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Importance of Renal Dietitians in Nutritional Counselling and Dietary Interventions in The Early Stages of Chronic Kidney Disease

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ABSTRACT

Chronic kidney disease (CKD) is becoming a public-health problem, at a global level. In CKD, patients progressively lose the ability to excrete phosphorus. Several observational studies have determined hyperphosphatemia emerging as an independent cardiovascular risk factor in CKD-Mineral and Bone Disorder (CKD-MBD). In early CKD, serum Klotho declines and fibroblast growth factor-23 (FGF-23) starts increasing which coincides with its effects on augmenting urinary phosphate excretion with reduced serum phosphate reabsorption and decreased levels of calcitriol. The Klotho/FGF23 axis should be a novel target for renal clinicians being pathogenic contributors to CKD progression and cardiovascular disease (CVD) development. The high phosphorous load has been found to increase serum FGF-23 levels in the early stages of CKD which further leads to CVD and increased mortality. To control hyperphosphatemia, a potentially simple and effective approach of dietary phosphate control should be incorporated to reduce the early clinical consequences of CKD-MBD. Along with the amount of dietary phosphorus intake, its type (organic vs. inorganic), its source (animal vs. plant derived), phosphorus-to-protein ratio and preparation of food by boiling should also be made aware to patients which is likely a neglected aspect of dietary counselling in CKD. A kidney-friendly diet plan is needed to protect kidneys from further damage which is rather an arduous period for making patients follow a phosphate-restricted diet. Here, the role of the renal dietitian appears mandatory in counselling and educating the patients to effectively integrate dietary interventions into the therapeutic approach of CKD-MBD.

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Introduction

At the global level, chronic kidney disease (CKD) has become a public health problem that should be managed in its early stages by general internists and specialists. The definition of chronic kidney disease is based on the presence of kidney damage (proteinuria) or decreased kidney function (i.e., glomerular filtration rate (GFR)<60 mL/min per 1•73 m^2) for 3 months or more [1]. In the majority, CKD can be detected with 2 simple tests: a urine test for the detection of proteinuria and a blood test to estimate GFR [2]. Because of the central role of GFR in the pathophysiology of complications, the disease is classified into five stages based on GFR: more than 90 mL/min per 1•73 m^2 (stage 1), 60–89 mL/min per 1•73 m^2 (stage 2), 30–59 mL/min per 1•73 m^2 (stage 3), 15–29 mL/min per 1•73 m^2 (stage 4), and less than 15 mL/min per 1•73 m^2 (stage 5) [3].

The three outcomes of CKD are a decline in renal function, increased risk for cardiovascular disease [2] and malnutrition which was found to be common in pre-dialysis CKD patients even in early CKD stages [4].

Prevalence of CKD

Worldwide, an alarming rise in the burden of CKD is being experienced. A study by Coresh J et al showed the prevalence of CKD stages 1 to 4, increased from 10.0% to 13.1% in 10 years 5. Whereas, in the US adult population it was 11% (19.2 million) [6].

Nathan R Hill et al performed a systemic review and meta-analysis on the prevalence of CKD globally and observed 13•4% in Stages 1 to 5 and 10•6% in stages 3 to 5 based on a comprehensive overview of the existing literature [7].

In India, a study from two of the largest cities (Delhi and Chennai) showed 1 in 12 individuals with CKD, putting them at high risk for adverse outcomes [8]. The prevalence of CKD was observed at 17.2% by Ajay K Singh et al with approximately 6% having CKD stage 3 and above in the SEEK (Screening and Early Evaluation of Kidney Disease) study [9].

Risk factors of CKD

The risk factors for the progression of renal disease include uncontrolled proteinuria [10], uncontrolled diabetes, hypertension, cardiovascular disease, a family history of CKD, older age [2], smoking and obesity [11]. Furthermore, several observational studies have determined hyperphosphatemia as an independent cardiovascular risk factor in CKD which is found to be associated with mineral and bone disorder (MBD) [12,13], soft tissue calcification and increased mortality rates in individuals with CKD [14,15]. Considering the clinical implications of hyperphosphatemia, maintenance of phosphorus concentrations within an optimum range has become of utmost importance in this patient population.

