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Original article

Phosphorus Counting Table for the control of serum phosphorus levels without phosphate binders in hemodialysis patients

Vivianne Rêis Bertonsello-Catto [a,*], Leandro Junior Lucca [b], José Abrão Cardeal da Costa [c]

[a] Graduate Program in Science, Department of Clinical Medicine, Ribeirão Preto Medical School – São Paulo University, Brazil
[b] CKD-MBD Unit, Nephrology Division, Department of Clinical Medicine, Ribeirão Preto Medical School – University of São Paulo, Brazil
[c] Nephrology Division, Department of Clinical Medicine, Ribeirão Preto Medical School – University of São Paulo, Brazil

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SUMMARY

Background and aims: Hyperphosphatemia constitutes one of the major problems faced by patients with chronic kidney disease, and nourishment plays a significant role in its control. The present study aimed to evaluate the maintenance of phosphorus serum levels by observing measurements before and after an intervention using the Phosphorus Counting Table (PCT), in hemodialysis patients lacking phosphate binder use.

Methods: The assessment included fifty individuals on hemodialysis who underwent phosphate binder suspension 30 days prior to the intervention. The participants received food and nutrition education on the PCT tool, which assists in the control of dietary phosphorus intake, and followed its instructions for two months. Fasting blood samples were collected at three moments for phosphorus, total calcium, and parathyroid hormone (PTH) analysis. The study sample was initially analyzed as a whole, then sub-classified into two groups: adherence and non-adherence.

Results: At the end of the study, no significant difference in serum phosphorus was observed in the total and the adherence groups ($p > 0.05$). The non-adherence group showed a substantial increase of 0.74 mg/dL in serum phosphorus levels and 6.16 mg^2/dL^2 in the calcium-phosphorus product after the intervention. Meanwhile, the calcium-phosphorus product improved from 56.42 ± 11.49 mg^2/dL^2 to 51.05 ± 10.67 mg^2/dL^2 in the adherence group. Serum calcium levels did not change throughout the study in the three groups. A significant increment in PTH serum levels was observed at the end of the study in all groups.

Conclusion: The PCT showed to be efficient in the maintenance of serum phosphorus in the individuals who adhered well to the tool, without the administration of phosphate binders. Such a method can assist in patient adherence to treatment and enables better diet flexibility.

The present trial was registered under the Brazilian Clinical Trials Registry (Rebec). Registration number: RBR-2vzd48.

1. Introduction

Hyperphosphatemia consists of a frequent problem among patients with chronic kidney disease (CKD). Its occurrence can lead to complications such as the development of mineral and bone disorders and soft tissue calcification, which may result in increased cardiovascular risk and mortality [1,2]. Removal by dialysis, reduction of intestinal absorption through chelation, and decreased phosphorus intake comprise the primary therapeutic strategies that aim to control the disorder [3,4].

Phosphorus is a mineral that is widely found in several foods, especially in protein sources, thus hindering its restriction. In its natural form, organic phosphorus can be detected in both animal and plant foods [3], while, in turn, the inorganic form of the mineral derives from food additives, such as processed foods [5,6]. These additives may significantly increase the phosphate load of protein-

Abbreviations: CKD, chronic kidney disease; PCT, Phosphorus Counting Table; PTH, parathyroid hormone.

* Corresponding author. Department of Clinical Medicine, Ribeirão Preto Medical School, University of São Paulo, Bandeirantes Ave 3900 – Campus Monte Alegre, Ribeirão Preto/SP, 14049-900, Brazil. Fax: +55 16 3315 0229.

E-mail addresses: vi.reisb@gmail.com (V.R. Bertonsello-Catto), leandro.ibene@gmail.com (L.J. Lucca), jacdcost@fmrp.usp.br (J.A.C. da Costa).

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rich food sources [7]. Since phosphorus is widespread among foods, meeting daily requirements becomes easy, and can lead to an even higher consumption than recommended for healthy individuals. In the United States, between 2001 and 2014, the estimated mean dietary phosphorus consumption was of 1373 mg/day [8].

