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Starvation Ketoacidosis due to the Ketogenic Diet and Prolonged Fasting – A Possibly Dangerous Diet Trend

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Patient: **Male, 60**
Final Diagnosis: **Starvation ketoacidosis**
Symptoms: **Nausea • syncope • vomiting**
Medication: —
Clinical Procedure: —
Specialty: **Metabolic Disorders and Diabetics**

Objective: **Challenging differential diagnosis**





Background: The low-carbohydrate, high-fat ketogenic diet has been popularized in the press recently, touting multiple health benefits such as weight loss and increased energy. In this diet, participants intentionally push themselves into a state of ketosis and usually do not develop metabolic complications or illness unless put under certain circumstances such as stress and prolonged fasting.

Case Report: We report a case of starvation ketoacidosis in a 60-year-old male with well-controlled diabetes mellitus type II following a strict ketogenic diet who then underwent prolonged fasting.

Conclusions: Although the ketogenic diet with or without periods of fasting might yield short-term weight loss, it has potentially dangerous side effects, including ketoacidosis. It is recommended that people, especially those with comorbidities such as diabetes mellitus type II, consult their physicians before initiating this diet. Clinicians must keep a broad differential when evaluating acute metabolic acidosis.

MeSH Keywords: **Acidosis • Diet Fads • Diet, Carbohydrate-Restricted • Fasting • Ketogenic Diet • Ketosis**

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Background

The ketogenic diet is a strict nutritional regimen consisting of low carbohydrates, high fat, and adequate protein [1]. Ketogenic diets have been used in the treatment of seizure disorders, neurodegenerative disorders, and more recently have become mainstream as a method for weight loss, although its weight loss implications have been described as early as the 1800s [2]. It can be modified by the addition of intermittent or prolonged fasting which will also restrict caloric intake. By reducing carbohydrate ingestion and exhausting the body's glucose reserve, there is a shift in metabolism into ketogenesis, primarily by the hepatic oxidation of fatty acids. The ketones produced then become an important alternative to glucose as the body's energy source [3].

In certain conditions, this ketosis can develop into overt ketoacidosis, causing a decrease in pH and serum bicarbonate level, leading to serious illness and hospitalization. While ketoacidosis is most frequently associated with diabetes mellitus type I and alcoholism, starvation, particularly in individuals following low-carbohydrate and/or low-caloric diets, should not be overlooked as a possible etiology. Malnutrition and poor dietary intake are ways to enter a state of starvation that may result in ketoacidosis [4]. Gastric banding has also been associated with a risk of starvation ketoacidosis [5]. Besides ketoacidosis, the ketogenic diet may lead to electrolyte abnormalities, hypoglycemia, acute pancreatitis, and dyslipidemia [6].

Case Report

A 60-year-old male with a history of well-controlled diabetes mellitus type II presented to the emergency department after having a witnessed syncopal episode at home. He was a follower of a vegetarian version of the popular ketogenic diet who engaged in intermittent fasting. While following this strict diet for roughly the past year and increasing his exercise, he reported losing 20 pounds and decreasing his hemoglobin A1C (HbA1C) from 11.5% to 7.0%. He decided to challenge himself by going on a multiple day fast by foregoing food and only drinking water. He intended to transition into ketosis at a quicker rate, thereby possibly helping him further manage his diabetes.

After 5 days of fasting, the patient broke his fast by eating soup and taking a chlorophyll supplement, which he usually took, which caused him to vomit and become dizzy. He later syncopized in front of his wife, hitting his head on the shower door and briefly lost consciousness. He presented to the emergency department with persistent nausea and vomiting. His only prescription medication was metformin 500 mg twice

a day, and he denied alcohol or recreational drugs. He did not take any alkalinizing supplements.

On evaluation, he was hemodynamically stable with baseline normal mental function. Physical examination was unrevealing. Laboratory evaluation was notable for glucose 133 mg/dL, serum bicarbonate 19 mEq/L, anion gap 15 mEq/L, venous lactic acid 1.8 mmol/L, a positive serum acetone in a diluted serum 1: 4, plasma osmolality 305 mOsm/kg, sodium 139 mEq/L, and HbA1C 7.0%. A urinalysis had 2+ ketones and was negative for glucose. pH from a venous blood gas on admission was 7.20.

Given the patient's history of intentional fasting, mild blood glucose elevation, and lack of alcohol use, the ketoacidosis was most probably due to starvation. He was started on intravenous hydration with dextrose 5%-0.9% normal saline. The next day, the patient's pH normalized on an arterial blood gas and anion gap decreased to 9. He reported resolution of symptoms and tolerated an oral diet. He was discharged home with instructions to follow up with his primary care physician for further management.