Herein, we review the pathophysiology of CKD along with the management of hyperphosphatemia by introducing careful dietary phosphorus intake at an early stage of CKD through dietary counselling and nutritional education based on emerging evidence from experimental, observational, and interventional studies suggesting high phosphorus intake may accelerate the course of CKD [16].

Pathophysiology of CKD

To reduce the CKD burden; researchers should have a deep insight into the early biomarkers so that early treatment can be given to slow the progression of CKD. Appropriate levels of phosphate are maintained by coordinated regulation of, bone-derived phosphaturic hormone, fibroblast growth factor-23 (FGF-23) with most of its functions occurring in the kidney through an FGF receptor (FGF-R) and its cofactor Klotho [17,18], one of the earliest biochemical abnormalities in CKD [19].

FGF-23 is an influential regulator of vitamin D metabolism and phosphate homeostasis [20]. In early CKD, FGF-23 levels start increasing which coincides with its effects on augmenting urinary phosphate excretion with reduced serum phosphate reabsorption by inhibiting the expression of type II renal sodium phosphate co-transporters (Npt2a and Npt2c) in cells of renal proximal tubules [21]. Further, FGF-23 directly suppresses renal 1a-hydroxylase, leading to decreased conversion of 25-hydroxyvitamin D to its active metabolite 1, 25-hydroxyvitamin D (1, 25$[OH]_2D_3$; calcitriol). Decreasing vitamin D levels in turn stimulates parathyroid hormone (PTH) secretion thereby facilitating the development of secondary hyperparathyroidism [22].

In the early stages of CKD progression, serum Klotho declines [23] followed by a rise in serum FGF23 [24]; before the increase of serum phosphate or PTH level [25]; both function as early biomarkers for kidney dysfunction and can also serve as predictors for risk of cardiovascular disease (CVD) and mortality in CKD patients and the general population [26,23,25].

As it is now evident that FGF-23 increases in the early stages of CKD, especially in response to declining renal function with normal or higher than normal dietary phosphorus load which inhibits renal 1α-hydroxylase directly. A decline in the circulating levels of calcitriol leads to relative hypocalcaemia; on account of depressed gut absorption of calcium, stimulating synthesis and secretion of PTH [27,28]. Burnett et al. observed 66 healthy males and females with dietary phosphate loading which increased the phosphate excretion and circulating FGF-23, thereby, suggesting that dietary phosphate is an important regulator for high FGF-23 levels in humans [29,30].

Need for early dietary intervention

High phosphate intake even in patients with early CKD results in an excessive load of phosphate causing renal damage and accelerating renal function deterioration due to renal tubular injury [31].

Thus, phosphate restriction may need to be initiated even earlier, so that FGF-23 can be maintained within normal limits [32]. Good control of dietary phosphorous intake in the early stages of CKD might potentially reduce the risk of the development of renal secondary hyperparathyroidism and all other clinical consequences of poorly controlled CKD mineral bone disorder [33]. Given the above, primary care physicians should take note of the importance of screening hypertensive and diabetic patients for identifying early kidney damage, followed by early intervention, to retard the progression of kidney disease and prevent cardiovascular damage to the vulnerable population [9,11].

Therefore, dietary phosphorus restriction (DPR) should be advised to CKD patients at an early stage for delaying the progression of CKD and preventing cardiovascular disease. Hence, optimizing the timing of the initiation of therapeutic strategies to target disordered phosphorus metabolism in the early stages of CKD is required.

Dietary phosphorous sources

Therefore, it is conceivable that intervention should aim to control phosphorus levels in CKD patients mainly by restriction of dietary phosphorus intake. It is noted that not just the amount of dietary phosphorus intake is important but also its type (organic vs. inorganic), source (animal vs. plant derived), protein-to-phosphorus ratio and the bioavailability of phosphorus from food. This qualitative aspect of the diet is likely a neglected aspect of dietary counselling in CKD [34].

