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(REVIEW ARTICLE)

Vegan diet to slow the progression of diabetic nephropathy: A review

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Abstract

Diabetic nephropathy (DN) is the major cause of renal disease that affects 40% of patients with diabetes. DN is characterized by the pathological urine albumin excretion rate (UAER), diabetic glomerular lesions, and loss of glomerular filtration rate (GFR). Several studies have found strong association of animal protein with the glucagon activation, insulin resistance, proteinuria, microalbuminuria, and progression of renal disease in diabetic patients. Vegan diet that excludes all animal foods such as meat (including fish, shellfish, and insects), dairy, eggs, and honey, as well as products such as leather has been found significantly beneficial on enhancing insulin sensitivity, reducing glucagon activation and incidence of chronic kidney disease (CKD), and slow the progression of DN. Other studies have suggested that avoiding animal food and shifting the source of dietary protein from animal-derived to plant-based products may be a better dietary approach than dietary protein restriction to reduce kidney disease and cardiovascular disease (CVD), particularly in CKD and diabetes patients with profound insulin resistance. Based on the literature search conducted in this study we concluded that the vegan diet is beneficial in patients with diabetes and CKD to slow the progression of the DN and renal failure. However, additional interventional studies in humans are needed to understand the mechanisms underlying the increased insulin sensitivity by vegan diets and further studies of efficacy and safety of vegan diets in patients with diabetes and DN are recommended.

Keywords: Vegan diet; Plant-based diet; Plant-based protein; Diabetes; Diabetic nephropathy; Chronic kidney disease

1. Introduction

More than 37 million Americans (about 1 in 10) have diabetes, and about 90-95% of them have type 2 diabetes (T2D) [1]. T2D results from the body's ineffective use of insulin, which is due to excess body weight and physical inactivity [2]. Common diabetes health complications include heart disease, chronic kidney disease (CKD), nerve damage, and other problems with feet, oral health, vision, hearing, and mental health [3].

Diabetic nephropathy (DN) is the major cause of renal disease in patients starting renal replacement therapy, which affects approximately 40% of type 1 diabetic (T1D) and T2D patients [4]. DN is characterized by the pathological urine albumin excretion rate (UAER), diabetic glomerular lesions, and loss of glomerular filtration rate (GFR) in diabetics [5].

The pathogenesis of DN is multifactorial with many diverse structural, physiological, hemodynamic, and inflammatory processes contributing to the progressive decline in GFR. Increased activity of the sodium-glucose transporter-2 (SGLT2) in the proximal tubule initiates many of these pathophysiological abnormalities. Inhibition of SGLT2 activities reverses many of these disturbances and markedly slow the progression of DN. Maintaining HbA1c <6.5% (upper limit of the prediabetic range) and ideally within the normal range (<5.7%) is the most definitive means of preventing DN.

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However, once the histological and clinical evidence of the DN is manifested, different measures targeting multiple pathophysiological disturbances simultaneously are required to slow the progression of DN to renal failure [6].

Many studies have indicated the effectiveness of carbohydrate diet restriction in T2D patients on insulin and incretin-based therapies to achieve glycemic control [7]. several other studies have suggested dietary protein restriction in diabetics to prevent renal complications. Animal protein is strongly associated with clinical features of DN and cardiovascular disease (CVD) whereas plant-based protein has a strong beneficial effect on both DN and CVD. Plant-based diet (PBD) has been found to be nutritionally safe in general population, diabetics, and renal patients [8]. The aim of this review based on the available research and review literatures was to analyze the benefits of the vegan (non-animal products) diets to prevent and slow the progression of the kidney disease in diabetic patients.

2. Methods of Literature Search

We used PubMed, Medline, and PubMed Central to search for relevant articles. The search terms we used for literature search include vegan diet, plant-based diet, vegetarian diet, animal proteins, and plant-based proteins combined with their outcomes such as diabetes, insulin sensitivity, insulin resistance, glomerular filtration rate (GFR), chronic kidney disease (CKD), diabetic nephropathy, microalbuminuria, glomerular filtration rate, and renal failure. As we are not doing a systematic review, we have not identified all the literature. Therefore, we acknowledge a publication bias.

3. Dietary Proteins and Diabetic Nephropathy (DN)

In a meta-analysis of randomized controlled trials done by Li XF et al [9] with a total of 690 DN patients in the low-protein diet (LPD) group and a total of 682 patients in the control group, moderate to robust evidence indicated that LPD was significantly effective for decreasing the UAER and proteinuria. However, their study didn't find any statistical differences in glycated hemoglobin (HbA1c), serum creatinine, and GFR between the two groups. In a case-control study done by Aziz M et al in 105 women with DN and 105 controls [10], they found a strong positive association between adherence to the Western-based Dietary Protein Sources (WDPS) and DN whereas Mediterranean-based Dietary Protein Sources (MDPS) was associated with lower odds of DN. WDPS pattern is rich in red and processed meats, eggs, and high-fat dairy and the MDPS pattern is rich in low-fat dairy, fish, poultry, soy, and legumes.

