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Let Them Eat Healthy: Can Emerging Potassium Binders Help Overcome Dietary Potassium Restrictions in Chronic Kidney Disease?



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Potassium-rich foods might provide many health benefits even to people who have declining renal function. The barrier to obtaining these health benefits has long been the concern over hyperkalemia. There are new and novel treatment options available which may enable patients with chronic kidney disease to obtain the health benefits of eating a diet that contains foods such as fruits and vegetables which are high in potassium while reducing the risk of hyperkalemia. We conclude by emphasizing the need for clinical trials with patients on hemodialysis to directly compare the current standard of care, including a potassium-restricted diet, to a potassium-liberalized diet with a potassium binder. The outcome measures would be serum potassium (<5.3 mmol/L), assessments of acidosis, blood pressure, constipation, glycemic control, overhydration, and azotemia, all of which might change in a favorable direction with vegetarian diets as well as quality of life and satisfaction.

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Introduction

FOR THE GENERAL adult population, a diet rich in fibers including fresh fruits and vegetables, whole grains, and plant-based protein is considered a healthy and nutritious diet. In fact, many of the tools used to determine dietary patterns and diet quality use these components for assessment of a healthy diet.¹ Conversely, the dietary recommendations for chronic kidney disease (CKD) patients are exceptionally restrictive and look very different from the accepted healthy diet for the general adult population.² Additionally, the restrictive nature of the CKD diet may in fact lead to worsening outcomes and survival,² which is the opposite of what is trying to be achieved by healthcare specialists for the CKD patient population. Thus, if it was possible to liberalize the diet for CKD patients without causing

subsequent harm to the patient, it is worth evaluating. Therefore, the purpose of this paper is to explore the literature which specifically documents the rationale for dietary restriction as well as provide references to studies demonstrating the health benefits associated with a plant-based, potassium enriched diet even in patients with CKD. We conclude this review by discussing the potential use of potassium binders with the renal diet in order to liberalize the diet and how this could alter the diet recommendations and nutrient profile for CKD patients. We conducted this review by searching relevant articles on PubMed using the following research terms: diet, CKD, potassium, potassium binders, health benefits, and plant-based diets. Articles were chosen to be discussed based on their scientific rigor, sample size, mesh with inclusion terms, and recency of publication.

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The Current Recommended Diet

Management of moderate to severe CKD includes dietary restrictions which have long been thought to delay progression of the disease. These restrictions, along with those recommended for concomitant conditions such as diabetes and hypertension, make the diet difficult to follow and often times is confusing for patients. This issue is further compounded for patients who develop stage 5 CKD requiring hemodialysis (HD), when more restrictions are added. The HD diet consists of restrictions in potassium (≤ 3 g/day), restrictions in phosphorus (≤ 800 mg/day), a fluid restriction (≤ 1 L + urine output/day), and a relatively high protein content (≥ 1.2 g/kg/day), among other requirements (Table 1).^{3,4} It is well established and accepted that the diet for HD patients is restrictive and challenging to follow.^{5,6} The severity of the restrictive renal diet causes it to lack many important nutritional components, including essential vitamins and minerals.^{7,8}

Potassium

Potassium is the body's major intracellular cation, maintaining an intracellular concentration of approximately 145 mmol/L and an extracellular concentration of only 3.8–5 mmol/L, maintained by the $\text{Na}^+/\text{K}^+ \text{ -ATPase}$ pump.⁹ Common foods high in potassium include leafy greens (cabbage, kale, spinach), fruit of vine-based plants (cucumbers, eggplant, pumpkin, tomatoes, zucchini), root vegetables (carrots, onions, radishes), beans and peas (chick peas, green beans, kidney beans, peas, soybeans), tree fruits (oranges, bananas, grapes, strawberries), tubers (potatoes, sweet potatoes, yams), and milk and yogurt (Table 2).⁹ What is perhaps underappreciated is that animal proteins are also high in potassium, especially those from organ meats and from cattle. It is important to note, depending on the food source, there may be differences in the relative rise in serum potassium.^{10,11} For example, potassium-rich foods that are also high in carbohydrates may impact serum potassium to a lesser degree than foods that are high in potassium and low in carbohydrates as the carbohydrate-rich foods would also stimulate insulin release which would decrease the initial rise in serum potassium.¹⁰

Potassium-rich foods are considered healthy due to their alkalinity, high micronutrient (vitamin and mineral), and fiber content.^{4,12,13} Studies have demonstrated a reduction in blood pressure when potassium consumption increases and sodium consumption decreases in the healthy adult population,¹⁴ while an insufficient intake of potassium increases the risk of cardiovascular disease and stroke.^{9,12} The Dietary Approaches to Stop Hypertension diet, which is rich in potassium, is commonly prescribed for patients with hypertension, and has been shown to lower blood pressure¹⁵ and low density lipoprotein cholesterol.¹⁶ Additionally, potassium intake has been associated with reduced risk of kidney stones and increased bone mineral density.^{9,12} However, in patients with advanced CKD, hyperkalemia

is a barrier to instituting this diet plan.^{2,17} To achieve the normal reference range for serum potassium of 3.5–5.5 mmol/L,⁹ the Dietary Reference Committee established an adequate intake for healthy adults to consume 4.7 g/day (120 mmol/day) of potassium.

