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CASE REPORT

Diabetic Ketoacidosis and Acute Mountain Sickness: Case Report and Review of Treatment Options in Type 1 Diabetes Mellitus

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A 30-year-old man with a 20-year history of well-controlled type 1 diabetes mellitus and no microvascular complications traveled from near sea level to an altitude of 3000 m within 6 hours. At altitude, his blood glucose levels began to rise, necessitating increased insulin delivery. Typical symptoms of acute mountain sickness (AMS) developed, and he became increasingly hyperglycemic and unwell. Upon presentation to an emergency clinic, diabetic ketoacidosis (DKA) was diagnosed and was managed with insulin, intravenous fluids with potassium, and acetazolamide orally. No other potential causes for diabetic ketoacidosis were identified. Hyperglycemia, ketosis, and acidosis resolved with treatment as expected, but an increased insulin requirement was noted for the next 48 hours, until returning to expected levels when acetazolamide was discontinued. This case describes an episode of mild diabetic ketoacidosis potentially precipitated by moderate to severe acute mountain sickness, and an apparent hyperglycemic effect of acetazolamide. Individuals with type 1 diabetes traveling to altitude and their physicians should be vigilant for this complication and should be aware of the effects of conventional first-line therapies for acute mountain sickness on insulin requirement, glycemic control, and preexisting microvascular diabetes complications.

Key words: diabetic ketoacidosis, DKA, acute mountain sickness, AMS, type 1 diabetes mellitus, T1DM, acetazolamide, dexamethasone

Introduction

Unacclimatized individuals who travel to altitudes of more than 2500 m in a single day are at risk of having acute mountain sickness (AMS).[1] Descent of 300 m to 1000 m is considered to be the single best treatment for AMS; however, treatment options such as supplemental oxygen therapy, the carbonic anhydrase inhibitor acetazolamide, or the synthetic glucocorticoid dexamethasone (both administered orally) are more usually used as first-line treatment. Individuals with type 1 diabetes mellitus require exogenous insulin, delivered either by multiple daily subcutaneous injections or continuous subcutaneous infusion through an insulin pump. The insulin dose or delivery rate is adjusted to maintain blood glucose at near-normal levels.[2] An increased requirement for insulin with increasing altitude is recognized among some individuals with type 1 diabetes.[3]

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Diabetic ketoacidosis (DKA) is a life-threatening complication of type 1 diabetes that occurs when insufficient insulin is delivered, requiring prompt administration of insulin, fluids, and electrolytes to restore normal metabolism.[4] There are few reports of DKA due to AMS in the literature, possibly reflecting the reluctance of those with diabetes to travel to such locations. Recent advances that facilitate optimized glycemic self-management in type 1 diabetes such as insulin pumps and continuous glucose monitors (reviewed by DeSalvo and Buckingham[5]) have led to an increasing number of individuals with type 1 diabetes traveling to altitude, often in remote locations. A thorough understanding of the optimum treatment of DKA due to AMS is, therefore, an essential goal. Metabolic decompensation (hyperglycemia) and increased insulin requirement is almost universally observed when supraphysiological doses of glucocorticoids are administered to patients with type 1 diabetes.[6] As there have been no randomized, placebo-controlled studies, the effects of acetazolamide on insulin

requirement and glycemic control of type 1 diabetes is less clear.

Here, I describe a case of DKA potentially due to severe AMS precipitated by rapid ascent to moderate altitude, and the subsequent effects of treatment with acetazolamide on insulin requirement. The potential adverse effects of conventional treatments for AMS are reviewed. On account of these potential adverse effects, alongside the morbidity and mortality associated with DKA, descent from altitude may be a safer alternative when DKA is precipitated by AMS in individuals with type 1 diabetes.

