

## Diagnosis and Management of Diabetic Ketoacidosis in Adults

Baligh Ramzi Yehia, MD

Kelly C. Epps, MD

Sherita Hill Golden, MD, MHS

A 38-year-old African American man with a history of type 1 diabetes, hypertension, and chronic kidney disease presented to the emergency department complaining of polyuria, polydipsia, and generalized weakness. He had not taken insulin in 2 days because he could not afford to refill his medications. The patient was afebrile with a blood pressure of 107/63 mm Hg, heart rate of 97 bpm, and respiratory rate of 25 breaths/min. Physical examination demonstrated a drowsy individual with dry mucosal membranes, decreased skin turgor, clear lung examination, and benign abdominal examination. Significant laboratory data included abnormal levels of glucose (300 mg/dL), sodium (130 mEq/L), potassium (4.5 mEq/L), magnesium (1.8 mg/dL), phosphate (2 mg/dL), blood urea nitrogen (30 mg/dL), bicarbonate (8 mEq/L), and creatinine (1.5 mg/dL); a calculated anion gap of 25 mEq/L; an arterial pH of 7.17; and a  $P_{CO_2}$  of 16 mm Hg. Urine and plasma were positive for ketones. White blood cell count and differential were in the normal range, with negative urinalysis, blood cultures, and chest radiograph. The patient was immediately started on intravenous (IV) fluids and an IV insulin drip. His electrolytes were closely monitored and replacement was infrequently required. The patient's mental status rapidly improved. He received a total of 7 L of normal saline and was transitioned from IV insulin to his home regimen. He was seen by a social counselor and discharged home with close follow-up.

**D**iabetic ketoacidosis (DKA) is a serious and potentially life-threatening complication of diabetes mellitus.<sup>1,2</sup> It represents a state of insulin deficiency with a concurrent elevation in counterregulatory hormones.<sup>2-6</sup> The annual incidence ranges from 4.6 to 8 cases per 1000 diabetic patients, and DKA carries a mortality rate of 2% to 10%.<sup>2</sup> DKA occurs more commonly in patients who have type 1 diabetes as compared with patients who have type 2 diabetes.<sup>5</sup> However, recent data suggest that African American and Hispanic patients are more likely to develop DKA in the setting of type 2 diabetes than are white patients.<sup>7,8</sup> Diagnosing DKA centers on identifying the classic triad of hyperglycemia, ketosis, and acidosis. Management focuses on treating the precipitating factors and correcting dehydration, hyperglycemia, and electrolyte abnormalities. Despite available guidelines, DKA has been shown to be inadequately managed in teaching hospitals.<sup>9,10</sup> This article reviews the approach to accurate diagnosis and timely management of DKA.

### PATHOPHYSIOLOGY

DKA results from a dysregulation of carbohydrate, protein, and lipid metabolism. Insulin deficiency along

with an increase in counterregulatory hormones (glucagon, cortisol, catecholamines, and growth hormone) lead to the development of hyperglycemia, ketosis, and acidosis.<sup>2,4,5,11,12</sup> Briefly, hyperglycemia develops secondary to an increase in glycogenolysis and gluconeogenesis. Although peripheral insulin resistance and decreased tissue utilization of glucose may also occur, they are not major contributors in DKA. An increase in circulating free fatty acids leads to hepatic production of ketone bodies, resulting in ketosis and metabolic acidosis. Hyperglycemia causes fluid and electrolytes to shift from the intracellular to the extracellular space, which leads to subsequent cellular dehydration and electrolyte abnormalities. In addition, hyperglycemia and ketosis create an osmotic diuresis, generating further hypovolemia.<sup>2,3,6,11-13</sup>

### PRECIPITATING FACTORS

The most common precipitating factors for DKA are infection, medication noncompliance, and new-onset

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*Dr. Yehia and Dr. Epps are internal medicine residents, and Dr. Golden is an associate professor of medicine and epidemiology; all are at Johns Hopkins University, Baltimore, MD.*