Epidemiologic studies have demonstrated an association between plasma potassium and greater progression of kidney disease with a reasonably low (< 4.0 mmol/L) and high (> 5.5 mmol/L) plasma potassium level.¹⁸ Furthermore, a high potassium concentration among long-term HD patients is associated with an increased mortality risk.^{19–21} There are studies which suggest that HD patients who consume high potassium foods have a modest, if any, increase in serum potassium.¹⁹ Because of the apparent risk of hyperkalemia in HD patients they have been advised to limit their potassium intake to less than 3 g/day⁴ due to the deleterious effects of hyperkalemia, most notably, cardiac arrhythmia, including sudden death.²² However, the recommended intake is almost 40% less than the adequate intake for healthy adults putting HD patients at risk for lacking essential vitamins and minerals normally found in potassium-rich food sources.^{7,8,23} Consequently, limiting high potassium containing foods causes a subsequent lack of intake in important micronutrients and fiber, resulting in a diet that causes greater constipation²⁴ and there are data to suggest that the colon might be an important potassium sensor and a critical organ for regulating potassium homeostasis especially as renal function declines.²⁵ Certain cooking techniques (i.e., boiling) can alter the amount of potassium in foods^{26,27}; however, the effect of a dietary potassium restriction on serum potassium levels remains uncertain due to lack of randomized trials.²⁴

Phosphorus

Certain potassium containing foods, including nuts, legumes, beans, and dairy products also contain phosphorus. Phosphorus occurs in 2 forms: organic (as phosphates) and inorganic (as salts).²⁸ Generally, organic phosphorus is naturally found in food whereas inorganic phosphorus salts are added to foods for purposes of moisture retention, longer shelf-life, and enhanced flavor.^{28,29} Of the previously mentioned potassium containing foods, fruits and vegetables contain very small amounts of organic phosphorus, while nuts, beans, and yogurt are richer in organic phosphorus.³⁰ Nonetheless, the absorption of phosphorus from the plant-based foods that contain organic phosphorus (and potassium) is less than 50%¹⁹ due to the phytic acid content.³¹ Organic phosphorus in plant-based foods is mostly in the storage form of phytates or phytic acid and humans do not possess the enzyme required to degrade phytates or phytic acid, thus the bioavailability of phosphorus from plant-based sources is low.³² However, these sources are still rich in potassium which has no barrier for absorption. Although high in phosphorus, these

Table 1. Recommended Dietary and Nutrient Intake in Adults With Ongoing Dialysis

Dietary Constituent	Amount
Protein (g/kg/day)	1.2-1.4; may require >1.5 if hypercatabolic
Sodium (g/day)	<3
Potassium (g/day)	<3; target high fiber intake
Phosphorus (mg/day)	<800; minimize added inorganic phosphorus; add phosphorus binder as needed
Calcium (mg/day)	<800
Fibers, alkali, and plant-based foods (g/day)	25-30 or more
Energy (kcal/kg/day)	30-35; target higher intake of PEW is present or imminent
Fats	Mostly unsaturated lipids, including n-3 fatty acids

PEW, protein energy wasting.

Adapted from Table 2 from Kalantar-Zadeh et al.⁴

plant-based foods do not significantly contribute to serum phosphorus levels as does inorganic phosphorus from food additives and phosphorus from animal-based sources.^{30,33,34} Moreover, it is well known that dialysis patients experience a high pill burden, with a majority of their daily pill intake from phosphorus binders.³⁵ An increased intake of these organic phosphorus containing and potassium containing foods could ultimately contribute to a reduced daily pill burden due to the reduced phosphorus bioavailability and lack of significant contribution to serum phosphorus levels, plausibly leading to a lower phosphorus binder requirement with greater phosphorus control while simultaneously leading to an improved nutrient profile.

Protein With a Plant-Based Diet

Nuts, beans, and legumes are plant-based protein sources as well as sources of potassium. Consumed individually, these foods do not comprise a complete protein (defined as a protein source that contains all of the essential amino acids). However, when eaten in combination with other foods, as typically eaten during a meal, these foods will provide all the essential amino acids required by the body. Research has shown a close correlation between serum potassium levels and nutritional markers, notably protein equivalent of nitrogen appearance (nPNA).³⁵ The relationship suggests that patients with better protein consumption are likely to have a higher serum potassium level (Fig. 1).²⁰

The consumption of plant-based protein does not contribute to metabolic acidosis, as does an animal-based diet.³⁶ Metabolic acidosis is a common problem among HD patients and can cause detrimental physiologic effects, including protein degradation,^{37,38} kidney stone

disease,³⁶ deleterious bone issues,³⁹⁻⁴¹ and insulin resistance.³⁶ Although only a few studies have directly compared a plant-based (vegetarian) diet to an animal-based diet in the HD population, a plant-based diet in HD patients has been shown to be equivalent to or more beneficial to an animal-based diet.^{42,43} When comparing non-vegetarian HD patients to vegetarian HD patients, activities of daily living and subjective global assessment scores were not significantly different.⁴² When measuring advanced glycation end products through skin autofluorescence in HD patients, Nongnuch and Daventport⁴³ found vegetarian HD patients to have a lower skin autofluorescence, suggesting a vegetarian diet may reduce exposure to dietary advanced glycation end products which could potentially reduce CVD risk compared to non-vegetarians.

It can be assumed that consuming more plant-based foods would result in a higher potassium intake. In the general population, many studies have shown that vegetarians have a lower risk of cardiovascular disease, hypertension, diabetes, and some forms of cancer.⁴⁴ Interestingly, in 2011, Moe et al.⁴⁵ conducted a crossover trial with 9 CKD patients (mean estimated glomerular filtration rate of 32 mL/min/1.73 m²) and directly compared meat and vegetarian diets. The diets contained the same amount of protein and the participants followed each diet for 7 days. Although the authors did not measure serum potassium or dietary potassium intake, they found that following the vegetarian diet for a week led to a lower serum phosphorus level and decreased fibroblast growth factor 23 levels, which is thought to improve bone health.

