ChiKD CHILDHOOD KIDNEY DISEASES

Review Article

Child Kidney Dis 2024;28(3):112-115
pISSN 2384-0242 · eISSN 2384-0250
https://doi.org/10.3339/ckd.24.017

Diet as a treatment for chronic kidney disease

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The management of chronic kidney disease (CKD) includes nutritional interventions aimed at slowing disease progression and mitigating complications. This review examines various dietary approaches for CKD treatment, focusing on carbohydrate intake modulation, ketogenic diets, and plant-based diets. Standard guidelines recommend carbohydrate intake within 45% to 65% of total calories, but there is growing interest in reducing carbohydrate consumption to preserve kidney function. Low-carbohydrate diets (<25% of total calories) have shown benefits in glycemic control and weight reduction but may pose long-term adherence challenges. High-protein, low-carbohydrate diets are discouraged due to associations with hyperfiltration and CKD progression. Limiting fructose intake has been linked to reductions in blood pressure and uric acid levels. Intermittent fasting and ketogenic diets, which promote ketone body production and reduce inflammation, have shown promise in animal models and some human studies, particularly in autosomal dominant polycystic kidney disease, though more research is needed. Plant-based diets, such as the Mediterranean and DASH (Dietary Approaches to Stop Hypertension) diets, offer cardiovascular benefits and may reduce CKD risk but require careful management of potassium intake. Overall, dietary interventions should be individualized, considering potential risks like hyperkalemia and ensuring nutritional adequacy.

Keywords: Carbohydrate-restricted diets; Children; Chronic renal insufficiency; Ketogenic diets; Plant-based diets

Introduction

The Kidney Disease Outcomes Quality Initiative (KDOQI) clinical practice guidelines for nutrition in children with chronic kidney disease (CKD) emphasize regular evaluation of growth and nutritional status, maintaining optimal nutrition, and avoiding uremic toxins [1]. The guidelines aim to sustain ideal nutritional health, prevent the accumulation of uremic toxins, correct metabolic imbalances, prevent undernutrition, and decrease the future risk of chronic illnesses and mortality. In this review, we discuss diet as a treatment for CKD. Most of the content is based on adult studies, which might apply to children in the future.

Carbohydrates

The KDOQI guidelines recommend that children with CKD consume carbohydrates within the acceptable macronutrient distribution ranges (AMDR) of the dietary reference intake (DRI), which is 45% to 65% [1]. A daily intake of carbohydrates exceeding 45% is considered a high-carbohydrate diet [2]. Consuming a diet high in carbohydrates (particularly monosaccharides like fructose) and low in fats tends to elevate plasma triglyceride levels and lower high-density lipoprotein cholesterol levels [1]. There is growing interest in recommending lower carbohydrate intake than standard guidelines to preserve kidney function in CKD patients [2].

Received: September 25, 2024; Revised: October 17, 2024; Accepted: October 22, 2024

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Low-carbohydrate diet

A daily intake of carbohydrates of less than 25% is considered a low-carbohydrate diet [2]. Such diets have been associated with better glycemic control, reduced body weight, and fewer cardiovascular events within 12 months in patients with or without type 2 diabetes mellitus. However, the long-term effects beyond 1 year are unclear, possibly due to adherence issues [3]. Methods to decrease carbohydrate intake include high-protein diet, ketogenic diet (KD), or plant-based diets [3].

Low-carbohydrate high-protein diet

The KDOQI guidelines recommend protein restriction in adult patients with CKD stages 3–5 and maintaining dietary protein intake at 100% to 140% of the DRI for ideal body weight in children with CKD children stage 3, and 100% to 120% of the DRI in stages 4 to 5 for adequate growth [1]. A low-carbohydrate, high-protein diet was associated with an increased glomerular filtration rate [4]. High-protein diets are reported to be associated with glomerular hyperfiltration and CKD progression [5]. The Tehran Lipid and Glucose Study showed that such diets were associated with the development of CKD in adults [5]. Therefore, we do not recommend a low-carbohydrate, high-protein diet, which might be harmful.

Low-fructose diet

Over the past century, fructose consumption from added sugars has surged dramatically and has been linked to hypertension, inflammation, and kidney disease [6]. Brymora et al. [6] reported that, while maintaining the total carbohydrate ratio for energy intake, restricting consumption of sucrose-sweetened and artificially sweetened drinks and food for 6 weeks lowered blood pressure and serum uric acid levels in patients with CKD stages 2 and 3. A low-fructose diet also lowered serum inflammatory markers [6]. Long-term fructose restriction might be beneficial for preventing CKD progression, as hypertension and hyperuricemia are known risk factors, although these effects were not evident in this short-term study [6]. Monosaccharide restriction instead of total carbohydrate restriction may help improve CKD prognosis, but further studies are needed for clarification.

Intermittent fasting

Intermittent fasting (IF) refers to regularly scheduled cycles of eating followed by fasting periods [2]. The benefits of IF arise from reduced calorie intake and the body's use of fatty acids to produce ketone bodies [2]. IF is effective in reducing body weight and insulin resistance [2]. There is a risk of electrolyte imbalance or decreased kidney function due to dehydration in CKD patients, so careful monitoring is needed [2]. IF can be considered a form of KD, which will be discussed further.

