Original Article

Phosphate binders, appetite and nutritional status in maintenance hemodialysis patients

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Background and Objectives: The potential side effects of common phosphate binders are gastrointestinal in practice. We hypothesized that regular use of phosphate binders may be associated with decreased appetite, dietary intake and consequently, poor nutritional status. **Methods and Study Design:** This was cross-sectional study of 78 patients (mean age 67.5±13.0, 34.6% women) undergoing maintenance hemodialysis (MHD) treatment. Participants were divided into three equal groups - sevelamer (n=25), lanthanum (n=24) and the control group (n=29). Eating motivation was assessed using visual analogue scales (VAS) and by a self-reported appetite assessment which was graded on a 5-point Likert scale. Main outcome measure was differences in VAS scores for appetite, dietary intake and nutritional status (malnutrition-inflammation score [MIS]) in the study groups. **Results:** Appetite, dietary intake, biochemical nutritional markers, anthropometric measures and MIS were similar in the three groups. A statistically significant difference was observed in sensation of fullness between the groups: multivariable adjusted ORs in the sevelamer carbonate group was 4.90 (95% CI: 1.12 to 21.43), p=0.04 and in the lanthanum carbonate group was 5.18 (95% CI: 1.15 to 23.30), p=0.03 versus the control group. However, no linear association was observed between MIS scores and VAS scores for appetite in any study group. **Conclusions:** Regular use of these phosphate binders was not associated with anorexia, decreased dietary intake and nutritional status in the study population. Therefore, there is no preference in the choice of phosphate binders in MHD patients with hyperphosphatemia, even those who are at nutritional risk.

Key Words: appetite, hemodialysis, lanthanum carbonate, malnutrition, sevelamer carbonate

INTRODUCTION

Hyperphosphatemia is associated with an increased risk of death in maintenance hemodialysis (MHD) patients.[1,2] To control phosphorus levels in this population, the kidney disease outcomes quality initiative (KDOQI) recommends a low-phosphorus diet and, if necessary, it should be combined with the use of phosphate binders.[3] The main limitation of dietary phosphorus restriction is malnutrition as a result of reduced protein consumption, which may increase the mortality risk in MHD patients.[4] Moreover, dietary restrictions of phosphorus are usually not sufficient to deal with hyperphospatemia.[5] Therefore, oral administration of phosphate binders is a standard treatment for hyperphosphatemia in MHD patients.

One of the explanations of the positive relationship between phosphate binder use and better survival of hemodialysis patients is that this treatment allows patients to reach dietary daily protein intake recommendations thus having a better nutritional status, while maintaining controlled blood levels of phosphorus.[2] However, it is also known that the potential disadvantages of common phosphate binders (calcium containing, lanthanum carbonate, sevelamer carbonate) are gastrointestinal side effects such as nausea, vomiting, abdominal pain, diarrhea and constipation.[5] Therefore, regular use of phosphate binders may lead to decreased appetite due to the aforementioned side effects, poor dietary intake and malnutrition.[6]

Appetite, the subjective desire to swallow food, is poor

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in the majority of dialysis patients.[7] This may lead to malnutrition, inflammation, resistance to erythropoietin and anemia, decreased quality of life, and, consequently, increased morbidity and mortality in MHD patients.[8-10] Decreased appetite pathogenesis in MHD patients is complex and involves factors associated with comorbidities, hormonal stimulants (ghrelin, leptin, cholcystocinin, YY peptide), as well as psychosocial factors.[7,11] There are no reports in the literature about the relationship between the use of phosphate binders and appetite in hemodialysis patients. Such an association is possible, at least with the use of a particular type of phosphate binder.

We hypothesized that regular use of phosphate binders (or at least of one of them) may be associated with poor appetite, decreased protein and calorie intake and consequently, poor nutritional status. The conceptual model of the study hypothesis is shown in Figure 1. Such information may be useful in selecting the type of phosphate binder in MHD patients with hyperphosphatemia, especially in those who are at nutritional risk. Therapeutic priority should be given to phosphate binders that are not associated or associated to a lesser degree to a decrease in appetite and food consumption. Our specific goal was to evaluate and compare appetite, dietary intake and consequential nutritional status between the groups of MHD patients taking either sevelamer carbonate or lanthanum carbonate (the currently most common phosphate binders) and to determine which of these preparations is more closely related to anorexia and accordingly to poor dietary intake in the study population.

