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Case Report

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Intermittent Fasting as a Trigger of Ketoacidosis in a Patient With Stable, Long-term Type 1 Diabetes

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Abstract

Diabetic ketoacidosis (DKA) is an acute complication of type 1 diabetes (T1DM) with a high morbidity and mortality. Diabetic ketoacidosis is usually triggered by metabolic stressors that increase insulin requirements like infection, trauma, surgery, or some medications. Ketogenic diets are nutritional regimes that drastically reduce the intake of carbohydrates in order to increase circulating ketones and reduce appetite. Intermittent fasting diets similarly aim to impact appetite and body weight, but through the restriction of feeding to specific periods of time or days. A 58-year-old woman with T1DM and no prior episodes of DKA since her diagnosis 16 years ago was admitted to the emergency room with severe metabolic acidosis, ketosis, dehydration, and back pain after 9 days of practicing a ketogenic, intermittent fasting diet on the advice of a friend. The standard management of DKA led to the resolution of the symptoms and metabolic alterations, but this might not be the case in other patients. This case highlights the relevance of close professional monitoring of dietary and insulin schemes in patients with T1DM, and of the adequate nutritional education of patients in order to avoid having them follow fashionable dietary trends without knowledge of their implications.

Key Words: intermittent fasting, ketoacidosis, type 1 diabetes

Among the many diets proposed both in popular culture and the medical literature for the management of diabetes, 2 of the most prominent are ketogenic, or "keto" diets, and intermittent fasting diets (IFDs). The main characteristic of ketogenic diets is that of a very low carbohydrate content, which leads to reduced insulin levels and increased lipolysis, beta-oxidation, and production of ketone bodies [1]. While in order to be truly ketogenic the diet must have a markedly low contribution from carbohydrates; the term low-carbohydrate diet encompasses any diet containing less than 130 g/day or 26% of total energy intake from carbohydrates [2]. Intermittent fasting diets also aim to stimulate ketogenesis, but through a different strategy involving the ingestion of any calories but only during certain hours of the day, or certain days of the week [3]. Evidence from animal models and human trials suggests that increased

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plasma ketones may reduce appetite and increase insulin sensitivity, leading to improvements in weight and glycemic levels [4]. Nonetheless, such benefits from ketones have been proven mostly for obesity or type 2 diabetes, not in the context of absolute insulinopenia that characterizes type 1 diabetes (T1DM).

Evidence on the safety and impact of low-carbohydrate diets (including ketogenic diets) among patients with T1DM is limited and of heterogeneous quality [2]. However, due to a flurry of recent reports in the mass media about the potential benefits of a ketogenic diet or IFDs on multiple medical conditions, many individuals have started to practice them on their own, without professional supervision or regards to potential adverse effects. We report the case of a patient with long-standing T1DM who never before had a hyperglycemic crisis requiring hospitalization, but who started a ketogenic, IFD and developed severe diabetic ketoacidosis (DKA).

Case Report

Patient history

A 58-year-old woman diagnosed with T1DM since April 2004 consulted to the Emergency Department of Fundación Santa Fe de Bogotá in Bogotá, Colombia, on January 17, 2020, after 24 hours of progressively increasing general malaise, chills, and lower back pain (10/10). The patient had never experienced any acute or chronic complications of T1DM. At 5:00 AM on the day of consultation, the patient presented with nausea and vomiting. At 9:30 AM her capillary blood glucose was 348 mg/dL; the PATIENT injected a 6-unit dose of insulin lispro and tried to rehydrate herself by drinking a bottle of water and a bowl of soup, but 3 hours later her capillary glucose was still 373 mg/dL, at which time the patient decided to attend the ER.

