[18,19]

Methods

In this study, we enrolled 34 patients with end-stage renal disease who were undergoing hemodialysis. Patients participated in either twice-weekly or thrice-weekly hemodialysis sessions, each lasting four hours (resulting in a total of 12 hours per week for thrice-weekly sessions and 8 hours per week for twice-weekly sessions).

We collected comprehensive demographic data from the patients' dialysis records, including information on name, gender, age, dialysis vintage (duration of dialysis), and details related to the dialyzer, such as type and surface area of the dialyzer membrane. Additionally, we recorded parameters such as the rate of blood flow during dialysis and the volume of ultrafiltration.

To assess daily phosphorus intake, we conducted interviews with each participant. Patients were categorized based on their daily phosphorus intake into three groups:

- < 900 mg/day
- 900-1200 mg/day
- 1200-1500 mg/day

Furthermore, patients who were taking non-calcium-containing phosphate binders were classified based on the dose of the drug:

- <1600 mg/day
- 1600-4800 mg/day

Throughout the study, the dialysate calcium levels were maintained at 1.25 mmol/L for all patients. Ethical considerations were addressed by obtaining informed consents from all participants, and the study was approved by the Institutional Review Board (IRB). Data analysis was performed using SPSS version 25.

Sample collection technique: Before initiating dialysis, blood samples for phosphate and urea were collected from the arterial side before connecting the arterial line. At the end of the dialysis session, additional samples were obtained from the arterial end after reducing the blood flow rate to 50 mL/min just before completing the dialysis process.

Results

The baseline demographics of the study population (n=34) as shown in table 1, revealed that the average age of patients was 59.6 years, with a range spanning from 17 to 87 years. Among the patients, 16 (47.1%) were female and 18 (52.9%) were males. 91.2% (31) of patients had hypertension, and 67.6% (23) were diabetic. The average duration of dialysis was 33.9 months, with a range from half a month to 79 months.

The dialysis parameters as shown in table 2 are as follows: 41.2% (14/34) received 12 hours of hemodialysis and 58.8% (20/34) received 8 hours of hemodialysis. Blood Flow Rate (BFR) of 350 ml/min was prescribed in 28 patients and 250 ml/min in the remaining 6 patients. The dialyzer type in 94.1% (32) of patients was FX10 dialyzer. 88.2% (30) patients had an arteriovenous fistula (AVF), 8.8% (3) had a temporary central venous catheter (CVC) and 2.9% (1) had a permanent CVC.

Table 1: *Baseline Characteristics (n=34)*

Characteristics		n	%
Gender	Female	16	47.1
	Male	18	52.9
Age (yrs)	<=40	2	5.9
	>40	32	94.1
HTN	NON HTN	3	8.8
	HTN	31	91.2
DM	NON-DM	11	32.4
	DM	23	67.6
Residual Urine Output (ml)/24hours	<250	22	64.7
	>250	12	35.3
Intake of Vitamin D	Yes	21	61.8
	No	13	38.2
Intake of phosphate binder (mg/day)	<1600	22	64.7
	1600-4800	12	35.3
Dietary phosphate intake (mg/day)	<900	19	55.9
	900-1200	15	44.1
	1200-1500	2	5.8

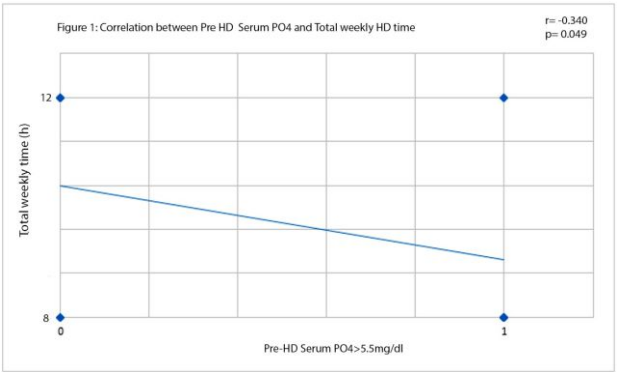
Phosphate management was done by using phosphate binder, dietary phosphate monitoring and vitamin D supplementation. Dose of phosphate binder was <1600 mg/day in 22 (64.7%) patients and 1600-4800 mg/day in 12 (35.3%) patients. A Dietary phosphate intake was <900 mg/day observed in 19 (55.9%) patients, 900-1200 mg/day in 15 (44.1%) and 1200-1500 mg/day in 2 (5.8%) patients. Vitamin D Supplements were taken by 21 (61.8%) patients.

