

PROFOUND HYPOKALEMIA IN DIABETIC KETOACIDOSIS: A THERAPEUTIC CHALLENGE

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ABSTRACT

Objective: To describe profound hypokalemia in a comatose patient with diabetic ketoacidosis.

Methods: We present a case report, review the mechanisms for the occurrence of hypokalemia in diabetic ketoacidosis, and discuss its management in the setting of hyperglycemia and hyperosmolality.

Results: A 22-year-old woman with a history of type 1 diabetes mellitus was admitted in a comatose state. Laboratory tests revealed a blood glucose level of 747 mg/dL, serum potassium of 1.9 mEq/L, pH of 6.8, and calculated effective serum osmolality of 320 mOsm/kg. She was intubated and resuscitated with intravenously administered fluids. Intravenous administration of vasopressors was necessary for stabilization of the blood pressure. Intravenous infusion of insulin was initiated to control the hyperglycemia, and repletion of total body potassium stores was undertaken. A total of 660 mEq of potassium was administered intravenously during the first 12.5 hours. Despite such aggressive initial repletion of potassium, the patient required 40 to 80 mEq of potassium daily for the next 8 days to increase the serum potassium concentration to normal.

Conclusion: Profound hypokalemia, an uncommon initial manifestation in patients with diabetic ketoacidosis, is indicative of severe total body potassium deficiency. Under such circumstances, aggressive potassium repletion in a comatose patient must be undertaken during correction of other metabolic abnormalities, including hyperglycemia and hyperosmolality. Intravenously administered insulin should be withheld until the serum potassium concentration is ≥ 3.3 mEq/L. (**Endocr Pract.** 2005;11:331-334)

Abbreviation:

ADA = American Diabetes Association

INTRODUCTION

Patients in diabetic ketoacidosis typically have total body potassium deficits of 3 to 5 mEq/kg (1-3). Despite this negative potassium balance, they usually present with hyperkalemia or normokalemia because of the movement of potassium from the intracellular space to the extracellular space, attributable to insulinopenia and hyperosmolality of the extracellular fluid (4). Hypokalemia (serum potassium level <3.5 mEq/L), however, has been known for years to occur in 3% to 4% of all cases of diabetic ketoacidosis (4-7). Recently, we saw a comatose young woman in diabetic ketoacidosis, who had severe hyperosmolality and profound hypokalemia (defined by us as a serum potassium concentration <2.5 mEq/L) at presentation. We discuss the management of profound hypokalemia in the setting of coma and severe hyperosmolality.

CASE REPORT

A 22-year-old white woman with a 3-year history of type 1 diabetes mellitus was taken to a local emergency department after being found unresponsive. On general physical examination, she was obtunded, with a body temperature of 36.1°C, height of 183 cm, weight of 67.9 kg, heart rate of 115 beats/min, and blood pressure of 110/75 mm Hg. She had good air entry into her lungs bilaterally, normal heart sounds without murmurs or rubs, and no pedal edema. On neurologic examination, she was responsive only to deep painful stimuli. Electrocardiography performed in the emergency department revealed sinus tachycardia with no U waves. The blood glucose level in the emergency department was >700 mg/dL.

Results of the first series of laboratory studies were as follows: blood glucose 747 mg/dL, calculated effective serum osmolality 320 mOsm/kg, arterial pH 6.8, measured Paco_2 8 mm Hg, calculated Paco_2 28 mm Hg, PaO_2 141

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mm Hg, sodium 139 mEq/L, potassium 1.9 mEq/L, chloride 120 mEq/L, total CO₂ 5 mEq/L, blood urea nitrogen 13 mg/dL, serum creatinine 0.7 mg/dL, and serum albumin 2.0 g/dL. Urinalysis revealed pH 5, specific gravity 1.013, 2+ glucose, 3+ ketones, and 1+ protein.

The patient received an initial intravenous infusion of 2 L of isotonic saline during a period of 60 minutes. Thereafter, isotonic saline with 20 mEq of potassium chloride per liter was infused at a rate of 200 mL/h. One ampule of sodium bicarbonate was administered at the local hospital because of the blood pH of 6.8 (1-3). A continuous intravenous infusion of insulin also was initiated at a rate of 0.1 U/kg per hour after administration of an initial bolus of 20 U. Because of the severe mental obtundation, she was intubated for airway protection and transferred to Tufts-New England Medical Center for further management.

