A Case of Diabetic Ketoacidosis with Refractory Metabolic Acidosis Successfully Treated with Continuous Hemodiafiltration

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Diabetic ketoacidosis (DKA) is a complex medical disorder characterized by abnormalities in electrolyte, acid-base, and volume status. Metabolic acidosis in mild and moderate DKA is corrected with insulin therapy. Bicarbonate therapy may be indicated in cases of severe metabolic acidosis, however the use of bicarbonate in severe DKA is controversial due to a lack of prospective randomized studies. Renal replacement therapy can be used for correction of systemic acidemia. Continuous renal replacement therapy (CRRT) is used in patients who are too hemodynamically unstable to tolerate conventional hemodialysis, but has also been used in treatment of patients with severe DKA. CRRT has never been used previously in DKA patients with refractory metabolic acidosis in Korea. Here, we describe the successful treatment of a DKA patient with refractory metabolic acidosis with CRRT.

Key Words: Diabetic ketoacidosis, Hemodiafiltration, Renal replacement therapy

Introduction

Diabetic ketoacidosis (DKA) is a serious, life-threatening complication of diabetes that occurs when large amount of ketones are released into the blood. Ketones are cleared within hours if insulin is given in sufficient doses, but clearance of ketones may lag because of conversion of β-hydroxybutyrate to acetoacetate as the acidosis resolves. The correction of acidosis with bicarbonate administration in the treatment of patients with DKA is controversial. On rare occasions, dialysis may be required to treat acidosis associated with renal failure. Although CRRT was previously performed to treat DKA patients with refractory metabolic acidosis, there is few case report of CRRT used for DKA in Korea. Here, we report a case of DKA with refractory metabolic acidosis that was successfully treated with CRRT.

Case Report

A comatose 26-year-old Korean woman was admitted to our hospital with respiratory insufficiency. She had no significant medical or surgical history, but had lost 20 kilograms of weight with diet and exercise in 3 years. She had a family history of type 2 diabetes mellitus. The patient began to complain of nausea and abdominal discomfort two days prior to admission. On arrival, her level of consciousness was E1V2M3 on the Glasgow coma scale. She had a temperature of 36°C, pulse rate of 114 beat/min, blood pressure of 78/41 mmHg, and respiratory rate of 44/min. Initial arterial blood gas analysis showed severe metabolic acidosis (pH = 6.800, pCO₂ = 12.0 mmHg, pO₂ = 145.0 mmHg, HCO₃⁻ = 0 mmol/L, and anion gap = 34 mEq/L). Her serum glucose and hemoglobin A1c levels were 667 mg/dL and 15.8%, respectively. Urinalysis showed glycosuria and strong positivity for ketonuria. Other laboratory studies produced the following results: serum osmolality, 332 mOsm/kg; serum sodium, 136 mEq/L; serum potassium, 3.8 mEq/L; serum calcium, 7.6 mg/dL; serum phosphate, 6.1 mg/dL; serum chloride, 101 mEq/L; lactate acid 0.8 mmol/L; ketone body, 9935.0 umol/L; serum myoglobin, 114.0 ng/mL; serum lactate dehydrogenase, 273 IU/L; serum creatine phosphokinase, 38 U/L; serum amylase, 207 U/L; serum lipase, 800 U/L. Blood urea nitrogen...
was 31 mg/dL (normal: 8–20 mg/dL) and serum creatinine 0.8 mg/dL (normal: 0.6–1.2 mg/dL). Urinary concentrations of sodium, potassium, chloride were 20 mEq/L, 19.5 mEq/L, and 11 mEq/L, respectively. Urine osmolality was 429 mOsm/kg. Her chest radiography and brain computed tomography appeared normal. Anti-glutamic acid decarboxylase (GAD), antibody (Ab) titer, anti-IA-2 Ab, and anti-insulin Ab were absent, but anti-islet cell Ab was positive.