METHODS

Study design and subjects

This was a cross-sectional study which was approved by the local ethics committee (0107-15-ASF). The study included ESKD patients on hemodialysis treatment for at least three months, who were 18 years or older and taking stable doses of the same phosphate binder (sevelamer or lanthanum carbonate) for at least three months prior to recruitment. Use of calcium compounds was allowed by protocol only as dietary supplements. All patients signed a local institutional review board approved consent form. Patients with an anticipated life expectancy less than six months (e.g., because of a metastatic malignancy) were excluded. A flow chart of the study is presented in Figure 2. In total, 78 patients undergoing MHD treatment at our outpatient HD clinic were included in the study. All patients underwent regular dialysis via their vascular access four hours three times per week at a blood flow rate of 250-300 ml/min and at a dialysis solution flow rate of 500 ml/min. All dialysis treatments were performed with biocompatible dialyzer membranes with a surface area of 1.4 to 1.9 m^2. The efficiency of dialysis was assessed according to the delivered dose of dialysis (Kt/V urea), using a single pool urea kinetic model.

Urine output was expressed as mL/24 hours. Residual renal function (RRF) was defined as measured urine volume >200 mL/day.

Dietary intake and appetite assessment

The patients completed three-day dietary histories (including a dialysis day, a weekend day and a non-dialysis day) as a food diary. Relying on these diaries, the dietary energy and protein intake were calculated and normalized for ideal body weight according to the European best practice guidelines.[12] Ideal weight in the present study was calculated from the Lorentz equations differently for men and women.

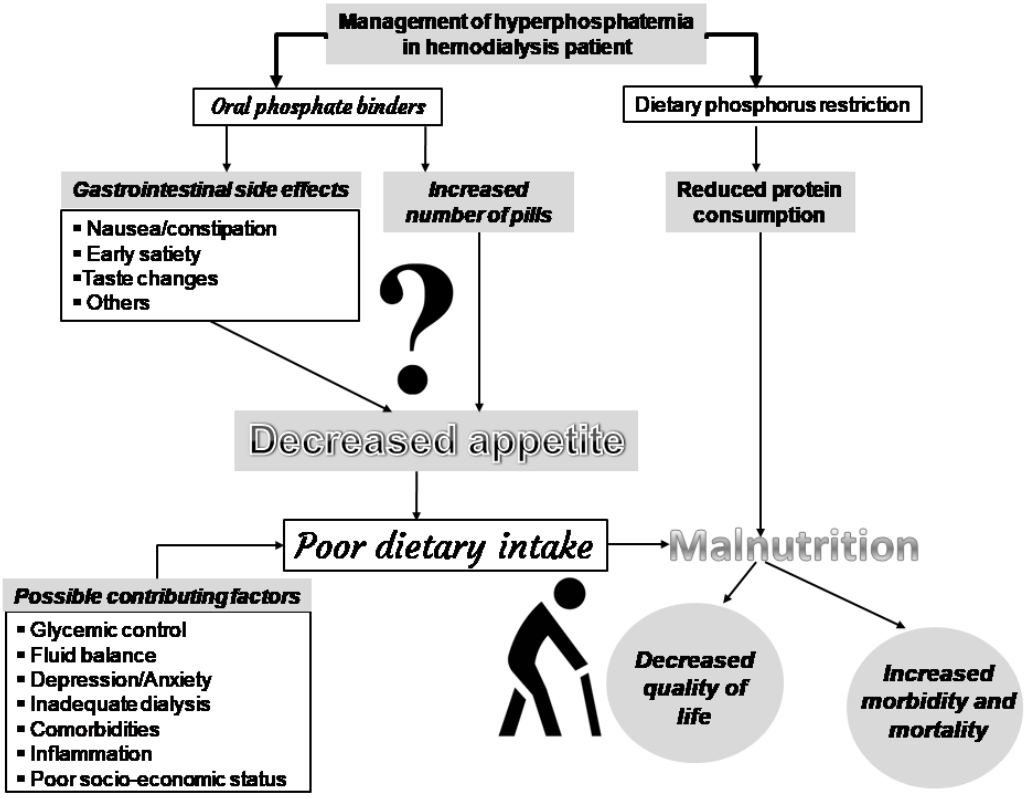

Figure 1. The conceptual diagram of possible association between phosphate binder use and malnutrition in hemodialysis patients.