The proportion of phosphorus which is absorbed throughout the gastrointestinal tract is 60% of the ingested phosphorus on average. Phosphorus in foods is provided in the form of either organic phosphate or inorganic phosphate. However, organic phosphorus from plant protein has a lower bioavailability of phosphorus, despite its high phosphorus content, than phosphorus from animal protein, ranging from 40 to 50% [27].

The reason is that phosphorus from plants such as seeds, nuts and legumes, is in the form of phytate and mammals lack the degrading enzyme phytase. Phosphorus in animal protein is in the form of organic phosphate, which is readily hydrolyzed and absorbed by [35] up to 60% to 80% [27].

A study by Ranjani N Moorthhi et al demonstrated that a diet composed of 70% protein from plants is far more effective than a meat-based diet which helped in decreasing the dietary phosphorous excretion and also found this diet safe and palatable for CKD patients [36,37] By contrast absorption of inorganic phosphorus found in additives and preservatives is very high, up to 100%. A large amount of phosphate is added to foods as preservatives as well as from common beverages such as soda (cola) drinks, with a high phosphate content [38].

Protein-rich foods are historically and naturally the main source of dietary phosphorus [27], hence; most scientific societies recommend reducing protein intake from early stages in patients with chronic renal disease, to reduce the input of phosphorus. Low dietary protein intake will help in slowing the CKD progression, especially in patients with proteinuria as dietary phosphorus intake

will also be decreased, which has been found to be directly related to CKD progression [39].

Because phosphorus is found in a wide variety of foods, complying with a dietary phosphorus restriction is very challenging for CKD patients. The direct relationship between protein and phosphorus dietary content is well known: on average, a mixed diet contains 12–14 mg of phosphorus per gram of protein [40]. To avoid foods with high phosphorus relative to protein, CKD patients should be educated with an effective-friendly approach which will help them in reducing the high phosphorus intake with adequate dietary protein to prevent malnutrition. Claudia D'Alessandro et al designed a phosphorous pyramid, to present the phosphate load of various foods. The pyramid was designed with six floors in which the foods were arranged based on the phosphorus content, phosphorus to protein ratio and phosphorus bioavailability [41].

Another method to reduce the phosphorus content is by preparing the phosphorous-rich foods by wet cooking methods such as boiling, which reduce phosphorus as well as sodium and potassium content, or by other types of cooking-induced demineralization [27].

Important to restrict high phosphorous diet

Some studies have shown the importance of dietary phosphorous restrictions in delaying CKD progression and reducing renal deaths [42].

Another study by Biagio Di Iorio et al performed a randomized, controlled crossover study with 32 patients and found that a very-low-protein diet (0.3 g/kg per day) supplemented with keto analogues reduced FGF-23 levels when compared with a low-protein diet (0.6 g/kg per day) in CKD patients not yet on dialysis [43]. Maintaining normal phosphate levels with dietary modification (low phosphorous diet) and phosphate binders in patients with CKD with declining Klotho expression is expected to reduce mineral and vascular derangements [44].

Role of educating and counselling

A kidney-friendly diet is needed help to protect kidneys from further damage. It is rather an arduous period for making CKD patients follow a phosphate-restricted diet. Here, the role of the dietitian appears mandatory in educating CKD patients through the management of nutrition counselling [45]. Several large studies have examined the association between educational attainment and outcomes in patients with kidney disease. There was an analysis of 61,457 study subjects in the Kidney Early Evaluation Program, who showed lower educational attainment which was found to be independently associated with reduced kidney function and increased mortality [46]. In addition, dietary-related education and counselling can play an important role in an integrated treatment approach to hyperphosphatemia which can help patients in their food selection low in phosphorus [47]. Here, the renal dietitian plays a pivotal role in counselling the patient on what to avoid, at the same time providing solutions and suggesting choices when making the dietary plan.