Table 2: *Dialysis related characteristics of studied patients*

Characteristics		n	%
Qb (ml/min)	250	6	17.6
	350	28	82.4
Qd (ml/min)	500	33	97.1
	800	1	2.9
Access	AVF	30	88.2
	CVC	1	2.9
	PC	3	8.8
Dialyzer flux	Low	32	94.1
	High	2	5.9
Total weekly time on dialysis (hrs)	12	14	41.2
	8	20	58.8

The average pre-hemodialysis phosphate was 6.01 mg/dl and average post-hemodialysis phosphate was 2.59 mg/dL. The average difference between pre- and post-dialysis phosphate Level was statistically significant ($p<0.01$). Average pre-dialysis urea was 120.6 mg/dL and post-dialysis urea was 28.9 mg/dl. Mean urea reduction ratio (URR) was calculated as 74.9%.

Several interesting correlations related to pre-HD phosphate levels were observed. Patients with a prolonged weekly time on HD showed a lower pre-HD phosphate level ($p = 0.049$, $r = -0.34$) for those with a pre-dialysis phosphate level exceeding 5.5 mg/dL as shown in figure 1. The p valve was statistically significant. Additionally, high pre-HD phosphate levels were positively correlated with pre-dialysis urea levels ($r = 0.568$, $p < 0.01$) and negatively correlated with serum bicarbonate ($r = -0.363$, $p = 0.041$). However, pre-HD phosphate levels did not significantly correlate with other parameters such as residual urine output, volume of blood passing through the dialyzer, hematocrit, Kt/V (dialysis adequacy), or dietary phosphate consumption.



The post-HD phosphate was lower in patients with higher Kt/V, URR and OCM ($r = -0.417$ $p = 0.014$, $r = -0.307$ $p = 0.07$, $r = -0.295$ $p = 0.091$ respectively).

Mean Phosphate Reduction Ratio (PRR) was 55.6% with SD +11.71. A higher predialysis serum phosphate and urea ($r = 0.608$, $p < 0.01$ and $r = 0.379$, $p = 0.027$ respectively) were seen in patients with a higher PRR20. Daily phosphate intake and PRR had a negative correlation ($r = -0.377$, $p = 0.028$). Kt/V, OCM, URR and blood volume passing through the dialyzer, UF volume, residual urine output, use of phosphate binders or hematocrit were not significantly correlated with PRR.

We observed interesting associations related to post-hemodialysis (HD) phosphate levels. Patients with higher Kt/V, higher URR, and higher OCM had lower post-HD phosphate levels. These correlations were statistically significant: Kt/V ($r = -0.417$, $p = 0.014$), URR ($r = -0.307$, $p = 0.07$), and OCM ($r = -0.295$, $p = 0.091$)[20]. Additionally, the mean Phosphate Reduction Ratio (PRR) was 55.6% with a standard deviation of +11.71. Patients with higher predialysis serum phosphate and urea showed a positive correlation with a higher PRR (serum phosphate: $r = 0.608$, $p < 0.01$; urea: $r = 0.379$, $p = 0.027$). However, daily phosphate intake negatively correlated with PRR ($r = -0.377$, $p = 0.028$). Other parameters such as Kt/V, OCM, URR, blood volume passing through the dialyzer, UF volume, residual urine output, use of phosphate binders, and hematocrit were not significantly correlated with PRR20.

Discussion

The aim of our study was to identify factors influencing

Table 3: *Mean values of Pre-HD and Post -HD phosphate and urea, URR and PRR.*

	Pre-HD phosphate	Post-HD phosphate	PRR(%)	Pre-HD Urea	Post-HD Urea	URR (%)
Mean	6.02	2.59	55.59	120.56	28.97	74.91
Std. Deviation	2.02	0.71	11.71	57.34	13.77	6.49
Minimum	2.90	1.40	22.50	32.00	6.00	60.40
Maximum	12.60	4.10	76.10	261.00	71.00	88.60

phosphate clearance in order to reduce pre-dialysis phosphate levels. Notably, an increased weekly duration of dialysis sessions was associated with a decrease in pre-dialysis phosphate levels, consistent with findings from studies conducted by Zhan et al and Ayus et al.[21,22]

In our region, most patients receive 8 to 12 hours of dialysis per week due to resource constraints. Therefore, we compared reduced dialysis hours (8hrs/week) to standard hours (12hrs/week). Interestingly, the ACTIVE Dialysis study by Zhan et al compared extended hours hemodialysis (≥24 h/week) to conventional hemodialysis (≤18 h/week) and reported lower phosphate levels in the extended hours group. Similarly, Ayus et al demonstrated that short daily hemodialysis (6 sessions/week, 3 hours each) achieved greater phosphorus clearance over 12 months, leading to improved mineral metabolism goals[22]. Although our study did not directly measure weekly phosphate clearance, the impact of increased HD duration on phosphate reduction aligns with these findings.

