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Phosphate-specific diet effect on serum phosphate levels in adults undergoing hemodialysis: A meta-analysis

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Abstract

Background

We performed a meta-analysis to evaluate the influence of a phosphate-specific intake on serum phosphate levels in hemodialysis subjects.

Methods

A systematic literature search up to November 2021 was done and 14 studies included 1284 hemodialysis subjects at the start of the study; 671 of them were provided with phosphate-specific intake, and 613 were control. We calculated the mean difference (MD) with 95% confidence intervals (CIs) to evaluate the influence of phosphate-specific intake on serum phosphate levels in hemodialysis subjects by the contentious method with a random or fixed-influence model.

Results

Phosphate-specific intake had significantly better serum phosphate levels change (MD, -0.66; 95% CI, -0.95- -0.36, $p<0.001$) with moderate heterogeneity ($I^2 = 71\%$) compared to control in hemodialysis subjects

Conclusions

Phosphate-specific intake had significantly lower serum phosphate levels change compared to control in hemodialysis subjects. Further studies are required.

Keywords: phosphate-specific diet; hemodialysis; control; serum phosphate levels change

Introduction

Extra nutritional phosphate consumption possibly adds to cardiovascular and bone illnesses in subjects with chronic kidney disease. [1] Chronic kidney disease-mineral and bone disease define the cardiovascular and bone diseases in subjects with chronic kidney disease, and the metabolic derange of phosphate and calcium metabolism add to these results. [2] The 2020 Kidney Disease Outcomes Quality Initiative Clinical Practice Guidelines for Nutrition in chronic kidney disease suggest that subjects with stages 3a–5D chronic kidney disease correct their nutritional phosphate consumption to sustain serum phosphate in the normal range (Grading of Recommendations, Assessment, Development, and Evaluations evidence 1B). [3] To treat hyperphosphatemia though treating other intake-associated disease problems, dietarians made nutritional interventions adjusted to a subject's specific requirements, benefits, and abilities. [4] Nutritional phosphate limitations are the main constituent of the intake given for subjects with kidney disease and are one of the chief emphases of counseling by kidney dietarians. [5] Though, even in clinics of hemodialysis with the presence of dietarians of kidney, subjects have information insufficiencies and show problems following nutrients especially phosphate, [6, 7] and about half of the subjects on hemodialysis have pre-dialysis hyper-phosphatemia (serum phosphate levels more than 5.5 mg/dl). [8, 9] With the restraints on dietarian time [10] and consistency of hyperphosphatemia, the influence of phosphate-specific intake treatment and its possible improvement influence on serum phosphate in such a population should be investigated. The present meta-analysis aimed to evaluate to phosphate-specific intake on serum phosphate levels in hemodialysis subjects.

Methods

This meta-analysis is organized according to the epidemiology statement, [11] following the established methodology.

Study selection

The main objective of this study is to compare the influence of phosphate-specific intake on serum phosphate levels in hemodialysis subjects.
using the following tools like odds ratio (OR), frequency rate or relative risk, and confidence interval of 95%.
The search was narrowed to English, only included, and inclusion criteria are not restricted by study type or size. Studies with no correlation have been exempted from the study, e.g., editorials, perspectives, letters, and commentary.
Figure 1 exhibits the mode of analysis.
The article inclusion criteria are classified and integrated into meta-analysis when
1. The study was a randomized control trial, prospective study, or retrospective study.
2. The target population was hemodialysis subjects
3. The intervention program was a phosphate-specific intake
4. The study comprised comparisons between phosphate-specific intake and control.
The following exclusion criteria were adopted among the intervention groups
1. Studies that did not determine the influence of phosphate-specific intake on serum phosphate levels in hemodialysis subjects
2. Studies with management other than phosphate-specific intake.
3. Studies did not concentrate on the influence of comparative outcomes.