Discussion

The ketogenic diet is a strict nutritional regimen consisting of low-carbohydrates, high-fat, and adequate protein that pushes one into a state of ketosis as the body's glucose reserve is depleted. Fat metabolism primarily in liver hepatocytes produces 2 ketone bodies, i.e., beta-hydroxybutyrate and acetoacetate, that serve as substrates for energy production. As acid anions, beta-hydroxybutyrate and acetoacetate can result in a decreased blood pH (acidemia), if present in higher levels. A third ketone, acetoacid is produced by the spontaneous decarboxylation of acetoacetate, acetone, and is neutral and cannot alter blood pH [7]. Acetone, however, has the ability to cross the alveolar membrane barrier of the lung and can be measured in one's breath, making it a convenient ketone biomarker [8].

One of the reasons for the increased popularity in the ketogenic diet is its effectiveness in weight loss. In a study that had obese adults undergo a 12-week ketogenic diet, significant weight loss was achieved (-18 ± 9 kg in men versus -11 ± 3 kg in women). There was also decreased emotional eating, increased body image satisfaction, and improved physical importance [9]. Another study that focused on individuals with diabetes mellitus type II found that participants who followed a very-low-calorie ketogenic diet compared to those following a hypocaloric diet had a significant reduction in weight loss and waist circumference and had better glycemic control [10].

It is hypothesized that using energy from protein in a ketogenic diet is more energy-intensive which results in the loss

of more calories [11]. Other proposed methods for weight loss in the ketogenic diet include a reduction in appetite due to a higher satiety effect of proteins, a possible direct appetite suppression from ketone bodies, and increased lipolysis [11]. By increasing his exercise and following a vegetarian ketogenic diet along with periods of fasting causing ketosis, our patient was able to lose about 10% of his total body weight and better manage his diabetes.

However, if the caloric intake is too low or a periodic fasting is performed, there is a chance to enter ketosis faster and possibly develop clinically significant ketoacidosis with symptoms such as fatigue, nausea, and vomiting. This is likely what happened to our patient. Other cases of ketoacidosis developing from low carbohydrate and high protein diets, such as the South Beach Diet and the Atkins Diet, have been reported [12,13].

Although there is data regarding the short-term success of low-caloric, low-carbohydrate diet, there is only limited data regarding the long-term success of the ketogenic diet – this might be due to the difficulty in maintaining a strict low-carbohydrate rule for longer periods of time. In studies on long-term (22 weeks) ketogenic diets in mice, the mice did not lose weight after an initial weight loss and had hepatic steatosis and glucose intolerance from decreased β -cell insulin secretion [14]. The high protein and fat diet is also unlikely to be cardioprotective, since it might cause an increase in LDL cholesterol and serum triglycerides [11].

Starvation ketoacidosis is an uncommon cause of acute metabolic acidosis. In our patient, our initial differentials were possible diabetic ketoacidosis (due to the fasting followed by vomiting) versus lactic acidosis (secondary to metformin use) versus acidosis due to herbal supplements (that sometimes contain unregulated additives). Through clinical and laboratory evaluation, we were able to diagnose his fasting while on a ketogenic diet as the cause of acidosis.

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In this patient with diabetes mellitus type II, diabetic ketoacidosis should be considered as the cause of his metabolic acidosis. Diabetic ketoacidosis is typically seen in poorly controlled disease, a consequence of the inability to use glucose due to insulin deficiency in type I diabetes or increased insulin resistance in type II diabetes [7]. However, it was believed that the patient's diabetes was well controlled as evidenced by his HbA1C of 7%. He also did not use a sodium-glucose cotransporter 2 inhibitor which has been reported to cause an increased risk of euglycemic diabetic ketoacidosis. This risk is particularly high for patients who participate in prolonged fasting, had large weight loss, or have major illness. Furthermore, euglycemic diabetic ketoacidosis typically presents with severe metabolic acidosis, while starvation ketoacidosis typically presents with a pH above 7.3 and serum bicarbonate more than 18 mEq/L [15]. Clinicians must remember to keep a broad differential when evaluating patients with acute metabolic acidosis.

Conclusions

Although the ketogenic diet and other low-carbohydrate, high-protein diets with or without periods of fasting might yield short-term weight loss, they have potentially dangerous side effects, including ketoacidosis. It is recommended that people wishing to start a ketogenic diet, especially those with comorbidities such as diabetes mellitus type II, first consult their physicians to discuss the risks and benefits. Furthermore, clinicians should remember to keep a broad differential diagnosis when evaluating patients with acute metabolic acidosis.

Conflict of interest

None.

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