On arrival of the patient at our institution approximately 4 hours after her initial presentation, intravenous administration of norepinephrine was initiated because of a systolic blood pressure of 80 to 90 mm Hg. She remained unconscious. Blood chemistry studies at our institution (5 hours after the first laboratory tests) showed the following: blood glucose 672 mg/dL, calculated effective serum osmolality 313 mOsm/kg, arterial blood gas results (with the patient breathing 100% O₂) of pH 6.8, Paco₂ 46 mm Hg, Pao₂ 549 mm Hg, and calculated total CO₂ 8 mEq/L (and repeated blood gas analysis approximately 1 hour later revealing a pH of 7.09, Paco₂ 24 mm

Hg, Pao₂ 519 mm Hg, and calculated total CO₂ 8 mEq/L), serum sodium 138 mEq/L, potassium 2.0 mEq/L, total CO₂ 10 mEq/L, serum calcium 7.1 mg/dL, serum phosphorus 1.7 mg/dL, serum magnesium 1.4 mg/dL, blood urea nitrogen 25 mg/dL, and serum creatinine 1.4 mg/dL.

The saline infusion was increased to 700 mL/h. During the next 8 hours, the patient received 6.5 L of isotonic saline. She also received approximately 400 mEq of sodium bicarbonate during the first 24 hours. Intravenous infusion of insulin was maintained at 0.1 U/kg per hour (see Discussion). Her profound hypokalemia proved a challenge to replete. A constant dose of potassium of 40 mEq/h was supplemented by additional boluses based on hourly serum potassium measurements. The course of her electrolyte imbalance and the sequential amounts of potassium infused, primarily through a central venous catheter, are shown in Table 1.

Despite the aggressive initial replacement with 660 mEq of potassium during the first 12.5 hours, a daily supplementation of 40 to 80 mEq intravenously was necessary for the next 8 days to maintain the serum potassium level at 3.5 to 4.0 mEq/L. The serum magnesium and phosphorus concentrations were returned to normal during the next 2 to 3 days. The patient began following commands by day 2 but became agitated on day 3 (coincident with a temperature elevation to 38.9°C) and needed intravenous sedation. She was subsequently extubated on day 5. Nonoliguric acute renal failure developed in conjunction with an increase in serum creatinine level to a peak of

Table 1
Hourly Laboratory Data and Potassium Repletion
During the First 12.5 Hours After Admission of Study Patient*

Hospital day (T-NEMC)	Time†	Glucose (mg/dL)	Effective serum osmolality (mOsm/kg)	Total CO ₂ (mEq/L)	Potassium (mEq/L)	Total amount of potassium infused (mEq)
1	1725	672	313	10	2.0	440 in 5.5 hours
	1850	550	317	10	2.7	
	2015	493	301	8	3.4	
	2150	479	304	8	2.9	
	2245	455	327	7	3.1	
2	0015	417	329	7	2.7	220 in ~7 hours
	0120	396	324	8	3.1	
	0230	368	324	8	2.7	
	0315	371	321	9	2.8	
	0441	347	325	8	3.7	
	0530	349	321	9	3.3	

*T-NEMC = Tufts-New England Medical Center.

†Shown in 24-hour system.

2.5 mg/dL on hospital day 2 attributable to acute tubular necrosis (diagnosed on the basis of urine sediment examination). The serum creatinine concentration gradually declined to 0.8 mg/dL on hospital day 5. The patient was dismissed from the hospital on day 17.

During the patient's hospitalization, interviews with friends revealed that she had been extremely noncompliant with administration of insulin and had not taken it at all for several weeks before hospitalization. The patient also had been diagnosed with bulimia as a teenager and used laxatives occasionally for alleged constipation.

DISCUSSION

Diabetic ketoacidosis is a common illness in patients with type 1 diabetes mellitus. Despite advances in clinical medicine, the mortality rate associated with severe diabetic ketoacidosis remains at 5% to 10%, depending on the degree of volume depletion, presence or absence of coma, and age of the patient (1,2,8,9). It is accompanied by several metabolic abnormalities beyond alterations in glucose metabolism and accelerated ketogenesis. The detailed recommendations by the American Diabetes Association (ADA) regarding overall management (intravenous administration of fluids, insulin, potassium, phosphate, and bicarbonate) of adult patients with diabetic ketoacidosis are clearly presented in recent publications (1,2). We focus here on the metabolic issues underlying potassium imbalance in the unusual patient with diabetic ketoacidosis, coma, severe hyperosmolality, and profound hypokalemia.

The total body content of potassium in normal adults is approximately 50 mEq/kg body weight (10). The vast majority of total body potassium (approximately 98%) is contained in the intracellular space. One of the most commonly used methods in estimating total body potassium has been the measurement of total exchangeable potassium. Early studies showed that exchangeable potassium was approximately 25% lower in adult patients with diabetes mellitus than in normal control subjects, irrespective of hyperglycemia and glucosuria (11).

