VIEWPOINT

The Ketogenic Diet for Obesity and Diabetes—Enthusiasm Outpaces Evidence

Shivam Joshi, MD
Division of General Internal Medicine, Department of Medicine, New York University School of Medicine, New York; and Department of Medicine, NYC Health + Hospitals/Bellevue, New York.

Robert J. Ostfeld, MD, MSc
Division of Cardiology, Montefiore Health System, Bronx, New York.

Michelle McMacken, MD
Division of General Internal Medicine, Department of Medicine, New York University School of Medicine, New York; and Department of Medicine, NYC Health + Hospitals/Bellevue, New York.

Corresponding Author: Shivam Joshi, MD, Division of General Internal Medicine, Department of Medicine, New York University School of Medicine, 550 First Ave, New York, NY 10016 (shivam.joshi@nyulangone.org).

The ketogenic diet has recently received much attention for its promise of treating obesity and type 2 diabetes. However, the enthusiasm for its potential benefits exceeds the current evidence supporting its use for these conditions. Although the temptation is great to recommend a potentially novel approach for otherwise difficult-to-treat diseases, it is important to remain grounded in our appraisal of the risks, benefits, and applicability of the diet to avoid unnecessary harm and costs to patients.

The ketogenic diet, or keto diet, emerged in popularity after a recent series of other low-carbohydrate diets, such as the Paleo and Atkins diets. The ketogenic diet is unique from other low-carbohydrate diets in that followers of the diet are encouraged to forgo nearly all carbohydrates, avoid excess protein, and consume high levels of fat (generally exceeding 70% of calories consumed), resulting in the production of ketones, giving the diet its name. The excitement for low-carbohydrate diets comes on the heels of what some have considered the failure of a low-fat diet to curb the obesity epidemic and its associated increase in type 2 diabetes. This enthusiasm is belied by the fact that the modern American diet is not truly low in fat (defined as less than 30% of total calories). Of more importance, from the early 1970s to the early 2000s, Americans increased total energy consumption by at least 240 calories per day (estimates vary by method and source), likely contributing to weight gain and the increased incidence of diabetes.

Is the ketogenic diet more effective for weight loss than other diets? In a meta-analysis of 13 studies lasting longer than a year, researchers found that the ketogenic diet was associated with less than a kilogram of additional weight loss over high-carbohydrate, low-fat strategies.[1] This difference, although statistically significant, may not be clinically significant. Furthermore, a meta-analysis of 32 controlled feeding studies found that energy expenditure and fat loss were greater with low-fat diets compared with ketogenic diets.[2]

Any diet that results in weight loss does so because it reduces calorie intake. The ketogenic diet, when used for weight loss, is no different. The salient questions are whether it is sustainable and whether it promotes long-term health. No studies, to our knowledge, have evaluated ketogenic diets for cardiovascular events or mortality, although observational studies in the broader low-carbohydrate diet literature suggest increased all-cause mortality.[3]

What about the role of a ketogenic diet in the treatment of type 2 diabetes? One well-publicized, nonrandomized study of the ketogenic diet in persons with type 2 diabetes showed a 1.3% reduction in glycosylated hemoglobin at 1 year in the ketogenic group.[4] These findings must be interpreted with caution, however, because the ketosis group was self-selected and received intensive technological and behavioral support not offered to the control group. Long-term (≥1 year) randomized studies tell a different story. A meta-analysis of randomized long-term studies comparing the ketogenic diet with low-fat diets for weight loss reported no difference in glycemic control among persons with type 2 diabetes.[1]

Type 2 diabetes is characterized by carbohydrate intolerance due to insulin resistance. Restriction of carbohydrates (as in the ketogenic diet) can transiently improve glycemic control, and weight loss by any means can improve insulin resistance. However, there is little if any evidence that ketogenic diets specifically improve carbohydrate intolerance independent of weight loss, unlike other dietary approaches in which glycemic control is improved despite the consumption of healthful carbohydrate-rich foods, such as legumes, whole grains, and fruits, even in the absence of weight loss.

Are there other possible benefits of a ketogenic diet? The ketogenic diet has been touted to have favorable effects on cardiovascular risk factors, such as serum lipid levels. However, evidence suggests that low-density lipoprotein cholesterol and apo-B–containing lipoprotein levels may fail to improve, or even significantly increase, with a ketogenic diet despite weight loss.[5] Although there may be a concurrent increase in high-density lipoprotein cholesterol level with a ketogenic diet, historically, various interventions used to increase high-density lipoprotein cholesterol level have not translated into reductions in cardiovascular events.

In terms of the risk-benefit balance of the ketogenic diet, the potential adverse effects may give one pause. A review of the literature[6,7] on ketogenic diets for the treatment of pediatric epilepsy reveals multiple adverse effects, ranging from the relatively benign but inconvenient "keto flu," an induction period of fatigue, weakness, and gastrointestinal disturbances, to the less common but deadlier occurrence of cardiac arrhythmias from selenium deficiency. Other documented adverse effects include nephrolithiasis, constipation, halitosis, muscle cramps, headaches, diarrhea, restricted growth, bone fractures, pancreatitis, and multiple vitamin and mineral deficiencies.

The greatest risk, however, of the ketogenic diet may be the one most overlooked: the opportunity cost of not eating high-fiber, unrefined carbohydrates. Whole grains, fruits, and legumes are some of the most health-promoting foods on the planet. They are not responsible for the epidemics of type 2 diabetes or obesity, and their avoidance

may do harm. In a systematic review and meta-analysis of 45 prospective studies, researchers found that whole grain intake was associated with a dose-dependent reduction in risk of coronary heart disease, cardiovascular disease, total cancer, and all-cause mortality.[8] Similar findings have been seen with fruits and legumes. Nearly all experts agree that highly processed, refined carbohydrate-rich foods should be avoided. Blurring the distinction between refined and unrefined carbohydrates and thus excluding both precludes the numerous health benefits of unrefined carbohydrates.

The risks posed by the ketogenic diet may explain why the majority of, if not all, populations consume enough carbohydrates to avoid chronic ketosis. Despite popular misconception, even the circumpolar Inuit, who historically have subsisted on a diet of minimal carbohydrates, have a widely prevalent genetic mutation to circumvent the production of ketones.[9] Although the reason for the genetic mutation is not known, it may have conferred a survival advantage, by minimizing ketone production. In contrast, some of the longest-living populations, the so-called Blue Zone communities (eg, Greece, Japan), subsist on a carbohydrate fare that exceeds 50% of daily calories.

Although the ketogenic diet has garnered much attention for the dietary treatment of chronic diseases such as obesity and type 2 diabetes, the evidence supporting its use is currently limited and the diet's potential risks are real. Physicians and patients should continue to judiciously appraise the benefits and risks of the ketogenic diet in accordance with the evidence, not the hype.

ARTICLE INFORMATION

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