### TAKE HOME POINTS

- Diabetic ketoacidosis (DKA) is an endocrinologic emergency marked by hyperglycemia, ketosis, and acidosis.
- Diagnosis is based on a serum glucose level exceeding 250 mg/dL, arterial pH below 7.3, a serum bicarbonate below 18 mEq/L, and positive serum or urine ketones.
- The mainstay of treatment is adequate fluid resuscitation, insulin therapy, and electrolyte replacement.
- Criteria for determining resolution of DKA include pH > 7.3 (or anion gap < 14 mEq/L), serum bicarbonate level of 18 mEq/L or higher, and serum glucose level < 200 mg/dL.
- Intravenous insulin infusion overlapping with subcutaneous insulin by 1 to 2 hours is recommended once DKA has resolved.
- Frequent monitoring of metabolic status is essential.

diabetes.<sup>2,4,5,11</sup> Urinary tract infections and pneumonia are frequently encountered infectious precipitants. Poor medication compliance and an ineffective outpatient medication regimen (ie, inadequate insulin dosing) often lead to DKA.<sup>2,4,5,11,12</sup> Age, ethnicity, and comorbidities play a role in insulin compliance.<sup>3,14,15</sup> For example, nearly 50% of all DKA cases in urban African Americans with known diabetes are due to insulin non-compliance.<sup>15</sup> Other inciting factors include myocardial infarction, stroke, acute pancreatitis, and medication toxicity (Table 1).<sup>2,4,5,11</sup>

### DIAGNOSIS

#### Clinical Presentation

The metabolic abnormalities associated with DKA develop rapidly, usually within 24 hours. However, signs and symptoms of poor diabetic control may precede DKA by several days.<sup>4,5</sup> Patients often present with polyuria, polydipsia, weakness, fatigue, and altered sensorium.<sup>2,4,5</sup> Abdominal pain, nausea, and vomiting are common features in DKA that usually resolve with correction of acidosis.<sup>1–5</sup> Persistence of these features after the resolution of DKA may signify the presence of an intraabdominal process. On physical examination, signs of hypovolemia are often present, including dry mucosal membranes, decreased skin turgor, tachycardia, and hypotension. Additionally, patients may have a fruity odor to their breath as a consequence of acetone release. Deep and labored breathing, or *Kussmaul's*

**Table 1.** Common Precipitating Factors of Diabetic Ketoacidosis

#### Most common

Infection (urinary tract infection, pneumonia)

Medication noncompliance

Inadequate insulin dosing

New-onset diabetes mellitus

#### Other

Acute myocardial infarction

Stroke

Acute pancreatitis

Trauma

Pregnancy

Surgery

Alcohol abuse

Medications (corticosteroids, thiazides, phenytoin,  $\beta$ -blockers, dopamine)

*respirations*, may also be observed and are an attempt to correct the metabolic acidosis with a compensatory respiratory alkalosis; however, the excess acid cannot be expired. Mental status can range from an intact sensorium to diabetic coma.<sup>2–5,11,12</sup>

#### Laboratory Findings

The initial laboratory evaluation in DKA includes measurement of serum glucose, electrolytes, blood urea nitrogen, and creatinine; urinalysis; testing for ketones in urine and serum; and assessment of serum osmolality and arterial blood gas values. Further testing may be done to identify potential infections or myocardial infarction as a DKA precipitant. These tests may include complete blood count with differential, urine and blood cultures, cardiac enzymes, electrocardiogram, and imaging studies such as chest radiographs.<sup>2,4–6,12</sup>

The hallmark laboratory findings in DKA are hyperglycemia (serum glucose > 250 mg/dL), ketosis (positive serum and/or urine ketones), and acidosis (arterial pH < 7.30 and/or serum bicarbonate < 18 mEq/L).<sup>4,5,12</sup> DKA can be classified into 3 categories: mild (arterial pH, 7.25–7.30; serum bicarbonate, 15–18 mEq/L; anion gap > 10 mEq/L; mental status, alert), moderate (arterial pH, 7.00 to < 7.25; serum bicarbonate, 10 to < 15 mEq/L; anion gap, > 12 mEq/L; mental status, alert/drowsy), and severe (arterial pH, < 7.00; serum bicarbonate, < 10 mEq/L; anion gap, > 12 mEq/L; mental status, stupor/coma).<sup>4,5</sup> The presence of a high anion-gap metabolic acidosis, a decreased level of serum sodium, and an elevated

potassium level are common features in DKA. Normal or low levels of potassium typically indicate total body potassium deficiency and require vigilant monitoring and repletion. In comparison with the high serum osmolality seen in hyperosmolar hyperglycemic state, serum osmolality is variable in DKA. Amylase elevation occurs in 21% to 79% of DKA cases, often from a nonpancreatic source.<sup>1</sup> Lipase can be elevated in DKA but can also be a marker of pancreatitis. Therefore, clinical judgment and follow-up of the patient's clinical status as DKA is treated are imperative to differentiate between the 2 processes.<sup>1,3–5</sup> Mild leukocytosis, ranging from 10,000 to 15,000 cells/ $\mu$ L, may be present due to dehydration, stress, and demargination of leukocytes. A higher white blood cell count is often indicative of infection.<sup>1</sup>