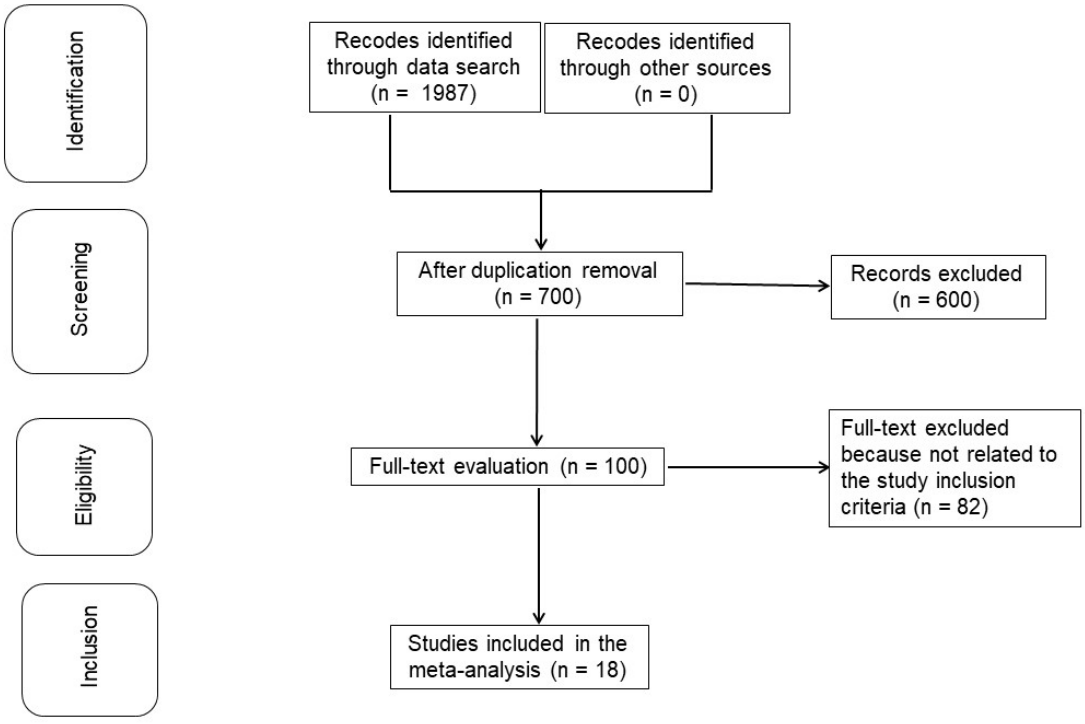

Figure 1. Schematic illustration of the study method

Identification

PICOS principle was the protocol for the search strategy [12] and asserted the critical elements of PICOS as P (population): hemodialysis subjects; I (intervention/exposure): phosphate-specific intake; C (comparison): phosphate-specific intake and control; O (outcome): serum phosphate levels change; and S (study design): had no limitation. [13] We conducted a systematic and brief search of MEDLINE/PubMed, Google Scholar, Embase, OVID, and Cochrane Library until November 2021, by a combination of keywords and correlated words for phosphate-specific intake, hemodialysis, control, serum phosphate levels change as shown in Table 1. The selected studies were pooled in EndNote software to exclude the duplicates. Additionally, a thorough screening on the title and abstracts are done to erase any data that did not show any the influence of phosphate-specific intake and control on the outcomes studied for hemodialysis subjects. Related pieces of information were collected from the remaining studies.

Table 1. Search Strategy for Each Database

Database	Search strategy
Pubmed	#1 "phosphate-specific intake"[MeSH Terms] OR "hemodialysis"[All Fields] #2 "control"[MeSH Terms] OR "serum phosphate levels change"[All Fields] #3 #1 AND #2
Embase	'phosphate-specific intake'/exp OR 'hemodialysis'/exp #2 'control'/exp OR 'ICBG'/exp OR 'serum phosphate levels change'/exp #3 #1 AND #2
Cochrane library	#1 (phosphate-specific intake):ti,ab,kw OR (hemodialysis):ti,ab,kw (Word variations have been searched) #2 (control):ti,ab,kw OR (serum phosphate levels change):ti,ab,kw (Word variations have been searched) #3 #1 AND #2

Screening

Subject-related and study-related data characteristics are considered for the collection and classification of data, and it is pooled into a standardized form. The categorization was made into the standard form like the surname of the first author, duration of the trial, place of practice, design of the study, subject type, sample size, categories, demography, and treatment methodology, information source, method of evaluation (both qualitative and quantitative), statistical analysis, and primary outcome evaluation [12].