A concern with recommending a more plant-based diet for dialysis patients could be that the diet will fall short of the required amount of protein and that a diet low in protein will (1) decrease the components for albumin synthesis and (2) could potentially result in malnutrition leading to protein-energy wasting (PEW).⁴⁶ Interestingly, vegetarian dialysis patients have lower inflammation (measured by C-reactive protein and white blood cell count) which may explain how patients following a vegetarian diet maintain their prealbumin and albumin levels, possibly indicating that visceral protein stores can be sustained in vegetarians despite a decrease in protein catabolic rate.⁴² PEW, a state of decreased body stores of protein and energy fuels, is common in patients with CKD and is one of the strongest predictors of mortality.⁴⁷ The diagnostic criteria of PEW are multi-factorial and include nutritional and non-nutritional mechanisms. There are 4 distinct categories of PEW: (1) biochemical indicators, (2) low body weight, reduced body fat or weight loss, (3) decreased muscle mass, and (4) low protein or energy intake.⁴⁸ Those eating primarily plant-based diets have been observed to consume approximately 0.7-0.9 g/kg/day of mostly plant-based protein without any negative effects⁴⁹; however, it is important to note that the evidence to

Table 2. Comparative Amounts of Approximate Potassium Content in Various Food Groups

Food Group	Potassium (mg/100 kcal)	Examples
Leafy greens	1,500	Spinach, lettuce, romaine, cabbage, kale
Fruit of vine-based plants	1,200	Tomatoes, cucumbers, zucchini, eggplant, pumpkin
Root vegetables	975	Carrots, radishes, turnips, rutabaga, onions
Beans and peas	500	Kidney beans, peas, green beans, chick peas, soybeans
Tree fruits	430	Apples, oranges, bananas, apricots, grapes, strawberries
Tubers	400	Potatoes, sweet potatoes, yams
Milk and yogurt	350	Skimmed milk, whole milk, yogurt
Meats	230	Beef, lamb, pork, poultry, fish, rabbit
Cheese	150	Edam, stilton, cottage, cheddar
Nuts	110	Walnuts, cashews, almonds, brazil nuts, hazelnuts
Eggs	90	Chicken eggs
Cereal grains	90	Wheat, rice, oats, rye

Adapted from Institute of Medicine.⁹

prescribe a lowered protein intake is still emerging. Nonetheless, using the 4 distinct criteria listed above, those eating a plant-based diet have improved biochemical indicators, do not have reductions in body weight or body fat mass, do not have reductions in muscle mass, and can maintain adequate protein consumption. Furthermore, consuming plant-based proteins have shown reductions in severity of hypertension, hyperphosphatemia, and metabolic acidosis. Plant-based proteins, when consumed in a varied diet, are not only nutritionally adequate but have pleiotropic effects which may favor their use in CKD patients.⁴⁹ Despite the seen benefits of those eating a plant-based diet, the evidence is limited and hence more research is needed.

Potential Health Benefits of a Liberalized Diet for Dialysis Patients

A reduction in cardiovascular disease is of the upmost importance in dialysis patients as it is the primary cause of death.⁵⁰ Certain micronutrients, including vitamin C and carotenoids, as well as fiber, can help protect against the development of cardiovascular disease; however, these micronutrients and fiber are also often restricted in dialysis patients due to the potential for hyperkalemia.⁵¹ In fact, when one analyses the nutrient composition of the diet most often consumed by dialysis patients it is actually atherogenic due to the high intake of saturated fat and a low intake of fiber and unsaturated fat.⁵² Liberalizing the diet by increasing consumption of fruits, vegetables, and fiber in

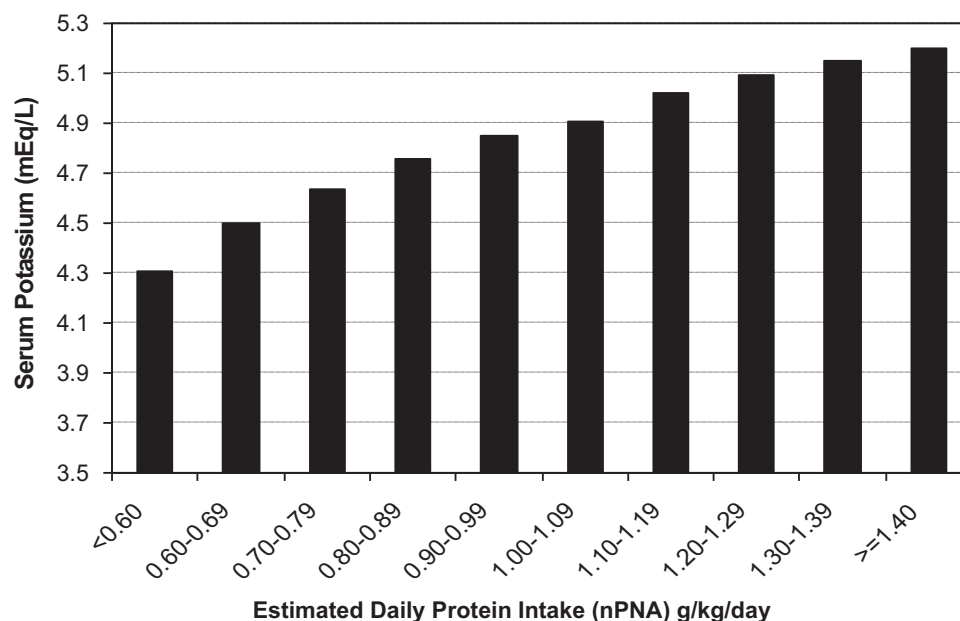


Figure 1. Relationship between estimated daily protein intake and predialysis serum potassium in HD patients. HD, hemodialysis. Adapted from Kovesdy et al.²⁰

the dialysis patient could lead to reductions in disease development most notably atherosclerosis.⁵¹

High-risk patients for cardiovascular disease are commonly treated by using angiotensin converting enzyme inhibitors and angiotensin receptor blockers; however, hyperkalemia is often a side effect.^{53,54} Hyperkalemia resulting from renin-angiotensin-aldosterone system (RAAS) blockers, including angiotensin converting enzyme inhibitors and angiotensin receptor blockers, can pose a therapeutic dilemma for physicians treating individuals with CKD because there are numerous health benefits associated with these medications such as reductions in mortality, slowed progression of kidney disease, and decreased risk of hospitalization in individuals who are receiving optimal therapeutic levels of these medications.^{53,54} Due to the risk of hyperkalemia, many of the patients who would most benefit from these drugs are suboptimally dosed. Recently, a large retrospective analysis of the general adult population found that 62% of patients received a lower than recommended dose of the RAAS inhibitor due to the risk of hyperkalemia, whereas only 22% were receiving the recommended dose, and 15% had actually had the medication discontinued due to hyperkalemia.⁵⁵

Pharmacological Management of Hyperkalemia: Can It Be Accomplished?