### Differential Diagnosis

Clinical presentation and laboratory data often provide the needed information for diagnosing DKA. Other causes of ketosis and high anion-gap metabolic acidosis besides DKA should be considered. Although less common, ketosis can occur in hyperosmolar hyperglycemic state. This clinical scenario is distinguished from classical DKA by an elevated effective serum osmolality ( $> 320$  mOsm/kg) and marked elevation in serum glucose ( $> 600$  mg/dL).<sup>3,4</sup> Starvation ketosis and alcoholic ketoacidosis can both produce serum ketones, but unlike DKA, serum glucose is not significantly elevated in these conditions. In addition, the acidosis associated with alcohol rarely results in serum bicarbonate levels lower than 18 mEq/L.<sup>4,5</sup> The differential diagnosis of high anion-gap metabolic acidosis should also include lactic acidosis, renal failure, and drug intoxication (methanol, ethylene glycol, paraldehyde, and salicylate). Measuring serum lactate and salicylate levels, obtaining a toxin screen (methanol, ethylene glycol, ethanol), and calculating an osmolal gap are often helpful in distinguishing these processes from DKA.<sup>4,5</sup>

### MANAGEMENT

The keys to successful management of DKA are fluid resuscitation, insulin therapy, correcting metabolic acidosis and electrolyte imbalances, and identifying and treating precipitating factors (**Figure** and **Table 2**).<sup>1,2,4,5</sup> Frequent monitoring is required to achieve these goals and avoid complications (**Table 3**).<sup>1–6,11,12</sup> A flow sheet tracking the metabolic progress of patients can be helpful.<sup>4,5,12</sup> Although elderly patients are most often affected by hyperosmolar hyperglycemic state, they require special attention since death due to DKA tends to occur at the extremes of age.<sup>4,5,16,17</sup> Treatment of DKA in elderly patients is similar to that of younger patients, although