Methodological quality was assessed by the "risk of bias tool "adopted from Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0. This meta-analysis recommended that if a trial with inclusion criteria is based on the standards mentioned earlier, any conflicts that arose during the data collection by two reviewers must be resolved through discussion and when and necessary by the "corresponding author" to ensure the quality of the methodology [14].

Level of risk of bias is counted in the assessment criteria

The level of risk was considered low if all quality parameters are met; it was considered moderate if one of the quality parameters is not met/or partially met; and was considered high if one of the quality parameters is not met/ not included. A reexamination of the original article addressed for its any inconsistencies.

Eligibility Criteria

The main eligibility criteria concentrated on the influence of a phosphate-specific intake on serum phosphate levels in hemodialysis subjects. An evaluation of the influence of phosphate-specific intake and control on serum phosphate levels change in hemodialysis and the data extracted forming a summary.

Inclusion

Studies reporting the influence of phosphate-specific intake on serum phosphate levels in hemodialysis subjects were only included in the sensitivity analysis. In comparison, the impact of phosphate-specific intake and control cooperated as a subcategory of sensitivity analysis.

Statistical analysis

The dichotomous method was used to compute the mean difference (MD) at 95% confidence interval (CI) on a fixed-influence or random-influence model. First, the I^2 index range was established between 0- 100%, when the I^2 index scale for heterogeneity is indicated nil, low, moderate, and high as 0%, 25%, 50%, and 75%, respectively [15]. Random-influence is considered if I^2 was > 50%, and if < 50%, as fixed-influence. The initial evaluation of the result is always stratified, and in sub-group analysis, a p-value <0.05 is reported statistically significant. Egger regression test is used quantitatively and qualitatively to assess the Publication bias (if p ≥0.05) by inspecting funnel plots of the logarithm of odds ratios compared with their standard errors [12]. The entire p-values were appeared two-tailed. The statistical analysis and graphs are done by " Reviewer manager version 5.3" (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark).

Results

A total of 2045 distinctive studies were found, of which 14 studies (between 2003 and 2021) satisfied the inclusion criteria and were comprised in the study. [16-29] This meta-analysis study based on 14 studies included 1284 hemodialysis subjects at the start of the study; 671 of them were provided with phosphate-specific intake, and 613 were control. All studies evaluated the influence of a phosphate-specific intake on serum phosphate levels in hemodialysis subjects.

The study size ranged from 30 to 297 hemodialysis subjects at the beginning of the study. The information of the 14

studies is shown in Table 2.
Phosphate-specific intake had significantly better serum phosphate levels change (MD, -0.66; 95% CI, -0.95- -0.36, p<0.001) with moderate heterogeneity (I^2 = 71%) compared to control in hemodialysis subjects as shown in Figure 2.
The stratified data did not examine the factors like age, gender, and ethnicity between the two groups because no studies adjusted or outlined these factors.
No publication bias (p = 0.87) was detected when the quantitative measurement was conducted using the Egger regression test and examination of the funnel plot as shown in Figure 3. There was; however, low methodological quality was observed in selected randomized control trials. No articles had selective reporting or incomplete data, which proved that selected articles devoid of selective reporting bias.

Table 2. Characteristics of the selected studies for the meta-analysis

Study	Country	Total	Phosphate-specific intake	Control
de Brito Ashurst, 2003 [16]	UK	58	29	29
Ford, 2004 [17]	USA	63	32	31
Morey, 2008 [18]	UK	48	27	21
Sullivan, 2009 [19]	USA	279	145	134
Lou, 2012 [20]	Spain	80	41	39
Karavetian, 2013 [21]	USA	61	37	24
Reese, 2015 [22]	USA	36	24	12
Tsai, 2016 [23]	Taiwan	61	30	31
Vrdoljak, 2017 [24]	Croatia	47	25	22
Rizk, 2017 [25]	UAE	246	116	130
de Fornasari, 2017 [26]	Brazil	131	66	65
Lim, 2018 [27]	Korea	70	48	22
Byrne, 2020 [28]	Ireland	74	35	39
Chen, 2021 [29]	Taiwan	30	16	14
	Total	**1284**	**671**	**613**

