

Effectiveness of Self-adjusted Phosphate Binder Dose According to Dietary Phosphate Content Method In Improving Hyperphosphatemia Among Hemodialysis Patients

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ABSTRACT

Serum phosphate level control is a major goal in the management of hyperphosphatemia among end stage kidney disease patients. This study aimed to evaluate the effectiveness of self-adjusted phosphate binder dose according to dietary phosphate content method (SPB method) in optimizing the phosphate level among hemodialysis patients.

This was a randomized controlled study conducted from September 2015 to October 2016 which involved eight hemodialysis centers in Penang, Malaysia. Ninety-eight hemodialysis patients who had serum phosphate level more than 1.8 mmol/L were recruited and randomly assigned to intervention and standard group. All patients underwent a standard low phosphate counseling. The 49 patients in intervention group underwent an additional counseling on how to adjust the calcium carbonate tablet dose based on their food intake with the help of a booklet. Meanwhile, the calcium carbonate dose was fixed to the meals among the patients in standard group. The change in serum phosphate levels in both groups at baseline, month-3, month-6 and month-9 were recorded.

The phosphate level at baseline for intervention (2.15 ± 0.22 mmol/L) and standard (2.22 ± 0.27 mmol/L) group were not differed significantly ($p = 0.19$). The intervention group showed significant lower phosphate level compared to standard group (month-3: 1.68 ± 0.43 mmol/L versus 2.10 ± 0.39 mmol/L; month-6: 1.58 ± 0.34 mmol/L versus 2.07 ± 0.38 mmol/L; month-9: 1.54 ± 0.36 mmol/L versus 1.96 ± 0.33 mmol/L; $P < 0.001$).

The SPB method demonstrated significant greater serum phosphate level reduction than the fixed-dose method. This new method in consuming phosphate binder dose should be introduced among the hemodialysis patients.

Key Words: Hemodialysis, hyperphosphatemia, phosphate binder, dietary phosphate content

Introduction

Hyperphosphatemia is a pervasive problem among dialysis patients with end stage kidney disease (ESKD). It has been associated with high morbidity, mortality and hospitalization rate (1). The abnormalities of the phosphate metabolism in these patients can lead to cardiovascular calcification, renal osteodystrophy and secondary hyperparathyroidism (2-6). Therefore, correction of phosphate level is a major goal in the management of hyperphosphatemia among ESKD patients.

Hyperphosphatemia can be controlled by phosphate removal through dialysis, dietary phosphate restriction and inhibition of gastrointestinal phosphate absorption by phosphate binder (7). Despite

complying to regular dialysis schedule and limiting the dietary phosphate intake as recommended by KDIGO (8), most of the patients requiring phosphate binder to achieve the phosphate balance. Hence, the non-compliance to phosphate binder was always associated with failure of achieving the target phosphate level (9). In normal practice, the phosphate binders were prescribed as a fixed dosing regimen such as two pills per meals and three times daily. The clinicians generally assumed that patients have only three main meals a day and the amount of dietary phosphate content are similar for all meals (10). Therefore, the mismatched of the phosphate binder to the dietary phosphate contents might be one of the factors which cause uncontrolled hyperphosphatemia.

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Extra phosphate load from food additive in convenient and processed food was another challenge for dialysis patients to control hyperphosphatemia (11). Phosphate additive usage had become prominent in recent years to enhance the freshness, color, flavor and texture for the processed foods particularly in meat, poultry, egg products, bakery products, cereals and beverage (12). Study showed that the phosphate additive was 90% absorbed into the intestinal compare to 40-60% absorption in animal protein and 10-30% in plant protein (13). Furthermore, the amounts of the phosphate additive in these foods were not reported in most of the food label. The patients would not know which food contained phosphate additive and the amount of phosphate additive in the food even if it is stated in the food label (14).

The used of fixed-dose phosphate binder might be insufficient to match and block the phosphate absorption from meal, as there are variations in meals and phosphate content in each meal among the dialysis patients. In Malaysia, calcium carbonate is commonly used among hemodialysis patients. This study was therefore aimed to evaluate the effectiveness of a newly invented self-adjusted phosphate binder (calcium carbonate) dose according to dietary phosphate content method (SPB method) in improving the serum phosphate level among the hemodialysis patients.

Materials and Methods

This was a randomized controlled study conducted in eight dialysis centers in Penang state, Malaysia, from September 2015 to October 2016. Among the dialysis centers, four centers were from government hospital while another four centers were from non-government organizations. The inclusion criteria were ESKD patients who undergo routine hemodialysis treatment for four hours, three times a week; with serum phosphate level of more than 1.8 mmol/L and taking calcium carbonate as phosphate binder. Patients who underwent parathyroidectomy surgery during the study period or having major acute disease which have affected the food intake were excluded.