Case Presentation

A 30-year-old man traveled from his home in Los Angeles, California (elevation 236 m [774 ft]), to Breckenridge, Colorado (elevation 2926 m [9600 ft]), above sea level over the course of 6 hours with no acclimatization. He had been diagnosed with type 1 diabetes at the age of 8 years and had maintained good glycemic control (hemoglobin A1C 48 to 53 mmol/mol [6.5% to 7%] over the past 12 months). In the 21 years he had type 1 diabetes, he had 3 hospital admissions with severe hypoglycemia (last episode 18 months earlier) and 3 previous episodes of DKA (last episode 3 years earlier), all with a clear precipitant. There was no evidence of microvascular or macrovascular complications. Insulin (lispro) was delivered via an insulin pump, and glycemia monitored using a continuous glucose monitor. Regular adjustments of insulin delivery allowed maintenance of blood glucose within a narrow range. He reported no symptoms suggestive of intercurrent illness during the week before travel and the week after this episode. Comorbidities included mild hypertension (treated with amlodipine, 2.5 mg daily) and post-traumatic stress disorder (treated with sertraline, 25 mg daily). He denied the use of any over-the-counter medication or supplements, and he had no known drug allergies. He reported no prior episodes of AMS.

Six hours after arriving at altitude, he developed mild generalized weakness, dizziness, nausea, frontal headache, and he was unable to sleep (Lake Louise Score = 9).[7] Blood glucose level was persistently elevated at 240 mg/dL (13.3mmol/L) in spite of an increased basal insulin infusion rate (150%) and two 3-unit correction boluses. His symptoms worsened, vomiting ensued, and he sought medical attention.

At the local primary care medical center (elevation approximately 3000 m [9800 ft]), the patient's blood pH was acidic, whole blood glucose was elevated at 350 mg/dL (19.5 mmol/L), and capillary beta hydroxybutyrate (ketone) was 1.4 mmol/L, indicating moderate ketoacidosis. Increased basal insulin infusion rate with 3 to 4 hourly correction boluses were continued. Three liters intravenous normal saline with potassium (40 mmol KCl/L) was administered over 4 hours. Intravenous antiemetic (ondansetron, 4 mg) was given, and oral acetazolamide, 125 mg twice daily, was begun. Within 90 minutes of beginning treatment, his blood glucose level was 250 mg/dL (13.9 mmol/L) and continued to fall. Ketones fell to 1.2 mmol/L, indicating resolving DKA. Once the intravenous fluid was completed, the patient's symptoms were significantly improved, and he was discharged.

Acetazolamide was continued for 48 hours during which time an increased basal insulin infusion rate of 130% was required to maintain the patient's between-meal euglycemia, and correction doses were required to prevent postprandial hyperglycemia. Symptoms of AMS completely resolved within 24 hours of presentation. When the acetazolamide was discontinued, his blood glucose level tended to fall toward the hypoglycemic range, necessitating a reduction in the basal infusion rate back to normal levels, and no more correction boluses were needed. Basal, mealtime bolus, and total daily insulin dose, shown in Figure 1, demonstrate increases in both basal and mealtime bolus dose requirements while acetazolamide was used. The drop in insulin requirement, from 130% of normal back to baseline levels, on discontinuation of acetazolamide was abrupt.

Discussion

Acute mountain sickness is a risk when travel to altitudes higher than 2500 m is undertaken, and predicting who will be affected is difficult.[1] A number of researchers have reported no difference in the incidence of AMS between healthy climbers and climbers with type 1

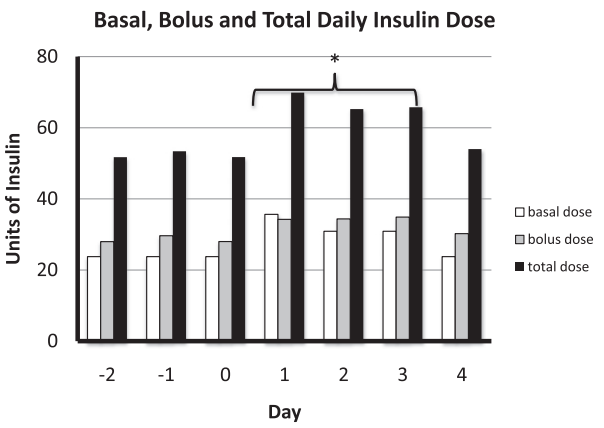

Figure 1. Total daily basal insulin dose (open bars), total daily bolus insulin dose (shaded bars), and total daily insulin dose (solid bars). Day 0 indicates travel day. *Indicates significantly increased insulin requirement on days 1 to 3 compared with other days ($P < .05$).