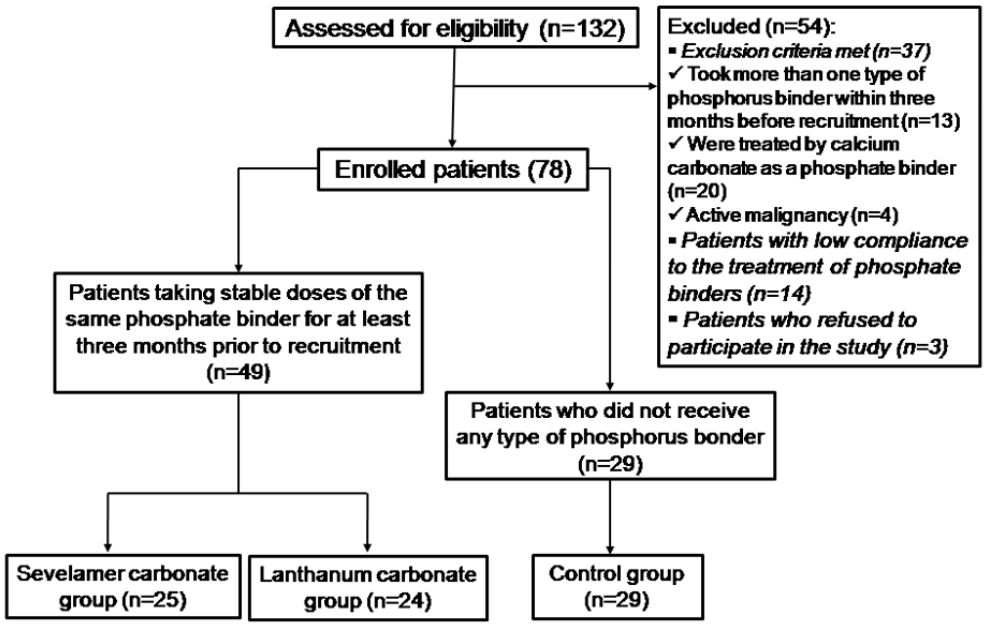

Figure 2. Flow diagram of the study.

Dietary protein intake was also approximated by determining normalized protein nitrogen appearance (nPNA) from the patient's urea generation rate by using urea kinetics modeling.[13] Single-pool model urea kinetics was used to estimate then PNA.

With respect to the self-reported appetite assessment, all patients were asked to grade their appetite during the past week according to a 5-point Likert scale: 1) very good, 2) good, 3) fair, 4) poor, and 5) very poor. These questionnaires were completed when blood samples were collected. The score was rearranged into two main groupings for further comparisons: diminished (combining fair, poor and very poor appetites) or non-diminished (combining very good and good appetites).

In addition, eating motivation was assessed using visual analogue scales (VAS). Subjects were familiarized with these scales prior to the commencement of the study. The VAS was 100 mm in length with words anchored at each end, expressing the most positive or the most negative ratings. The VAS was used to assess hunger, satiety, fullness, prospective food consumption, desire to eat something fatty, salty, sweet or savory, and the palatability (five questions) of the test meal.[14] The questionnaire was completed after a test meal, a standard meal that dialysis patients usually receive during dialysis. Subjects were requested to make a vertical mark on each line that best matched how they were feeling at the time. Each score was determined by measuring the distance from the left side of the line to the mark. Subjects did not discuss or compare their ratings with each other and could not refer to their previous ratings when marking the VAS.

Anthropometric measurements

All measurements were performed after dialysis, when the patient was at dry weight (the right upper arm was used whenever possible, with exceptions for patients whose dialysis access placement, injury, or stroke precluded measurement). The same dietitian performed all anthropometric measurements. Body mass index, triceps skinfold thickness (TSF), and calculated midarm muscle circumference (MAMC) were measured as anthropometric variables. MAMC was estimated as:

MAMC (cm) = midarm circumference (cm) - 0.314 XTSF (mm).

Nutritional assessment and Comorbidity index

Overall nutritional assessment was performed using the malnutrition-inflammation score (MIS). MIS has been described in detail in several previous studies[15] and has also been shown to be a valid tool for longitudinal observations of MHD patient nutritional status.[16] It is a subjective global assessment (SGA) based method that consists of 10 components. The sum of all 10 components results in an overall score ranging from 0 (normal) to 30 (severely malnourished).