Educational interventions focused on controlling serum phosphorus in maintenance hemodialysis have rendered significant results, as demonstrated by several studies found in the literature [9–13].

Considering the complexity found in the management of hyperphosphatemia, new strategies and tools should be developed to identify its cause, as well as to improve patient treatment adherence.

2. Materials and methods

2.1. Participants

The study protocol was approved by the Research Ethics Committee of the Clinical Hospital of the Ribeirão Preto Medical School, at the University of São Paulo - USP (HCRP protocol no. 3781/2010), and registered under the Brazilian Clinical Trials Registry (Rebec) as RBR-2vzd48.

A total of 50 out of 88 recruited patients on maintenance hemodialysis completed the survey. The involved participants were from the Clinical Hospital of the Ribeirão Preto Medical School – USP, the Nephrology Service of Ribeirão Preto, and the Lund Nephrology Clinic. The inclusion criteria comprehended patients with chronic kidney disease and mineral and bone disorders on hemodialysis; age range greater than or equal to 18 years; literate or had literate careers; serum phosphorus levels less than or equal to 7.8 mg/dL after thirty days of phosphate binder interruption; signed a written informed consent form. The upper limit of 7.8 mg/dL of serum phosphorus was established because studies have shown that calcium-phosphorus product levels >72 mg^2/dL^2 are associated with significant increases in the relative risk of mortality when compared to calcium-phosphorus product <52 mg^2/dL^2 [14–16]. Patients using anti-inflammatory hormones, with neoplasias or active infectious diseases, were excluded from the trial.

2.2. Study design

This study comprised a non-randomized clinical treatment trial and was carried out between January and September 2012. Its primary objective was to evaluate the maintenance of serum phosphorus levels by observing measurements taken before and after the intervention, using the Phosphorus Counting Table (PCT), in hemodialysis patients lacking phosphate binder use.

2.3. Phosphorus Counting Table

The PCT, a tool developed to aid in the control of dietary phosphorus consumption in hemodialysis patients, consists of a food list divided into food groups, which indicates fixed phosphorus contents, with pre-established and proportional scores. Only the processed food group presents variable phosphorus content, due to its diversity. Thus, the participants were encouraged to consume foods complying with a score range between 276 and 333 points daily, which would supply 800–1000 mg of phosphorus/day and protein intake of 68.83 g–77.01 g/day, respectively.

The tool provides patients with more choices and flexibility when planning meals. Each food group list offers options that allow the individuals to select preferred foods and, consequently, respect their dietary habits.

2.4. Intervention

The assessment spanned three months, and the same dietician followed-up with the patients. Demographical (age, gender, educational level, and period on dialysis), clinical (cause of end-stage renal disease), nutritional (weight, height, and body mass index [BMI]), and biochemical data were collected. At the beginning of the study, the patients underwent phosphate binder suspension thirty days prior to the intervention.

After such period, blood samples were collected, and patients with serum phosphorus levels less than or equal to 7.8 mg/dL were excluded from the study. The remaining subjects were recommended to control their food consumption using the PCT. Each individual received a chart to record the daily scores consumed over two months of intervention, in addition to a pen and a calculator for note-taking and calculations. The dietician monitored the participants biweekly (Fig. 1) and, after 30 and 60 days of intervention, blood samples were again collected. Also, at the beginning and end of the study, the dietary intake was assessed using a 3-D food record.

Given adherence to treatment comprises a significant factor to evaluate the PCT effect, the sample was analyzed by two approaches: 1) patients in a single group; and 2) patients subdivided into adherence and non-adherence groups. The non-adherence patients were those who, according to the 3-D food record, consumed a minimum of two portions of phosphorus-rich processed foods at the end of the study, and/or did not report the daily consumed score, and/or presented scores that did not correspond to the actual food consumption throughout the intervention - for example some participants recorded scores less than 90 points daily during intervention without signs of low food intake, characterizing underreporting.