The sample size was calculated for addressing the primary objective of this study, which was the detection of difference in serum phosphate level between intervention and standard group. A previous study revealed that the mean difference of 0.35 mmol/L is considered clinically significant reduction in serum phosphate level (6). According to the formula for experimental study comparing two groups (15), 88 patients (44 patients for each group) were required to detect mean difference of 0.35

mmol/L in serum phosphate level with 90% statistical power and 5% significant level. After considering a 20% possible drop-out rate, 106 patients were needed.

This study was conducted in accordance with the Declaration of Helsinki and approved by Medical Research Ethic Committee, Ministry of Health Malaysia (approval number NMRR-15-782-25554) in September 2015. All patients gave written consent before enrollment. A total of 117 eligible patients who fulfilled the inclusion criteria were invited to participate in the study. All the patients were stratified and assigned into 34 groups followed their dialysis days and shifts. These groups were randomly assigned to intervention and standard groups. The patients were blinded about the assigned group. The patient's demographic data was obtained from the medical record file. There were 60 patients in intervention group and 57 patients in standard groups.

A self-adjusted phosphate binder dose booklet (SPB booklet) was developed (by the first author) from 80 items of commonly eaten foods among dialysis patients in Penang. The food items were chosen based on the expert opinions of three senior dietitians which had experiences in counseled the dialysis patients for more than ten years in Penang. The phosphate contents in the booklet were referred to the 4th edition of Nutrition Composition of Malaysia food (16) and the Food Composition Guide Singapore (17). All the foods phosphate content was adjusted for the phosphate additive and the percentage of intestinal phosphorus absorption.

Diet assessment was carried out at baseline and at the end of study (month-9) by using 24 hours diet recall to capture the foods and beverages that consumed by the patients in the past 24 hours, from midnight to midnight on the day prior to the interview (18). The two days 24 hours diet recall (one weekday and one weekend) was chosen as a previous study showed that this method was able to estimate patients' diet intake (19). After the baseline diet recall, all patients (in both intervention and standard groups) received a diet counseling on low phosphate diet. However, the intervention group received an additional diet counseling on using the SPB booklet in adjusting their calcium carbonate dose. The total daily dose of calcium carbonate in both intervention and standard groups were determine and adjusted by physician throughout the study period. The patients must strictly comply to the total daily dose of calcium carbonate prescribed by the physician. The patients in intervention group were advised to divide their calcium carbonate dose (flexible dosing) according to the number of meals per day and based on the estimated dietary phosphate content for each meal

with the help of the SPB booklet. Meanwhile, the calcium carbonate dose for standard group was fixed to the meals. After the counseling, all patients went for a phosphate knowledge test to ensure their understanding about low phosphate diet. The patients were followed up for nine months and the phosphate, corrected calcium, calcium x phosphate products (Ca x P) and albumin level were recorded at baseline, month-3, month-6 and month-9 for both intervention and standard groups.

Statistical Analysis: The collected data were entered into SPSS version 18.0 for analysis. The demographics and biochemical measures of the patients between intervention and standard groups were compared by using the independent sample t-test (for normally distributed data) or Mann-Whitney U test (for non-normally distributed data) for continuous variables. Pearson Chi square was used for categorical variables. The one-way repeated measures ANOVA was performed to compare the phosphate, corrected calcium and Ca x P between and within the intervention and standard groups at four different time periods (baseline, month-3, month-6 and month-9). Post hoc pairwise comparisons by using a Bonferroni adjustment were conducted for between and within subjects' comparison that considered the four different time periods and the group (intervention and standard) effects. Additionally, the comparison within the group for the total calories, protein and dietary phosphate intake at baseline and month-9 was performed by using paired t-test. Meanwhile, the comparison between intervention and standard groups for the total calories, protein and dietary phosphate intake at baseline and month-9 were conducted by using independent sample t-test. The statistical significant was defined as $P < 0.05$ for all the statistical tests.

Results

A total of 98 patients (49 patients from each group) had completed the study. There were 11 and 8 dropouts from intervention and standard groups respectively (Figure 1). There was no significant difference between the intervention and standard groups in term of age, body weight, height, body mass index, gender, ethnicity, number of years of dialysis, education level and working status at baseline of study. The concurrent used of calcitriol (active vitamin D), ranitidine, omeprazole and lanthanum were compared between the groups as these medications might affect the phosphate absorption in the gastrointestinal tract. The results showed no significant difference between intervention and standard group in the number of patients who

prescribed with these four medications respectively at baseline of study. Nevertheless, the standard group showed significant higher medium number of calcium carbonate 500 mg tablet prescribed to the patients throughout the study as compared to intervention group. Considering the biochemical measures (serum phosphate, calcium, Ca x P and albumin level), both groups showed no significance difference at baseline of study (Table 1).