We also calculated the comorbidity index, developed recently by Liu et al[17] and validated specifically for dialysis patient populations, as a measure of comorbid conditions.

Laboratory evaluation

Predialysis blood samples and postdialysis serum urea nitrogen were obtained from non-fasting patients on a mid-week day. All biochemical analyses were measured by an automatic analyzer. Serum high sensitivity C-reactive protein (CRP) was measured by a turbidimetric immunoassay.

Statistical analysis

Data are expressed as mean ± standard deviation (SD), or as median with interquartile range (IQR) for variables that did not follow a normal distribution, or as frequencies for categorical data.

Differences between study groups, according to the type of phosphate binder used, were analyzed by analysis of variance (ANOVA) using a one-way ANOVA, Kruskal-Wallis test, or a chi-square test, where appropriate. Associations between two parameters were assessed us-

Table 1. Baseline demographics, clinical, and laboratory values in total (n=78) and according to phosphate binder treatment in the study population†

Variable	Phosphate binder group				*p* value
	Total (n=78)	Sevelamer (n=25)	Lanthanum (n=24)	Control (n=29)	
Demographic and clinical characteristics					
Age (y)	67.5±13.0	64.4±13.2	66.1±13.8	71.3±11.6	0.13
Gender (female %)	34.6	28.0	33.3	41.4	0.58
Dialysis vintage (mo)	28.5 (13.0-62.8)	38.0 (12.5-112.0)	30.0 (16.0-64.3)	27.0 (9.5-45.5)	0.16
DM (yes %)	61.5	64.0	58.3	62.1	0.92
Comorbidity index	5.5 (3.0-8.3)	5.0 (1.5-9.0)	5.0 (4.0-7.8)	7.0 (3.0-9.0)	0.39
Smoking (yes %)	12.8	12.0	4.2	20.7	0.20
Kt/V	1.34±0.28	1.32±0.28	1.39±0.33	1.33±0.24	0.67
Daily urine volume (mL)	0.0 (0.0-300)	0.0 (0.0-400)	0.0 (0.0-250)	0.0 (0.0-450)	0.06
RRF (yes)	35.9	32.0	25.0	48.3	0.19
Hemoglobin (mmol/L)	6.83±0.68	6.95±0.81	6.83±0.62	6.70±0.68	0.41
Appetite (diminished %)	41.0	32.0	54.2	37.9	0.26
Body composition					
BMI (kg/m^2)	27.5±6.3	26.0±4.8	27.7±5.9	28.4±7.5	0.45
Waist-hip ratio	1.01±0.09	1.00±0.1	1.03±0.1	1.00±0.09	0.48
TSF (mm)	15.4±5.8	15.2±5.7	15.3±6.7	15.6±5.3	0.97
MAC (cm)	27.1±4.2	27.4±4.0	27.0±4.2	26.9±4.6	0.92
MAMC (cm)	22.6±3.6	22.9±3.2	22.5±3.7	22.5±3.9	0.93
Dietary intake					
DEI (kcal/kg/d)	20.1±7.2	22.0±6.5	19.3±8.3	19.2±6.6	0.37
DPI (g/kg/d)	0.90±0.33	1.02±0.34	0.82±0.27	0.87±0.07	0.11
nPNA (g/kg/d)	1.00±0.26	1.02±0.25	1.00±0.29	0.97±0.25	0.75
Biochemical measurements					
Albumin (g/L)	37.0±3.1	38.2±3.3	38.1±4.1	36.3±3.2	0.08
Creatinine (mmol/L)	0.66±0.21	0.73±0.19	0.71±0.23	0.56±0.19	0.005
Uric acid (umol/L)	315±65.4	315±71.4	327±89.2	309±65.4	0.61
Cholesterol (mmol/L)	3.66±0.88	3.39±0.67	3.76±0.97	3.82.8±0.93	0.16
TG (mmol/L)	1.47 (1.02-2.07)	1.92 (1.1-2.24)	1.42 (1.06-2.11)	1.44 (0.92-1.79)	0.30
Bicarbonate (mmol/L)	21.3±2.6	20.9±2.5	20.9±2.4	21.9±2.7	0.24
Calcium (mmol/L)	2.07±0.19	2.03±0.15	2.13±0.21	2.05±0.19	0.16
Phosphorus (mmol/L)	1.81±0.48	1.97±0.42	1.78±0.45	1.68±0.52	0.047
PTH (pmol/L)	40.6 (24.1-64.3)	49.2 (28.8-99.9)	46.2 (20.0-72.8)	33.4 (21.0-52.5)	0.15
CRP (nmol/L)	66.7 (33.3-166)	57.1 (34.3-143.8)	91.4 (46.7-231)	54.3 (18.1-132)	0.19
Nutritional assessment					
MIS	7.30±3.7	7.35±3.7	7.37±3.6	7.22±3.9	0.99
Concomitant medicators					
Number of pills/24h	11 (8-13)	11 (9-14)	12 (10-14)	8 (5.5-12)	0.006
Alphacalcidol (%)	29.5	28.0	37.5	24.1	0.56
Paricalcitol (%)	33.3	36.0	25.0	37.9	0.58
Cinacalcet (%)	12.8	24.0	16.7	0.0	0.03
H2 blockers (%)	12.8	12.0	8.3	17.2	0.62
PPIs (%)	43.6	44.0	54.2	37.9	0.46

