Original Paper

Phosphate Removal During Conventional Hemodialysis: a Decades-Old Misconception

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Key Words

Phosphate removal • Hemodialysis • Dialysate • Hyperphosphatemia

Abstract

Background/Aims: Hyperphosphatemia is associated with high mortality rate in patients on dialysis. Conventional hemodialysis (HD) is a limit technique in removing phosphate (P). There is a widespread belief that P is removed mainly in the first hour of HD. The aim of this study was to certify the percentage of 1-hour removal of P as compared to the entire procedure. **Methods:** data from the first dialysis of the week of 21 patients (13 men, age 44 ± 15 years), for 3 consecutive dialysis sessions were evaluated. Fresh dialysate samples were collected at 1 hour and at the end of the session from a partial spent dialysate collection method. **Results:** Pre dialysis serum P was 4.7 ± 1.7 mg/dl. Reduction rate of serum P was 47.4 ± 14.3 and $45.1 \pm 10.8\%$ in 1- and 4-hour of HD, respectively ($p=0.322$). P removal was 194 (145, 242) mg in 1-hour ($p<0.0001$), which represents $25.0 \pm 0.2\%$ of the total removed during the entire HD. Patients with pre dialysis P ≥ 5.5 mg/dl had higher P removal during HD than those with P < 5.5 mg/dl [975 (587, 1354) vs. 776 (580, 784) mg, $p=0.025$], although the percentage of removal in 1 hour was not different from those with P < 5.5 mg/d (24.9 ± 0.3 vs. $25.0 \pm 0.1\%$, $p=0.918$). P removal during dialysis correlated with pre dialysis serum P ($r=0.455$, $p=0.001$), parathormone ($r=0.264$, $p=0.037$) and ultrafiltration volume ($r=0.343$, $p=0.019$). **Conclusion:** despite the P serum concentration normalizing in the first hour of hemodialysis, the removal in the same period reaches only 25% of the entire session.

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Introduction

It is no longer argued that high serum phosphate (P) is associated with high mortality rate among patients on dialysis [1, 2]. Despite that, one of the greatest frustrations of the

nephrologist community worldwide is that serum P levels tend to be poorly controlled in dialysis patients.

Conventional thrice-weekly hemodialysis (HD), the most commonly used method of renal replacement therapy, is a rather limited technique in removing P [3]. Some authors have suggested an increase in dialysis frequency, instead of an increase in dialysis length, based on an assumption that the higher amount of P is removed during the first 1 or 2 hours [4].

In the present study, we examined the amount of P removed during the first hour of dialysis, as compared to the total amount removed in a 4-hour HD procedure, to confirm the hypothesis of a higher removal of P in the first hour of a conventional HD.

Materials and Methods

Twenty-one patients were submitted to a high-flux HD three times per week, with new high-flux polysulphone dialyzers FX80 (Fresenius Medical Care) each studied HD session. The first dialyses of the week, for 3 consecutive weeks were chosen for analysis. Blood flow was set to 350 ml/min and dialysate flow to 800 mL/min; bicarbonate dialysate/infusate with potassium 2 mEq/L was used (Fresenius Medical Care).

The study conforms to the provisions of the Declaration of Helsinki and was approved by the Local Ethics Committee (Cappesq #14052813.4.0000.0068). All patients signed informed consent before study enrolment.

Phosphate removal

Blood samples for phosphate concentration were taken pre dialysis, after 1 hour and at the end of the 4-hour dialysis session. Fresh dialysate samples were collected at 1 hour and at the end of the session from a partial spent dialysate collection method, which accurately reflects the total spent dialysate collection [5-7]. In this technique, spent dialysate and ultrafiltrate were continuously sampled by a reversed automatic injection pump, located in the waste tubing just before the drain, throughout the complete dialysis procedure at a rate of 1L/h as previously described. This system ensured a constant volume of fluid ejecting it at a 5L capacity recipient. At 1 hour and at the end of procedure all collected fluid was homogenized in the vessel and an aliquot was withdrawn for analysis of phosphate removal.

Reduction rate of P was calculated using the equation: (serum P at 4 hour of HD – predialysis serum P and serum P at 1 hour of HD – predialysis serum P) divided by predialysis serum P; results were expressed as %.

Statistical Analysis

Continuous variables were expressed as mean $\pm$ standard deviation or median and percentiles (25; 75), according to the D'Agostino & Pearson omnibus normality test. Spearman rank correlation was used to access relationships between independent variables. Friedman test was used as appropriate to compare variables at baseline (pre dialysis), after 1 hour and post dialysis. Comparisons were done using Student t-test or Mann-Whitney as appropriate. Statistical analysis was performed with GraphPad Prism 5.0 (Ca, USA). Significance was assigned at p values < 0.05.

Results

Chronic glomerulonephritis, diabetes and nephrosclerosis accounted for the 66.5% of ESRD etiology. All patients had an arteriovenous fistula as vascular access.

A total of 3 HD sessions from 21 stable patients (13 men; 44 ± 15 years) were analyzed. Pre dialysis serum P was 4.7 ± 1.7 mg/dl (range 1.5 to 10 mg/dl) and reduced significantly in 1 and 4 hours of dialysis. Table 1 shows serum P, reduction rate and P removal at 1 and 4-hour HD. The reduction rate of P at 4-hour of HD was higher among patients who started

dialysis with P serum levels ≥ 5.5 mg/dl. In this subgroup of patients, serum levels of P were higher in 1- and 4-hour of HD than in same moment for those with P levels < 5.5 mg/dl. P removal, as measured through the dialysate, was lower in 1 hour of HD than in the entire 4-hour procedure. This result is reflecting the relative removal of P, which was only 25% of the total during the first hour of HD. Patients with pre dialysis serum levels of P ≥ 5.5 mg/dl presented a higher removal of P in the entire HD than those with serum levels < 5.5 mg/dl, although the relative removal remained the same (75.0 ± 0.1 vs. $75.0 \pm 0.3\%$, respectively, $p=0.715$). P removal during dialysis correlated with pre dialysis serum P ($r=0.455$, $p=0.001$), parathormone ($r=0.264$, $p=0.037$) and ultrafiltration volume ($r=0.343$, $p=0.019$).