The one-way repeated measures ANOVA test demonstrated significant different of serum phosphate and Ca x P between intervention and standard group at month-3, month-6 and month-9 (Table 2). The intervention group showed a significant lower phosphate level than the standard group at month-3 (1.68 ± 0.43 mmol/L versus 2.10 ± 0.39 mmol/L; $P < 0.001$), month-6 (1.58 ± 0.34 mmol/L versus 2.07 ± 0.38 mmol/L; $P < 0.001$) and month-9 (1.54 ± 0.36 mmol/L versus 1.96 ± 0.33 mmol/L; $P < 0.001$). The Ca x P showed similar trend whereby the level in intervention group was significantly lower than the intervention group at month-3 (3.87 ± 1.03 mmol²/L² versus 4.93 ± 1.10 mmol²/L²; $P < 0.001$), month-6 (3.48 ± 0.78 mmol²/L² versus 4.61 ± 0.88 mmol²/L²; $P < 0.001$) and month-9 (3.40 ± 0.85 mmol²/L² versus 4.81 ± 3.06 mmol²/L²; $P < 0.001$). Post hoc pairwise comparison within subjects showed a significant reduction in phosphate and Ca x P levels between baseline and month-9 for both the intervention and standard group. However, the intervention group demonstrated a significant greater decrement in phosphate and Ca x P levels compared to standard group (Table 2, Figure 2 and Figure 3). The corrected calcium and albumin level were not differed significantly between the two groups throughout the study. Besides, comparison within subjects that considered the interaction between the time periods and the groups showed no significant difference in the corrected calcium and albumin level (Table 2).

The total dietary calories, protein and phosphate intake of the patients were calculated from their two days diet history at baseline and month-9. The intake of these three dietary measures was not differed significantly between intervention and standard group at baseline. Besides, the pair-t test showed no significant difference in the intake of these three dietary measures from baseline to month-9 for both intervention and standard group (Table 3).

Discussion

Over the study period, both intervention and standard groups showed a significant reduction of serum phosphate and Ca x P. Nevertheless, the