DM: diabetes mellitus; RRF: residual renal function; BMI: body mass index; TSF: triceps skinfold thickness; MAC: midarm circumference; MAMC: midarm muscle circumference calculated; DEI: daily energy intake; DPI: daily protein intake; nPNA: normalized protein nitrogen appearance; PTH: parathyroid hormone; CRP: C-reactive protein; MIS: malnutrition-inflammation score; PPI: protein pump inhibitor.

†Continuous variables are expressed as mean±SD or median with interquartile range in case of non-normally distributed data, and categorical variables are expressed as a percentage.

ing Pearson correlation coefficients or Spearman rank order correlation coefficients in cases of skewed distributions of data. Multivariate linear regression analyses were performed to obtain adjusted (partial) correlations.

We used a stepwise logistic regression with backward elimination to develop an initial set of predictors that would show a strong association with VAS scores. Multivariate logistic regression was used to determine whether a significant association between the phosphate binder and VAS scores remained significant after adjustments to other significant predictors of appetite in a study population. The calculated sample size was 22 patients in each group, which allowed us to detect a difference of 5 points in VAS score between groups, with a standard deviation of 5 points, with α=0.05 and statistical strength equal to 90%.

All statistical analyses were performed using SPSS software, version 18.0 (SPSS Inc, Chicago, IL).

RESULTS

Demographic and clinical characteristics of the study population are presented in Table 1. There were 78 MHD patients (34.6% women, mean age 67.5±13.0 years) selected for this study. The cohort had a median dialysis vintage of 28.5 months and over half of the participants (61.5%) had diabetes. The patients were divided into three equal groups, two treatment groups and a control group. One treatment group took sevelamer carbonate

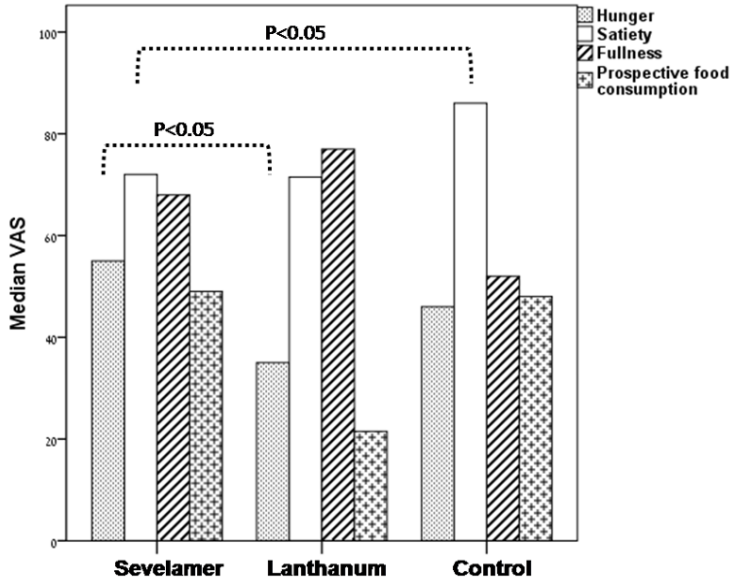

Figure 3. Median VAS scores for appetite in the study groups.

