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Comparing the Effects of Vegan Diets versus Ketogenic Diets on Glycemic Control in Type 2 Diabetes Mellitus

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REVIEW

April McCune et al

Comparing the Effects of Vegan Diets versus Ketogenic Diets on Glycemic Control in Type 2 Diabetes Mellitus

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Abstract

Purpose: The purpose of this review is to explore whether plant-based (vegan) diets result in greater reductions in hemoglobin A1c (HbA1c) than high-fat carbohydrate-restricted (ketogenic) diets in adults with type 2 diabetes mellitus. **Search Criteria**: PubMed and Cochrane library databases were systematically searched for all relevant studies using MeSH terms (("diet, high fat" AND "diet, carbohydrate restricted") OR "diet, ketogenic" OR "diet, vegan") AND "diabetes mellitus, type 2/therapy". Limiting the research to meta-analyses and systematic reviews narrowed the results to six articles. One systematic review was excluded because it examined the effects of ketogenic diets on the quality of life of adults with chronic disease, not specifically glycemic control in patients with type 2 diabetes mellitus. **Results**: Eight randomized controlled trials reported a reduction of HbA1c between 0.3-1.4% after a vegan diet, but only two of the eight studies showed a statistically significant mean difference between the intervention and control groups. In a separate review, eight of thirteen studies showed a reduction of HbA1c ranging from 0.6-3.3% with a mean reduction of 1.07% following a ketogenic diet but offered no controls for comparison. A meta-analysis of fourteen trials revealed that a ketogenic diet provided an average of 0.5% greater reduction in HbA1c compared to control (primarily low-fat) diets. The last two reviews agreed that vegan diets appear promising, but one included the benefits of ketogenic diets while the other found the studies on ketogenic diets inconclusive. **Conclusion:** While the results of some of the selected studies appear promising, the consensus among the systematic review and meta-analyses is that further research is needed to determine which eating patterns are most effective for improving glycemic control in type 2 diabetes.

Keywords: plant-based, vegan, carbohydrate-restricted, ketogenic, type 2 diabetes mellitus, glycemic control, hemoglobin A1c, HbA1c,

Introduction

Diabetes occurs when the body is no longer capable of adequately regulating glucose levels in the blood. Hemoglobin is a protein found in red blood cells which is responsible for oxygen transport and is glycated in proportion to the concentration of glucose in the blood. Measuring the percentage of glycated hemoglobin (HbA1c) provides an estimated average blood glucose over the preceding eight to twelve weeks,[1] which is the average lifespan of red blood cells. According to the CDC,[1] 11.3% of the US population suffers from diabetes, which is defined as having a HbA1c of 6.5% or greater. An additional 38% of the adult population has prediabetes[1] with a HbA1c between 5.7% and 6.4%. Uncontrolled diabetes, especially when combined with high blood pressure and/or high cholesterol increases the risk of heart disease, stroke, blindness, kidney failure, amputations of the legs and feet, certain types of cancer, Alzheimer's disease, and early death.[1] There is currently no cure for type 2 diabetes, however eating well, exercising, and losing weight can help reduce blood glucose.[2] It is important for healthcare providers to use evidence-based research when advising their patients on dietary changes to manage their diabetes in addition to or in lieu of antihyperglycemic medications.

Background

Dietary carbohydrates are broken down into glucose, which is the primary source of energy for the human body.[3] In response to carbohydrate intake, a healthy pancreas releases insulin which binds to receptors on cell membranes to facilitate the movement of glucose into cells.[3] Insulin also promotes the uptake of glucose by the liver to be stored in the form of glycogen and by adipose tissue to be converted and stored as fat.[3] Insulin, therefore, prevents blood glucose from getting too high. When blood glucose levels drop, either between meals or when dietary intake of carbohydrates is restricted, a healthy pancreas releases glucagon which stimulates the liver to break down glycogen into glucose in a process called glycogenolysis.[3] Glucagon also promotes gluconeogenesis, which is the process of making glucose by breaking down other sources of energy such as fats and proteins.[3] Both glycogenolysis and gluconeogenesis release glucose into the bloodstream, thereby preventing blood glucose from getting too low.[3] In this way, insulin and glucagon oppose each other to maintain glucose homeostasis.[3] To protect cells from metabolic and oxidative stress caused by excess glucose influx, cells can partially downregulate their insulin signaling pathways in response to chronically elevated insulin levels.[3] This contributes to a condition called "insulin resistance" resulting in decreased uptake of glucose by cells and hyperglycemia.[3] Type 2 diabetes (DM2) is caused by a combination of insulin resistance and insufficient production of insulin by the pancreas.