Studies of patients with diabetic ketoacidosis have shown that the serum potassium concentration at presenta-

tion is either normal or high in more than 95% of cases (4-6). Hypokalemia at the time of initial assessment of patients with diabetic ketoacidosis is an uncommon complication, occurring in <5% of patients, and results from a combination of factors (4-7,12). The most important cause is kaliuresis from prolonged glucosuria and osmotic diuresis. Kaliuresis also is driven by secondary hyperaldosteronism from profound losses of sodium and extracellular volume but continued delivery of sodium to the distal nephron because of the osmotic diuresis. Profound hypokalemia (serum potassium level <2.5 mEq/L) in diabetic ketoacidosis is extremely rare. Its occurrence indicates severe total body potassium depletion. The total body potassium deficit in diabetic ketoacidosis can reach 10 mEq/kg (1-3), and it is likely at its maximum in patients with a serum potassium concentration <2.5 mEq/L. In the literature, we found only 3 well-documented cases of diabetic ketoacidosis with associated profound hypokalemia (7,13,14) (Table 2). Young or adolescent patients with diabetic ketoacidosis frequently have an underlying eating disorder or noncompliance with administration of insulin (or both), and severe hypokalemia is likely to be more common in this setting (1,2,15). Moreover, administration of insulin and the β_2 -adrenergic agonist norepinephrine, as was done in the current case, can further decrease serum potassium levels. In fact, the ADA strongly recommends increasing the serum potassium concentration to ≥ 3.3 mEq/L before initiation of insulin therapy because the decline in blood glucose level may lead to movement of fluid out of the extracellular fluid compartment and may cause hypotension (1,2).

Severe hypokalemia is associated with undesirable consequences including cardiac arrhythmias, such as ventricular tachycardia and fibrillation from increased automaticity, and respiratory failure from neuromuscular weakness. In general, the recommended rate of intravenous administration of potassium is 10 to 20 mEq/h in patients with mild to moderate hypokalemia (1,2,16). In our patient, we estimated the minimal total body potassium deficit as 10 mEq/kg or ~ 680 mEq (weight \times maximal observed deficit in the literature of 10 mEq/kg). The potassium deficit was repleted at an initial rate of ~ 40 mEq/h, with additional supplementation of 10 to 40 mEq each

Table 2
Profound Hypokalemia in Diabetic Ketoacidosis: Summary of Published Cases

Reference	Case	Age (yr) and sex	Glucose (mg/dL)	Potassium (mEq/L)	Total CO ₂ (mEq/L)	pH
Abramson & Arky (7)	1	42 M	2,030	2.3	13.0	7.31
Manzano & Kozak (13)	2	51 F	900	2.0	2.0	7.14
Leventhal & Goldman (14)	3	15 F	420	2.2	5.5	...

hour based on hourly measurement. A total of 440 mEq of potassium was administered as both potassium chloride (290 mEq) and potassium phosphate (150 mEq) during the first 5.5 hours at our institution (Table 1), in accordance with the ADA recommendations (1,2). After the first 5.5 hours of aggressive potassium repletion, we decreased the rate to 20 to 30 mEq/h. Typical patients with hypokalemia have required a mean of 5 days for return of their serum potassium levels to normal (12,13). Our patient required a daily supplementation of potassium of 40 to 80 mEq for 8 days to maintain normal levels.

In unusual patients such as ours, the risks of worsening hypokalemia by administration of insulin need to be balanced against the benefits of reducing blood glucose levels and plasma osmolality, thereby ultimately leading to improved mentation. Coadministration of large amounts of potassium (Table 1) and insulin allowed correction of both metabolic defects during a period of 24 to 48 hours. In profound hypokalemia, as in our patient, aggressive potassium repletion at rates substantially greater than the usual recommended rate of 10 to 20 mEq/h may be necessary until the serum potassium level increases to >3.0 to 3.3 mEq/L (16,17). Such rapid administration of potassium is potentially dangerous and necessitates continuous electrocardiographic monitoring and measurement of serum potassium levels hourly.

CONCLUSION

Profound hypokalemia (serum potassium levels <2.5 mEq/L) at presentation of patients with diabetic ketoacidosis is a life-threatening condition that remains a therapeutic challenge, particularly in a comatose patient with severe hyperglycemia. Treatment must be directed at infusing potassium in amounts and rates arguably greater than in any other clinical setting, withholding intravenously administered insulin until the serum potassium is at least 3.3 mEq/L, and subsequently correcting the hyperglycemia with insulin for restoration of normal mentation.

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