Monitoring of nutritional status

More frequent nutritional monitoring may be done in patients with changing clinical status or after therapeutic interventions which might help an individual to keep their health status in check. Patients should be evaluated for nutritional status using subjective global assessments, diet diaries, hand grip strength, anthropometric measurements such as body weight, BMI, waist-to-hip ratio, mid-upper arm circumference and skin folds measurements (biceps, triceps, suprailiac and subscapular skin folds). The results obtained can help renal dietitians in making a therapeutic nutrition plan which will be appropriate for each patient. A renal laboratory evaluation can be assayed for estimating eGFR which is widely accepted as the best index of kidney function in health and disease [48].

Conclusion

A high phosphorous load has been found to increase serum FGF-23 levels in the early stages of CKD patients which further leads to CVD and increased mortality. To control hyperphosphatemia, a potentially beneficial and simple approach to dietary phosphate control may reduce the early clinical consequences of CKD-MBD. Unfortunately, dietary phosphorus control is quite challenging in a real-life setting. Therefore, nutrition-related information, education and counselling are needed to effectively integrate dietary interventions into the therapeutic approach of CKD-MBD. To conclude, the renal dietitian should be one of the principal specialists for educating patients about diet, selection of the right food and how to prepare their food. Proper dietary counselling can make better control of phosphorus intake by motivating patients to stick to dietary prescriptions and to avoid nutritional errors which can accelerate kidney function deterioration. Nutritional education and dietary counselling along with intensive nutritional intervention underlie the importance of a phosphate-controlled diet as an integrated therapeutic approach to prevent hyperphosphatemia in CKD patients.

Conflict of Interests

Authors declare no conflict of interest.

Ethical considerations

Ethical issues (including plagiarism, and double publication) have been completely observed by the authors.

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Core Tip

High phosphorous load in the early stages of chronic kidney disease (CKD) patients has been found to increase serum FGF-23 levels that lead to cardiovascular disease and increased mortality which can be delayed by restricting dietary phosphorous intake with the help of the renal dietitian through nutritional counselling and educating the patients to effectively integrate dietary interventions to prevent hyperphosphatemia in CKD patients.

References

1. Lamb EJ, Levey AS, Stevens PE (2013) The Kidney Disease Improving Global Outcomes (KDIGO) guideline update for chronic kidney disease: evolution not revolution. Clin Chem. 59: 462-465.
2. Vassalotti JA, Stevens LA, Levey AS (2007) Testing for chronic kidney disease: a position statement from the National Kidney Foundation. Am J Kidney Dis. 50:169-180.
3. Levey AS, Coresh J (2012) Chronic kidney disease. Lancet. 379: 165-80.
4. Oluseyi A, Enajite O (2016) Malnutrition in pre-dialysis chronic kidney disease patients in a teaching hospital in Southern Nigeria. Afr Health Sci. 16: 234-241.
5. Coresh J, Selvin E, Stevens LA, Manzi J, Kusek JW, et al. (2007) Prevalence of chronic kidney disease in the United

