Adequacy of Plant-Based Proteins in Chronic Kidney Disease

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Concerns regarding protein and amino acid deficiencies with plant-based proteins have precluded their use in chronic kidney disease (CKD) patients. Many of these concerns were debunked years ago, but recommendations persist regarding the use of "high-biological value" (animal-based) proteins in CKD patients, which may contribute to worsening of other parameters such as blood pressure, metabolic acidosis, and hyperphosphatemia. Plant-based proteins are sufficient in meeting both quantity and quality requirements. Those eating primarily plant-based diets have been observed to consume approximately 1.0 g/kg/day of protein, or more. CKD patients have been seen to consume 0.7-0.9 g/kg/day of mostly plant-based protein without any negative effects. Furthermore, those substituting animal-based proteins for 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.

Introduction

IN SOME CIRCLES within the nephrology and nutrition communities, plant-based proteins have been viewed as nutritionally inadequate and even hazardous for the management of patients with chronic kidney disease (CKD). Select literature in other fields of medicine, such as cardiology and endocrinology, suggest that plant-based proteins are not only nutritionally adequate but also possess pleiotropic benefits that can be beneficial for management of several acute and chronic disease states, such as diabetes and heart disease. Some experts and opinion leaders in nephrology and renal nutrition have maintained that plant-based proteins may cause harm to nondialysis CKD patients. In this article, we argue the opposite and present data and opinions suggesting that plant-based proteins are both nutritionally adequate and beneficial to patients with CKD.

Protein Quantity in the General Population

A common myth is that those who do not eat enough animal-based foods will become protein deficient; the evidence, however, would suggest otherwise. In the largest study of those eating plant-based diets, the Adventist Health Study-2 involving 96,335 participants, those who were eating the highest amount of plant-based foods (strict vegetarians) exceeded their minimum requirement for protein, consuming an average of 72.3 g of protein per day.[1]

A somewhat smaller–but still relatively large–study, the British EPIC-Oxford study of 65,429 participants found those eating entirely plant-based diets averaged 12.9% of their energy from protein, exceeding the minimum recommendation of 9% for British and 10% for American guidelines for protein derived from energy.[2-4] A subset analysis of the Epic-Oxford study participants further confirmed adequate protein intake. Not only did participants ingest more than the recommended dietary allowance (RDA) for all the essential amino acids, they also had serum amino acid levels that exceeded the lower limit of reference ranges.[4-6]

According to the Institute of Medicine, the estimated average requirement and RDA for protein are 0.66 and 0.8 g/kg of body weight per day, corresponding to the needs for the 50th and 95th percentiles of the population, respectively.[4] A 1999 cross-sectional study of Californians found those eating exclusively plant-based diets averaged a protein intake of 1.04 g/kg of body weight per day.[7] Another study of Bostonian women showed an averaged protein intake of 1.0 g/kg of body weight per day.[8] These studies show that modern plant-based diets provide adequate amounts of protein.

Protein Quality in the General Population

Another reason plant-based proteins are believed to be nutritionally inadequate stems from the common (but inaccurate) belief that plants lack essential amino acids. In addition, animal-based proteins are believed to be nutritionally

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superior as they contain more essential amino acids per serving and better gastrointestinal bioavailability. In reality, all foods contain essential amino acids including plants (with the exception of gelatin which lacks tryptophan), although the composition and proportion may be different from animal products.[9,10] The clinical significance of this is that although there are differences in the amino acid content, digestibility, and availability between plant and animal protein foods, these differences may not be clinically significant for adults eating varied diets in sufficient quantity.[10,11] A meta-analysis of nitrogen balance studies found no significant difference in protein needs due to the source of protein being consumed.[12]