Ketogenic diet

Lowering carbohydrate intake might be beneficial, but replacing carbohydrates with high-protein seems harmful [5]. High-fat intake may be considered to maintain a low-carbohydrate and low-to-moderate protein diet. The extreme form of low-carbohydrate, high-fat diet is the KD [2]. The KDOQI guidelines recommend balanced calories from unsaturated fats within the physiological ranges of the AMDR of the DRI (25%–35% in children aged 4–18 years) [1]. KD typically sources at least 70% of its calories from fats while limiting carbohydrates to no more than 15% of total caloric intake [2]. In KD, fat is metabolized as the body's primary energy source instead of glucose, and gluconeogenesis is minimized due to reduced blood glucose concentration [7].

The KD is known to be effective in the treatment of several diseases, such as epilepsy, cancer, and Alzheimer disease [2]. It is also helpful in treating obesity and type 2 diabetes mellitus [2]. KD might be effective in inhibiting CKD progression. Consuming less protein results in reduced proteinuria, fewer uremic toxins, and less hyperphosphatemia in CKD patients [8]. KD is associated with inhibition of reactive oxygen species, nuclear factor kappa B, and p62 signaling, which might be related to inhibiting inflammation in the kidney [8]. Keto acid supplementation might help improve oxidative damage and mitochondrial dysfunction by inhibiting the proteins p66Shc and FoxO3a [8].

The effect of KD on autosomal dominant polycystic kidney disease (ADPKD) has been actively researched recently. Altered glucose metabolism is reported to be involved in kidney cyst formation [9]. Glucose consumption was increased, and glycolysis was enhanced in the polycystic kidney disease mouse model. The severity of cystic disease was reduced after administration of a nonmetabolized glucose analog, which inhibits glycolysis [9]. KD intervention (food restriction) significantly re-

duced cyst growth in polycystic kidney disease animal models [10,11]. However, human study results are not definitive yet. In the REST-PD study, a pilot trial on short-term ketogenic interventions in patients, total liver volume decreased significantly, but total kidney volume did not change after KD (IF group) [12]. Authors expected kidney volume to decrease after longer-term interventions [12]. The KETO-ADPKD study also showed similar results [13].

The KD may be complicated with hyperlipidemia, metabolic acidosis, nephrolithiasis, or increased risk for cardiovascular disease [2]. Further studies and clinical considerations are needed to elucidate the benefits of KD in CKD.

Plant-based diet

A plant-based diet is an eating pattern of foods mainly derived from plants and may or may not include small to moderate amounts of meat, fish, seafood, eggs, and dairy [2]. Examples are Mediterranean or DASH (Dietary Approaches to Stop Hypertension) diets [2]. Plant-based diets are effective in treating hypertension and improving cardiovascular biomarkers [2].

In clinical practice, plant foods are not usually recommended for CKD patients due to the risk of hyperkalemia [2]. KDOQI guidelines limit CKD patients' potassium intake but do not inhibit plant foods [1]. The guidelines discuss the advantages of plants as a protein source in controlling hyperphosphatemia due to a lack of degrading enzyme phytase and low bioavailability [1]. Kontessis et al. [14] reported that fractional clearance of albumin and plasma glucagon increments was lower in vegetable protein diets than in the animal diet group. Renal vascular resistance was lower, and glomerular filtration rate and renal plasma flow were higher in the animal protein diet group, indicating hyperfiltration [14]. The change in protein type could have affected membrane size, charge selectivity, and the pressure gradient across the glomerular barrier [14]. A meta-analysis of studies in the general population demonstrated a 10% reduction in the odds of developing CKD for every 1-point increase in adherence to the Mediterranean Diet Scale [15]. In the CORDIOPREV randomized controlled trial, coronary heart disease patients on a long-term Mediterranean diet showed less decline in kidney function compared to baseline [16]. Plant-based diets may be considered in CKD patients with preserved renal potassium excretion. However, adherence may be difficult as plant-based diets are unfamiliar in many people [2].

Conclusions

Diet plays a crucial role in the management of CKD, with various approaches offering potential benefits in slowing disease progression and improving patient outcomes. Reducing carbohydrate intake, particularly sugars like fructose, may help preserve kidney function and mitigate cardiovascular risks. While KD and IF show promise, especially in specific conditions like ADPKD, their long-term safety and efficacy require further investigation. Plant-based diets emerge as a favorable option due to their cardiovascular benefits and potential to reduce CKD incidence, though attention must be paid to potassium levels and patient adherence. High-protein diets are generally discouraged due to their association with hyperfiltration and CKD progression. Personalized dietary plans, developed in consultation with healthcare professionals, are essential to balance the benefits and risks of these interventions, ensuring optimal nutritional status while minimizing complications. Future research should focus on long-term outcomes of these dietary strategies in both adult and pediatric CKD populations.

Conflicts of interest

Joo Hoon Lee is an editorial board member of the journal but was not involved in the peer reviewer selection, evaluation, or decision process of this article. No other potential conflicts of interest relevant to this article were reported.

Funding

None.

Author contributions

All the work was done by JJ and JHL.

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