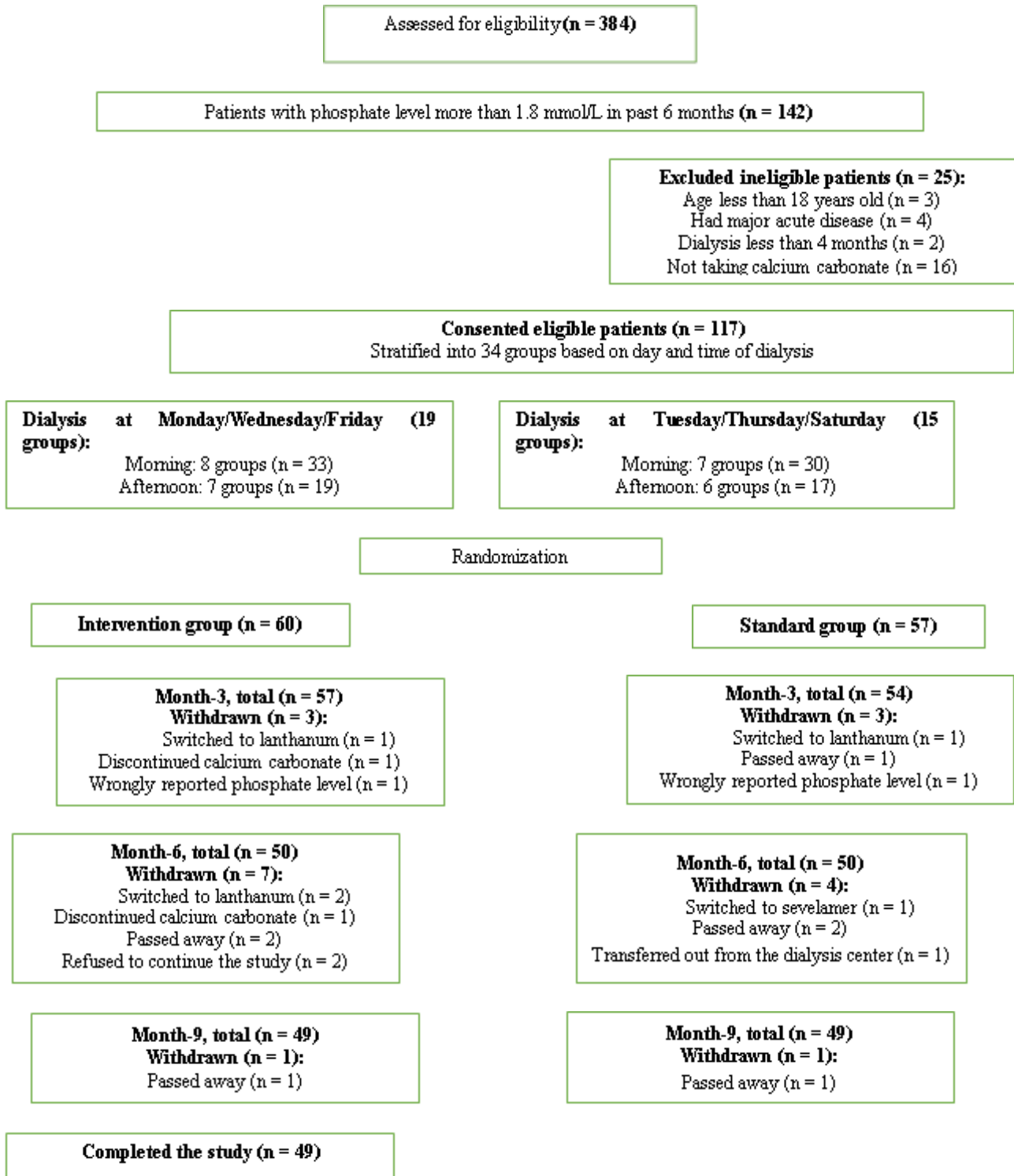


Fig. 1. Patients’ recruitment flow chart

intervention group demonstrated greater reduction of serum phosphate (mean reduction of 0.61 mmol/L versus 0.26 mmol/L) and Ca x P (mean reduction of 1.45 mmol²/L² versus 0.28 mmol²/L²) as compare to standard group. Indeed, the intervention group demonstrated faster reduction in serum phosphate and Ca x P than the standard group particularly

within the first three months of study. These findings indicating that the SPB method is more effective in controlling the serum phosphate and Ca x P than the conventional method of administering calcium carbonate. Previous studies had showed a strong association between high serum phosphate and Ca x P with cardiovascular mortality (2,20,21). Therefore,

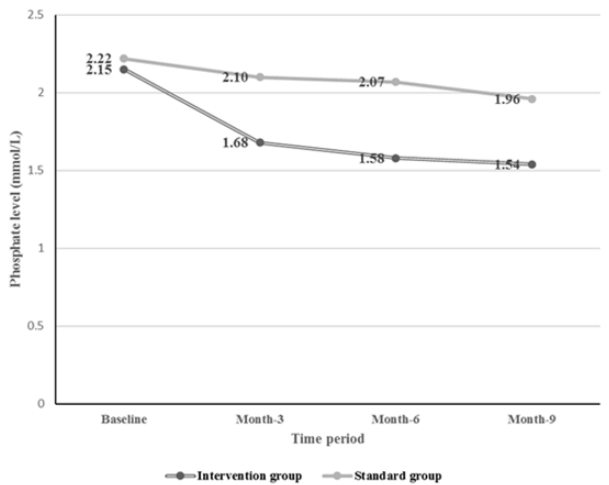


Fig. 2. Comparison of mean serum phosphate level for intervention and standard group at different time periods

the greater decrement in serum phosphate and Ca x P by the SPB method could further reduce the risk of mineral and bone disorder and vascular calcification among dialysis patients.

To the best of our knowledge, currently there was only one published study available on SPB method which was conducted by Ahlenstiel *et al.* on 16 children with chronic kidney disease (CKD) in year 2010 (22). The study involved phosphate binder dosage adjustment based on eye-estimated dietary phosphate content using a newly defined phosphate unit (PU) (1 phosphate unit = 100 mg phosphate). The study revealed a significant reduction of serum phosphate from 1.94 mmol/L to 1.78 mmol/L within 24 weeks. However, the small sample size in the study had limited the validity of the SPB method. Therefore, the present study that using more powerful study design and larger number of patients could further supported the use of SPB method in managing the hyperphosphatemia among ESKD patients.

The present study involved more simplified method in adjusting the phosphate binder dose. The method used by Ahlenstiel *et al.* involved the need of patients to record the daily food diary and higher literacy to estimate the total phosphate unit in daily meals (22). Indeed, there is a need of an expert to adjust the phosphate binder/PU ratio from time to time based on the serum phosphate level (22). All these steps might had cause this intervention hardly to be implemented in real practice. Additionally, there was no limit of phosphate binder intake in the intervention group where the number of phosphate binder was based on the total daily estimated PU. It carried the risk of uncontrolled excessive calcium-based phosphate binder intake that can lead to hypercalcemia and vascular calcification. Conversely, the patients in the present study must strictly follow

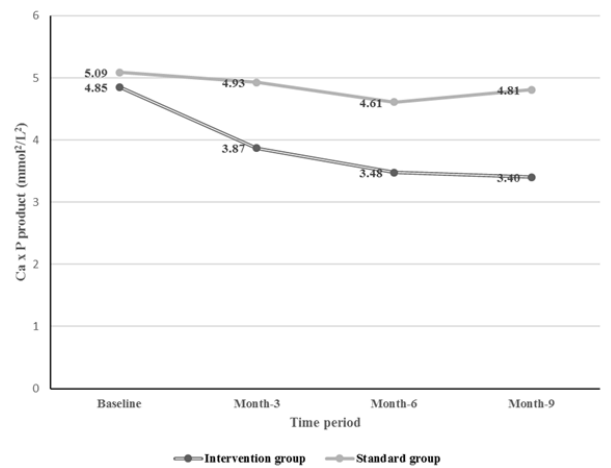


Fig. 3. Comparison of mean calcium x phosphate product for intervention and standard group at different time periods

the total prescribed daily calcium carbonate dose, but they can adjust the timing and number of tablets accordingly to their meals. Therefore, the risk of excessive calcium carbonate intake was minimized.