(n=25) and the second took lanthanum carbonate (n=24). The control group (n=29) received neither sevelamer carbonate nor lanthanum carbonate. Demographic and clinical data showed no statistically significant difference between the three groups except the trend in daily urinary volume (as a measure of the residual renal function) to be highest in the control group. However, this difference between the study groups did not reach statistical significance. There was also no significant statistical difference between the groups in body composition indices and daily consumption of calories or protein. For nutritional biochemical markers, significant differences were seen in serum creatinine levels, with the lowest level in the control group (apparently, this result is a reflection of the better renal function in this group compared to the sevelamer carbonate or lanthanum carbonate groups). The phosphorus level was not in the range of therapeutic targets in the sevelamer carbonate group compared with the lanthanum carbonate or control groups ($p<0.05$). Both CRP, as a measure of inflammatory response, and MIS as an overall nutritional assessment, were similar in the three groups. The amount of pills per day and the use of cinacalcet were lowest in the control group compared to the two treatment groups ($p=0.006$ and $p=0.03$, respectively). There were no differences in the use of alphacalcidol, paricalcitol, PPIs, or H2 blockers.

In comparison of median VAS scores for appetite by univariate analysis, feeling of hunger was higher ($p<0.05$) in the sevelamer carbonate group compared to the lanthanum carbonate group and satiety was lower ($p<0.05$) in the sevelamer carbonate group compared to the control group (Figure 3). Ratings were very similar in all study groups for visual appeal, taste, smell, aftertaste or overall palatability (data not shown).

The aforementioned differences in VAS scores for hunger or satiety didn't stand to multivariable adjustments. However, in a multivariate logistic regression analysis, a statistically significant difference was observed in sensation of fullness between the groups. ORs in the sevelamer carbonate group was 4.90 (95% CI: 1.12 to 21.43), $p=0.04$ and in the lanthanum carbonate group was 5.18 (95% CI: 1.15 to 23.30), $p=0.03$ versus control group (Table 2).

In these models of multivariate logistic regression, adjustments were made for age, sex, diabetes, comorbidity index, vintage, urinary volume per day, amount of pills per day and cinacalcet use. In VAS scores for specific foods, multivariate analysis showed a decreased desire to eat salty food in the lanthanum carbonate group compared to the control group. This desire was the same between the sevelamer carbonate and the control group.

Multivariate logistic regression showed no statistically significant differences in VAS scores for any parameter of test meal palatability between the study groups (data not shown).

We further tested univariate and adjusted (for all relevant confounders) correlations between the parameters of dietary intake and VAS scores for appetite in the study groups (Table 3). Sevelamer carbonate and lanthanum carbonate groups were motivated to eat. Hunger and prospective food consumption in these groups were positively and significantly associated with daily calorie and protein intake, but not in the control group. Moreover, MHD patients in the control group had an inverse relation between VAS scores for hunger and nPNA (r=-0.52, $p=0.03$). In other words, control group patients report hunger but did not eat enough protein. The feeling of fullness was inversely correlated with the daily protein and calorie intake in the sevelamer carbonate group and with the daily calorie intake in the control group, whereas in the lanthanum carbonate group the correlation between feeling of fullness and dietary intake parameters was positive (Table 3). No linear association was observed between MIS scores and VAS scores for appetite in any study group (data not shown).

DISCUSSION

The primary aim of this study was to explore the relationship between food intake and VAS ratings of appetite sensations, such as hunger or fullness, in MHD patients taking phosphate binders compared with control MHD patients. We found that hunger ratings are good predictors

Table 2. VAS ratings for appetite and specific foods in the study groups according to univariate and multivariate† logistic regression analysis (the group of MHD patients (n=29) who did not receive sevelamer carbonate or lanthanum carbonate i.e. the control group was used as a reference)