Pan Yu et al [11] in their meta-analysis of randomized control trial did not find the LPD to be associated with a significant improvement of renal function in patients with DN. Instead, LPD resulted in lower serum albumin concentrations in a subgroup analysis. However, Zeller K et al [12] concluded that the dietary restriction of protein and phosphorus can slow the progression of chronic renal failure in patients with DN. A low-protein diet was associated with a significant improvement in GFR. This effect was consistent across the subgroups of type of diabetes, stages of nephropathy, and intervention period. However, GFR was improved only when diet compliance was fair. Proteinuria and serum albumin were not differed between the groups. HbA1c was slightly but significantly decreased in the low-protein diet group [13]. Hansen et al [14] concluded that moderate dietary protein restriction improves prognosis in T1D patients with progressive DN in addition to the beneficial effect of antihypertensive treatment and indicated a wider use of dietary protein restriction in patients with DN.

4. Vegetarian vs Vegan Diets

A PBD excludes all animal products such as red meat, poultry, fish, eggs, and dairy products. It is based on foods derived from plants that contain minimal amounts of processed food and more fruits, vegetables, whole grains, legumes, nuts, seeds, herbs, and spices. Though vegetarian diet is a PBD avoiding all animal flesh–based foods and animal-derived products, some modified versions allow eggs (Ovo), dairy products (lacto), or a combination of both. However, vegan diet excludes all animal foods such as meat (including fish, shellfish, and insects), dairy, eggs, and honey, as well as products such as leather [15].

Several previous studies have reported vegetarian diets to be effective not only in the prevention but also in the treatment of T2D resulting in dramatic reduction in medication and in plasma glucose concentrations in response to a combination of PBD with the exercise [16, 17]. Other studies reported that the vegetarian diets are almost twice as effective even without exercise to reduce body weight and blood lipids and to improve glycemic controls compared to a conventional diabetic diet in the treatment of T2D [18, 19]. Kahleova H et al [20] demonstrated that a vegetarian diet increased insulin sensitivity, reduced volume of visceral fat, and improved plasma concentrations of oxidative stress markers more than a conventional diabetic diet. Therefore, properly planned vegetarian diets are not only healthy and

nutritionally adequate, but also effective in controlling weight and blood glucose, have metabolic and cardiovascular benefits, and reduce diabetes complications [21].

Bernstein AM et al [22] concluded that substitution of vegetable protein or fish protein for animal protein may protect against the development of proteinuria in patients with diabetes. Vegetable protein diets meet protein requirements and provide adequate nutrition in people with CKD [22]. Vegan diets that are lower in protein intake compared with all other diet types have gained popularity, especially in the last decade. Vegan diets have a low glycemic load and are low in vitamins B2, Niacin (B3), 12, D, iodine, zinc, calcium, potassium, and selenium. However, vegan diets not related to deficiencies in vitamins A, B1, B6, C, E, iron, phosphorus, magnesium, copper, and folate [23].

5. Benefits of Vegan Diets in Diabetes

Diabetic patients typically experience excessive glucagon secretion that induces insulin resistance and increases glomerular filtration rate (GFR) [8]. Vegetable protein consumption enhances insulin sensitivity as opposed to the intensification of insulin resistance and glucagon activation with consumption of animal proteins. Reducing or excluding animal food and increasing plant-based protein is significantly beneficial on insulin sensitivity and consequently PBD patterns are effective in the prevention of T2D [24].

Vegan diets rich in dietary fibers and soy proteins reduce total cholesterol due to the absence of cholesterol in the vegetable domain, compared to dietary patterns that contain animal products [25-28]. Soy-based diet reduces the GFR and total and LDL cholesterol in the young adults with T1D and glomerular hyperfiltration [26]. Accordingly, PBD patterns improve the clinical expression of insulin resistance (one of the components of the metabolic syndrome) and are beneficial to hypertension, dyslipidemia, obesity, and glycemic control [29]. In a 12-week randomized clinical trial, Lee Y-M et al [30] found the use of a vegan diet for 3 months to be more effective for glycemic control among T2D, as compared to a conventional diabetes diet recommended by the Korean Diabetic Association (KDA).