There was a trial on developing a ‘phosphate counting program’ in Canada to simplifying the SPB method among peritoneal dialysis patients (23). A mobile application (App) for Apple iPod handheld device was created for patients to enter their food intake into the App to calculate the number of phosphate binder that are required for each meal (23,24). However, the estimated cost of this project was around USD 156,000. Furthermore, the food items in the device might not be tailor with the Malaysian local foods and create the same positive outcomes among Malaysian dialysis patients.

The SPB booklet which does not require high cost, high literacy to estimate the PU of the meals or an expert in adjusting the phosphate binder/PU ratio appeared to be more users friendly and affordable for Malaysian population. The patients only need to refer how much phosphate binder should be taken for the common food that they plan to consume. Besides, the development of the SPB booklet involved consideration of the bioavailability of the phosphate, food additive, the recommendation of daily phosphate intake and the daily calcium intake. Therefore, it can reduce the problem of mismatch of phosphate binder to dietary phosphate contents and avoid higher usage of calcium-based phosphate binder as mentioned in a previous meta-analysis (25).

Hypercalcemia was associated with all-cause mortality (26). Previous studies had revealed the cautions on using the calcium-based phosphate binder in management of hyperphosphatemia. The use of calcium-containing phosphate binder in lowering the phosphate level could worsen the survival prognosis

Table 1. Comparison of demographic characteristics and biochemical measures for intervention and standard group at baseline

Characteristics	Intervention group (n = 49)	Standard group (n = 49)	Statistical analysis and P value
Age (year), mean±SD	54.5±13.3	50.3±14.7	t(96) = -1.60, P = 0.113*
Weight (kg), mean±SD	62.5±10.3	58.8±11.1	t(96) = -1.07, P = 0.091*
Height (m), mean±SD	1.63±9.40	1.61±8.50	t(96) = -1.45, P = 0.151*
Body Mass Index (kg/m ²), mean±SD	23.5±3.7	22.7±3.3	t(96) = -1.17, P = 0.244*
Gender, n (%)			
Male	34(69.4)	33(67.3)	X ² (1) = 0.05, P = 0.828†
Female	15(30.6)	16(32.7)	
Ethnic, n (%)			
Chinese	35(71.5)	34(69.5)	X ² (1) = 0.05, P = 0.825†
Others	14(28.5)	15(30.5)	
Years of dialysis, n (%)			
1 to 5 years	22(44.9)	15(30.6)	X ² (1) = 2.13, P = 0.145†
More than 5 years	27(55.1)	34(69.4)	
Education level ^b , n (%)			
Primary	14(28.6)	13(26.5)	X ² (2) = 2.58, P = 0.275†
Secondary	26(53.1)	32(65.3)	
Diploma or higher	9(18.3)	4(8.2)	
Working status, n (%)			
Yes	17(34.7)	22(44.9)	X ² (1) = 1.07, P = 0.302†
No	32(65.3)	27(55.1)	
Concurrent Medication, n (%)§			
Calcitriol	30(61.2)	22(44.9)	X ² (1) = 2.62, P = 0.105†
Ranitidine	6(12.2)	3(6.1)	X ² (1) = 1.10, P = 0.294†
Omeprazole	7(14.3)	11(22.4)	X ² (1) = 1.09, P = 0.297†
Lanthanum	7(14.3)	7(14.3)	X ² (1) = 0.00, P = 1.000†
Calcium carbonate, medium (IQR)			
Baseline	6(6)	9(3)	Z = -2.82, P = 0.005‡
Month 3	6(5)	9(4)	Z = -2.16, P = 0.031‡
Month 6	6(6)	8(3)	Z = -2.50, P = 0.013‡
Month 9	6(6)	8(3)	Z = -2.43, P = 0.015‡
Phosphate level (mmol/L), mean±SD	2.15±0.22	2.22±0.27	t(96) = 1.32, P = 0.191*
Corrected calcium (mmol/L), mean±SD	2.26±0.19	2.30±0.24	t(96) = 1.02, P = 0.311*
Ca x P (mmol ² /L ²), mean±SD	4.85±0.59	5.09±0.75	t(96) = 1.79, P = 0.077*
Albumin (g/dL), mean±SD	38.51±3.99	38.04±3.92	t(96) = -0.59, P = 0.558*

*Independent sample t-test, †Pearson Chi square test, ‡Mann Whitney U test, §Number and percentage of patients who were prescribed with these medications, ||Medium number of calcium carbonate 500 mg tablet prescribed to the patient. The data was not normally distributed and presented as medium (interquartile range).

