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Phosphorus Consumption Within 1 Hour Prior to Blood Work and Associated Serum Levels of Phosphate, Calcium, and PTH in Adult Patients Receiving Hemodialysis Treatment

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Abstract

Background: While dietary intake is known to influence serum markers of chronic kidney disease–mineral and bone disorder (CKD-MBD), the effects of recent food and beverage intake, particularly phosphorus consumption on these serum markers (phosphate, calcium, and parathyroid hormone [PTH]), are unknown in hemodialysis patients. An understanding of these effects could have direct and important implications on the management of CKD-MBD.

Objective: To determine whether serum phosphate, calcium, and PTH levels were higher in hemodialysis patients who had consumed dietary phosphorus within 1 hour prior to their routine dialysis-related blood work (non–phosphorus-fasted) compared with patients who did not (phosphorus-fasted).

Design: Observational, cross-sectional study.

Setting: Kingston Health Sciences Center—Kingston General Hospital Site and its affiliated satellite hemodialysis units.

Patients: Two hundred fifty-four adult patients receiving outpatient hemodialysis treatment for end-stage kidney disease were recruited.

Measurements: The main measurements for this study included an assessment of dietary phosphorus intake as well as serum phosphate, calcium, PTH, albumin, Kt/V, and urea reduction ratio.

Methods: A direct patient interview was performed to assess dietary phosphorus intake within 1 hour prior to routine dialysis-related blood work. The Canadian Nutrient File was then used to estimate dietary phosphorus based on the specific foods and beverages (including portion sizes and brands where applicable) identified in the interview. Serum measures of phosphate, PTH, calcium, albumin, and dialysis adequacy (Kt/V and urea reduction ratio) were obtained from participants' routine dialysis-related blood work.

Results: Non–phosphorus-fasted participants had nonsignificantly higher serum PTH levels compared to phosphorus-fasted participants (61.2 $\pm$ 64.7 vs 47.9 $\pm$ 39.7, $P = .05$). Non–phosphorus-fasted participants with PTH levels at the Kidney Disease Improving Global Outcomes (KDIGO) "target" (between 15 and 60 pmol/L) had significantly higher serum phosphate levels relative to phosphorus-fasted participants (1.6 $\pm$ 0.3 vs 1.4 $\pm$ 0.4, $P = .006$). In non–phosphorus-fasted participants, there was a nonsignificant association between the number of items containing inorganic phosphate additives and higher levels of serum phosphate and lower levels of serum calcium.

Limitations: Some limitations include the cross-sectional nature of this study, self-reporting biases and estimates (as opposed to direct measurements) related to the dietary assessment, and the use of single (and not serial) assessments of serum measures.

Conclusions: Dietary phosphorus intake in close proximity to blood work may contribute to subtle alterations in some key serum CKD-MBD parameters in adult outpatient hemodialysis patients but may not meaningfully alter CKD-MBD management.

Abrégé

Contexte: Alors que l'alimentation est connue pour influencer les marqueurs sériques des troubles minéraux et osseux associés à l'insuffisance rénale chronique (TMO-IRC), les effets d'une consommation récente de nourriture et de boisson,