States. JAMA. 298: 2038-2047.
6. Coresh J, Astor BC, Greene T, Eknoyan G, Levey AS (2003) Prevalence of chronic kidney disease and decreased kidney function in the adult US population: Third National Health and Nutrition Examination Survey. Am J Kidney Dis. 41: 1-12.
7. Hill NR, Fatoba ST, Oke JL, Hirst JA, O'Callaghan CA, et al. (2016) Global Prevalence of Chronic Kidney Disease - A Systematic Review and Meta-Analysis. PLoS One. 11: e0158765.
8. Anand S, Shivashankar R, Ali MK, Kondal D, Binukumar B, et al. Prevalence of chronic kidney disease in two major Indian cities and projections for associated cardiovascular disease. Kidney Int. 2015;88(1):178-85.
9. Singh AK, Farag YM, Mittal BV, Subramanian KK, Reddy SR, et al. (2013) Epidemiology and risk factors of chronic kidney disease in India - results from the SEEK (Screening and Early Evaluation of Kidney Disease) study. BMC Nephrol. 14: 114.
10. Peterson JC, Adler S, Burkart JM, Greene T, Hebert LA, et al. (1995) Blood pressure control, proteinuria, and the progression of renal disease. The Modification of Diet in Renal Disease Study. Ann Intern Med. 123: 754-762.
11. Kazancioglu R (2013) Risk factors for chronic kidney disease: an update. Kidney Int Suppl (2011). 3: 368-371.
12. Hruska KA, Mathew S, Lund R, Qiu P, Pratt R (2008) Hyperphosphatemia of chronic kidney disease. Kidney Int. 74: 148-157.
13. Shaman AM, Kowalski SR (2016) Hyperphosphatemia Management in Patients with Chronic Kidney Disease. Saudi Pharm J. 24: 494-505.
14. Savica V, Santoro D, Monardo P, Mallamace A, Bellinghieri G (2009) [Management of hyperphosphatemia in patients with chronic kidney disease]. G Ital Nefrol. 26: 58-61.
15. Palmer SC, Hayen A, Macaskill P, Pellegrini F, Craig JC, et al. (2011) Serum levels of phosphorus, parathyroid hormone, and calcium and risks of death and cardiovascular disease in individuals with chronic kidney disease: a systematic review and meta-analysis. JAMA. 305: 1119-1127.
16. Chang AR, Anderson C (2017) Dietary Phosphorus Intake and the Kidney. Annu Rev Nutr. 37: 321-46.
17. Juppner H, Wolf M, Salusky IB (2010) FGF-23: More than a regulator of renal phosphate handling? J Bone Miner Res. 25: 2091-2097.
18. Urakawa I, Yamazaki Y, Shimada T, Iijima K, et al. (2006) Klotho converts canonical FGF receptor into a specific receptor for FGF23. Nature. 444: 770-4.
19. Papagianni A (2017) Fibroblast Growth Factor-23: A Novel Biomarker for Cardiovascular Disease in Chronic Kidney Disease Patients. Pril (Makedon Akad Nauk Umet Odd Med Nauki). 38: 19-27.
20. Shimada T, Hasegawa H, Yamazaki Y, Muto T, Hino R, et al. (2004) FGF-23 is a potent regulator of vitamin D metabolism and phosphate homeostasis. J Bone Miner Res. 19: 429-35.
21. Erben RG (2017) Pleiotropic Actions of FGF23. Toxicol Pathol. 45: 904-910.
22. Moorthi RN, Moe SM (2011) CKD-mineral and bone disorder: core curriculum 2011. Am J Kidney Dis. 58:1022-1036.
23. Lu X, Hu MC (2017) Klotho/FGF23 Axis in Chronic Kidney Disease and Cardiovascular Disease. Kidney Dis (Basel). 3: 15-23.
24. Prie D, Friedlander G (2010) Reciprocal control of 1,25-dihydroxyvitamin D and FGF23 formation involving the FGF23/Klotho system. Clin J Am Soc Nephrol. 5: 1717-1722.
25. Wolf M (2009) Fibroblast growth factor 23 and the future of phosphorus management. Curr Opin Nephrol Hypertens. 18: 463-468.
26. Hu MC, Shi M, Zhang J, Quinones H, Griffith C, et al. (2011) Klotho deficiency causes vascular calcification in chronic kidney disease. J Am Soc Nephrol. 22: 124-36.
27. Cupisti A, Kalantar-Zadeh K (2013) Management of natural and added dietary phosphorus burden in kidney disease. Semin Nephrol. 33: 180-90.