The discrepancy between the drop in serum P concentration and the actual P removal, calculated through the spent dialysate is illustrated in the Fig. 1. As shown, while serum levels decreased by 47%, solute removal accounted for only 25% of the entire session during the first hour of HD.

Table 1. Levels of serum phosphate, reduction rate compared to pre dialysis levels and phosphate removal derived from 63 hemodialysis (HD) sessions. P = phosphate; HD = hemodialysis. Values are expressed as mean $\pm$ SD or median (25,75), as appropriate. "a" $p<0.05$ vs. baseline; "b" $p<0.05$ vs. 1 hour; "*" $p < 0.05$ vs. P < 5.5 mg/dl

	Baseline	After 1 hour of HD initiation	At the end of the 4-hour HD	P
Serum P, mg/dl	4.5 (3.5, 5.4)	2.5 (2.0, 3.0) ^a	2.3 (1.9, 2.8) ^{ab}	<0.0001
Pre HD P ≥ 5.5 mg/dl	6.5 (6.0, 7.6)	3.3 (3.0, 4.1) ^{a*}	2.9 (2.5, 3.2) ^{ab}	<0.0001
Pre HD P < 5.5 mg/dl	4.4 (3.2, 1.8)	2.2 (1.8, 2.6) ^a	2.1 (1.6, 2.6) ^a	<0.0001
Reduction rate of serum P, %		47.4 $\pm$ 14.3	45.1 $\pm$ 10.8	0.322
Pre HD P ≥ 5.5 mg/dl	-	49.1 $\pm$ 8.3	57.3 $\pm$ 8.3*	0.015
Pre HD P < 5.5 mg/dl	-	43.9 $\pm$ 11.2	44.3 $\pm$ 14.3	0.887
Phosphate removal, mg		194 (145, 242)	776 (581, 973)	<0.0001
Pre HD P ≥ 5.5 mg/dl	-	241 (146, 337)	975 (587, 1354)*	<0.0001
Pre HD P < 5.5 mg/dl	-	193 (145, 196)	776 (580, 784)	<0.0001
Phosphate removal, %		25.0 $\pm$ 0.2	100	-
Pre HD P ≥ 5.5 mg/dl	-	24.9 $\pm$ 0.3	100	-
Pre HD P < 5.5 mg/dl	-	25.0 $\pm$ 0.1	100	-

Fig. 1. A dual y-axis chart illustrating serum Phosphate (P) and P removal during conventional hemodialysis. Mean and 95% IC of serum P is represented in left y-axis with filled symbols; P removal is represented in right y-axis with empty symbols. P serum concentration has reduced by 47% from baseline values in 1 hour ($p=0.0001$); the P removed in the same period was 25% of the total. * $p<0.0001$ 1 hour vs. baseline and 4 hour vs. baseline.

Discussion

We found that despite a major drop in serum P concentration in the first hour of HD, only a quarter of the total P removal occurred in the same period. Despite the fact that total P mass removal was higher among patients with hyperphosphatemia, the percentage of mass removal in the first hour was virtually equal to that observed in patients without hyperphosphatemia.

As stated in the literature, P kinetics during HD is a 2-phase pattern, in which the first phase lasts 1.5-2 hours. In this phase, the decline of P is mainly explained by removal from the extracellular compartment. A relatively stable P level characterizes the second phase, which occurs when P levels dropped to about 40-50% of baseline predialysis levels [8]. Studies based on P mass removal, calculated through the spent dialysate, however, are scarce. A previous study stacked through decades has reinforced an erroneous concept of a greater P removal at the beginning of HD than the remainder of the procedure [4]. Of note, this study enrolled only 6 patients, dated from 1993, and has enrolled patients performing 3:00 and 4 hours of HD duration. In agreement with our data, Sampaio et al [9]. have demonstrated a linear P mass removal throughout the conventional HD procedure.

The fact that patients usually present higher levels of serum phosphate before the first dialysis of the week, and therefore a higher chance of greater removal, was the main determinant to choose this dialysis session for research proposal. If P removal were greater during the first 2 hours of dialysis, daily dialysis schedule would be the best method to control serum P. The advantage of daily HD, however, is mainly based on a weekly removal of P, since if only the first 2 h of dialysis had been considered, weekly P removal would not be significantly different from the conventional HD [10]. Therefore, an increase in the frequency of HD can indeed remove greater amount of P since is performed 5-6 times a week, not because it removes P mass during the first 1-2 hours of HD.

We are aware of several limitations of the present study, which include the lack of nutritional parameters and the small sample size. However, we simply wanted to readdress classical concepts of serum concentration and mass removal of P during HD. And by that note, nephrologists should be aware that to remove P, longer HD time is needed, despite the serum concentration normalizing in 1 or 2 hours.

Conclusion

The pre-established concept that serum P has greater removal during the first hour of HD should be rethought. Although there is a greater reduction of serum levels of P in the first hour of HD, this does not translate into greater removal of this solute during this period. Indeed, removal of P appears to be continuous during the conventional hemodialysis procedure, explaining why longer therapies are the best option to remove this solute.

Disclosure Statement

The authors declare they have no conflicts of interest.

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