SD: Standard deviation, IQR: Interquartile range, Ca x P: Calcium x phosphate product

among dialysis patients (25-28). The SPB method in the present study was useful to the Malaysian population because it included the need of counsel dialysis patients on correct dosing and timing when using the calcium carbonate. This was support by the finding that there was no increment in the median

number of calcium carbonate prescribed by the nephrologist throughout the study, but it led to better control of phosphate level. Indeed, there was no significant difference in the mean corrected calcium level between baseline and month-9 for both groups in the present study. Conversely, in the Ahlenstiel et

Table 2. Comparison of the biochemistry measures for intervention and standard group at different time periods

	Intervention group (n = 49)				Standard group (n = 49)			
	Baseline	Month-3	Month-6	Month-9	Baseline	Month-3	Month-6	Month-9
Phosphate level (mmol/L)*,†	2.15±0.22	1.68±0.43	1.58±0.34	1.54±0.36	2.22±0.27	2.10±0.39	2.07±0.38	1.96±0.33
Corrected calcium (mmol/L)	2.26±0.19	2.32±0.23	2.22±0.24	2.23±0.19	2.30±0.24	2.32±0.17	2.24±0.20	2.24±0.22
Ca x P (mmol ² /L ²)‡,§	4.85±0.59	3.87±1.03	3.48±0.78	3.40±0.85	5.09±0.75	4.93±1.10	4.61±0.88	4.81±3.06
Albumin (g/dL)	38.51±4.00	37.18±3.10	38.22±4.89	38.57±4.65	38.04±3.92	36.80±3.10	38.37±4.35	37.88±4.26

One-way repeated measures ANOVA test results:

*Comparison between subjects showed a significant difference of mean serum phosphate level between intervention and standard group ($F = 52.48$, $P < 0.001$). Post hoc pairwise comparison showed a significant difference between intervention and standard group at month-3 ($P < 0.001$), month-6 ($P < 0.001$) and month-9 ($P < 0.001$).

†Comparison within subjects that considered the interaction between the time periods (baseline, month-3, month-6 and month-9) and the groups (intervention and standard group) showed a significant difference of mean serum phosphate level ($F = 11.36$, $P < 0.001$). Post hoc pairwise comparison showed a significant reduction of mean serum phosphate level for intervention group between baseline and month-3 ($P < 0.001$), baseline and month-6 ($P < 0.001$), and baseline and month-9 ($P < 0.001$). Post hoc pairwise comparison showed a significant reduction of mean serum phosphate level for standard group between baseline and month-9 ($P < 0.001$).

‡Comparison between subjects showed a significant difference of mean Ca x P level between intervention and standard group ($F = 42.81$, $P < 0.001$). Post hoc pairwise comparison showed a significant difference between intervention and standard group at month-3 ($P < 0.001$), month-6 ($P < 0.001$) and month-9 ($P < 0.001$).

§Comparison within subjects that considered the interaction between time periods (baseline, month-3, month-6 and month-9) and the group (intervention and standard group) showed a significant difference of mean Ca x P ($F = 9.51$, $P < 0.001$). Post hoc pairwise comparison showed a significant reduction of mean Ca x P level for intervention group between baseline and month-3 ($P < 0.001$), baseline and month-6 ($P < 0.001$), baseline and month-9 ($P < 0.001$), and month-3 and month-9 ($P = 0.005$). Post hoc pairwise comparison showed a significant reduction of mean Ca x P level for standard group between baseline and month-6 ($P = 0.002$), baseline and month-9 ($P < 0.001$), and month-3 and month-9 ($P = 0.005$).

Ca x P: Calcium x phosphate product. Values are presented as mean±standard deviation

Table 3. Comparison of total dietary calories, protein and phosphate intake for the intervention and standard groups

	Intervention group (n = 49)			Standard group (n = 49)			Independent sample t-test statistic, t & P value	
	Baseline	Month-9	Paired t-test statistic, t & P value	Baseline	Month-9	Paired t-test statistic, t & P value	Baseline	Month-9
Calories (kcal/day)	1402.5±234.1	1428.9±197.8	t = 1.193, P = 0.239	1419.9±262.5	1442.8±160.1	t = 0.885, P = 0.380	t = 0.348, P = 0.729	t = 0.383, P = 0.703
Protein (g/day)	44.9±7.7	46.5±6.3	t = 1.788, P = 0.080	42.6±7.3	43.7±5.2	t = 1.309, P = 0.200	t = 1.492, P = 0.139	t = 2.399, P = 0.018
Phosphate (mg/day)	930.4±142.6	945.2±146.8	t = 0.822, P = 0.415	949.9±159.4	968.9±127.9	t = 1.10, P = 0.277	t = 0.638, P = 0.525	t = 0.849, P = 0.398

Values are presented as mean±standard deviation

al. study, there was an increment in the number of phosphate binder consumed by the patients from 6.3 ± 2.9 to 8.2 ± 5.4 pills after the study period of 24 weeks (22).

