Benefits of ketogenic diets

Dear Sir:

In this age of the obesity epidemic, some careful work reported in the May issue of the Journal by Johnston et al (1) provides more information to help solve the problem. With strict controls in a 6-wk trial, they directly compared 2 diets: a ketogenic very-low carbohydrate (KLC) diet and a nonketogenic low-carbohydrate (NLC) diet. They concluded that the KLC and NLC diets were equally effective in reducing body weight and insulin resistance, but the KLC diet was associated with several adverse metabolic and emotional effects. Thus, the use of ketogenic diets for weight loss is not warranted. This conclusion is amplified by the article's title and by its final sentence: "Patients should know that there is no apparent metabolic advantage associated with ketosis during dieting."

As shown in Table 1 of the article by Johnston et al, the 2 diets were equal in energy content (1500 kcal/d). The major nutrients provided daily by the KLC and NLC diets, respectively, were as follows: 33 and 157 g carbohydrate, 125 and 117 g protein, 100 and 50 g total fat, 35 and 13 g saturated fat, 34 and 16 g monounsaturated fat, 14 and 7 g polyunsaturated fat, 15 and 30 g fiber, and 620 and 230 mg cholesterol. Could some of the adverse metabolic effects reported in this study support the long-expressed concerns about the high-fat Atkins diet? Specifically, should the conclusion of Johnston et al have been that a ketogenic diet that is high in saturated fat and cholesterol is not warranted for weight loss? It can be shown that a blanket rejection of ketogenic diets for weight loss is not warranted.

It is safe to assume that no species could have survived millions of years if its members could not tolerate occasional brief periods of natural starvation, which itself is ketogenic. In fact, everyone approaches ketogenesis in the sleep portion of every diurnal cycle. If only water is ingested, stores of liver glycogen decrease steadily to zero in the first 12–24 h (2, 3). The body then must rely heavily on its vital gluconeogenesis capability to meet the needs of the body for glucose when carbohydrate is not available in sufficient amounts from the diet or from glycogen reserves. A supply of glucose is necessary, especially for the nervous system and erythrocytes. Death usually results if gluconeogenesis fails (2). At the same time, concentrations of insulin and glucose decrease (glucose decreases toward ≈3 mmol/L) while glucagon increases. These changes initiate a strong increase in the concentration of free fatty acids as the body switches from the fed state to the starved state. Although slightly delayed, the concentration of blood ketone bodies increases from a negligible value to ≈2 mmol/L (2, 3). As noted decades ago, after ≈3 d, hunger decreases considerably as the concentration of these ketone bodies continues to increase to >4 mmol/L (3, 4). Ketosis arises because the major fuel being burned is fat from body stores. The brain spares some glucose by using these ketone bodies. This mild ketosis is the body's natural adaptation to starvation and is not to be confused with the dangerous ketoacidosis associated with untreated type 1 diabetes. When zero calories are ingested, the maximum possible rate of weight loss occurs, and there will likely not be a flat weight-loss plateau. Of course, the ingestion of zero calories for an extended time is not healthful because of the total lack of vital nutrients of all kinds.

The protein-sparing modified fast (PSMF) is a human-engineered variation on natural starvation designed to extend the period of rapid weight loss and low hunger while preventing the body from catabolizing itself. Because of the special biochemical importance of glucose, essentially the same changes as described above for starvation take place if little glucose-producing food (carbohydrate) is ingested, despite the fact that protein and fat are still being ingested. Ketostix (Bayer Corporation, Elkhart, IN) can be used to verify the presence of ketosis in ≈3 d. Enough protein must be eaten to provide for the usual daily needs for amino acids plus enough to supply the now-required gluconeogenesis. The total amount of protein needed is not large, ≈1.3 g protein/kg ideal body wt (5). In this 1976 article, Bistrian et al conclude that "For diabetics with some endogenous insulin reserve, the PSMF offers significant advantages for weight reduction, including preservation of lean body mass (as reflected in nitrogen balance) and withdrawal of exogenous insulin." The small amount of carbohydrate allowed must be chosen carefully to maximize the nutrients per gram of carbohydrate.

