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CASE REPORT

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Severe anion gap metabolic acidosis associated with initiation of a very low-carbohydrate diet

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ABSTRACT

Low carbohydrate diets have been popularized as an effective solution for weight loss. Although rare, life-threatening anion gap metabolic acidosis has been reported in patients on these diets. We present a case of a 31-year-old man with atypical symptoms of chest pain and shortness of breath found to have severe metabolic acidosis after starting low carbohydrate diet for a week.

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KEYWORDS
Low carbohydrate diet; metabolic acidosis; anion gap; dialysis

1. Introduction

Obesity is being increasingly recognized as a global epidemic [1]. According to the World Health Organization (WHO) estimates in 2016, there are 1.6 billion overweight adults and 650 million obese adults [2]. Obesity increases the risk for cardiovascular diseases, diabetes mellitus, hyperlipidemia and some cancers such as of esophagus, colon, breast, endometrium, and kidney. As a result, people are constantly attempting to lose weight and sometimes by trying various diets like low carbohydrate diet. Low carbohydrate diets became popular in the US during the 1960s. Interest has grown recently as a solution for rapid short-term weight loss. However, people start them without consulting a physician or dietitian which can lead to unfavorable effects, of which, ketoacidosis can be life threatening [1]. We present a case of severe metabolic ketoacidosis after a week of low carbohydrate diet.

2. Case description

A 31-year-old man was admitted to our hospital for generalized weakness along with subjective fever, chills, and sore throat. He had acute kidney injury with creatinine 1.55 (reference range: 0.6–1.3 mg/dL) up from baseline of 1 and bicarbonate of 15.4 (reference range: 22.0–27.0 mEq/L) on presentation. His acute kidney injury was suspected to be pre-renal from decreased oral intake. His creatinine (1.32 mg/dL) and bicarbonate (18.1 mEq/L) had improved by next day with hydration and he was discharged. However, he presented to the emergency department the very next day with shortness of breath and palpitations. He denied chest pain, cough or other respiratory symptoms. He denied any alcohol or illicit drug use. He had quit alcohol 7 months back and was on disulfiram for prevention of relapse. He had been smoking a half pack a day for past 10 years. His past medical history included dural vein thrombosis on coumadin, seizure disorder, and bipolar disorder. The patient had dural vein thrombosis at the age of 29. It was in the setting of alcohol intoxication. He was never worked up for hypercoagulability. His home medications included bupropion, buspirone, trazodone, quetiapine, topiramate, disulfiram, and pravastatin. On examination, vital signs revealed a heart rate of 136 beats per minute, blood pressure of 107/78 mm Hg, and respiratory rate of 30 per minute with a saturation of 97% on room air. His BMI was 37.6 kg/m^2. He was somnolent but arousable. The examination was otherwise unremarkable.

Relevant labs included serum bicarbonate of 9.2 mEq/L and an anion gap of 20 mEq/L (corrected anion gap = 20.75) consistent with mixed high and normal anion gap metabolic acidosis (discussed below). Arterial blood gas revealed pH of 7.35, pCO2 of 10 mmHg, pO2 of 120 mmHg and calculated bicarbonate of 5.7 mEq/L. Serum osmolality was 292 mOsm/kg (reference range: 280–290 mOsm/kg). Serum osmolar gap was 11 mOsm/kg (reference range: <10 mOsm/kg). Volatile screen for acetone, isopropanol, methanol, and ethanol was negative. Serum acetaminophen, salicylate, and ethanol levels were negative. The urine drug screen was negative. Urinalysis was unremarkable. Blood glucose was 86 mg/dL (reference range: 70–99 mg/dL), serum ketones were 2+, and serum lactate was 1.4 mEq/L (reference range: 0.5–2.2 mEq/L). Abdominal ultrasound was unremarkable. Hemoglobin A1c was 5.0% (reference range: 4.9–6%). He received IV 150 mEq of 8.4% sodium bicarbonate with 5% dextrose water for 12 hours. Sequential bicarbonate every 3–4 hours was 6.4, 12.8, 10.4 and 14.3 meq/L. Although his bicarbonate levels were steadily rising, the patient underwent

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hemodialysis with concern for ingestion when the volatile compound screen was not back. Post-dialysis, his creatinine was 0.94 mg/dL (reference range: 0.60–1.30 mg/dL), bicarbonate was 26.9 mEq/L, and anion gap was 9 mEq/L. Patient endorsed that his shortness of breath and palpitations had improved, and he felt a lot better.

On further questioning, he mentioned being on a low carbohydrate diet (less than 20 grams of carbohydrate) for the past one week to lose weight. He had only been eating one meal a day. He mentioned that he was compliant for the entire period. Being a non-diabetic, his ketosis was thought to be secondary to fasting, but this degree was unlikely. We think his high anion gap metabolic acidosis was secondary to being on a very low carbohydrate fat diet and that normal anion gap metabolic acidosis was related to chronic topiramate use. His slow improvement in bicarbonate could also be related to topiramate.