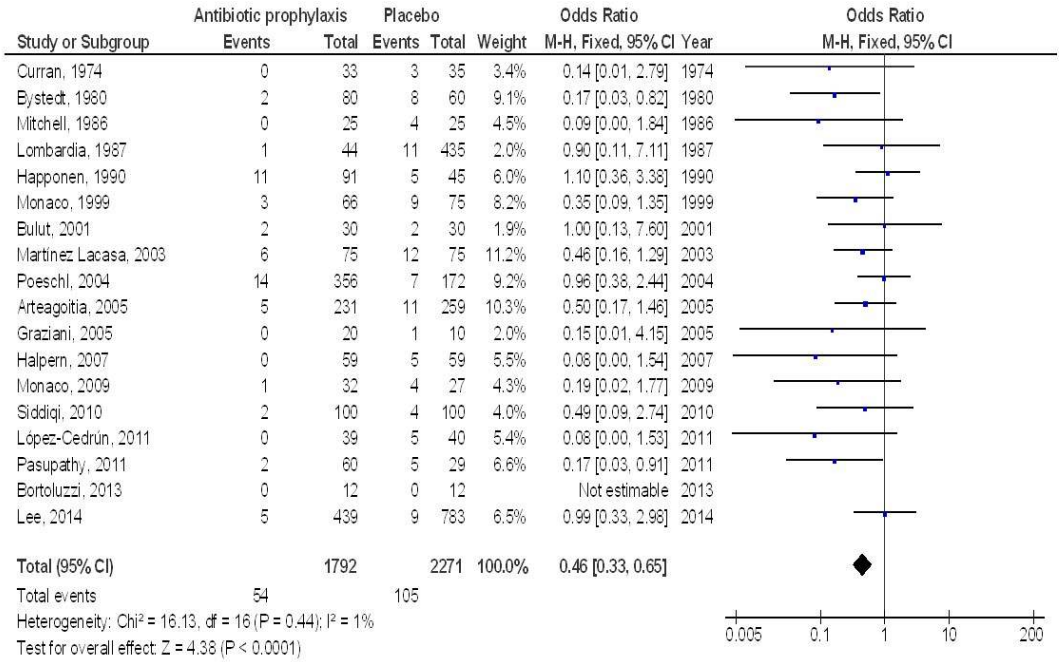

Figure 2. A forest plot of the serum phosphate levels change in hemodialysis subjects with the phosphate-specific intake compared to the control

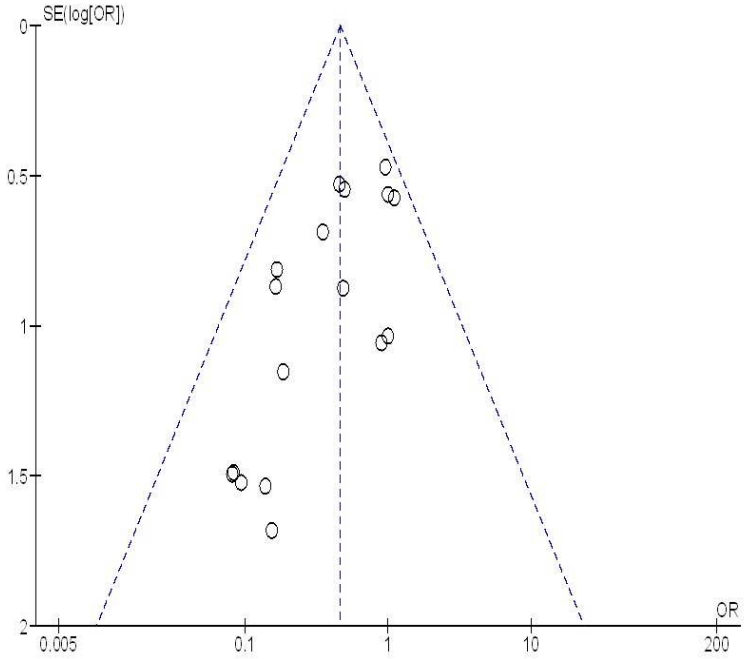

Figure 3. The funnel plot of the serum phosphate levels change in hemodialysis subjects with the phosphate-specific intake compared to the control

Discussion

This meta-analysis study constructed on 14 studies included 1284 hemodialysis subjects at the start of the study; 671 of them were given with phosphate-specific intake, and 613 were control. [16-29] Phosphate-specific intake had significantly better serum phosphate levels change compared to control in hemodialysis subjects. However, the analysis of outcomes should be performed with consideration because of the low number of selected studies and the low sample-size of some of the selected studies found for the meta-analysis, 11 out of 14 studies with ≤ 100 subjects as sample size; recommending the need for other studies to confirm these findings or perhaps to significantly impact confidence in the influence evaluation.