particulièrement de phosphore, sur ces mêmes marqueurs sériques (phosphate, calcium et hormone parathyroïde [PTH]), demeurent inconnus chez les patients hémodialysés. Une meilleure connaissance de ces effets pourrait avoir une influence majeure et directe sur la prise en charge des TMO-IRC.
Objectif: Déterminer si les taux sériques de phosphate, de calcium et de PTH sont plus élevés chez les patients hémodialysés ayant consommé des aliments contenant du phosphore dans l'heure précédant les analyses sanguines de routine liées à la dialyse (analyse sanguine de routine), lorsque comparés aux taux des patients n'en ayant pas consommé (patients à jeun).
Type d'étude: Une étude transversale observationnelle.
Cadre: Le Kingston Health Sciences Centre, sur le site de l'hôpital général de Kingston, et ses unités satellites d'hémodialyse.
Sujets: L'étude porte sur 244 patients adultes atteints d'insuffisance rénale terminale et recevant des traitements ambulatoires d'hémodialyse.
Mesures: Les principales mesures incluaient l'évaluation de l'apport en phosphore alimentaire, la mesure des taux sériques de phosphate, de calcium, de PTH et d'albumine, de même que le Kt/V et le taux de réduction de l'urée.
Méthodologie: Les patients ont été questionnés sur leur consommation de phosphore dans les heures précédant l'analyse sanguine de routine liée à la dialyse. Le Fichier canadien des éléments nutritifs a par la suite été employé pour estimer la quantité de phosphore alimentaire selon les aliments et les boissons consommés (portions et marque du produit, lorsque disponibles). Les mesures sériques de phosphate, de PTH, de calcium et d'albumine, de même que l'efficacité de la dialyse (Kt/V et taux de réduction de l'urée) ont été obtenues par les analyses sanguines de routine.
Résultats: Les participants qui avaient consommé du phosphore n'ont pas présenté un taux de PTH sérique plus élevé que les patients à jeun (61,2 ± 64,7 contre 47,9 ± 39,7; $P = 0,05$). Les sujets ayant consommé du phosphore et dont les taux de PTH sériques se situaient dans la « cible » du KDIGO (*Kidney Disease Improving Global Outcomes*), soit entre 15 et 60 pmol/L, présentaient des taux de phosphate sérique significativement plus élevés que les sujets à jeun (1,6 ± 0,3 contre 1,4 ± 0,4; $P = .006$). En outre, chez les patients ayant consommé du phosphore, une association non significative a été observée entre le nombre d'aliments contenant des additifs phosphatés inorganiques qui avaient été consommés et des taux sériques plus élevés en phosphate et plus faibles en calcium.
Limites: La nature transversale de l'étude, de possibles biais et estimations dus à l'auto-évaluation des apports alimentaires (par rapport à une mesure directe) et le recours à des mesures uniques (et non en série) pour les analyses sanguines constituent les limites.
Conclusion: La consommation de phosphore alimentaire dans les heures précédant l'analyse sanguine est susceptible d'introduire de légères altérations pour certains paramètres sériques clés du TMO-IRC chez les adultes recevant des traitements ambulatoires d'hémodialyse, sans toutefois altérer la gestion du TMO-IRC de façon significative.

Keywords
hemodialysis, dietary phosphorus, phosphate, calcium, parathyroid hormone

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What was known before

High serum phosphate levels are associated with a greater risk of cardiovascular disease and mortality in patients with end-stage kidney disease (ESKD). While serum measures (phosphate, calcium and parathyroid hormones [PTH]) of chronic kidney disease-bone mineral disorder (CKD-MBD) are known to be affected by dietary intake, it is not currently part of standard clinical practice for patients to fast (ie, avoid dietary phosphorus consumption) prior to routine dialysis-related blood work.

What this adds

By examining the effects of recent dietary phosphorus consumption on CKD-MBD serum markers, the results of this study, together with future studies, have potential to impact CKD-MBD management. Specifically, it will be important

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to determine whether the conditions (ie, dietary intake) prior to routine dialysis-blood work should become more formally assessed and controlled as part of standard of care.

Introduction

Among patients with chronic kidney disease (CKD), cardiovascular disease (CVD) is the leading cause of death, and the more advanced the CKD, the higher the risk of mortality from CVD.[1,2] The elevated risk in this population is due in part to the consequences of vascular calcification, which has been linked to alterations in the metabolism of divalent ions and abnormalities in bone remodeling.[3] In this population, elevated phosphate levels have been consistently linked to the onset and development of vascular calcification.[4]

At present, the management of CKD-MBD is largely driven by laboratory values with the understanding that responding to trends, as opposed to single values, is important. First-line treatment for CKD-MBD includes dietary phosphorus restriction and the administration of pharmacological agents that reduce phosphate absorption.[5] Phosphate binders include calcium- as well as noncalcium-based phosphate binders. Calcium effectively binds phosphate in the intestine and is the primary agent used in many countries as noncalcium-based phosphate binders are not universally available.[6] However, the calcium in these pharmacological preparations may also be absorbed and contribute to the progression of vascular calcification; thus, limiting calcium exposure is of critical importance.[7] Kidney Disease Improving Global Outcomes (KDIGO) clinical practice guidelines recommend 'restricting the dose of calcium in patients ESKD whilst KDOQI guidelines recommend a daily ceiling dose of 1500 mg of elemental calcium/day.[8,9]

Secondary hyperparathyroidism frequently accompanies abnormalities in divalent ions in patients with ESKD. When PTH levels approach ~60 pmol/L and above or 9 times the upper limit of normal for the specific manufacturer's assay, a vitamin D analogue such as calcitriol may be prescribed to suppress PTH secretion.[8] Calcitriol, however, increases intestinal absorption of calcium and phosphate and may also have direct procalcific actions on vascular smooth muscle cells. Although randomized controlled trials addressing this question in humans are lacking, this conclusion has been borne out in several animal models.[10,11] Given the frequency with which patients are prescribed calcium and calcitriol, our understanding of the factors that alter the management of CKD-MBD needs to be optimized to reduce harm.