Ketogenic Diets

Ketogenic diets drastically reduce dietary intake of carbohydrates, forcing the body to break down fat for energy once glycogen stores are depleted.[4] Ketone bodies are a byproduct of fat metabolism that replace glucose as the body's primary source of energy in times of glucose deprivation,[4] hence the term "ketogenic diet." The body will remain in a ketogenic state as long as dietary carbohydrates continue to be restricted.[4] Ketogenic diets are typically high-fat (55-60% of total energy intake), moderate-protein (30 to 35% of total energy intake), and very low-carbohydrate (5-10% of total energy intake).[4] Each gram of carbohydrate contains four kilocalories (kcal), therefore a 2000 kcal per day ketogenic diet allows only 25-50 grams of carbohydrates per day. The typical American diet contains 200-300 grams of carbohydrates daily.[4] Ketogenic diets also limit protein intake to prevent the conversion of protein to glucose from inhibiting the breakdown of fats.[4] Fat intake and total caloric intake are not restricted.[4]

Ketogenic diets aid in glycemic control in patients with DM2 by decreasing intake of carbohydrates and improving insulin sensitivity.[4] Unlike diabetic ketoacidosis, a life-threatening condition where ketone bodies are produced in extremely high concentrations sending blood pH into an acidotic state, nutritional ketosis produces ketones in relatively small concentrations that do not alter blood pH and is considered quite safe.[4] Insulin and oral antihyperglycemic medications must be appropriately adjusted to prevent severe hypoglycemia in diabetic patients beginning a ketogenic diet.[4] Patients with pancreatitis, liver failure, disorders of fat metabolism, primary carnitine deficiency, carnitine palmitoyl transferase deficiency, carnitine translocase deficiency, porphyria, or pyruvate kinase deficiency must not follow a ketogenic diet.[4] Kidney function should be monitored while on a ketogenic diet,[4] especially in diabetic patients who are already at high risk of kidney disease.

Vegan Diets

Plant-based (vegan) diets include fruits, vegetables, whole grains, nuts, seeds, and legumes while excluding all animal-derived foods including meat, fish, poultry, eggs, and dairy products. Some also discourage the use of honey. Vegan diets are not defined by specific macronutrient distributions, but they tend to be very high in carbohydrates, low in proteins, and very low in saturated fats.[5] Portions and calories are generally not restricted.[5] Vegan diets have been shown to decrease insulin resistance and improve glycemic control in patients with diabetes.[5] Although not fully understood, there are several proposed mechanisms.[5] Plant-based diets are low in saturated fats, which are associated with oxidative stress, mitochondrial dysfunction, inflammation, and insulin resistance.[5] Saturated fats contribute to the accumulation of toxic fat metabolites in hepatic and skeletal muscle cells, which impairs insulin signaling and decreases glucose uptake.[5] It is proposed that eliminating saturated fats from the diet detoxifies the liver and improves insulin sensitivity.[5]

Advanced glycated end products are oxidants that have been implicated in the development of insulin resistance.[5] They are found in high levels in meats, low levels in plants, and reducing their intake has been shown to reduce insulin resistance in patients with type 2 diabetes.[5] Iron from animal sources is an oxidant that leads to increased glucose output by the liver, impaired insulin signaling, and is directly toxic to the pancreas.[5] Plant-based diets are rich in fiber, antioxidants, and magnesium, all of which promote insulin sensitivity.[5] Fiber improves insulin signaling and glucose response.[5] Fiber cannot be digested by humans and therefore promotes weight loss by decreasing the caloric density of foods and increasing satiety.[5] Antioxidants are thought to stimulate insulin secretion and enhance glucose uptake by cells.[5] Perhaps most significantly, vegan diets promote weight loss and lower total body fat, both of which are highly protective against insulin resistance.[5] However, it is important to note that plant-based diets have been shown to improve insulin sensitivity even after controlling for weight loss.[5]