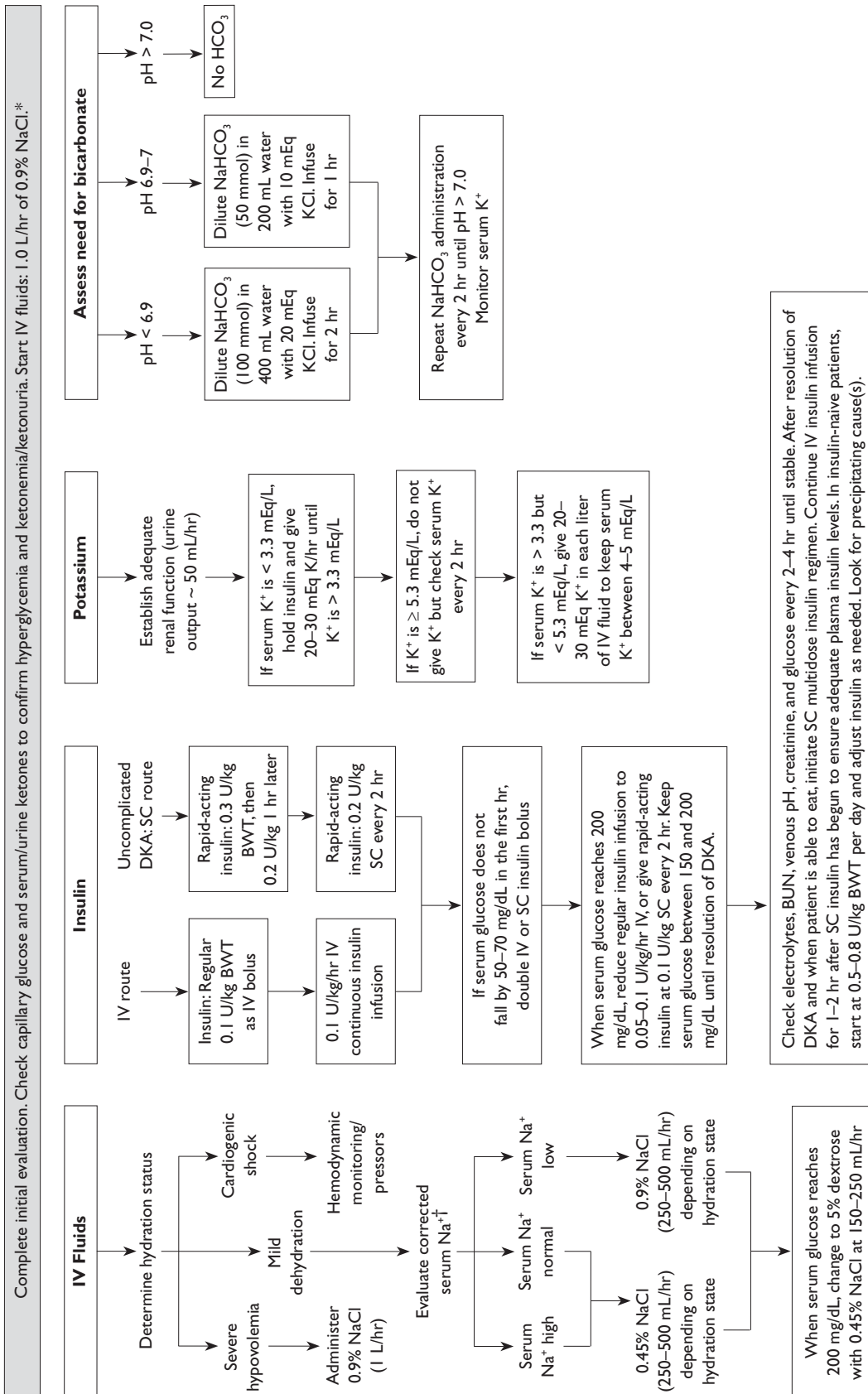
fluid resuscitation should be followed more closely in order to prevent volume overload.<sup>16</sup>

### Fluid Resuscitation

Patients in DKA have a total body water deficit of approximately 5 to 8 L,<sup>4–6</sup> and correcting this deficit will result in significant metabolic improvement. Fluid resuscitation with isotonic saline (0.9% NaCl) at 15 to 20 mL/kg/hr for the first hour is recommended for all patients. Therapy should then be tailored based upon volume status and serum sodium concentration. In patients with hypovolemic shock, infusion of 0.9% NaCl should be continued and the addition of a plasma expander should be considered. When hypovolemia is mild (ie, stable blood pressure and adequate urine output), fluid should be selected based on the serum sodium concentration. Low serum sodium requires 0.9% NaCl at a rate of 4 to 14 mL/kg/hr. If sodium levels are normal to high, changing to a lower salt content infusate, such as 0.45% NaCl, at a rate of 4 to 14 mL/kg/hr is recommended. The aim is to correct the total body water deficit in the first 24 hours. Because rehydration will lower plasma glucose and osmolality, serum levels must be monitored closely. When blood glucose falls to below 250 mg/dL, 5% dextrose should be added to the NaCl infusion to prevent iatrogenic hypoglycemia. Dextrose supplementation, with a target blood glucose concentration between 150 and 250 mg/dL, should continue as long as insulin infusion is required to treat acidosis.<sup>1–6,11–13</sup> To avoid complications of rapid fluid shifts, the change in osmolality should be no greater than 3 mOsm/kg of free water per hour, and sodium changes should not exceed 1 mmol/hr.<sup>1</sup>

### Insulin Therapy

Regular insulin administered intravenously is the optimal choice for treatment of DKA.<sup>2–6,18–20</sup> Previous controversy over the use of a high-dose versus low-dose insulin regimen has been resolved. Several studies have shown that low-dose insulin effectively corrects metabolic acidosis without precipitating rapid declines in plasma osmolality, glucose, and potassium.<sup>2,4,5,19,20</sup> A low-dose protocol with a bolus of 0.1 U/kg followed by a continuous infusion at a rate of 0.1 U/kg/hr should be initiated. If plasma glucose does not decrease by 50 to 75 mg/dL in the first hour, the rate of the insulin infusion should be doubled every hour until the goal reduction is achieved. Once blood glucose is less than 200 mg/dL, the rate of insulin infusion can be decreased. Because ketoacidosis typically takes longer to resolve than hyperglycemia, insulin infusion should continue until acidosis resolves.<sup>2–6,11,12</sup> Serum and urine