6. Effects of Vegan Diets on Diabetic Nephropathy (DN)

Plant-based protein is renal protective, and its consumption reduces the risk of incident CKD whereas animal protein intake elevates GFR, increases albuminuria, and accelerates the rate of kidney function decline resulting in the increased risk of incident CKD [31]. Vegan diet significantly enhances insulin sensitivity and mediates their remarkable vascular advantages. Avoiding animal food and shifting the source of dietary protein from animal-derived to plant-based products may be a better dietary approach than dietary protein restriction to reduce kidney disease and CVD, particularly in CKD and diabetes patients with profound insulin resistance [32].

Non-vegetarian diet evokes renal vasodilatory response resulting in increased GFR while plant-based protein has no effect on GFR. Prolonged consumption of plant-based protein does not modify GFR whereas ingestion of animal protein results in persistently elevated GFR [33, 34]. Plant-based proteins induce renal changes like those obtained by protein restriction and prevent the vasodilatory and proteinuric effects of meat products mediated by hormonal changes involving glucagon secretion and renal prostaglandin production. Modification in sources of protein, rather than protein restriction, in the diets may prove advantageous in the long-term treatment of chronic renal failure [35].

In a systematic review that included 7 interventional nutritional clinical trials and 161 patients with diabetes, a PBD was found to be associated with a reduction in albuminuria and GFR in T1D patients with glomerular hyperfiltration [36]. Wiseman MJ et al [37] concluded that the vegan diet is associated with glomerular and systemic hemodynamic changes which may be beneficial in the prevention of glomerular sclerotic changes in health and disease. The study done by Jibani MM et al [38] in eight T1D patients with an UAER in excess of 30 micrograms min-1 concluded that a predominantly vegetarian diet may have important beneficial effects on DN without the need for a heavily restricted total protein intake.

Nettleton JA et al [39] found that nondairy animal food intake was positively associated with urinary albumin-to-creatinine ratio (UACR) and concluded that a high intake of low-fat dairy foods and a dietary pattern rich in whole grains, fruit, and low-fat dairy foods were both associated with lower UACR. In a study done by Azadbakht L et al [40] in 14 patients with total urine protein excretion between 300 and 1000 mg/day, serum creatinine between 1 and 2.5 mg/dl and blood urea nitrogen between 20 and 40 mg/dl, the dietary soy protein significantly reduced proteinuria, urinary urea nitrogen and phosphorus. Interventional studies have confirmed the specific role of animal protein in increasing UAER by showing the decrease in albuminuria in T1D patients with exclusive reduction in animal protein

consumption and concluded that the long-term vegetarian diets have renal protective effect in patients with DN [41, 42].

7. Discussion

Restriction or elimination of animal protein from the diet is crucial to prevent or to slow the progression of CKD. Higher animal fat and two or more servings per week of red meat is associated with the increased risk for microalbuminuria whereas lower sodium and higher β-carotene intake is associated with the reduced risk for eGFR decline. Higher intake of plant-based protein and lower intake of red meat has been found to be significantly associated with markedly reduced risk of CKD [43, 44]. A reversible decline in GFR and albuminuria has been induced with dietary protein restriction for four weeks in T1D patients with DN [45].

Cross-sectional analyses in Japanese patients and participants in the Diabetes and Lifestyle Cohort Twente-1 (DIALECT-1) study found an independent association of meat intake with a higher prevalence of renal failure among T2D patients. Similarly, a PBD pattern has been found to be associated with a decreased incidence of renal failure, compared to an animal-derived diet, in a prospective study of 3088 European T2D patients. Furthermore, replacement of dietary animal protein with plant-based protein is inversely associated with renal failure in diabetics [46, 47].

The main benefit of the PBD is to enhance the insulin sensitivity in diabetic patients with marked insulin resistance. Hence, PBD patterns may be more effective to slow the progression of DN [48]. Specific restriction or exclusion of animal-derived products and promoting consumption of vegan diet to enhance insulin sensitivity is a better nutritional approach to prevent the development or slow the progression of renal failure in diabetic patients [49].

8. Conclusion

Based on the literature search conducted in this study, we found that the animal-derived diet has significant association with the increased risk of CKD specifically in diabetic patients. The animal-based protein increases insulin resistance and GFR and results in microalbuminuria in diabetic patients. Vegan diet has an inverse association with CKD and renal failure in diabetic patients than in general population. Vegan diet increases insulin sensitivity, reduces risk for eGFR decline, decreases microalbuminuria in diabetic patients. Therefore, the vegan diet is beneficial in patients with diabetes and CKD to slow the progression of the DN and renal failure. However, additional interventional studies in humans are needed to understand the mechanisms underlying the increased insulin sensitivity by vegan diets and further studies of efficacy and safety of vegan diets in patients with diabetes and DN are recommended.

Compliance with ethical standards

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RP: developed the research plan, wrote the article; KRP: read, reviewed, and approved the final manuscript; and both authors: conducted the literature search, had primary responsibility for final content.

Disclosure of conflict of interest

The authors declare no conflict of interest.

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