

Source Matters: From Phosphorus Load to Bioavailability

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Phosphorus plays crucial roles in the development of mineral and bone disorders including secondary hyperparathyroidism and vascular calcification, which eventually result in high risk for cardiovascular events and effect on survival in patients with chronic kidney disease (CKD) (1). Such an effect of phosphorus load on survival has also been demonstrated in general populations. Contribution of phosphorus load to abnormal mineral metabolism already starts from the early stages of CKD, still without significant increase of its serum level (2,3). Such effects of phosphorus load in early stages of CKD are presumably mediated by the increase of fibroblast growth factor 23 (FGF23) secretion from the bone (3,4). Although diurnal variation in serum phosphorus including postprandial changes may also contribute to the development of mineral and bone disorders and their related outcomes, these data support the importance of controlling dietary phosphorus load as well as of its serum concentration.

Except for several trials to inhibit active phosphate transport from the intestine through Na/Pi IIb (5), control of phosphorus load has been traditionally attempted by restriction of dietary phosphorus intake, mostly by that of protein, and by the use of phosphate binders (6). In addition to such strategies, recent reports suggested that the source of phosphorus, not just its content, should be considered in food (7).

Phosphorus in food is provided in the form of either inorganic phosphate or organic phosphate. Inorganic phosphate is readily absorbable. Thus, its overload by food additives and preservatives has recently emerged as another serious issue for patients with CKD (8,9). Absorption of organic phosphate derived from protein is lower. Moreover, absorption of phosphorus derived from plants may be different from that derived from meat. Phosphorus in meat is present within the cells as organic phosphates, which is easily hydrolyzed and absorbed. By contrast, phosphorus in plants, such as seeds, nuts, and legumes, is mostly in the form of phytate (10). Because mammals lack the degrading enzyme phytase, bioavailability of phosphorus from plant-derived foods is relatively low, despite their high phosphorus content.

Such difference in the bioavailability of phosphorus should be of great importance especially in patients with CKD. As a pilot study of an animal

model, Moe *et al.* (11) showed lower bioavailability of phosphorus in rats that had CKD and were fed grain-based chow compared with those that were fed casein-based chow with comparable contents of protein and phosphorus. In this issue of *CJASN*, they further demonstrated the decreased bioavailability of phosphorus from a vegetarian source than from a meat source in patients with stage 3/4 CKD and normal levels of serum phosphorus (12). In this crossover trial, which compared the effects of 1 week of vegetarian and meat diets with equivalent phosphorus content on mineral metabolism, Moe *et al.* found lower serum phosphorus levels, a trend toward decreased urine 24-h phosphorus excretion, and significantly decreased FGF23 levels in the vegetarian diet group compared with the meat diet group. Although more precise effects of phytate on absorption of other nutrients including calcium need to be clarified in the future, these observations will certainly have an effect on the new strategies for diet therapy in patients with CKD.

Despite its beneficial effects on the control of serum phosphorus, higher risk for malnutrition has recently been recognized in severe dietary protein restriction (13). By considering dietary phosphorus sources in more detail, it may become possible to control actual phosphorus load without the risk for malnutrition (14). Furthermore, ethnic differences in CKD progression and its manifestation may possibly be explained by the differences in food sources (7,10). For this reason, information of phosphorus bioavailability needs to be provided for food frequency questionnaires, food tables, and nutritional database, in addition to the contents of phosphorus, phosphorus–protein ratio (7), and food additives. Only after such information is routinely available for nutritional assessments will it become possible to manage actual phosphorus burden adequately while simultaneously maintaining protein intake in patients with CKD. Whether such management strategy provides survival benefit to dialysis patients as well as predialysis patients with CKD and whether measuring FGF23 levels is useful to guide phosphorus management in this situation (15) are interesting and worthy of further investigation.

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Disclosures

None.

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See related article, “Vegetarian Compared with Meat Dietary Protein Source and Phosphorus Homeostasis in Chronic Kidney Disease,” on pages 257–264.