Over the past 50 years, management of hyperkalemia has relied upon dietary potassium restriction, the use of potassium excreting diuretics, eliminating RAAS blockers, and a potassium binder, specifically sodium polystyrene sulfonate (Kayexalate); unfortunately, Kayexalate has been associated with gastrointestinal (GI) toxicity and is not well tolerated.¹² Within the past few years, 2 new potassium binders have been approved for use in the United States: patiromer (Vifor Fresenius Medical Care Renal Pharma Ltd., St. Gallen, Switzerland) and sodium zirconium cyclosilicate (AstraZeneca Pharmaceuticals LP, Wilmington, DE).^{56,57} Both are of powder consistency and should be dissolved in water prior to consuming.

Patiromer binds potassium in the GI tract, notably the colon, in exchange for calcium, and excretes potassium through the feces⁵⁶ within 24-72 hours after administration.⁵⁸ Patiromer has been demonstrated to be efficacious in patients with CKD and/or heart failure who are receiving optimal doses of RAAS inhibitor to reduce the incidence of hyperkalemia.⁵⁹⁻⁶¹ Due to potential drug/binder interactions, it is recommended to separate the binder and drugs by 3 hours.⁶² The reported adverse effects include constipation (7.2%), hypomagnesemia (5.3%), diarrhea (4.8%), hypokalemia <3.5 mEq/L (4.7%), nausea (2.3%), abdominal discomfort (2%), and flatulence (2%). Additional conditions to consider before administering patiromer include the following: (1) it binds many orally administered medications which could decrease their GI absorption and lead to reduced efficacy, (2) avoid use

with severe constipation, bowel obstruction, or impaction, including abnormal postoperative bowel motility disorders; patiromer may be ineffective with these conditions present and may worsen GI conditions, (3) patients with a history of bowel obstruction or major GI surgery, severe GI disorders, or swallowing disorders were not included in clinical trials, and (4) it binds to magnesium in the colon which can lead to hypomagnesemia; monitor serum magnesium and consider magnesium supplementation if low serum magnesium levels are observed.

Sodium zirconium cyclosilicate binds potassium in the lumen of the GI tract in exchange for hydrogen and sodium, and increases fecal potassium excretion.⁵⁷ Sodium zirconium cyclosilicate has a rapid onset of action (within 1 hour) and like patiromer, this drug is effective in lowering plasma K⁺ concentration in a dose-dependent manner with greater reductions in those with the highest K⁺ levels. Sodium zirconium cyclosilicate has been shown to be efficacious in phase 2 and 3 studies in a wide range of patients, including a high proportion of patients with CKD receiving RAAS inhibitor therapy.⁶³⁻⁶⁶ Due to potential drug/binder interactions, it is recommended to separate sodium zirconium cyclosilicate and drugs by 2 hours. Because sodium zirconium cyclosilicate can transiently increase gastric pH, oral medications with pH-dependent solubility should be administered at least 2 hours before or 2 hours after sodium zirconium cyclosilicate. Spacing is not needed if it has been determined that the concomitant medication does not exhibit pH-dependent solubility. Common adverse effects (among ≥5% of patients) reported during the extended dosing phase were hypertension, peripheral edema, urinary tract infection, nausea, constipation, anemia, and upper respiratory tract infection.⁶⁷ Edema may be associated with retention of sodium as well. Both binders are generally well tolerated with an incidence of GI adverse events similar to placebo. Hypokalemia is uncommon and resolves with dose reductions or discontinuation of the use of the binders.

It is important to note that dietary potassium was not controlled in clinical trials for either patiromer or sodium zirconium cyclosilicate; however, patients were counseled to maintain a low potassium intake (≤3 g/day) during the patiromer clinical trial⁵⁹ and to continue their usual diet during the sodium zirconium cyclosilicate clinical trials.^{12,64} To the best of our knowledge, the DIALIZE study has been the only study to evaluate the effectiveness of a potassium binder in the HD patient population.⁶⁸ In this phase 3b randomized, double-blind, placebo-controlled trial, a significantly higher proportion of HD patients achieved a predialysis serum potassium between 4.0 and 5.0 mmol/L when taking sodium zirconium cyclosilicate compared to the placebo group (41.2% compared to 1%, respectively). Although these results are promising, these potassium binders have yet to be carefully studied through randomized trials in the dialysis patient population who

have been encouraged to liberalize their diet while taking these potassium binders. Therefore, it is plausible that the use of these binders could change and improve the nutrient profile of dialysis patients. More specifically, the use of potassium binders could allow for liberalization of foods otherwise avoided in this patient population, including fruits, vegetables, and beans. Theoretically, consuming more of these foods would expand the current nutrient profile of these patients. We believe that the use of new K^+ binding drugs as a way to maintain normokalemia during liberalization of the diet in patients at risk for hyperkalemia is an area deserving of additional exploration. In line with the authors' suggestion of additional exploration, the newly released for comments 2019 update to the Kidney Disease Outcomes Quality Initiative Clinical Practice Guidelines for Nutrition in Chronic Kidney Disease also suggests a need for further research evaluating the optimal intake of dietary potassium when taking potassium binders.⁶⁹