Levels of calcium, phosphate, and PTH are typically monitored every 4 to 6 weeks in hemodialysis patients, and changes to the dosage of calcium and calcitriol are made by the attending nephrologist upon blood work review with consideration of previous values and trends. The 2017 KDIGO guidelines for CKD-MBD management recommend that phosphate be "lowered toward the normal range" and that hypercalcemia be avoided.[9] Target PTH is approximately 2 to 9 times the upper normal limit for the assay which translates approximately to between 15 pmol/L and 60 pmol/L.[9,12]

It is widely acknowledged that serum phosphate levels are influenced by the time of day, food intake, adherence to phosphate binders, individual differences in the efficacy of phosphate binders, as well as dialytic removal.[13] With a focus on dietary intake, we recently provided a 500 mg bioavailable phosphorus challenge to nondialyzed participants with low kidney function (measured glomerular filtration rate [GFR] less than 60 mL/min) and identified that PTH and phosphate both rose significantly and peaked at 60 minutes.[14] While it is recommended that patients should restrict their food intake for the duration of their dialysis shift due to potential adverse effects (including decreased blood volume, increased aspiration risk and gastrointestinal symptoms),[15-17] it is not routinely recommended that patients fast (ie, avoid dietary phosphorus) *before* routine blood work. We hypothesized that fasting status could influence blood levels of phosphate, calcium, and PTH. The objective of this study was to determine whether dietary phosphorus consumed within 1 hour prior to routine dialysis-related blood work was associated with higher levels of phosphate, calcium, and PTH in adult hemodialysis patients.

Methods

Adult patients receiving maintenance hemodialysis treatment on an outpatient basis were recruited from Kingston Health Sciences Center–Kingston General Hospital site or one of its affiliated dialysis units. Written informed consent was obtained for all interested patients prior to their participation in this study. Inclusion criteria included adult patients with ESKD receiving maintenance hemodialysis treatment for any length of time. Patients were excluded if they were receiving hemodialysis treatment on an inpatient basis, if they were unable to speak English, or if they were unable to provide informed consent for participation in the study. Two hundred fifty-four patients were enrolled into this study. The Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board (HSREB) reviewed and approved this study.

Dietary Assessment

On the day of routine dialysis-related blood work assessment, upon arrival to the hemodialysis unit, trained research assistants conducted a direct interview with each enrolled patient. Participants were specifically asked what they had to eat and drink (including an estimate of portion size) in the previous 1 hour leading up to the time at which they presented to the dialysis unit. If patients had *not* consumed phosphorus within 1 hour of presenting to the dialysis center, they were classified as "phosphorus-fasted" and if they had consumed phosphorus within this hour, they were classified as "non–phosphorus-fasted."

Table 1. Baseline Demographics, Serum Laboratory Values, Medications, and Hemodialysis Shifts of All, Phosphorus-Fasted, and Non–Phosphorus-Fasted Participants.

	All (n = 254)	Phosphorus-fasted (n = 185)	Non–phosphorus-fasted (n = 69)	*P*
Demographics				
Sex (male), n (%)	145 (57.1)	105 (56.8)	40 (58.0)	.86
Age (years)	66.8 ± 14.5	67.0 ± 14.0	66.2 ± 15.7	.68
Diabetes, n (%)	140 (55.1)	104 (56.2)	36 (52.2)	.57
Serum laboratory values				
URR % (n = 249)	0.8 ± 0.1	0.8 ± 0.1	0.8 ± 0.1	.42
Ca mmol/L	2.3 ± 0.2	2.3 ± 0.2	2.2 ± 0.2	.18
PO4 mmol/L	1.5 ± 0.4	1.5 ± 0.4	1.6 ± 0.3	.26
PTH pmol/L	51.5 ± 48.0	47.9 ± 39.7	61.2 ± 64.7	.05
Albumin g/L	32.0 ± 3.2	31.9 ± 3.2	32.1 ± 3.3	.63
Medications				
Ca daily dose (mg/day) (n = 252)	1578.0 ± 1188.4	1585.7 ± 1226.6	1556.7 ± 1084.4	.87
Calcitriol daily dose (µg/day) (n = 253)	0.1 ± 0.2	0.1 ± 0.2	0.1 ± 0.2	.94
Hemodialysis shifts				
07:30, n (%)	100 (39.4)	68 (36.8)	32 (46.4)	.21
12:30, n (%)	96 (37.8)	70 (37.8)	26 (37.7)	
17:30, n (%)	58 (22.8)	47 (25.4)	11 (15.9)	