A controlled study compared reports of appetite and symptoms in 28 obese subjects randomly assigned to either a 500-kcal PSMF or a 1200-kcal balanced diet (6). During the first comparison month, the subjects who consumed the PSMF lost significantly more weight and reported significantly less hunger than did the subjects who consumed the balanced diet; the former group reported significantly greater problems with cold intolerance, constipation, dizziness, dry skin, and fatigue. A ketogenic diet was developed early in the 20th century to successfully treat children with drug refractory epilepsy (7). A direct comparison showed that saturated fat is undesirable even when a high-fat ketogenic diet is required, as in special treatments of refractory epilepsy (8). A 2-wk carefully controlled inpatient study showed that a ketogenic diet was beneficial for the control of weight and blood glucose concentrations in diabetic patients. Cutting carbohydrate consumption to ≈20 g/d produced a spontaneous reduction in calories of ≈1000 kcal/d with little change in hunger, diet satisfaction, or energy levels (9).

Clearly, one major advantage of the ketogenic diet is that it allows the calorie intake to be cut drastically without producing ravenous hunger. A suggestion for extending the benefits of ketogenic weight-loss diets would be to alternate 1–3 wk of the PSMF with longer periods of the Heller plan (10). The Heller plan allows for one full, healthful, balanced meal plus snacks daily that follow a PSMF protocol. This would enable the consumption of useful amounts of vital plant foods while taking the body back and forth through the entire cycle of emptying (23 h) and refilling (1 h) the liver's glycogen stores.

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Reply to NJ Krilanovich

Dear Sir:

We thank Krilanovich for his comments regarding our recent study (1). Low-carbohydrate diets have withstood recent scientific scrutiny (2, 3) and may soon become the "diet of choice" for effective weight loss. We challenged the view that the metabolic advantage of these diets is related to ketosis, and we showed that dietary protein (≈1.2 g/kg body wt) generates the metabolic milieu for efficient weight loss (1). That is, dietary protein—not ketosis or dietary fat or carbohydrate—corresponds to reduced hunger and elevated energy expenditure during active weight loss (1, 4).

The protein-sparing modified fast (PSMF) developed in the 1970s by Bistrian et al (5) permits the consumption of only lean meat, fish, and poultry at a level to provide 1.2–1.4 g protein/kg ideal body wt. Dietary carbohydrate is prohibited, dietary fat is restricted to that present in the protein source, and vitamin and mineral supplementation is necessary. Although Krilanovich agrees that ketogenic diets high in saturated fat and cholesterol (eg, the Atkins diet) may be unhealthful, he suggests that ketogenic PSMF diets would be the preferred diet for weight reduction because these diets promote "rapid weight loss and low hunger." Yet, the rate of weight loss with a PSMF diet, ≈1 kg/wk at energy intakes near 800–900 kcal/d (6, 7), is similar to that reported for nonketogenic, low-carbohydrate, high-protein diets (1, 8), and both diets appear to effectively control hunger (4, 8, 9).

Thus, there is no apparent advantage to restricting dietary carbohydrates to a level that is ketogenic. Vegetables and low-fat dairy products contain numerous nutrients and phytochemicals that reduce the risk of chronic disease; therefore, the restriction of these foods in the diet is simply not wise. Furthermore, a recent article provides evidence that ketosis increases blood methylglyoxal concentrations 2-fold (10). Methylglyoxal and its byproducts are considered a significant cause of blood vessel damage. We continue to claim that the use of ketogenic diets for weight loss is not warranted.

SLT, the research chef, received consulting fees from the Inflammation Research Foundation. HH is an employee of Zone Labs Inc. BS is a stockholder and serves on the boards of directors of Zone Labs Inc and Zone Cuisine Inc and is also on the boards of directors of Zone Café and ZoneNet. None of the other authors had any personal or financial conflict of interest.

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