To evaluate the nutrient differences between the current recommend diet⁷⁰ and a more liberalized diet for HD patients, nutrient comparison was completed using Food Processor (ESHA, 11.3.2, Salem, OR). Table 3 compares two 1-day menus for HD patients, while Table 4 provides a nutrient comparison of the current diet prescription to a liberalized diet. As seen in Table 4, the liberalized diet is far superior to the current recommended diet for a number of nutrients. Notably, the liberalized diet provides a substantial more amount of fiber, omega-3 fatty acids, vitamin A, vitamin B6, vitamin C, copper, magnesium, manganese, potassium, and zinc. Furthermore, by liberalizing the diet to include more potassium-rich foods, the Dietary Reference Intake recommendation is met for 8 nutrients that, with the current recommended diet, are deficient. It is also important to note that the phosphorus content of the liberalized diet is slightly more than the current diet; however due to greater organic sources of phosphorus in the liberalized diet, less phosphorus will be absorbed.

The restrictive nature of the current prescribed diet for HD patients is not ideal and difficult to maintain. Furthermore, a disconnect exists between the restrictive prescription of the HD diet, what the patients actually consume, and what is recommended for a heart healthy diet. Dietary non-compliance of HD patients is quite prevalent^{5,71} with phosphorus restrictions being the most frequently broken.⁷¹ Interestingly, approximately 75% of patients are knowledgeable of the dietary restrictions required of them, and patients with better knowledge of the medical consequences of non-adherence were less likely to be compliant with the diet, specifically with phosphorus and sodium/fluid.⁷¹ The need for diet re-evaluation and liberalization of dialysis patients has previously, albeit briefly, been discussed and a more individualized method to dietary restrictions consisting of a more balanced diet should be implemented.² To further strengthen the argument for a

Table 3. Comparison of a One-Day Meal Plan With the Current Recommended HD Diet and a Proposed Liberalized HD Diet

Meal	Diets		
	Current Diet	Liberalized Diet	
Breakfast	2 scrambled eggs	2 scrambled eggs	
	1 cup of coffee	1 cup of coffee	
	2 slices, soft white toast	2 slices, whole wheat toast	
	2 tsp margarine	2 tbsp butter	
	2 tbsp sugar free maple syrup	1/2 cup fresh strawberries	
	1/2 cup unsweetened grape juice	1/2 cup fresh blueberries	
	Snack		15 grapes
			10 walnut halves
	Lunch	3 oz grilled salmon	3 oz grilled salmon
		1 cup pasta	1 cup pasta
1 piece cornbread		1/2 cup steamed broccoli	
1 tsp margarine		Salad with tomatoes, carrots, cucumber	
Small salad		2 tsp olive oil	
2 tsp olive oil		1 tsp balsamic vinegar	
Snack	1 tsp balsamic vinegar		
	15 grapes	Baby carrots	
Dinner	1/2 cup Sprite Zero	1/4 cup hummus	
		1 medium apple	
	4 oz steak	4 oz steak	
	1/2 cup mushrooms	1/2 cup mushrooms	
	1/4 cup onion	1/4 cup onion	
	1/2 cup boiled green beans	1/2 cup green beans	
	1/2 cup spaghetti	1/2 baked sweet potato, with skin	
	1 large dinner roll	1 chocolate chip cookie	
	1 tsp margarine		
	1 individual cup sugar-free Jell-O		
Snack	1/2 cup sugar free lemonade		
	3 cups popcorn	3 cups popcorn	
	1 tsp margarine	1 tsp margarine	

HD, hemodialysis.

more liberalized diet, more research is needed. Furthermore, the small number of studies conducted to date on a liberalized diet makes scientific rigor of prior studies limited as well. It has also been suggested that clarity of the severely restricted dietary prescriptions on improved outcome measures has not been well established, has the potential to be harmful, and may contribute to the development of atherosclerosis. Therefore, it is plausible to think that a more liberalized diet will lead to better compliance and overall improved health.

Conclusion

Incorporating more plant-based and potassium-rich foods for HD patients might provide multiple benefits.

Table 4. Nutrient Analysis Comparison for a One-Day Meal Plan With the Current Recommended HD Diet and a Proposed Liberalized HD Diet

Nutrients	Diet		DRI
	Current	Liberalized	
Macronutrients			
Calories (kcal)	2,013	1,976	
Protein (g)	70	73.4	
Carbohydrate (g)	229	215.3	130
Fiber (g)	16	34.8	21-38*
Fat (g)	91.5	97.6	ND
Saturated fat (g)	26	28.4	
Omega-3 (g)	1.2	2.6	1.1-1.6*
Omega-6 (g)	13.3	14.5	11-17*
Vitamins			
VitA (mcg RAE)	250.7	1,847	700-900
Vit B1 (mg)	1.43	1.4	1.1-1.2
Vit B2 (mg)	1.63	1.7	1.1-1.3
Vit B3-NE (mg)	20	20.1	14-16
Vit B6 (mg)	0.7	1.4	1.3-1.7
Vit B12 (mcg)	1.3	1.1	2.4
Vit C (mg)	15	135	75-90
Vit D (mcg)	2.3	2.3	15-20
Vit E-a-Toco (mg)	5.3	6.06	15
Folate (mcg DFE)	531.4	480	400
Vit K (mcg)	76.3	104	90-120*
Pantothenic acid (mg)	4.3	5.2	5*
Biotin (mcg)	32	41.06	30*
Minerals			
Calcium (mg)	453.7	450	1,000-1,200
Chromium (mcg)	6.27	5.9	20-35*
Copper (mcg)	850	1,900	900
Fluoride (mg)	0.4	0.2	3-4*
Iodine (mcg)	59.5	56	150
Iron (mg)	13.7	15.3	8-18
Magnesium (mg)	170.9	233.1	310-420
Manganese (mg)	2.4	4.7	1.8-2.3*
Phosphorus (mg)	884.1	950.3	700
Potassium (g)	1.5	2.8	4.7*
Selenium (mcg)	122.4	103.5	55
Sodium (g)	2.3	2.2	1.2-1.5*
Zinc (mg)	5.4	7.4	8-11

DFE, dietary folate equivalents; DRI, Dietary Reference Intake; HD, hemodialysis; ND, not determined; NE, niacin equivalents; RAE, retinol activity equivalents.