2.5. Laboratory analyses

Fasting blood samples were collected at baseline (T0), and after 30 days (T1), and 60 days (T2) of intervention. Serum phosphorus was analyzed by the molybdate U.V. method, and calcium and parathyroid hormone (PTH) by colorimetric and chemiluminescence, respectively.

2.6. Statistical analysis

The statistical analysis was performed using SPSS software, version 17.0, for Windows (SPSS, Inc. Chicago, IL), and the results

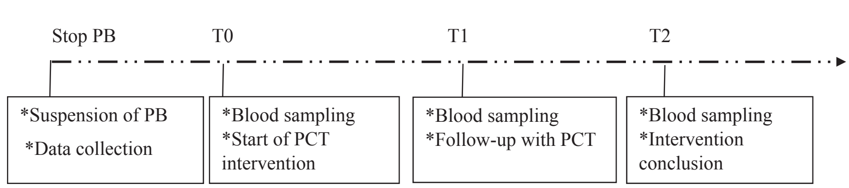

Fig. 1. – Study design. Stop PB: Period of phosphate binder suspension; T0: baseline; T1: 30 days of intervention; T2: 60 days of intervention. Abbreviations: PB: phosphate binders; PCT: Phosphorus Counting Table.

were expressed as means and standard deviation (minimum and maximum). The Spearman test was employed in the correlation analysis, and the Wilcoxon signed-rank test was used for paired samples. In case of repeated measures, ANOVA (analysis of variance) was applied, and the Bonferroni post-hoc test was conducted for comparisons between groups. A significance level of $p < 0.05$ was adopted in the study's entirety.

3. Results

Regarding the 88 patients recruited in the study, 23 dropped out after 30 days of phosphate binder suspension; 13 withdrew after the first month of intervention, and 2 abandoned the survey during the last month. The reasons for exclusion or patient withdrawal were pruritus (n = 10), serum phosphorus levels >7.8 mg/dL (n = 7), change of view concerning participation in the research (n = 17), difficulty reading the PCT due to visual problems (n = 1), restarted the use of phosphate binders (n = 1), renal transplantation (n = 1), and complaint of malaise after phosphate binder suspension (n = 1). Of the 50 patients who completed the study, 25 were assigned to the adherence group and 25 to the non-adherence group. The baseline characteristics of the patients are summarized in Table 1. Significant differences were not observed considering each parameter between the two groups (Table 1). It is noteworthy that 48% of the patients from the total group did not complete elementary school. No alterations in nutritional status were verified after the intervention.

At the end of the study, no significant difference regarding the intervention in the total group concerning serum levels of phosphorus, calcium, and calcium-phosphorus product was observed (Table 2). Only the non-adherence group showed an increment of 0.74 mg/dL in serum phosphorus levels and 6.16 mg^2/dL^2 in calcium-phosphorus product after the intervention. The adherence group presented an improvement in calcium-phosphorus product levels at the end of the trial.

The serum levels of PTH showed a considerable increase at the end of the study in the total sample and the adherence and non-adherence groups, although no significant difference between the latter two ($p = 0.86$) for the variable was observed. However, at T0, the PTH levels showed a positive correlation with serum calcium ($p = 0.003$) and calcium-phosphorus product ($p = 0.02$) at T2 in the total group.

At baseline, the protein intake was 1.0 ± 0.39 g protein/kg in the total group; 1.04 ± 0.29 g protein/kg in the adherence group, and 0.97 ± 0.45 g protein/kg in the non-adherence group. No changes in protein consumption were observed after the intervention in the total (0.98 ± 0.34 g protein/kg), adherence (1.06 ± 0.34 g protein/kg), and non-adherence (0.9 ± 0.34 g protein/kg) groups.

4. Discussion

The Phosphorus Counting Table is an unpublished tool that is applicable to hemodialysis patients. The serum phosphorus levels remained stable in the total group after the intervention with the PCT (note: the patients did not receive phosphate binders for three months). It is noteworthy that the mean phosphorus values were close to the National Kidney Foundation recommendation [17], and the serum calcium levels were normal within all three groups throughout the study. The adherence group showed improvements in calcium-phosphorus product at the end of the assessment.