Nevertheless, animal-based proteins are still believed to be nutritionally superior for the aforementioned reasons, which is true despite being less meaningful clinically. Regardless, these ideas led to the rise of the protein-complementing myth that plant proteins need to be specifically paired according to their amino acid levels to ensure adequate intake of amino acids with each meal.[13] However, this has also been shown to be not quite necessary. The body is capable of maintaining storage pools of amino acids over hours to days rendering the practice of protein-pairing superfluous.[10,14-17]

It is important to note that amino acid deficiency is possible in those who are eating a restrictive diet limited to one or two food sources, creating a situation such that attaining the RDA for an amino acid may exceed the number of servings than is humanly possible. A stark example of this can be illustrated by the low tryptophan content of an apple. A medium-sized (100 g) apple contains 1 mg of tryptophan.[18] Based on the RDA for tryptophan (5 mg/kg/day), a 70-kg person would need on average 350 mg of tryptophan per day.[4] To meet this, a person eating a diet exclusively of apples would need to eat 350 apples daily to meet the RDA for tryptophan, which is not possible in a real-world scenario. Hypothetically, anyone subsisting exclusively on apples would ultimately develop a deficiency in tryptophan, if he or she averaged less than 350 apples per day, which is illustrative of the dangers of extremely restrictive diets without food variety. Those eating multiple types of plants, however, will reliably avoid the issue of amino acid deficiency.[19] Of note, it is also possible to be deficient in the case of starvation. Those not meeting minimum dietary energy (caloric) requirements will incur deficiencies of amino acids, along with other nutrients.

Real-world evidence from the EPIC-Oxford cohorts and the Seventh Day Adventists of California support the idea that well-balanced and diverse plant-based diets are nutritionally adequate for all stages of the life cycle from birth to death in everyday life situations[20,21] More importantly as it relates to the question of diet in CKD, these diets may indeed be preferred for those with CKD for the reasons mentioned in the following.[22]

Plant-Based Proteins in CKD and End-Stage Renal Disease Populations

Some nephrologists prescribing low-protein diets to manage CKD tend to recommend using animal-based proteins for at least half of the daily protein intake based on the idea that animal-based proteins are of "high-biologic[al] value."[23,24] The so-called "biological value" of a protein is an antiquated method of measuring protein quality that is a ratio of retained and absorbed nitrogen content; there are other metrics and techniques that may be more appropriate, including the protein digestibility-corrected amino-acid score (PDCAAS).[10,11]

The PDCAAS is currently the preferred method for measuring protein quality by the Food and Agricultural Organization of the United Nations and World Health Organization.[25] The PDCAAS measures the protein quality of a specific food group based on comparing the amino acid profile of that food against a standard amino acid profile. The scoring is based on the nutritional requirements of a child aged 2-5 years (the most nutritionally demanding age).

Animal-based proteins do have higher PDCAAS score than plant proteins, but the lower plant-protein scores do not preclude their use (See Table 1). Even when using the PDCAAS to assess plant protein quality, plant proteins have been found to be of adequate quality for consumption, especially when consumed from diverse sources.[10] Concerns regarding malnutrition or protein-energy wasting using plant-based proteins in CKD are unfounded: Total and near-total plant-based diets have been used in CKD without adverse effect, as described below.

A 1996 Italian study placed 37 patients with stage III/IV CKD on a low-protein (0.7 g/kg/day), "special vegan diet" comprised of a prespecified combination of cereals and legumes based on the now-discarded idea of protein complementation.[27] A subset (22) of the patients was followed for a mean of 13 months and did not show any signs of nutritional deficiency, while on an exclusively plant-based

Table 1. Protein Digestibility-Corrected Amino Acid Scores (PDCAAS) for Selected Foods[25,26]