Dietary Reference Intake is issued by the Food and Nutrition Board of the Institute of Medicine, National Academy of Sciences, and is set for nutrient intakes of healthy people. The references above are ranges to incorporate men and women 19 years and older. They represent the recommended dietary allowances unless otherwise noted by an asterisk (*) which denotes adequate intake.

Specifically, in conjunction with a potassium binder, the dialysis patient would be able to liberalize and alter their diet composition by incorporating more nutrient dense foods, such as fruits, vegetables, nuts, beans, legumes, seeds, peanut butter, and dairy products. By increasing intake of these foods, it is plausible to hypothesize that dietary phosphorous could be controlled more easily and with a decreased amount of phosphorus binders taken daily.

Furthermore, a diet higher in fruits, vegetables, and plant protein, and lower in animal protein, would lend itself well to a more alkaline diet while still obtaining the necessary amount of protein. A diet high in fruits and vegetables would provide a greater amount of fiber and reduce the incidence of constipation in the HD patient population. Finally, as we previously mentioned, the HD diet is very difficult to follow and leads to a poor quality of life, liberalization of the diet would allow for a greater variety of foods to be consumed thereby enhancing dietary compliance and patient satisfaction. For all of these reasons, the benefit of a liberalized potassium diet, in conjunction with a potassium binder, and a decrease in animal protein warrant further research.

Practical Application

Ingestion of K⁺-rich foods is beneficial as it reduces the incidence of stroke, hypertension, nephrolithiasis, and osteoporosis. Currently, patients who would most benefit from increasing their intake of K⁺-rich foods are the very patients who are unable to do so because of reductions in kidney function. Additionally, therapy to reduce hypertension and provide cardiorenal protection is often suboptimally dosed due to the risk of hyperkalemia. There are 2 new therapeutic options to chronically treat hyperkalemia, affording for the speculation these drugs may allow for dietary liberalization of K⁺ in the diet and optimal dosing of cardiorenal protective drugs in those who would most benefit.

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References

1. Reedy J, Krebs-Smith SM, Miller PE, et al. Higher diet quality is associated with decreased risk of all-cause, cardiovascular disease, and cancer mortality among older adults. *J Nutr.* 2014;144:881-889.
2. Kalantar-Zadeh K, Tortorici AR, Chen JLT, et al. Dietary restrictions in dialysis patients: is there anything left to eat? *Semin Dial.* 2015;28:159-168.
3. Ikizler TA, Hakim RM. Nutrition in end-stage renal disease. *Kidney Int.* 1996;50:343-357.
4. Kalantar-Zadeh K, Fouque D. Nutritional management of chronic kidney disease. *N Engl J Med.* 2017;377:1765-1776.
5. Kugler C, Vlaminc H, Haverich A, Maes B. Nonadherence with diet and fluid restrictions among adults having hemodialysis. *J Nurs Scholarsh.* 2005;37:25-29.
6. Kara B, Caglar K, Kilic S. Nonadherence with diet and fluid restrictions and perceived social support in patients receiving hemodialysis. *J Nurs Schol- arsh.* 2007;39:243-248.
7. Morena M, Cristol JP, Bosc JY, et al. Convective and diffusive losses of vitamin C during haemodiafiltration session: a contributive factor to oxidative stress in haemodialysis patients. *Nephrol Dial Transplant.* 2002;17:422-427.
8. Tonelli M, Wiebe N, Hemmelgarn B, et al. Trace elements in hemodialysis patients: a systematic review and meta-analysis. *Bmc Med.* 2009;7:25.
9. Institute of Medicine (US) Standing Committee on the Scientific Evaluation of Dietary Reference Intakes. *Dietary reference intakes for water, potassium,*