Discussion

The systematic review by Pollakova et al[6] compiled the results of seven observational studies and eight randomized controlled trials to explore the impact of vegan diets in the prevention and treatment of type 2 diabetes. Analysis of seven observational studies revealed that a vegan diet is associated with a lower prevalence or incidence of DM2 compared to non-vegan diets.[6] Eight randomized controlled trials reported a reduction of HbA1c between 0.3-1.4% after a vegan diet, five of which were statistically significant compared to a reduction of HbA1c between 0.14-1.0% in control groups, three of which were statistically significant.[6] Only two of the eight studies showed a statistically significant mean difference from baseline to final values between the intervention and control groups.[6] Duration of the interventions varied between 6 to 74 weeks and controls included typical American, conventional low-fat, conventional diabetic, and portion-controlled diets.[6] Failure to control for confounding variables such as duration of disease, baseline HbA1c, medication regimens, medication changes during interventions, baseline BMI, etc. was a major limitation of the included studies.[6] The authors discussed potential mechanisms to explain how a vegan diet might improve blood glucose levels despite being high in carbohydrates and also expressed concerns regarding adverse effects of long term exclusion of certain nutrients including proteins, vitamin B12, calcium, vitamin D, iron, zinc, and omega-3.[6] They concluded that a following a vegan diet may be an efficient way to lose weight and maintain glycemic control for some patients with DM2, but that further research is needed to confirm the effectiveness and safety of vegan diets for diabetic patients.[6]

The systematic review and meta-analysis by Yuan et al[7] compiled thirteen studies to explore the effects of ketogenic diets on glycemic control, insulin resistance, and lipid metabolism in patients with DM2. Eight of the thirteen studies showed a reduction of HbA1c after a ketogenic diet ranging from 0.6-3.3% with a mean reduction of 1.07% (95% CI: 0.73-1.37),[7] but the analysis offered no controls for comparison. Duration of interventions varied between 1 to 56 weeks and the data were analyzed without comparing studies based on duration.[7] Another major limitation was that all studies included in the meta-analysis were conducted on Caucasian diabetic patients.[7] The authors concluded that a ketogenic diet can reduce HbA1c and contribute to therapeutic effects regardless of duration.[7]

The meta-analysis by Choi et al[8] compiled fourteen randomized controlled trials investigating the impact of ketogenic diets on fasting glucose, HbA1c, BMI, and lipids in overweight and obese patients with or without DM2. Data analysis revealed that following a ketogenic diet provided an average of 0.5% greater reduction in HbA1c in patients with DM2 relative to comparison (primarily low-fat) diets.[8] Weaknesses included small sample sizes and varying comparison interventions and study durations.[8] The authors concluded that ketogenic diets may be more beneficial for losing weight and improving glucose and lipid metabolism relative to (primarily) low-fat diets, but that they should be thoroughly evaluated for long-term safety and sustainability.[8]

The systematic review by Papamichou et al[9] compiled the results of twenty randomized controlled trials to examine the effectiveness of six or more months of low-carbohydrate, macrobiotic, vegan, vegetarian, Mediterranean, and intermittent fasting diets compared to low-fat diets on diabetes control and management in adult patients with type 2 diabetes. Vegan diets demonstrated improved glycemic control (-0.4% HbA1c) compared to low-fat diets (-0.01% HbA1c) while only four of fifteen low-carbohydrate diet studies could claim the same.[9] Duration of interventions ranged from six months to four years.[9] Limitations included small sample sizes and inconsistency in the definition of low-carbohydrate diet interventions varying from a very low-carbohydrate intake of 20-50 grams/day to as high as 45% of total energy intake.[9] The authors suggested that subjects' inability to achieve and maintain strictly limited carbohydrate intake may have explained lack of improvement in HbA1c in the low-carbohydrate intervention groups.[9] They concluded that mounting evidence supports the implementation of vegan, vegetarian, and Mediterranean diets for the management of DM2, but that evidence for the long-term efficacy of low-carbohydrate diets is inconclusive.[9] They acknowledged that further long-term research is needed.[9]