Note. Data are represented as mean ± standard deviation unless otherwise specified. URR = urea reduction ratio; Ca = calcium; PO4 = phosphate; PTH = parathyroid hormone.

Estimate of Phosphorus Consumption

To obtain an estimate of dietary phosphorus in milligrams, dietary intake (food and beverage) information provided by each participant was cross-referenced with food and beverage composition tables in the Canadian Nutrient File (publicly available via the Health Canada website).

Laboratory Analysis

The following laboratory values were obtained from the dialysis-related monthly blood work: serum phosphate (mmol/L), serum calcium (mmol/L), PTH (pmol/L), serum albumin (g/L), Kt/V, and urea reduction ratio (n = 249).

Medical History and Medications

Dialysis vintage, history of diabetes, daily dose of calcium and calcitriol, and phosphate binder use within the hour prior to dialysis-related monthly blood work were determined via direct participant interviews and medical chart reviews as applicable.

Statistical Analysis

Baseline variables were expressed as mean with standard deviation for continuous variables and frequencies with percentages for categorical variables. Baseline variables were compared by fasting status (non–phosphorus-fasted vs phosphorus-fasted) with respect to phosphorus intake and by level of PTH using an independent *t* test, analysis of variance (ANOVA), chi-square test or a Kruskal-Wallis test where appropriate. Pearson product moment correlation was used to assess the relationship between the number of food or beverage items containing inorganic phosphate additives and the level of phosphate and calcium. Multivariate linear regression was used to assess the independent predictors (non–phosphorus-fasted status, phosphate binder use, and calcitriol use) of PTH values.

Results

The baseline characteristics of the 254 participants overall and by phosphate-fasted status are presented in Table 1. Compared with phosphorus-fasted participants, non–phosphorus-fasted participants had similar levels of phosphate and calcium with a nonsignificant trend of higher levels of PTH (Table 1).

Table 2 demonstrates participant characteristics and laboratory variables stratified by KDIGO PTH categories. Overall, participants with a PTH value greater than 100 pmol/L were significantly younger, had significantly higher serum phosphate levels, and had a significantly higher average daily prescribed dose of calcium and calcitriol relative to participants with PTH values equal to or less than 100 pmol/L. Participants with KDIGO "target" PTH values between 15 to 60 pmol/L were on the lowest daily dose of calcium compared with participants in all other PTH categories. Participants with PTH less than 15 pmol/L had significantly higher serum calcium and, as expected, were

Table 2. Participant Demographics, Estimated Phosphorus Intake, Serum Laboratory Values, and Medications Stratified by KDIGO PTH Levels.

	<15 pmol/L (n = 42)	15-60 pmol/L (n = 136)	61-100 pmol/L (n = 52)	>100 pmol/L (n = 24)	*P*
Demographics					
Sex (male) n (%)	22 (52.4)	79 (58.1)	29 (55.8)	15 (62.5)	.88
Age (years)	63.8 ± 12.0	68.8 ± 14.4	66.5 ± 15.3	61.2 ± 15.4	.04
Diabetes	21 (50.0)	73 (53.7)	34 (65.4)	12 (50.0)	.39
Phosphorus intake					
One hour estimated phosphorus intake (mg)	44.7 ± 114.1	60.8 ± 134.3	37.7 ± 97.4	129.9 ± 241.0	.05
Serum laboratory values					
URR (%) (n = 249)	0.8 ± 0.1	0.8 ± 0.1	0.8 ± 0.1	0.8 ± 0.1	.59
Serum Ca (mmol/L)	2.3 ± 0.2	2.3 ± 0.2	2.2 ± 0.2	2.3 ± 0.2	.03
Serum PO4 (mmol/L)	1.6 ± 0.4	1.4 ± 0.4	1.7 ± 0.4	1.7 ± 0.5	<.01
Serum PTH (pmol/L)	8.4 ± 4.2	35.3 ± 13.0	78.0 ± 10.5	161.6 ± 70.1	<.001
Serum albumin (g/L)	31.8 ± 3.1	31.9 ± 3.6	31.9 ± 2.4	32.9 ± 3.0	.56
Medications					
Daily Ca dose (mg) (n = 252)	1864.3 ± 1402.2	1346.6 ± 1079.7	1780.8 ± 1129.5	1929.2 ± 1286.2	.01
Daily Calcitriol dose (μg) (n = 253)	0.1 ± 0.2	0.1 ± 0.2	0.2 ± 0.2	0.2 ± 0.3	<.001