Nasih et al. [18], while conducting a study in Canada, developed the “Phosphorus Point System Tool” (PPS), a method that is similar to the PCT. After using the tool for one month in ten patients on peritoneal dialysis, a significant reduction was observed in serum phosphorus levels (5.1–4.48 mg/dL; $p = 0.019$), and the calcium-phosphorus product decreased from 3.92 to 3.22 $mmol^2/L^2$. However, the use of phosphate binders was stimulated in their study, unlike the current research [18]. Degen [19] employed the PPS in pre-dialysis patients for 12 weeks, and the obtained results were compared to those of patients that received standard nutritional guidance (permitted and unacceptable food) during the same period. The PPS group was provided material containing pictures of portions, cups, and tablespoons for standardization, as well as classes on the correct intake of phosphate binders, phosphorus metabolism, and risks of hyperphosphatemia. Both groups were oriented regarding phosphorus-based additives. At six weeks, the participants were allowed to choose between continuing to track daily phosphorus points or only to use the PPS as a reference for the diet. No significant alterations in serum levels of phosphorus, total calcium, and calcium-phosphorus product were reported at the end of the 6th and 12th week of intervention when comparing the initial dosages in both groups [19]. The main limitation of that study was the small sample size, which included less than 17 participants.

Ahlenstiell et al. [20] applied the “Phosphate Education Program - PEP” in 16 children with CKD, who were followed-up for 24 weeks. The PEP consisted of meal phosphorus content eye-estimates that were classified into “phosphate units” to enable the self-adjustment of the phosphate binder dosage. The serum levels of phosphorus showed a significant reduction between the 7th and 12th week, but not between the 19th and 24th week [20]. Their findings were similar to those obtained in the present study,

Table 1
Patient characteristics at baseline.

Characteristic	Total Group (n = 50)	Adherence Group (n = 25)	Non-adherence Group (n = 25)
Gender (male/female)	26/24	14/11	12/13
Illiterate (%)	2 (1)	4 (1)	0 (0)
Completed elementary school (%)	12 (6)	16 (4)	8 (2)
Completed middle school (%)	24 (12)	32 (8)	16 (4)
Completed higher education (%)	8 (4)	12 (3)	4 (1)
Age (years, median)	54 (20–84)	55 (20–74)	52 (20–84)
Cause of end-stage renal disease (%)			
- Hypertension	44 (22)	36 (9)	52 (13)
- Diabetic nephropathy	24 (12)	24 (6)	24 (6)
- Other	32 (16)	40 (10)	24 (6)
Duration of hemodialysis (years)			
- Mean	5.26 ± 6.49	4.28 ± 4.24	6.24 ± 8.13
- Median	2 (0.5–26)	2 (0.5–18)	2 (0.5–26)
Weight (kg)	67 ± 18.53	66.3 ± 17.5	67.69 ± 19.84
BMI (kg/m^2, mean)	24.98 ± 6.22	24.97 ± 6.43	24.99 ± 6.14

BMI: body mass index.

Table 2
Laboratory analyses during the intervention.

Group		T0	T1	T2
Total (n = 50)	Phosphorus (mg/dL)	5.71 ± 1.17	5.56 ± 1.05	5.9 ± 1.14
	Calcium (mg/dL)	9.35 ± 0.91	9.11 ± 0.78	9.11 ± 1
	Ca x P Product (mg^2/dL^2)	53.38 ± 12.2	50.7 ± 10.6	53.78 ± 12.24
	PTH (pg/mL)	265 (11–2182)	–	444 (33–2465)[a]
Adherence (n = 25)	Phosphorus (mg/dL)	5.92 ± 0.94	5.5 ± 0.89	5.55 ± 0.92
	Calcium (mg/dL)	9.49 ± 0.89	9.22 ± 0.74	9.21 ± 1.09
	Ca x P Product (mg^2/dL^2)	56.42 ± 11.49	50.88 ± 9.68[a]	51.05 ± 10.67[a]
	PTH (pg/mL)	245 (24–2182)	–	466 (44–2409)[a]
Non-adherence (n = 25)	Phosphorus (mg/dL)	5.5 ± 1.35	5.62 ± 1.22[b]	6.24 ± 1.25[a]
	Calcium (mg/dL)	9.2 ± 0.93	8.99 ± 0.81	9.02 ± 0.91
	Ca x P Product (mg^2/dL^2)	50.35 ± 12.36	50.53 ± 11.65[b]	56.51 ± 13.29[a]
	PTH (pg/mL)	282 (11–1451)	–	389 (33–2465)[a]