Food	PDCAAS
Egg	1.00
Cow's milk	1.00
Beef	0.92
Soy protein, concentrate	0.99
Chickpeas (canned)	0.71
Pea flour	0.69
Kidney beans (canned)	0.68
Pinto beans (canned)	0.63
Rolled oats	0.57
Black beans (canned)	0.53
Lentils (canned)	0.52
Peanuts	0.52
Wheat	0.42

diet. Another study of 15 Israeli, stage III/IV CKD patients on a near-total plant-based diet consuming 0.75 g/kg/day of protein for 6 months also did not show any nutritional deficits.[28] Further, those consuming a plant-based diet actually had better dietary compliance and caloric intakes than their animal-protein diet counterparts, which may be related to the decreased development of uremic toxins (thought to act as appetite suppressants) with plant-based proteins.[29]

Patients on plant-based diets do not need supplementation with keto or amino acids if they are achieving at least 0.6 g/kg/day of protein.[30] For those with CKD, those consuming 0.6-0.8 g/kg/day of protein have been considered to be on a "low protein diet", while those consuming 0.3-0.4 g/kg/day of protein have been designated as being on a "very low protein diet" (VLPD).[24] Those on VLPD diets do need to be supplemented, however, to remain in nitrogen balance.[31] Of note, when patients need to be placed on a VLPD diet, a strict vegan diet is often the only choice.

However, in CKD patients, unrestricted vegan diets can readily attain 0.7 to 0.9 g/kg/day of protein, which does not require supplementation in CKD or non-CKD populations.[32] Non-CKD cohorts have reported vegan protein intakes as high as 1.04 g/kg/day on exclusively plant-based proteins, and even higher amounts can be attained as needed with minor dietary alterations, for example, by increasing legume consumption.[7] Patients on dialysis eating vegetarian diets have been able to attain even higher amounts of protein intake, estimated at 1.1 to 1.25 g/kg/day of protein without signs of compromise.[33,34]

Of note, plant-based diets are almost universally lower in protein content than the standard American diet, which contains an average of 1.2 to 1.5 g/kg/day of protein and meets the definition of a high-protein diet (>1.2 g/kg/day).[23,35,36] High-protein diets may lead to maladaptive changes in the kidney like glomerular hyperfiltration, increased proteinuria, and accelerated progression of CKD, which has led some nephrologists to recommend against high-protein diets in CKD.[23,24] Serendipitously, the quantity of protein deemed to be a "low-protein diet" within the CKD community, that is, 0.6-0.8 g/kg/day, is the same, or similar, in those studied eating plant-based diets. By comparison to omnivorous diets, plant-based diets are less likely to lead to protein overload and are closer to estimated average requirement in RDA for non-CKD populations and closer–if not identical–to the goals set for "low-protein" diets in CKD populations.[24]

Plant-based proteins may not only attenuate the maladaptive changes seen in CKD by delivering lower protein loads to the glomerulus but also have other theoretical and demonstrable benefits that are relevant to CKD patients (see Table 2 and below).

Pleiotropic Benefits of Plant-Based Proteins in CKD

The other benefits of plant-based diets in CKD are reviewed elsewhere in detail but are discussed here briefly, including those related to improved control of serum phosphate levels, metabolic acidosis, and hypertension.[37]

Directing patients with CKD to eat more animal-based proteins may worsen serum phosphorus levels, which may promote CKD progression and worsen secondary hyperparathyroidism with deleterious effects on bone health and vascular calcification.[38,39] Although plant-based food items have more phosphorus, they are stored in a nonabsorbable form as phytate. The phosphorus in plant foods is thought to be only one-third bioavailable because human gut lacks the enzyme phytase, whereas animal-based foods are approximately two-thirds bioavailable.[39-41] In both animal and human studies of CKD, serum phosphorus and FGF-23 levels worsened on diets when protein was

Table 2. Overview of the Advantages and Disadvantages of Plant-Based Diets for Management of CKD Patients