Note. Data are represented as mean ± standard deviation unless otherwise indicated. KDIGO = Kidney Disease Improving Global Outcomes; PTH = parathyroid hormone; URR = urea reduction ratio; Ca = calcium, PO4 = phosphate.

prescribed significantly less calcitriol than participants with PTH values equal to or greater than 15 pmol/L.

Levels of phosphate and calcium were evaluated in response to phosphate-fasted status within 1 hour by KDIGO PTH categories (Table 3). When comparing serum phosphate levels by categories of PTH, non–phosphorus-fasted participants with KDIGO "target" PTH levels (15-60 pmol/L) had significantly higher serum phosphate levels compared with phosphorus-fasted participants (1.6 ± 0.3 vs 1.4 ± 0.4, $P = .006$). When comparing non–phosphorus-fasted participants with phosphorus-fasted participants who fall in the greater than 100 pmol/L PTH category, there was a trend toward lower calcium levels in non–phosphorus-fasted participants. Non–phosphorus-fasted participants also consumed significantly more phosphorus relative to participants with lower (<100 pmol/L) PTH levels.

With a multivariate linear regression model (Table 4), the association between non–phosphorus-fasted status and PTH remained significant after adjustment for whether a phosphate binder had been concurrently taken and whether the patient was on calcitriol (although the variance explained was low).

Due to the recognized diurnal rhythm of phosphate homeostasis, these parameters were also evaluated by the shift (07:30, 12:30, and 17:30) that each patient was receiving their hemodialysis treatment. Overall, there was no difference in the 1-hour fasting status between shifts, and other than age, no other variables were significantly different. There was also no significant difference in serum phosphate levels between phosphorus-fasted and non–phosphorus fasted participants based on shift (data not shown).

Last, in non–phosphorus-fasted participants (n = 76), an analysis was performed to determine whether the consumption of food items containing inorganic phosphate additives (n = 36) was associated with higher levels of serum phosphate and PTH compared with intake of foods and beverages containing phosphorus but without inorganic phosphate additives (n = 33). In a 1-way ANOVA, there was a nonsignificant trend between the number of food items consumed containing inorganic phosphate additives within 1 hour prior to dialysis-related blood work and higher serum phosphate level ($P = .068$). Participants consuming more food items containing inorganic phosphate additives also had nonsignificantly lower serum calcium levels ($P = .056$).

Discussion

In this study, non–phosphorus-fasted participants were found to have nonsignificantly higher levels of PTH and significantly higher levels of serum phosphate in participants with PTH levels within the KDIGO recommended target range compared with phosphorus-fasted participants. These results suggest that, in some patients, fasting status could have a subtle influence on the levels of serum values which are routinely monitored by nephrologists and used to make clinical decisions with regard to CKD-MBD management. For instance, higher PTH levels may prompt greater usage of calcitriol and other vitamin D analogues, agents believed to accelerate vascular calcification.

There are a multitude of factors that are linked to serum phosphate levels including many factors unaccounted for in our study. It is often assumed that high phosphate levels reflect

Table 3. Participant Demographics, Estimated Phosphorus Intake, Serum Laboratory Values, and Medications Stratified by KDIGO PTH Levels and Phosphorus-Fasted Status.