On admission, the patient reported having started an intermittent fasting, ketogenic diet on the advice of a friend since 9 days before, with the aim of losing some weight and improving her glycemic control. She had personally changed her insulin scheme from insulin degludec 20 UI in the morning plus lispro insulin 1–8 units with each meal, according to carbohydrate counting, to a single shot of 17 UI degludec in the morning with very little or no rapid-action insulin before meals. During the intermittent fasting, ketogenic diet, the patient omitted breakfast every day and had a lunch that included only meat, poultry, or fish, a vegetable salad, and a glass of water at about 1:00 PM. Her afternoon snack included unsweetened coffee and approximately 30 g of nuts (peanuts, walnuts, or other), and her last meal (at about 7:00 PM) was pretty much identical to her lunch. Over these 9 days the patient constantly wore a flash-continuous glucose monitoring sensor (FreeStyle Libre, Abbott Diagnostics, Lake Forest, IL). During the first 2 days of the diet, her glycemic levels were within the target range (70–140 mg/dL) 100% of the time, and the patient injected herself with 0.1–1.5 UI of lispro insulin with her 7:00 PM meal. However, on the night of the second day of the diet, Continuous Glucose Monitoring (CGM) readings ranged between 50 and 60 mg/dL for 3 hours (10:00 PM to 1:00 AM). The patient thought that this could be due to the small dose of lispro with her evening meal and decided to suspend rapid action insulin altogether. For the next 5 days, her CGM readings were within the target range 95% to 97% of the time. On day 8 of the diet, the patient presented with a hyperglycemic excursion reaching a peak of 238 mg/dL, 1 hour after lunch. The patient administered herself a 6.5 UI correction dose of insulin lispro and her glycemia returned to the target range 1 hour later. Her glycemic levels started to surge again around 7:00 PM that same day, reaching 348 mg/dL the next morning (day 9), as referred above. During these 9 days, the patient was entirely asymptomatic. The patient denied any respiratory, urinary, or gastrointestinal symptoms, or behavioral changes. Her body mass index was 24.4 Kg/m^2, and she was afebrile but had grade II dehydration. Laboratory values were HbA1c 8.26%, plasma glucose 396 mg/dL, urinary ketones 150 mg/dL, glycosuria > 300 mg/dL, pH 7.23, pCO_2 21 mmHg, bicarbonate 8.8 mEq/L, base excess -18.8 mEq/L, and lactate 1.9 mmol/L; renal function, plasma electrolytes, amylase, EKG, chest X-ray, and abdominal ultrasound were all normal. The patient was diagnosed with DKA and management was promptly begun.

Management and outcome

The patient received fluid replacement with saline, insulin infusion at 0.125 UI/Kg/h, and potassium replacement, with good clinical response and normalization of arterial gases and pH. The next day, insulin infusion was suspended and the patient started oral nutrition and a basal/bolus insulin scheme with good tolerance and maintenance of glycemic range goals. The patient was discharged with strict instructions to consult with her attending physician regarding any modifications to her diet or insulin regime. Despite some initial hyperglycemia after her discharge, she quickly achieved good glycemic control (Fig. 1).

Discussion

Type 1 diabetes is a very serious disease, and DKA is an acute, life-threatening complication that should be avoided to the largest possible extent. Usual triggers for DKA are