Additionally, John T Daugirdas et al found that 6 sessions/week resulted in reduction in mean serum phosphorus compared to 3 sessions/week.[23] Strategies such as extended treatment times, hemodiafiltration, and increased dialysis frequencies can enhance phosphate removal, despite the intracellular location of most inorganic phosphorus.[24, 25] our study underscores the importance of optimizing dialysis duration to effectively manage phosphate levels.

In our study, we observed that neither pre-dialysis phosphate levels nor the phosphate removal rate (PRR) significantly correlated with various factors, including residual urine output, blood volume passing through the dialyzer, hematocrit, ultrafiltration (UF) volume, Kt/V, online clearance monitor (OCM), urea reduction ratio (URR), dietary phosphate consumption, or intake of phosphate binders. However, P. Gallar et al. discovered a noteworthy correlation between phosphate removal and the volume of blood passing through the dialyzer during each session (with a correlation coefficient of $r = 0.001$).[19] interestingly, they did not find a significant correlation between phosphate removal and other parameters such as KT/V, dialysate flux, or ultrafiltration. This highlights the complexity of phosphate removal during hemodialysis and suggests that factors beyond the commonly measured parameters may influence phosphate clearance.

We investigated the correlation between the phosphate removal rate (PRR) and various parameters in hemodialysis patients. Notably, we found positive associations between PRR and predialysis serum phosphate levels ($r = 0.608$, $p < 0.01$) as well as pre dialysis urea ($r = 0.379$, $p = 0.027$). However, PRR did not significantly correlate with other factors, including Kt/V (a measure of dialysis adequacy), online clearance monitor (OCM), urea reduction ratio (URR), blood volume passing through the dialyzer, ultrafiltration (UF) volume, residual urine output, use of phosphate binders, or hematocrit. Interestingly, a separate study by Yu Q et al. reported contrasting findings[18]. They observed positive correlations between PRR and effective blood flow rate, predialysis serum phosphate, clearance reduction ratio (CRR), blood chamber volume, and membrane surface area of the dialyzer. However, PRR was negatively correlated with hematocrit ($r = 0.493$, 0.386, 0.368, 0.482, 0.303, and −0.225, respectively, and $P < 0.05$). These divergent results highlight the complexity of phosphate removal during hemodialysis and underscore the need for further research to better understand the factors influencing this process.

This study has a few notable limitations. Firstly, the small sample size compared to other studies may limit the generalizability of the findings. Additionally, the blood flow rates and duration of dialysis were not increased beyond a specified range, which could impact the observed outcomes. Another limitation is the lack of monitoring of dialysate effluent phosphate during the dialysis sessions.

Duration of a single hemodialysis session plays a crucial role in controlling serum phosphate levels in patients with end-stage renal disease (ESRD). While achieving a frequency of dialysis sessions exceeding 12 hours per week may be challenging in some regions, striving for at least 12 hours of dialysis per week could lead to better phosphate control in dialysis patients. Improved phosphate management has the potential to enhance the survival of ESRD patients by reducing the risk of cardiovascular disease within this population.[26] It underscores the importance of optimizing dialysis practices to benefit patient outcomes.

Conclusion

Predialysis phosphate levels were lower in patients with increased total weekly dialysis time compared to those who consumed less phosphate, took higher doses of phosphate binders, and achieved a higher Kt/V during a single session. This suggests that the frequency and duration of dialysis sessions play a crucial role in controlling serum phosphate.

Inability to comply with the prescribed three dialysis sessions per week may contribute to elevated phosphate levels. While achieving more frequent dialysis sessions (beyond the standard three times per week) might be challenging, striving for at least 12 hours of dialysis per week could lead to better phosphate control in patients undergoing hemodialysis. Improved phosphate management has the potential to enhance the survival of ESRD patients by reducing the risk of cardiovascular compli-

cations within this population.

These findings underscore the importance of optimizing dialysis practices and tailoring treatment regimens to individual patient needs. By addressing phosphate levels effectively, we can positively impact patient outcomes and overall well-being.

Disclosure

Only the abstract of this article was published in KI reports https://doi.org/10.1016/j.ekir.2020.02.227

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