Although the baseline phosphate level was not differed significantly between the study groups, lower median phosphate binder dose was found in intervention group as compare to standard group. The lower phosphate binder dose in intervention group at baseline was happened by chance through random sampling. However, throughout the study period (from baseline to month-9), the median dose of phosphate binder in intervention group was lower than the standard group. This finding suggested that the intervention group required lower phosphate binder dose, but it resulted in better phosphate level compare to standard group. It also reflects the mismatch of the phosphate binder dose to the dietary phosphate content in the standard group which showed higher phosphate level although higher phosphate binder dose was prescribed to them. This finding was supported by a study by Leung et al. which showed that the variation of dietary phosphate intake in ESKD patients can led to mismatch of dietary phosphate intake with the fix phosphate binder dose (29). The study revealed that the meal phosphate variability can be ranged from 0 to 798 mg for breakfast, 0 to 1853 mg for lunch, 0 to 1523 mg for supper, and 0 to 463 mg for snack with some patients even consuming three snacks per day. Hence, the standard fixed dose of phosphate binder at meals is an inappropriate management strategy for controlling hyperphosphatemia.

There was no significant change in total dietary calories, protein and phosphate intake from baseline to month-9 for both groups. This finding showed that the diet counseling at baseline did not led to changes in the diet intake among the patients. The strict phosphate restriction might had hindered the patients from any further changes in their current diet. Serum albumin is positively correlated with the protein intake even after accounted the confounding factor such as ages and diabetic disease (30). Therefore, the unchanged of total protein intake throughout the study in both groups could explain the none significant change in the albumin level in the patients. Ordinarily, the albumin level acted as one of the predictors for mortality rate in ESKD patients which reflecting the poor nutrition or malnutrition (31). The mean albumin level in the patients was ranged from 36.80 to 38.57 g/dL which showed that the patients were having poor nutrition. This finding was consistent to the mean serum albumin level (38.5 g/L) reported in the 22th Report of the Malaysian Dialysis and Transplant Registry among the Malaysian

hemodialysis patients in year 2014. The report showed that only 41% of Malaysian patients achieved the normal albumin level (> 40.0 g/dL). The percentage had dropped from 56% to 41% since 2005. This showed that the issue of malnutrition is getting worse among Malaysian dialysis patients (32). Therefore, it is essential to implement an innovative education that can improve the protein intake of the dialysis patients while on the other hand control the phosphate level.

Limitation: The SPB booklet only included the local foods in Penang which might not be generalized to the foods in other states of Malaysia or other countries. The portion size and different cooking method for the same food might lead to different phosphate content. Thus, the others state of Malaysia or other countries needs to create their own booklet which is match to their local food. Besides, the SPB booklet is specifically designed for calcium carbonate dosage adjustment and cannot be applied on other types of phosphate binders.

Conclusion: The SPB method gave a significant positive impact on lowering the serum phosphate level and $\text{Ca} \times \text{P}$ which can reduce the risk of mineral bone disease and cardiovascular events among the hemodialysis patients. Therefore, this new method in consuming phosphate binder dose should be introduced among the hemodialysis patients.

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References

1. Cupisti A, Gallieni M, Rizzo MA, Caria S, Meola M, Bolasco P. Phosphate control in dialysis. *Int J Nephrol Renovasc Dis* 2013;6: 193-205.
2. Block GA, Klassen PS, Lazarus JM, Ofsthun N, Lowrie EG, Chertow GM. Mineral metabolism, mortality, and morbidity in maintenance hemodialysis. *J Am Soc Nephrol* 2004;15: 2208-2218.
3. Block GA, Raggi P, Bellasi A, Kooienga L, Spiegel DM. Mortality effect of coronary calcification and phosphate binder choice in incident hemodialysis patients. *Kidney Int* 2007; 71: 438-441.
4. Shaman AM, Kowalski SR. Hyperphosphatemia management in patients with chronic kidney disease. *Saudi Pharm J* 2016; 24: 494-505.
5. Nadkarni GN, Uribarri J. Phosphorus and the kidney: What is known and what is needed. *Adv Nutr* 2014; 5: 98-103.
6. Kalantar-Zadeh K. Patient education for phosphorus management in chronic kidney