	<15 pmol/L		15-60 pmol/L		61-100 pmol/L		>100 pmol/L	
	Phosphorus-fasted (n = 34)	Non–phosphorus-fasted (n = 8)	Phosphorus-fasted (n = 98)	Non–phosphorus-fasted (n = 38)	Phosphorus-fasted (n = 39)	Non–phosphorus-fasted (n = 13)	Phosphorus-fasted (n = 14)	Non–phosphorus-fasted (n = 10)
Demographics								
Sex (male), n (%)	17 (50.0)	5 (62.5)	57 (58.2)	22 (5.9)	22 (56.4)	7 (53.8)	9 (64.3)	6 (60.0)
Age (years)	64.6 ± 12.4	60.4 ± 10.6	68.8 ± 14.0	68.8 ± 15.4	67.5 ± 14.6	63.6 ± 17.4	59.1 ± 13.7	64.0 ± 17.9
Diabetes, n (%)	18 (52.9)	3 (37.5)	51 (52.5)	22 (57.9)	28 (71.8)	6 (46.2)	7 (50.0)	5 (50.0)
Phosphorus intake								
One hour estimated phosphorus intake (mg)	0	44.6 ± 114.1	0	60.8 ± 134.3	0	37.7 ± 97.4	0	129.9 ± 241.0*
URR (%)	0.8 ± 0.1	0.7 ± 0.1	0.8 ± 0.1	0.7 ± 0.1	0.8 ± 0.1	0.8 ± 0.1	0.8 ± 0.1	0.8 ± 0.1
Serum Ca (mmol/L)	2.3 ± 0.2	2.3 ± 0.1	2.3 ± 0.2	2.3 ± 0.2	2.2 ± 0.2	2.2 ± 0.2	2.3 ± 0.2	2.2 ± 0.2
Serum PO4 (mmol/L)	1.6 ± 0.5	1.5 ± 0.2	1.4 ± 0.4	1.6 ± 0.3**	1.7 ± 0.4	1.6 ± 0.4	1.8 ± 0.5	1.6 ± 0.3
Albumin (g/L)	31.9 ± 2.8	31.6 ± 4.4	31.9 ± 3.7	31.8 ± 3.3	31.7 ± 2.1	32.4 ± 3.0	32.6 ± 3.0	33.3 ± 2.9
Hemodialysis shifts								
07:30, n (%)	9 (64.3)	5 (35.7)	40 (70.2)	17 (29.8)	14 (66.7)	7 (33.3)	5 (62.5)	3 (37.5)
12:30, n (%)	11 (84.6)	2 (15.4)	39 (73.6)	14 (26.4)	15 (75.0)	5 (25.0)	4 (66.7)	2 (33.3)
17:30, n (%)	14 (93.3)	1 (6.7)	19 (73.1)	7 (26.9)	5 (50.0)	5 (50.0)	10 (90.9)	1 (9.1)

Note. Data are represented as mean ± standard deviation unless otherwise indicated. KDIGO = Kidney Disease Improving Global Outcomes; PTH = parathyroid hormone; URR = urea reduction ratio; Ca = calcium; PO4 = phosphate.
*$P < .05$. **$P < .01$.

Table 4. Multivariate Linear Regression Model for Parathyroid Hormone.

Predictors	*B*	β	*P*	Lower 95%	Upper 95%
Constant	38.74		<.001	26.45	51.03
Non–phosphorus fasted status	13.83	0.13	.039	0.71	26.95
Phosphate binder use	−6.27	−0.07	.3	−18.02	5.49
Calcitriol use	21.95	0.23	<.001	10.2	33.70

Note. Model summary: Adjusted R^2: .06, $P < .0001$.

nonadherence to diet and phosphate binder therapy. There is a well-described diurnal rhythm as well as interindividual differences in the absorption of phosphate, the efficacy of phosphate binders, and the degree of dialytic removal. Residual kidney function is rarely considered. Furthermore, patients with significant hyperparathyroidism often have significant endogenous sources of phosphate. Interestingly, in our study, serum phosphate was only significantly different by phosphorus fasting status in patients whose PTH fell in the recommended KDIGO range. Perhaps at moderate levels of hyperparathyroidism, phosphate intake may have a greater modifying influence on the level of serum phosphate than at more advanced stages of CKD-MBD where other factors, such as endogenous phosphate sources, increasingly come into play. Furthermore, it is possible that phosphorus intake 1 hour prior to a dialysis session may reflect nutritional habit, thus influencing PTH levels through more extended exposure to dietary phosphorus. For example, the amount of phosphorus consumed within 1 hour was significantly higher in patients with the highest level of PTH.