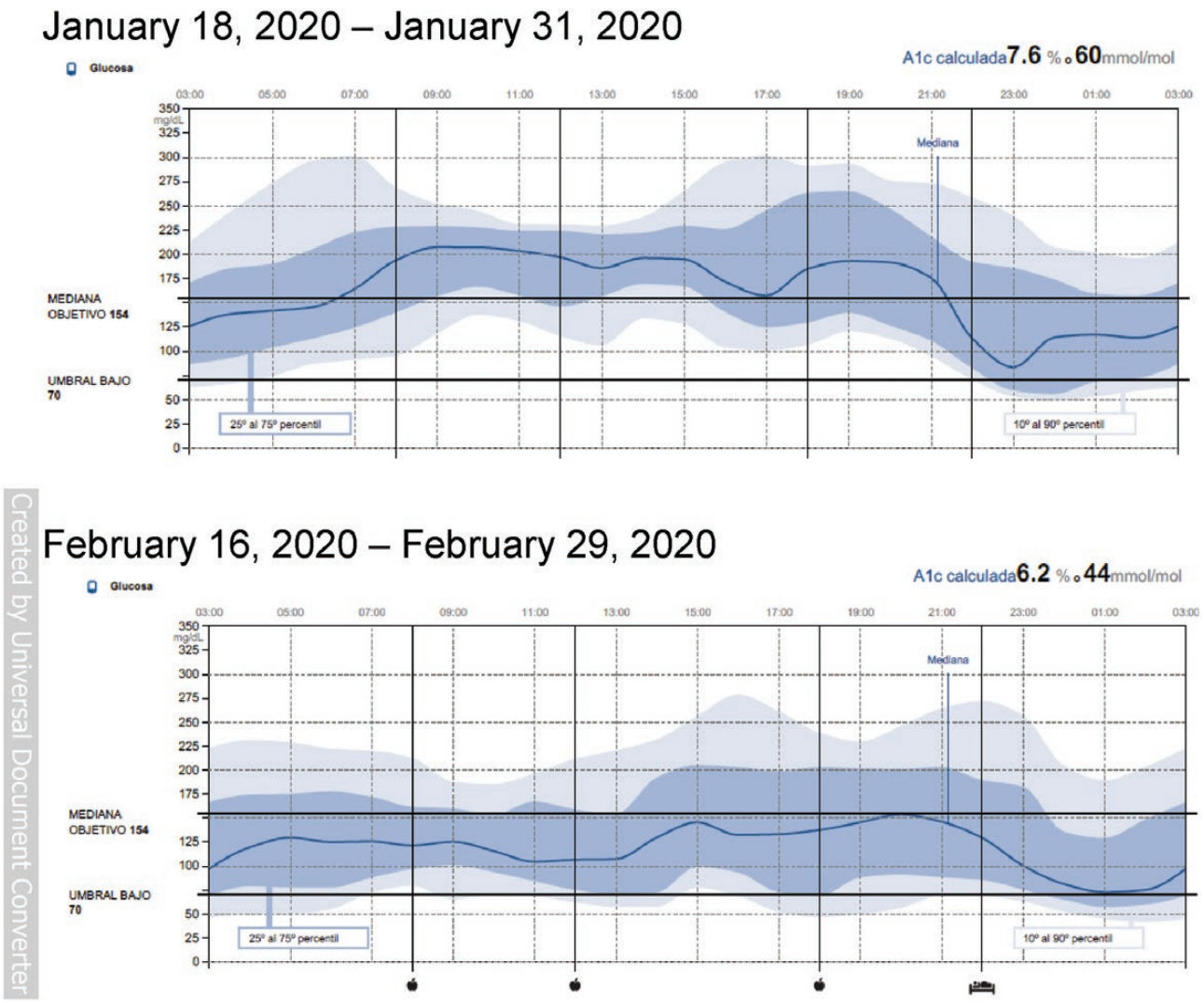

Figure 1. Twenty-four hour glycemic profile of the patient during the 2 weeks immediately after her ketoacidosis (top) and 1 month after admission (bottom).

infection, trauma, surgery, or other metabolic stressors [5], but DKA may also be provoked by omission of insulin doses or by a mismatch between the dynamic physiological demands for insulin and the amount provided by medical treatment. Insufficient insulin provision causes derepression of hormone-sensitive lipase, release of free fatty acids from adipose tissue, and a saturation of hepatic capacity for the beta-oxidation of fatty acids, leading to deregulated ketogenesis [6].

Many patients with T1DM may feel tempted to start a ketogenic or intermittent fasting diet out of legitimate concerns for increased weight gain or metabolic syndrome with insulin-only treatment [7]. However, this case illustrates the risks involved in starting a fashionable diet without proper advice or supervision. For example, in part due to their training in carbohydrate counting, many patients with T1DM mistakenly think that a meal with minimal carbohydrate content means that no prandial insulin is needed. A systematic review concluded that the fat and protein content of meals does affect postprandial glycemic excursions and prandial insulin requirements in T1DM [8]. Our case also highlights the importance of urine ketone tests or blood ketone tests for patients with T1DM, as these could opportunely alert patients about increased ketosis before the onset of full-blown DKA.

Evidence for the use of ketogenic diets in T1DM includes only 2 clinical trials: one a feasibility trial including 10 patients in New Zealand [9] and the other a crossover study, also of 10 patients, in which carbohydrate intake in the low-carbohydrate phase was actually 39% of total energy intake [10]. Concerning IFD, a recent 1-group trial in Muslim patients with T1DM who experienced intermittent fasting periods because of Ramadan showed that if performed under close medical surveillance, including

continuous glucose monitoring, dietary education, and frequent contact, this type of diet might be safely practiced by patients with T1DM [11]. However, the recent appearance of widely publicized reports both in the scientific [12] and lay press [13] has led to an exponential increase in the popularity of IFD, and many T1DM patients may attempt to start them without proper professional counseling or follow-up.

Upon starting her new diet, our patient continued her basal insulin and initially used a small dose of prandial insulin in her evening meal, but when she noticed low blood glucose during the late night/early morning hours, she decided to suspend all prandial insulin. Then, the enhanced ketosis from both a ketogenic diet and an insufficient suppression of ketosis by exogenous insulin, precipitated DKA. The onset of DKA was somewhat delayed relative to the start date of the diet and insulin changes, probably because of the long half-life of degludec. This may be a common situation for patients with T1D who embark on a ketogenic/intermittent fasting diet: the diet provides so little carbohydrate and imparts such prolonged periods of fasting that the use of an insulin dose that would be sufficient for complete suppression of ketogenesis in a T1DM patient may result in hypoglycemia. On the other hand, the omission of insulin reduces risk of hypoglycemia but may precipitate DKA, especially with such a diet. The patient is then walking a very thin line between DKA and hypoglycemia.

Conclusion

We report the case of a patient with long-standing T1DM who never before had a hyperglycemic crisis requiring hospitalization, but who started a ketogenic, IFD and developed severe DKA. This case highlights the key importance of instructing patients with T1DM to consult with a qualified health professional before undertaking any drastic changes to their diet or insulin treatment.

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Additional Information

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