- disease. *Patient Prefer Adherence* 2013; 7: 379-390.
7. Daugirdas JT, Blake PG, Ing TS. *Handbook of Dialysis*. (5th ed). Philadelphia: Wolters Kluwer Health, 2015.
 8. Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Work Group. KDIGO clinical practice guideline for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease-mineral and bone disorder (CKD-MBD). *Kidney Int* 2009; 76: 1-130.
 9. Kuhlmann MK. Management of hyperphosphatemia. *Hemodialysis Int* 2006; 10: 338-345.
 10. Kuhlmann MK, Hoechst S, Landthaler I. Patient empowerment in the management of hyperphosphatemia. *Int J Artif Organs* 2007; 30: 1008-1013.
 11. Uribarri J. Phosphorus additives in food and their effect in dialysis patients. *Clin J Am Soc Nephrol* 2009; 4: 1290-122.
 12. Karalis M, Murphy-Gutekunst L. Patient education. Enhanced foods: hidden phosphorus and sodium in foods commonly eaten. *J Ren Nutr* 2006; 16: 79-81.
 13. Noori N, Sims JJ, Kopple J, et al. Organic and inorganic dietary phosphorus and its management in chronic kidney disease. *Iran J Kidney Dis* 2010; 4: 89-100.
 14. Cupisti A, Kalantar-Zadeh K. Management of natural and added dietary phosphorus burden in kidney disease. *Semin Nephrol* 2013; 33: 180-190.
 15. Suresh KP, Chandrashekar S. Sample size estimation and power analysis for clinical research studies. *J Hum Reprod Sci* 2012; 5: 7-13.
 16. Tee ES, Azudin MN, Idris K. *Nutrient composition of Malaysian foods*. (4th ed). Kuala Lumpur: Institute for Medical Research, 1997.
 17. Singapore Health Promotion Board. *Food Composition Guide Singapore*. Singapore: Health Promotion Board, 2003.
 18. Ma Y, Olendzki BC, Pagoto SL, et al. Number of 24-hour diet recalls needed to estimate energy intake. *Ann Epidemiol* 2009; 19: 553-559.
 19. Bross R, Noori N, Kovesdy CP, et al. Dietary assessment of individuals with chronic kidney disease. *Semin Dial* 2010; 23: 359-364.
 20. Ganesh SK, Stack AG, Levin NW, Hulbert-Shearon T, Port FK. Association of elevated serum PO₄, Ca × PO₄ product, and parathyroid hormone with cardiac mortality risk in chronic hemodialysis patients. *J Am Soc Nephrol* 2001; 12: 2131-2138.
 21. Young EW, Albert JM, Satayathum S, et al. Predictors and consequences of altered mineral metabolism: the Dialysis Outcomes and Practice Patterns Study. *Kidney Int* 2005; 67: 1179-1187.
 22. Ahlenstiel T, Pape L, Ehrlich JH, Kuhlmann MK. Self-adjustment of phosphate binder dose to meal phosphorus content improves management of hyperphosphataemia in children with chronic kidney disease. *Nephrol Dial Transplant* 2010; 25: 3241-3249.
 23. Zimmerman DL, McCormick B. Development of a 'Phosphate Counting Program' on an iTouch to simplify self-management of dietary phosphate by patients with end stage renal disease (ESRD) treated with peritoneal dialysis. Ottawa: Ottawa Hospital Research Institute, 2017. Available at: <https://clinicaltrials.gov/ct2/show/NCT01643486> (accessed 19 June 2018).
 24. Hayashi A, Yamaguchi S, Waki K, et al. Testing the feasibility and usability of a novel smartphone-based self-management support system for dialysis patients: A pilot study. *JMIR Res Protoc* 2017; 6: 63.
 25. Jamal SA, Fitchett D, Lok CE, Mendelssohn DC, Tsuyuki RT. The effects of calcium-based versus non-calcium-based phosphate binders on mortality among patients with chronic kidney disease: a meta-analysis. *Nephrol Dial Transplant* 2009; 24: 3168-3174.
 26. Inaguma D, Koide S, Takahashi K, et al. Relationship between serum calcium level at dialysis initiation and subsequent prognosis. *Ren Replace Ther* 2017; 3: 2.
 27. Hill KM, Martin BR, Wastney ME, et al. Oral calcium carbonate affects calcium but not phosphorus balance in stage 3-4 chronic kidney disease. *Kidney Int* 2013; 83: 959-966.
 28. Jamal SA, Vandermeer B, Raggi P, et al. Effect of calcium-based versus non-calcium-based phosphate binders on mortality in patients with chronic kidney disease: an updated systematic review and meta-analysis. *Lancet* 2013; 382: 1268-1277.
 29. Leung S, McCormick B, Wagner J, et al. Meal phosphate variability does not support fixed dose phosphate binder schedules for patients treated with peritoneal dialysis: a prospective cohort study. *BMC Nephrol* 2015; 16: 205.
 30. Sridhar NR, Josyula S. Hypoalbuminemia in hemodialyzed end stage renal disease patients: risk factors and relationships - a 2 year single center study. *BMC Nephrol* 2013; 14: 242.
 31. Phelan PJ, O'Kelly P, Walshe JJ, Conlon PJ. The importance of serum albumin and phosphorous as predictors of mortality in ESRD patients. *Ren Fail* 2008; 30: 423-429.
 32. National Renal Registry. 22nd report of the Malaysian dialysis and transplant registry 2014. Kuala Lumpur: National Renal Registry 2014.