	Sevelamer (n=25)			Lanthanum (n=24)		
	OR	95% CI	*p* value	OR	95% CI	*p* value
VAS for appetite scores‡						
Hunger (>48 mm)						
Univariate	2.13	0.72-6.32	0.18	1.20	0.40-3.57	0.75
Multivariate	2.23	0.57-8.71	0.25	1.09	0.28-4.25	0.90
Satiety (>79 mm)						
Univariate	0.35	0.11-1.04	0.06	0.52	0.17-1.55	0.24
Multivariate	0.60	0.15-2.47	0.48	0.69	0.16-2.94	0.62
Fullness (>66.5 mm)						
Univariate	1.33	0.46-3.90	0.60	1.46	0.49-4.31	0.50
Multivariate	4.90	1.12-21.4	0.04*	5.18	1.15-23.3	0.03*
Prospective food consumption (>37.5 mm)						
Univariate	0.90	0.31-2.65	0.85	0.35	0.12-1.09	0.07
Multivariate	1.41	0.34-5.85	0.63	0.33	0.08-1.42	0.14
VAS for desires for specific foods‡						
Sweet (>82.5 mm)						
Univariate	1.57	0.53-4.60	0.41	1.23	0.42-3.64	0.71
Multivariate	2.05	0.55-7.66	0.29	1.40	0.37-5.32	0.62
Salty (>51.5 mm)						
Univariate	0.90	0.31-2.65	0.85	0.35	0.12-1.09	0.07
Multivariate	0.86	0.22-3.97	0.83	0.23	0.05-0.97	0.04*
Savory (>65.5 mm)						
Univariate	1.01	0.35-2.95	0.98	0.79	0.27-2.34	0.67
Multivariate	0.99	0.27-3.62	0.99	1.35	0.36-5.02	0.66
Fatty (>15.5 mm)						
Univariate	2.62	0.86-7.97	0.09	0.74	0.25-2.23	0.59
Multivariate	1.68	0.40-7.14	0.48	0.35	0.08-1.52	0.16

OR: odds ratio; CI: confidence interval; VAS: visual analogue scales; MHD: maintenance hemodialysis.
†Adjusted for age, gender, DM, vintage, comorbidity index, daily urine volume, number of pills and cinacalcet use.
‡VAS scores for appetite and specific foods were dichotomized (according to their median levels) and modeled as dependent variables, with sevelamer carbonate or lanthanum carbonate use being independent variables. All covariates included in the regression models are continuous except for categorical variables.
*Statistically significant OR values ($p<0.05$).

of dietary intake in sevelamer carbonate and lanthanum carbonate groups compared to controls, but no difference was observed among the study groups in hunger sensation and consequently in daily food intake. Treatment by both sevelamer carbonate and lanthanum carbonate were associated with a sensation of fullness. However, an increase in this feeling was accompanied by an increase in daily dietary intake in the lanthanum carbonate group and inversely, by a decrease in daily food intake of the sevelamer carbonate group. These differences were not however translated as differences in appetite, dietary intake and overall nutritional status between the study groups.

Our finding that hunger ratings are good predictors of food intake in MHD patientsis in agreement with a study by Flint et al.[14] However, not all studies show similar results. For example, Barkeling et al[18] tested the predictive validity of subjective motivation to eat using VAS and found that only "desire to eat" and "prospective consumption" predicted forthcoming food intake. In addition, an association between hunger sensation and food consumption can be even negative. It is well known that inadequate dietary protein intake itself leads to increased hunger in men.[19] This is a possible explanation of the inverse relation between hunger sensation and nPNA, as a surrogate measure for protein intake, in the control group of our study.

Fullness ratings were strongly associated with dietary intake in the three groups of our study, with the sevelamer carbonate and control groups having an inverse relationship. The inverse association between fullness sensation and daily consumption of food is known from studies conducted in the general population.[20] "Abdominal distension" was a major side effect of sevelamer carbonate versus placebo in a randomized controlled trial.[21] Apparently the feeling of fullness even before meal may be the result of this side effect of sevelamer carbonate. A meta-analysis of randomized trials examining phosphate binders in MHD patients[22] found gastrointestinal effects as major side effects of sevelamer carbonate and lanthanum carbonate, with a high frequency of constipation in sevelamer carbonate patients and of nausea in patients treated with lanthanum carbonate. Nausea, constipation, or abdominal swelling are symptoms that can translate into a sense of fullness and reduced daily food consumption, as seen in the sevelamer carbonate and control groups. In addition, the volume, nutrient composition, and the sensory aspects of the meal affect fullness and satiety.[23] Several interventional studies have demonstrated that high scores of fullness are associated with high protein consumption which may explain the reduction in body weight by high-protein diets.[24,25] Perhaps this partially explains the strong positive association between fullness ratings, daily

Table 3. Raw and adjusted† correlation coefficients between VAS for appetite ratings and dietary intake parameters in the study groups