The systematic review by Emadian et al[10] compiled the results of eleven randomized controlled trials to determine which dietary interventions are best for achieving glycemic control while controlling for weight loss in overweight and obese adults with type 2 diabetes. Interventions included low-fat vegan, American Diabetes Association (ADA), low glycemic index, high-protein, standard protein, low-fat, low-carbohydrate, low glycemic load, low-carbohydrate Mediterranean, traditional Mediterranean, high-carb/fiber, and modified lipid diets.[10] Duration of interventions ranged from 40 weeks to 4 years.[10] Only four of eleven studies showed greater improvement in HbA1c in one diet over another after controlling for weight loss.[10] One study found that the low-glycemic load diet group experienced a reduction in HbA1c of 0.8% compared to 0.1% in the low-fat diet group while also accounting for changes in glucose-lowering medications.[10] A three-arm study found that the low-carb Mediterranean diet subjects experienced a reduction in HbA1c of 2.0% compared to 1.8% in the traditional Mediterranean diet group and 1.6% in the 2003 ADA recommended diet group, however this study failed to adjust for diabetic medications.[10] A third study reported a mean HbA1c decrease of 0.4% in the low-fat vegan group versus 0.1% for the ADA group after adjusting for medications.[10] A fourth study involving only newly diagnosed patients who were not taking any form of glucose-lowering medications when the study began found that a low-carb Mediterranean diet led to a mean decrease in HbA1c of 0.9% compared to 0.5% in the low-fat diet group.[10] The authors concluded that while Mediterranean, vegan, and low-glycemic index diets appear promising, further research is needed to determine if any particular diet is superior in treating overweight and obese patients with DM2 while controlling for weight loss and the effects of diabetic medications.[10]

Conclusion

The incidence of type 2 diabetes is closely associated with obesity and excess nutrient intake.[7] Treatment of DM2 may require glucose-lowering medications, but some patients can be managed with diet and exercise alone.[2] To determine which, if any, specific dietary interventions are superior for improving HbA1c in diabetic patients, it is essential to control for variables such as age, sex, race, duration of disease, comorbidities, baseline HbA1c, medication regimen, medication changes during interventions, duration of adherence to interventions, baseline BMI, caloric intake, energy expenditure, weight loss during interventions, etc. The prevalence, morbidity, and mortality associated with diabetes should merit sufficient funding to design and carry out a large-scale randomized controlled trial that accounts for all these variables to facilitate meaningful comparisons between various dietary interventions and their impact on glycemic control. There is no one-size-fits-all diet for the management of type 2 diabetes mellitus. Ideological, environmental, ethical, political, financial, cultural, and religious concerns all impact what recommendations patients are willing and able to implement.[1] However, as medical providers we should seek to become educated on the risks and benefits of diabetic therapy so we can provide evidence-based guidance to our patients and their families. While the results of some of the selected studies appear promising, the consensus among the systematic review articles is that further research is needed.

Next Steps

The best way to determine which eating plans are most effective at improving glycemic control in adults with type 2 diabetes is to perform a large-scale study comparing various diets while controlling for confounding variables such as those previously discussed in this review. This could be achieved by recruiting a large number of volunteers with type 2 diabetes to participate in a long-term clinical trial that begins with six months of strictly monitored dietary interventions. Volunteers would be provided free lodging and dietician-approved meals prepared for each participant's particular dietary intervention in a self-contained campus where study personnel could record each participant's caloric intake, energy expenditure, weight changes, and metabolic parameters such as glycemic markers, blood pressure, and lipids. Subjects would be sorted into different arms of the study based on characteristics such as age, sex, race, baseline BMI, comorbidities, duration of diabetes, and baseline HbA1c and results would be analyzed to control for confounding variables.

After returning home, patients would be tracked over time to evaluate continued improvements, long-term sustainability, health benefits, and negative effects of various dietary restrictions. A study of this scale would require a tremendous amount of funding and planning, but the worldwide prevalence, morbidity, and mortality associated with diabetes justifies the investment. If dietary interventions could reduce or eliminate the need for lifelong antihyperglycemic medications, diabetes could be prevented and treated rather than simply managed and endured.

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Abbreviations: DM2, type 2 diabetes mellitus; HbA1c, hemoglobin A1c