3. Discussion

Different low carbohydrate diets such as Atkins Diet, the South Beach Diet, and the Zone Diet have been tried effectively for weight loss [3]. The carbohydrate content in these diets is less than 200 grams per day. In very low carbohydrate diet, carbohydrates are greatly reduced to ≤ 20–50 grams per day with an increase in dietary fats and proteins. These diets are believed to promote weight loss through various mechanisms. High-fat content promotes early satiety [1]. Limitation of choices with low carbohydrate diet decreases appetite [4]. Low carbohydrate diet increases glucagon levels and decreases insulin levels which, in turn, activates phosphoenolpyruvate carboxykinase, fructose 1,6-biphosphatase, and glucose 6-phosphatase that favor gluconeogenesis and inhibits pyruvate kinase, 6-phosphofructo-1-kinase, and glucokinase that slow down the glycolytic pathway [5]. This maintains a steady glucose supply to tissues with an obligatory glucose requirement such as red blood cells and brain [1,3]. There is increased protein turnover to provide amino acids as substrates for glucose production. This requires increased energy expenditure contributing to weight loss [3].

After 3–4 days without carbohydrate consumption, alternate fuel sources such as fatty acid are utilized for ketone bodies formation [6,7]. During well-fed state, fatty acids undergo β-oxidation to produce acetyl CoA which undergoes oxidation to CO2 and H2O in the citric acid cycle. However, during periods of low carbohydrate intake, acetyl CoA is converted to ketone bodies: acetoacetate and 3-hydroxybutyrate. Ketone bodies can regulate their own rate of formation by controlling insulin and glucagon secretion preventing abnormally high levels of ketone bodies [5]. This helps maintain ketonemia without acidemia in patients on low carbohydrate diets [6,7]. There should be no ketoacidosis with ketogenic diet if the

Table 1. Baseline characteristics of cases presenting with anion gap metabolic acidosis on a low carbohydrate diet.

S. N.	Authors \Headings	Age (years)/ Sex	BMI (kg/m^2)	Type/Duration of diet	History	pH/bicarbonate (mmol/L)	Anion gap (mmol/L)	Treatment	Complications
1.	Basnet et al	31/male	37.6	Low carbohydrate, high protein Atkins diet/1 week	Shortness of breath and palpitations	7.35/9.2	20	Intravenous 150 mEq of 8.4% sodium bicarbonate with 5% dextrose and hemodialysis	None
2.	Chen et al	40/female	-	Low carbohydrate, high protein Atkins diet (meat, salad, cheese)/one month	Nausea, vomiting, shortness of breath	7.19/8	26	5% dextrose with 150 mEq/L sodium bicarbonate at a rate of 30 ml/hr	None
3.	Geijer et al	32/female	-	Low carbohydrate diet, less than 20 g per day/ 10 days	Malaise	7.20/-	-	10% glucose infusion @ 125 ml/hr and insulin	None
4.	Shah et al	51/female	21.7	No carbohydrate diet/several months	Vomiting	7.2/-	33	Intravenous fluids and insulin	None
5.	Freeman et al	42/female	25.6	Low carbohydrate, high protein Dukan diet/3 days	Nausea, vomiting	7.21/10	24	Intravenous normal saline	None
6.	Chalasni et al	30/male	27.1	No carbohydrate South Beach diet/3 weeks	Nausea, vomiting and diffuse abdominal pain	7.43/12	21	Intravenous saline infusion and insulin	None

rate of hepatic ketone bodies production is matched by the rate of ketone bodies utilization by tissues [6]. Yancy et al in their study had 27 cases on a low-carbohydrate ketogenic diet for 24 weeks. There was a mild decrease in mean arterial pH from 7.43 at week 0 to 7.40 at week 24 with a small transient decrease in serum bicarbonate along with mild ketosis. There was no noted significant metabolic derangement [8]. Nonetheless, there have been a few documented cases of ketoacidosis in patients on a low carbohydrate diet. All the cases are presented in a table. (Table 1) Out of the 5 cases, 4 were females. They all had a similar presentation with nausea and vomiting [9–13], along with abdominal pain [11–13]. They were treated with intravenous insulin and fluids with a resolution of ketoacidosis and symptoms [9,11–13]. In contrast, our patient presented with shortness of breath and palpitations and had to be dialyzed for correction of acidosis. The diagnosis was based on ketoacidosis in the absence of another identifiable cause. Our patient was also on topiramate which can lead to hyperchloremic non-anion gap metabolic acidosis by increasing HCO3- loss from the gastrointestinal tract and by decreasing H +excretion or HCO3- absorption in the urinary tract [14].

4. Conclusion

Severe ketotic states from low carbohydrate diets may be a potential health hazard and can result in a protracted acidosis as was seen in our case. Given that very low carbohydrate diets have appeared frequently throughout time and have been touted by some to be a treatment for many diseases, physicians caring for patients with protracted acidosis should consider dietary manipulation in the differential of protracted unexplained acidosis.

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Disclosure statement

No potential conflict of interest was reported by the authors.

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