	Sevelamer (n=25)			Lanthanum (n=24)			Control group (n=29)		
	DEI r(p)	DPI r(p)	nPNA r(p)	DEI r(p)	DPI r(p)	nPNA r(p)	DEI r(p)	DPI r(p)	nPNA r(p)
Hunger									
Univariate	0.04 (0.88)	0.40 (0.08)	0.36 (0.07)	0.41 (0.07)	0.52 (0.02)*	-0.16 (0.47)	-0.13 (0.53)	-0.35 (0.08)	-0.23 (0.25)
Multivariate	0.62 (0.04)*	0.81 (0.003)*	0.62 (0.04)*	0.59 (0.07)	0.90 (<0.001)*	0.08 (0.84)	-0.01 (0.96)	-0.36 (0.15)	-0.52 (0.03)*
Satiety									
Univariate	-0.10 (0.68)	0.03 (0.90)	0.08 (0.70)	0.24 (0.32)	0.11 (0.64)	0.13 (0.55)	-0.16 (0.44)	-0.21 (0.30)	-0.16 (0.43)
Multivariate	0.13 (0.71)	0.21 (0.53)	-0.14 (0.67)	0.40 (0.25)	0.37 (0.29)	-0.29 (0.41)	0.22 (0.38)	0.09 (0.74)	0.06 (0.80)
Fullness									
Univariate	-0.46 (0.04)*	-0.24 (0.30)	-0.14 (0.51)	0.21 (0.38)	0.10 (0.67)	-0.23 (0.30)	-0.17 (0.39)	-0.16 (0.42)	-0.19 (0.33)
Multivariate	-0.54 (0.08)	-0.66 (0.03)*	-0.61 (0.04)*	0.70 (0.02)	0.70 (0.03)*	-0.19 (0.61)	-0.51 (0.03)*	-0.43 (0.07)	-0.17 (0.50)
Prospective food consumption									
Univariate	0.49 (0.03)*	0.43 (0.06)	0.39 (0.05)*	0.38 (0.10)	0.52 (0.02)*	-0.15 (0.49)	0.28 (0.16)	0.06 (0.78)	-0.32 (0.10)
Multivariate	0.74 (0.009)*	0.72 (0.01)*	0.62 (0.04)*	0.43 (0.22)	0.34 (0.33)	-0.39 (0.26)	0.23 (0.35)	-0.03 (0.90)	-0.43 (0.08)

VAS: visual analogue scales; DEI: daily energy intake; DPI: daily protein intake; nPNA: normalized protein nitrogen appearance.
†Adjusted for age, gender, DM, vintage, comorbidity index, daily urine volume, number of pills and cinacalcet use.
*Statistically significant OR values (p<0.05).

calories and protein consumption in the lanthanum carbonate group. A feeling of fullness seems to be secondary to the sensory aspects of the meal and possibly to a protein-rich diet. As for the sevelamer carbonate group, the direction of the relationship between fullness sensation and daily consumption of energy and protein seems to be reversed: feeling of fullness could be secondary to constipation or other gastrointestinal effects that may lead to decreased food intake. However, since our study is observational, we cannot prove the direction of the phenomenon (causal effect), but only a link between the variables.

Finally, the lack of significant differences in other components of appetite (feeling of hunger, satiety, prospective food consumption, or palatability) among the study groups explain the similarity of these groups in respect to dietary intake and consequential nutritional status.

The current study is limited by its observational nature, which does not allow for conclusions to be drawn about possible mechanisms. Second, the calculated sample size enabled us to detect a 5 mm or greater difference in the VAS score between the groups, with α=0.05 and statistical power equal to 90%. This precluded us to detect more subtle differences in appetite VAS scores among the study groups. Third, the VAS questionnaire was completed in the morning, noon or evening depending on the shift in which the participant performed dialysis treatments and not at a fixed time. This can affect the results of the study to some degree. Dietary intake assessed by three-day food records is another limitation of the study, as results can be subjective and incomplete. Despite these limitations, the availability of a wide array of nutritional parameters applied, which include appetite and dietary intake assessment, anthropometrics, biochemical markers, inflammatory biomarkers, and overall nutritional assessment for each participant, strengthened the study.

In summary, regular use of common phosphate binders (sevelamer carbonate, lanthanum carbonate) was not found to be associated with anorexia and decreased dietary intake in the study population. Although treatment by phosphate binders was found to be associated to a certain extent to fullness sensation (one of the domains examined by VAS scores for appetite), it did not translate to dietary intake and overall nutritional status. Therefore, there is no preference in the choice of phosphate binder in MHD patients with hyperphosphatemia, even for those who are at nutritional risk.

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AUTHOR DISCLOSURES

The authors declare no conflict of interest.

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