Meta-analysis is a methodology adapted to statistically pool and studies the findings from several independent randomized controlled trials. [30] The 2020 Kidney Disease Outcomes Quality Initiative Clinical Practice Guidelines for Nutrition in Kidney Disease Outcomes Quality Initiative workgroup emphasizes personalizing suggestions after suitable assessment of the subject's daily consumption. [3] Nutrition evaluation is a key character of the tailored intake-treatment method that is usually used by dietarians in clinical practice. Certainly, the Kidney Disease Outcomes Quality Initiative guidelines additionally note that intake treatment needs expert (if possible session with a kidney dietarian) [3] and the United States of America-based National Institutes of Diabetes and Digestive and Kidney Diseases states that it is important to involve and refer to a registered dietarian. [31] Regardless of this, most intake-treatment interventions seemed to utilize a one-size-fits-all method, which fails to influence the sole instruction and training of dietarians. Only four studies showed nutritional evaluation elements to the intervention. [16-18, 26] Though guidelines promoter strong support for kidney dietarians, a 2005–2007 Centers for Medicare and Medicaid Services Medical Evidence Report of incident hemodialysis subjects in the United States (n=192,307) and reported that most of them met a kidney dietarian for at least one time in the year when starting or after starting hemodialysis. [32] Regrettably, no studies in the non-dialyzed people met the inclusion criteria in the meta-analysis, even though calls were initiated in 2009 and in 2017 to prioritize study to assess the clinical assistances related to the use of nutritional interventions in subjects with Kidney Disease Outcomes Quality Initiative stages 3–5D; [2] and Kidney Disease Improving Global Outcomes clinical practice guidelines for Kidney Disease Outcomes Quality Initiative-MBD; [2] the call for the study was rebounded in the 2020 Kidney Disease Outcomes Quality Initiative nutrition guidelines. [3]

Regarding the dose, it seems that almost 0.5 hour/month of phosphate-specific intake treatment was enough to decrease serum phosphate in subjects on hemodialysis with persistent hyperphosphatemia, as long as it is sustained, for up to six months. This intake treatment dose go beyond the total amount of time accessible by almost 50% (almost 21 min/month), based on the latest study of United States of America kidney dietarians, [10] showing the moderate dose of intake treatment shown in this study was, in practice, high. The significance of subject interaction is supported by the results from the second treatment group of the trial by Rizk et al. [25] In this group, the dietarians of the hospital who deliver care by referral (< one time per six months) get thirty-two hours of professional training in nutrition but had no extra interaction with participants outside the normal care referrals.

In summary, the phosphate-specific intake had significantly better serum phosphate levels change compared to control in hemodialysis subjects. More studies are essential to confirm these outcomes.

Limitations

There may be a collection bias in this meta-analysis since several studies found were excluded from the meta-analysis. Though, the studies excluded did not satisfy the inclusion criteria of the meta-analysis. Furthermore, we could not decide if the results were linked to age, gender, and ethnicity or not. The study designed to assess the relationship between the influence of phosphate-specific intake and control on the outcomes of hemodialysis subjects was depending on data from former studies, which may result in bias brought by incomplete details. The meta-analysis was depending on 14 studies; 11 studies of them were small, ≤ 100. Features comprising the age, gender, obedience, ethnicity, and nutritional condition of subjects were also likely bias-encouraging features. Several unpublished studies and lost data may result in a pooled influence bias. Subjects were using diverse chief pharmacological medicines, treatment schedules, doses, and health care schemes. The length of phosphate-specific intake and control treatment of the included studies were varying. The comprised studies did not sufficiently assess the hospital costs and quality of life of the subjects studied, which are vital results.

Conclusions

Phosphate-specific intake had significantly better serum phosphate levels change compared to control in hemodialysis subjects. However, the analysis of outcomes should be done with consideration because of the low number of selected studies and the low sample size of some of the selected studies found for the meta-analysis; recommending the need for added studies to confirm these results or perhaps to significantly influence confidence in the effect evaluation. More studies are essential to confirm these outcomes..

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