Ca x P product: Calcium–phosphorus product; PTH: parathyroid hormone; T0: baseline; T1: 30 days of intervention; T2: 60 days of intervention.
[a] $p \leq 0.05$ compared with T0.
[b] $p \leq 0.05$ compared with T2.

although the population differed in age, stage of CKD (pre-dialysis patients), and the form of dialysis therapy (hemodialysis and peritoneal dialysis). The aim of the study was the self-adjustment of phosphate binder dosages.

Regarding the increment in serum PTH levels, it is believed that one of the reasons for such an increase was hypocalcemia, although serum calcium remained normal throughout the study. Moreover, at T2, the PTH showed a positive correlation with serum calcium, contrasting with what was expected. One hypothesis for such an increase was the fact that the studied sample was composed of patients undergoing long-standing dialysis treatment, and some had severe secondary hyperparathyroidism. Changes in serum phosphorus, especially in the non-adherence group, may have contributed to the increment in serum PTH. Emphasis should be given to the fact that the presence of severe secondary hyperparathyroidism may lead to an increase in bone remodeling and influence serum phosphorus levels [21]. The serum levels of PTH analyzed in the study conducted by Degen [19] did not present significant differences between the beginning and end of the assessment. However, the population was predialytic, and the treatment with phosphate binders had not been suspended.

Since phosphorus intake is associated with protein consumption, it's noteworthy that the PCT rendered the participants a protein supply ranging between 1.02 and 1.14 g protein/kg. However, the 3-D food record demonstrated low protein intake, mainly in the total and non-adherence groups at beginning and terminal of study. Nutritional education is essential for the adequate control of serum phosphorus levels in hemodialysis patients [9–12,22,23]. The results obtained in the present study corroborate those found in the literature, particularly in the adherence group, demonstrating that those who correctly followed the PCT were able to maintain and/or reduce the serum levels of phosphorus, calcium, and the calcium-phosphorus product. The PCT aids in nutrition education and may help patients adhere to treatment, in addition to enabling better diet flexibility. Such autonomy may improve the patients' knowledge and understanding of the method, contributing to the control of serum phosphorus levels.

The limitations of this study comprised the small sample size and the complexity involved in changing eating habits, which may have been one of the reasons why some participants dropped out of the trial. The individual's educational level constitutes another limiting factor that hinders the application of the PCT in any hemodialysis patient. The results obtained herein were similar to others found in the literature, in which most patients with CKD are poorly educated [24–27]. Regarding protein consumption, some adjustments may be necessary to achieve adequate intake in some patients. Another limitation was the number of patients with severe secondary hyperparathyroidism.

In conclusion, the PCT demonstrated to be an efficient tool in the maintenance of serum phosphorus levels for the individuals who retained good adherence to the material, since they maintained the parameter throughout the entire study, without the use of phosphate binders. Therefore, the use of the PCT can enable the non-use of phosphate binders or their use in reduced dosages. Nevertheless, more studies that evaluate the association between the tool and the use of phosphate binders are required.

Statement of authorship

VRBC elaborated the Phosphorus Counting Table, designed the study protocol, and conducted the research, data collection, analysis, and manuscript preparation. LJL contributed to the study design and aided in data collection, analysis, and manuscript preparation. JACC coordinated the study design, data collection, analysis, and drafting of the manuscript. All authors read and approved the final manuscript.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clnesp.2019.03.008.

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