Criteria	Advantage	Disadvantage
Protein quantity	Meets EAR and RDA Avoids protein overload Can be adjusted up or down to meet desired needs	Dietary planning may be necessary in patients with unusually high protein requirements
Protein quality	More than adequate in a balanced diet	Cannot depend on 1 or 2 staple foods
Blood pressure	Improved	None
Phosphate	Improved	None
Metabolic acidosis	Improved	None
Uremic toxins	Likely improved	None
Potassium	Plant foods increase bowel movements and potassium excretion	Plant foods contain potassium
Microbiome	Improved gut barrier, reduced inflammation, and CKD progression	None
Diabetes	Improved	None
Heart disease	Improved	None

CKD, chronic kidney disease; EAR, estimated average requirement; RDA, recommended dietary allowance.

derived from animal-based sources and improved with plant-based sources.[42–45]

Animal-based proteins increase the dietary acid load, worsening acidemia in patients with CKD.[46] Plant-based foods are generally acid-neutral or base-producing, while animal-based foods are acid-producing–so much so that they are the primary contributor to net acid loads in human diets.[47] Conversely, those adhering to a purely plant-based diet can attain an acid-neutral state.[48] As demonstrated in a pair of landmark trials, even a partial increase in the amount of consumed plant-based foods can reduce dietary acid loads, improve acidemia, and reduce the amount of alkali supplementation needed in patients with varying stages of CKD, which may slow the progression of CKD.[49,50]

Another important modifiable risk factor for CKD is hypertension, which is also improved with plant-based diets. Those most adherent to plant-based diets (vegans) have had some of the lowest blood pressures documented in industrialized societies.[51,52] Studies have also shown a dose-dependent effect, with reduced risks of hypertension (or lower blood pressure measurements) with increasing plant consumption.[51,53-55] Several trials have also had similar findings.[56,57] A recent study showed that the consumption of certain amino acids, such as methionine and alanine, which are naturally found in higher concentrations in animal-based products are associated with a higher odds of hypertension, whereas such amino acids as threonine and histidine, which are commonly found in plants, are associated with lower odds.[58]

Utilization of plant-based proteins in CKD may also generate fewer uremic toxins, reduce proteinuria, and even temper GFR decline through a variety of mechanisms other than those related to lower dietary protein intake including alterations in the microbiome.[29,59-64] Plant-based diets in CKD have been shown to favorably shift gut bacteria from a proteolytic profile to a sacchrolytic profile, thereby promoting the production of short-chain fatty acids, which strengthen intestinal barrier integrity, reduce bacterial translocation and inflammation, and improve overall immunity.[65,66] This shift also reduces the production of key uremic toxins, p-cresol, and indoxyl sulfate that have been shown to promote CKD progression. In contrast, a Western-style diet, rich in animal-based proteins, favors proteolytic bacteria, resulting in dysbiosis, increased inflammation, and disease progression.

Importantly, plant-based diets have also been shown to be helpful in treating and even reversing diabetes by reducing the amount of refined carbohydrates consumed and enabling long-term weight loss.[67,68] Similarly, these diets have also been shown to treat and reverse heart disease by favorably altering lipids, reducing inflammation, and decreasing atherosclerosis.[69,70]

Finally, plant-based diets, despite their relatively higher potassium contents, have not been shown to induce hyperkalemia in patients with advanced CKD, probably due to their high fiber content that facilitates gastrointestinal transition time allowing less potassium to be absorbed, as opposed to animal-based proteins that often worsen constipation and subsequent risk of hyperkalemia.[27,28,50]

Conclusion

Vegetarian diets, by taking out meat, as well as vegan diets, by taking out all food from animal source, including milk and eggs, are compatible with normal growth, health, pregnancy, and physical activity, including competitive sports.[22] These types of diets are also a feasible goal in dietary management of CKD. Plant-based proteins are not only adequate but are safe for patients with CKD including those with proteinuria. Many of the prevailing fears regarding their use have been debunked years, if not decades, ago, given the studies discussed previously. Patients eating plant-based diets can reliably avoid protein or amino acid deficiencies by eating a varied diet. Instead, they might be pleased to find improved control of their phosphorus levels, blood pressure, and degree of metabolic acidosis.

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