- sodium, chloride, and sulfate. Washington (DC): National Academies Press (US); 2005.
10. Bazzano L, Green T, Harrison T, Reynolds K. Dietary approaches to prevent hypertension. *Curr Hypertens Rep.* 2013;15:694-702.
 11. Picard K. Potassium additives and bioavailability: are we missing something in hyperkalemia management? *J Ren Nutr.* 2019;29:350-353.
 12. Palmer BF, Clegg DJ. Achieving the benefits of a high-potassium, paleolithic diet, without the toxicity. *Mayo Clinic Proc.* 2016;91:496-508.
 13. Tennant DR, Davidson J, Day AJ. Phytonutrient intakes in relation to European fruit and vegetable consumption patterns observed in different food surveys. *Br J Nutr.* 2014;112:1214-1225.
 14. Cook NR, Obarzanek E, Cutler JA, et al. Joint effects of sodium and potassium intake on subsequent cardiovascular disease: the Trials of Hypertension Prevention follow-up study. *Arch Intern Med.* 2009;169:32-40.
 15. Appel LJ, Moore TB, Obarzanek E, et al. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. *N Engl J Med.* 1997;336:1117-1124.
 16. Obarzanek E, Sacks FM, Vollmer WM, et al. Effects on blood lipids of a blood pressure-lowering diet: the Dietary Approaches to Stop Hypertension (DASH) trial. *Am J Clin Nutr.* 2001;74:80.
 17. Dunn JD, Benton WW, Orozco-Torrentera E, Adamson RT. The burden of hyperkalemia in patients with cardiovascular and renal disease. *Am J Manag Care.* 2015;21(15 Suppl):s307.
 18. Chen Y, Sang Y, Ballew SH, et al. Race, serum potassium, and associations with ESRD and mortality. *Am J Kidney Dis.* 2017;70:244-251.
 19. Noori N, Kalantar-Zadeh K, Kovesdy CP, et al. Dietary potassium intake and mortality in long-term hemodialysis patients. *Am J Kidney Dis.* 2010;56:338-347.
 20. Kovesdy CP, Regidor DL, Mehrotra R, et al. Serum and dialysate potassium concentrations and survival in hemodialysis patients. *Clin J Am Soc Nephrol.* 2007;2:999-1007.
 21. Pun P, Lehrich R, Honeycutt E, Herzog C, Middleton J. Modifiable risk factors associated with sudden cardiac arrest within hemodialysis clinics. *Kidney Int.* 2010;79:218.
 22. Rastergar A, Soleimani M. Hypokalaemia and hyperkalaemia. *Postgrad Med J.* 2001;77:759-764.
 23. Montazerifar F, Hashemi M, Karajibani M, Dikshit M. Hemodialysis alters lipid profiles, total antioxidant capacity, and vitamins A, E, and C concentrations in humans. *J Med Food.* 2010;13:1490-1493.
 24. St-Jules DE, Goldfarb DS, Sevick MA. Nutrient non-equivalence: does restricting high-potassium plant foods help to prevent hyperkalemia in hemodialysis patients? *J Ren Nutr.* 2016;26:282-287.
 25. Epstein M, Lifschitz MD. The unappreciated role of extrarenal and gut sensors in modulating renal potassium handling: implications for diagnosis of dyskalemias and interpreting clinical trials. *Kidney Int Rep.* 2016;1:43-56.
 26. Bethke PC, Jansky SH. The effects of boiling and leaching on the content of potassium and other minerals in potatoes. *J Food Sci.* 2008;73:H80-H85.
 27. Asimwe J, Sembajwe LF, Senoga A, Bakiika E, Muwonge H, Kalyesubula R. Overnight soaking or boiling of "Matooke" to reduce potassium content for patients with chronic kidney disease: does it really work? *Afr Health Sci.* 2013;13:546-550.
 28. Institute of Medicine (US) Standing Committee on the Scientific Evaluation of Dietary Reference Intakes. *Dietary reference intakes for calcium, phosphorus, magnesium, vitamin D, and fluoride.* Washington (DC): National Academies Press (US); 1997.
 29. Sullivan C, Sayre SS, Leon JB, et al. Effect of food additives on hyperphosphatemia among patients with end-stage renal disease: a randomized controlled trial. *JAMA.* 2009;301:629-635.
 30. Kalantar-Zadeh K, Gutekunst L, Mehrotra R, et al. Understanding sources of dietary phosphorus in the treatment of patients with chronic kidney disease. *Clin J Am Soc Nephrol.* 2010;5:519-530.
 31. Sandberg AS, Andersson H, Kivistö B, Sandström B. Extrusion cooking of a high-fibre cereal product. 1. Effects on digestibility and absorption of protein, fat, starch, dietary fibre and phytate in the small intestine. *Br J Nutr.* 1986;55:245.
 32. Uribarri J, Calvo MS. Hidden sources of phosphorus in the typical American diet: does it matter in nephrology? *Semin Dial.* 2003;16:186-188.
 33. Bell RR, Draper HH, Tzeng DY, Shin HK, Schmidt GR. Physiological responses of human adults to foods containing phosphate additives. *J Nutr.* 1977;107:42-50.
 34. Lei X, Porres J. Phytase enzymology, applications, and biotechnology. *Biotechnol Lett.* 2003;25:1787-1794.
 35. Mullon C, Sussman E, Ginsberg N, et al. 200: Amount of fluid ingested with phosphate binders (PB) in hemodialysis-dependent chronic kidney disease (HDD-CKD) patients. *Am J Kidney Dis.* 2010;55:B81.
 36. Adeva MM, Souto G. Diet-induced metabolic acidosis. *Clin Nutr.* 2011;30:416-421.
 37. Kraut JA, Kurtz I. Metabolic acidosis of CKD: diagnosis, clinical characteristics, and treatment. *Am J Kidney Dis.* 2005;45:978-993.
 38. Reaich D, Channon SM, Scrimgeour CM, Daley SE, Wilkinson R, Goodship THJ. Correction of acidosis in humans with CRF decreases protein-degradation and amino-acid oxidation. *Am J Physiol.* 1993;265:E230-E235.
 39. Mora Palma FJ, Ellis HA, Cook DB, et al. Osteomalacia in patients with chronic renal failure before dialysis or transplantation. *Q J Med.* 1983;52:332.
 40. Burton RF. The roles of intracellular buffers and bone mineral in the regulation of acid-base balance in mammals. *Comp Biochem Physiol Comp Physiol.* 1992;102:425.
 41. Green J, Kleeman CR. The role of bone in the regulation of systemic acid-base balance. *Contrib Nephrol.* 1991;91:61.
 42. Wu TT, Chang CY, Hsu WM, et al. Nutritional status of vegetarians on maintenance haemodialysis. *Nephrology (Carlton).* 2011;16:582-587.
 43. Nongnuch A, Davenport A. The effect of vegetarian diet on skin autofluorescence measurements in haemodialysis patients. *Br J Nutr.* 2015;113:1040-1043.
 44. Fraser GE. Vegetarian diets: what do we know of their effects on common chronic diseases? *Am J Clin Nutr.* 2009;89:S1607-S1612.
 45. Moe SM, Zidehsari MP, Chambers MA, et al. Vegetarian compared with meat dietary protein source and phosphorus homeostasis in chronic kidney disease. *Clin J Am Soc Nephrol.* 2011;6:257-264.
 46. Fouque D, Kalantar-Zadeh K, Kopple J, et al. A proposed nomenclature and diagnostic criteria for protein-energy wasting in acute and chronic kidney disease. *Kidney Int.* 2008;73:391.
 47. Kalantar-Zadeh K, Ikizler TA, Block G, Avram MM, Kopple JD. Malnutrition-inflammation complex syndrome in dialysis patients: causes and consequences. *Am J Kidney Dis.* 2003;42:864-881.
 48. Jadeja YP, Kher V. Protein energy wasting in chronic kidney disease: an update with focus on nutritional interventions to improve outcomes. *Indian J Endocrinol Metab.* 2012;16:246.
 49. Joshi S, Shah S, Kalantar-Zadeh K. Adequacy of plant-based proteins in chronic kidney disease. *J Ren Nutr.* 2019;29:112-117.
 50. U.S. Renal Data System. *USRDS 2013 annual data report: atlas of chronic kidney disease and end-stage renal disease in the United States, National Institutes of Health.* Bethesda, MD: National Institute of Diabetes and Digestive and Kidney Diseases; 2013.
 51. Kalantar-Zadeh K, Kopple JD, Deepak S, Block D, Block G. Food intake characteristics of hemodialysis patients as obtained by food frequency questionnaire. *J Ren Nutr.* 2002;12:17-31.
 52. Khoeiry G, Waked A, Goldman M, et al. Dietary intake in hemodialysis patients does not reflect a heart healthy diet. *J Ren Nutr.* 2011;21:438-447.
 53. Palmer BF, Clegg DJ. Treatment of abnormalities of potassium homeostasis in CKD. *Adv Chronic Kidney Dis.* 2017;24:319-324.
 54. Palmer BF. Managing hyperkalemia caused by inhibitors of the renin-angiotensin-aldosterone system. *New Engl J Med.* 2004;351:585-592.
 55. Epstein M, Reaven NL, Funk SE, McGaughey KJ, Oestreicher N, Knispel J. Evaluation of the treatment gap between clinical guidelines and