The current recommended daily phosphorus intake for patients with ESKD is 700 mg a day for an adult.[9] The growing use of fully bioavailable phosphate containing food additives is increasingly contributing to a large gap between the amount of phosphorus consumed versus that which is estimated and/or recommended. Phosphate additives are present at very high levels in processed foods but the contribution to total intake, at present, is difficult to estimate given the absence of reporting regulations. Consumption of food and beverages prior to blood work that contains high amounts of inorganic phosphate additives would presumably have the greatest impact on blood values based on the expected rapid and complete absorption. For example, in a study we conducted where we provided 500 mg of bioavailable phosphorus to individuals across a spectrum of kidney function, PTH was significantly elevated over baseline within 30 minutes of the phosphorus load and peaked at 60 minutes in 90% of participants.[14] In those participants with a measured GFR < 30 mL/min, the PTH increased on average by 31% over

baseline by 60 minutes. Given that calcitriol is prescribed in response to elevated PTH levels, it is conceivable that a habit of consuming foods containing inorganic phosphate additives prior to hemodialysis-related blood work could influence calcitriol prescription—a potentially problematic situation when one considers the significant toxic potential of calcitriol. We attempted to address inorganic phosphate intake by identifying the foods consumed within 1 hour that contained inorganic phosphate additives recognizing that the actual amount of phosphorus consumed by this approach is not possible to estimate given that this information is largely not available. We therefore looked at the number of individual food items consumed that contained inorganic phosphate additives and observed nonsignificant trends in relationships with serum levels of phosphate and calcium despite the relatively small sample size. Inorganic phosphate additives are becoming a growing public health concern as they are predominantly present in inexpensive processed foods and "convenience foods." It is concerning that these types of foods are consumed at a proportionally higher rate by people from lower socioeconomic tiers. In the Chronic Renal Insufficiency Cohort study, serum phosphate levels were higher in the lowest income class group by a factor of 2.5 to 2.7, suggesting that the most vulnerable people may be at highest risk.[18]

Phosphate follows a diurnal variation characterized by a nadir in the morning, a rise in the early afternoon and a peak at night.[19] Although incompletely understood, this circadian rhythm is thought to be related to a complex interplay between varying phosphorus intake, renal handling, and phosphate fluxes into and out of cells. However, we found no differences in phosphate, calcium, and PTH levels related to the time of hemodialysis shifts.

There are limitations to our study. The data were collected on a single day in a cross section of hemodialysis patients. The recently updated KDIGO recommendations indicate that clinical decisions should be made upon serial assessment of blood work trends as opposed to single values.[5] As such, one would not make clinical decisions on the basis of a single value. Whether the dietary habits of patients immediately prior to hemodialysis treatments are consistent from month to month is not known. It is acknowledged that food recall can be highly variable; however, trained research assistants interviewed the participants immediately upon arrival to the unit and questioned them about their food consumption within the previous hour. The reported foods consumed were cross-referenced with the Canadian Nutrient File. The amount of phosphorus ingested in our study is an estimate based on very short-term patient recall and ability to access exact food ingredients in the database. It would be informative to evaluate phosphate values in individuals longitudinally based on fasting status as serum phosphate levels are influenced by multiple factors including food and beverage ingestion. Finally, it is important to recognize that the results may differ across individuals with different dialysis vintages and severity of CKD-MBD.

Conclusions

The results of this study showed that the non–phosphorus-fasted adult hemodialysis patients had nonsignificantly higher levels of PTH overall and higher levels of phosphate in patients at KDIGO target PTH levels. Whether these subtle differences would actual alter CKD-MBD management is not known. Whether dietary phosphorus intake and, in particular, foods containing inorganic phosphate additives in close proximity to blood work based on their enhanced bioavailability influence the management of CKD-MBD and clinical outcomes in these patients is unknown. With future studies, the conditions (ie, dietary intake) surrounding routine dialysis-blood work may become more formally assessed and controlled as part of standard of care.

Ethics Approval and Consent to Participate

Ethics approval (REB#: DMED-1893-16) for this study was granted by the Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board (HSREB).

Consent for Publication

All authors consent for publication.

Availability of Data and Materials

Data and materials may be made available to qualified investigators upon written request to the corresponding author. Reasonable requests for data access will be assessed in consultation with the appropriate Research Ethics Board.

Declaration of Conflicting Interests

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