28. Hill Gallant KM, Spiegel DM (2017) Calcium Balance in Chronic Kidney Disease. Curr Osteoporos Rep. 15: 214-21.
29. Martin KJ, Gonzalez EA (2011) Prevention and control of phosphate retention/hyperphosphatemia in CKD-MBD: what is normal, when to start, and how to treat? Clin J Am Soc Nephrol. 6: 440-446.
30. Gutierrez OM (2010) Fibroblast growth factor 23 and disordered vitamin D metabolism in chronic kidney disease: updating the "trade-off" hypothesis. Clin J Am Soc Nephrol. 5: 1710-176.
31. Santamaria R, Diaz-Tocados JM, Pendon-Ruiz de Mier MV, Robles A, Salmeron-Rodriguez MD, et al. (2018) Increased Phosphaturia Accelerates The Decline in Renal Function: A Search for Mechanisms. Sci Rep. 8: 13701.
32. Eddington H, Hoefield R, Sinha S, Chrysochou C, Lane B, Foley RN, et al. (2010) Serum phosphate and mortality in patients with chronic kidney disease. Clin J Am Soc Nephrol. 5: 2251-2257.
33. Molony DA, Stephens BW (2011) Derangements in phosphate metabolism in chronic kidney diseases/endstage renal disease: therapeutic considerations. Adv Chronic Kidney Dis. 18: 120-131.
34. Adema AY, de Borst MH, Ter Wee PM, Vervloet MG, Consortium N (2014) Dietary and pharmacological modification of fibroblast growth factor-23 in chronic kidney disease. J Ren Nutr. 24: 143-50.
35. Fukagawa M, Komaba H, Miyamoto K (2011) Source matters: from phosphorus load to bioavailability. Clin J Am Soc Nephrol. 6: 239-240.
36. Moorthi RN, Armstrong CL, Janda K, Ponsler-Sipes K, Asplin JR, et al. (2014) The effect of a diet containing 70% protein from plants on mineral metabolism and musculoskeletal health in chronic kidney disease. Am J Nephrol. 40: 582-591.
37. Moe SM, Zidehsarai MP, Chambers MA, Jackman LA, Radcliffe JS, et al. (2011) Vegetarian compared with meat dietary protein source and phosphorus homeostasis in chronic kidney disease. Clin J Am Soc Nephrol. 6: 257-264.
38. Noori N, Sims JJ, Kopple JD, Shah A, Colman S, et al. (2010) Organic and inorganic dietary phosphorus and its management in chronic kidney disease. Iran J Kidney Dis. 4: 89-100.
39. Gonzalez-Parra E, Gracia-Iguacel C, Egido J, Ortiz A (2012) Phosphorus and nutrition in chronic kidney disease. Int J Nephrol. 2012: 597605.
40. Kalantar-Zadeh K, Gutekunst L, Mehrotra R, Kovesdy CP, Bross R, et al. (2010) Understanding sources of dietary phosphorus in the treatment of patients with chronic kidney disease. Clin J Am Soc Nephrol. 5: 519-30.
41. D'Alessandro C, Piccoli GB, Cupisti A (2015) The "phosphorus pyramid": a visual tool for dietary phosphate management in dialysis and CKD patients. BMC Nephrol. 16: 9.
42. Fouque D, Laville M, Boissel JP. Low protein diets for chronic kidney disease in non diabetic adults. Cochrane Database Syst Rev. 2006: CD001892.
43. Di Iorio B, Di Micco L, Torraca S, Sirico ML, Russo L, Pota A, et al. Acute effects of very-low-protein diet on FGF23 levels: a randomized study. Clin J Am Soc Nephrol. 7: 581-587.

44. Kuro OM. Phosphate and Klotho. Kidney Int Suppl. 2011: S20-3.
45. Anderson CAM, Nguyen HA (2018) Nutrition education in the care of patients with chronic kidney disease and end-stage renal disease. Semin Dial. 31: 115-21.
46. Choi AI, Weekley CC, Chen SC, Li S, Kurella Tamura M, et al. (2011) Association of educational attainment with chronic disease and mortality: the Kidney Early Evaluation Program (KEEP). Am J Kidney Dis. 58: 228-34.
47. Locatelli F, Fouque D, Heimburger O, Drueke TB, Cannata-Andia JB, et al. (2002) Nutritional status in dialysis patients: a European consensus. Nephrol Dial Transplant. 17: 563-72.
48. Stevens LA, Levey AS (2009) Measured GFR as a confirmatory test for estimated GFR. J Am Soc Nephrol. 20: 2305-13.