the utilization of renin-angiotensin-aldosterone system inhibitors. *Am J Manag Care*. 2015;21(11 Suppl):S212.

56. *Veltassa*® [package insert]. Redwood City, CA: Relypsa Inc.; 2015.

57. *Lokelma*™ [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2018.

58. Jung HK, Kim DY, Moon IH, Hong YS. Colonic transit time in diabetic patients—comparison with healthy subjects and the effect of autonomic neuropathy. *Yonsei Med J*. 2003;44:265–272.

59. Weir MR, Bakris GL, Bushinsky DA, et al. Patiromer in patients with kidney disease and hyperkalemia receiving RAAS inhibitors. *New Engl J Med*. 2015;372:211–221.

60. Bakris GL, Pitt B, Weir MR, et al. Effect of patiromer on serum potassium level in patients with hyperkalemia and diabetic kidney disease: the AMETHYST-DN randomized clinical trial. *JAMA*. 2015;314:151–161.

61. Pitt B, Anker SD, Bushinsky DA, Kitzman DW, Zannad F, Huang IZ. Evaluation of the efficacy and safety of RLY5016, a polymeric potassium binder, in a double-blind, placebo-controlled study in patients with chronic heart failure (the PEARL-HF trial). *Eur Heart J*. 2011;32:820–828.

62. Lesko LJ, Offman E, Brew CT, et al. Evaluation of the potential for drug interactions with patiromer in healthy volunteers. *J Cardiovasc Pharmacol Ther*. 2017;22:434–446.

63. Ash SR, Singh B, Lavin PT, Stavros F, Rasmussen HS. A phase 2 study on the treatment of hyperkalemia in patients with chronic kidney disease suggests that the selective potassium trap, ZS-9, is safe and efficient. *Kidney Int*. 2015;88:404–411.

64. Packham DK, Rasmussen HS, Lavin PT, et al. Sodium zirconium cyclosilicate in hyperkalemia. *N Engl J Med*. 2015;372:222–231.

65. Kosiborod M, Rasmussen HS, Lavin P, et al. Effect of sodium zirconium cyclosilicate on potassium lowering for 28 days among outpatients with hyperkalemia: the HARMONIZE randomized clinical trial. *JAMA*. 2014;312:2223–2233.

66. Spinowitz BS, Fishbane S, Pergola PE, et al. Sodium zirconium cyclosilicate among individuals with hyperkalemia: a 12-month phase 3 study. *Clin J Am Soc Nephrol*. 2019;14:798.

67. Hoy S. Sodium zirconium cyclosilicate: a review in hyperkalaemia. *Drugs*. 2018;78:1605–1613.

68. Fishbane S, Ford M, Fukagawa M, et al. A phase 3b, randomized, double-blind, placebo-controlled study of sodium zirconium cyclosilicate for reducing the incidence of predialysis hyperkalemia. *J Am Soc Nephrol*. 2019;30:1723–1733.

69. National Kidney Foundation. *Clinical practice guideline for nutrition in chronic kidney disease: 2019 update*. Public Review Draft 2019. <https://www.kidney.org/professionals/kdoqi-guidelines-commentary-nutrition>. Accessed November 10, 2019.

70. Dietary guidelines for adults starting on hemodialysis. National Kidney Foundation. https://www.kidney.org/atoz/content/dietary_hemodialysis. Accessed May 22, 2019.

71. Durose CL, Holdsworth M, Watson V, Przygodzka F. Knowledge of dietary restrictions and the medical consequences of noncompliance by patients on hemodialysis are not predictive of dietary compliance. *J Am Diet Assoc*. 2004;104:35–41.