Upon the diagnosis of DKA, insulin was infused at 6–10 U/h and isotonic saline was given at 1000 mL/h for two hours. Even though fluid replacement with half saline was continued, the patient’s metabolic acidosis did not improve. Thus, we administered sodium bicarbonate 250 mEq and continued the infusion of intravenous insulin. The patient’s central venous pressure was 11–13 mmH2O, urine output was 50–250 mL/h, and echocardiography showed good left ventricular systolic function without pulmonary hypertension. After twelve hours of treatment, we started norepinephrine (80 mg, mixed with 5% dextrose 500 mL, 30 mL/hour) and dopamine (1600 mg, mixed with dextrose saline, 5 mL/hour) because her blood pressure had remained low (<80/60 mmHg). However, arterial blood pH remained as low as 6.9.

Therefore, we started continuous veno-venous hemodialfiltration (CVVHDF) using the Prismaflex® system (Gambro Lundia AB, Sweden) on the first day of admission at the following settings: blood flow, 150 mL/min; replacement volume, 700 mL/h; and dialysate, 1700 mL/h. The total amounts of fluid were 7410 mL and intravenous insulin were 50 IU just before CVVHDF.

The patient’s metabolic acidosis was corrected 90 hours after the initiation of CVVHDF (Fig. 1). Arterial blood pH already increased above 7.3 and urine output and serum creatinine were maintained within the normal range. As soon as CVVHDF was stopped, however, arterial pH decreased rapidly despite insulin therapy and high anion gap metabolic acidosis and low levels of bicarbonate lasted for several days. Accordingly we continued CVVHDF. On the fourth day of dialysis, the bicarbonate level was higher than 15 mmol/L with a gradual stabilization of the blood pressure.

On day 4, the patient regained consciousness and on day 6, we stopped CVVHDF. After supportive care, the patient was discharged from the ICU on day 7.

**Discussion**

DKA is one of the most common and serious acute complications of diabetes, and is characterized by abnormalities in electrolyte, acid-base, and volume status. In Western countries, the annual incidence rate of DKA estimated from population-based studies ranges from 4.6-8.0 episodes per 1000 diabetic patients. The incidence of DKA increased seven-fold in Korea between 1982 and 2002\(^3\). The mortality rate for diabetic emergencies associated with mixed states of ketoacidosis and hyperosmolality is considerably higher than that with DKA alone\(^5\). Therefore, our patient was at high risk of mortality because of refractory acidosis, higher levels of serum osmolality, and comatose consciousness.

Insulin deficiencies and elevated levels of counter-regulatory hormones stimulate lipolysis and inhibit lipogenesis, resulting in the conversion of abundant free fatty acid to ketone bodies\(^6\). Thus, insulin treatment is a cornerstone of the management of DKA. Bicarbonate therapy in patients with DKA remains controversial, but may be considered for the treatment of patients who exhibit marked decreases in their levels of consciousness or advanced renal dysfunction\(^7\). In our case, the patient was comatose on arrival, and her plasma pH did not improve despite insulin therapy. Severe acidemia may be associated with decreased cardiac contractility\(^8\), diminished responses to endogenous and administered cate-
cholamines, and predisposition to cardiac arrhythmias\(^8\), all of which may contribute to hemodynamic instability. The hypotension observed in our case might have been caused by refractory acidosis. However, there is no standard treatment for DKA in patients with refractory metabolic acidosis.

Renal replacement therapy can be used to correct systemic acidemia. Continuous renal replacement therapy (CRRT) has been used to treat patients who are too hemodynamically unstable to tolerate hemodialysis. Kawata et al\(^2\) reported that a DKA patient with refractory metabolic acidosis was treated successfully with CRRT\(^2\). In our case, the patient had refractory metabolic acidosis and hypotension, and the acidosis was reversed after CRRT without any complications, such as cerebral edema or pulmonary edema. Therefore, CRRT was also effective in treatment of the DKA patient with refractory metabolic acidosis.

In summary, we report a case of refractory acidosis associated with DKA and hyperosmolality. The patient improved following treatment with CVVHDF and appropriate supportive care. Renal replacement therapy is one of the treatment options for patients with refractory acidosis associated with DKA.

REFERENCES