**Figure.** American Diabetes Association management protocol for adults with diabetic ketoacidosis. BUN = blood urea nitrogen; BWT = body weight; DKA = diabetic ketoacidosis; IV = intravenous; SC = subcutaneous. \*After history and physical examination, obtain capillary glucose and serum or urine ketones (nitroprusside method). Begin 1 L of 0.9% NaCl over 1 hr and draw arterial blood gases, complete blood count with differential, urinalysis, serum glucose, BUN, electrolytes, chemistry profile, and creatinine levels STAT. Obtain electrocardiogram, chest radiograph, and specimens for bacterial cultures, as needed. †Serum Na<sup>+</sup> should be corrected for hyperglycemia (for each 100 mg/dL, add 1.6 mEq to sodium value for corrected serum sodium value.). (Adapted with permission from The American Diabetes Association. Kitabchi AE, Umpierrez GE, Murphy MB, Kreisberg RA. Hyperglycemic crises in adult patients with diabetes: a consensus statement from the American Diabetes Association. Diabetes Care 2006;29:2743. Copyright © 2006 American Diabetes Association.)

ketones may remain positive after correction of acidosis, evidenced by closure of the anion gap, due to conversion of  $\beta$ -hydroxybutyrate to acetoacetate.<sup>2</sup> Criteria for resolution of DKA include pH greater than 7.3 (or anion gap < 14 mEq/L), a serum bicarbonate concentration of 18 mEq/L or less, and a blood glucose level less than 200 mg/dL.<sup>1</sup>

Once DKA has resolved, the transition to subcutaneous insulin can begin. The American Diabetes Association (ADA) recommends that basal subcutaneous insulin and insulin infusion be overlapped for 1 to 2 hours to prevent rebound hyperglycemia or recurrence of DKA.<sup>4,5</sup> In practice, a longer overlap period may be required, depending on the pharmacokinetics of the basal insulin selected (ie, 2–4 hr for neutral protamine Haegdorn [NPH] or glargine). Known diabetic patients should return to their home insulin regimen, which can be adjusted as needed to control hyperglycemia. Newly diagnosed diabetic patients should receive a mixture of long-acting and short-acting subcutaneous insulin.<sup>1–6,11,12</sup> Most patients with type 1 diabetes require a total daily dose of insulin of 0.5 to 1 U/kg/day. Half of the dose should be administered as basal insulin (once daily glargine or detemir or divided equally in 2 doses of NPH insulin). The remaining half should be administered in 3 equally divided doses of a rapid-acting insulin analog before each meal (ie, aspart, lispro, or glulisine).<sup>21</sup>

### Electrolyte Repletion

Patients in DKA have a total body potassium deficit of 3 to 5 mEq/L.<sup>2,4,5,22</sup> However, serum potassium is commonly normal or elevated at presentation. If serum potassium is less than 3.3 mEq/L, insulin administration should be deferred and potassium should be repleted to prevent the life-threatening complications of hypokalemia, such as cardiac arrhythmias and respiratory muscle weakness. If serum potassium is between 3.3 and 5.3 mEq/L, 20 to 40 mEq of potassium can be added to each liter of intravenous fluids once good urine output is assured. If serum potassium is greater than 5.3 mEq/L, potassium repletion is unnecessary; however, potassium levels should still be monitored closely. The target serum potassium is 4 to 5 mEq/L during treatment for DKA.<sup>1–6,11,12</sup>

The total body phosphate deficit in DKA averages 1 mmol/kg of body weight.<sup>4,5</sup> Several studies failed to show a benefit from phosphate replacement.<sup>23,24</sup> However, the ADA recommends repletion in patients with cardiac dysfunction, respiratory depression, or serum phosphate less than 1 mg/dL.<sup>4,5</sup>

Because acidosis typically resolves with treatment for

**Table 2.** Highlights of Diabetic Ketoacidosis Management

### Fluid resuscitation

Start 0.9% NaCl at 15–20 mL/kg/hr for first hr (add colloid if hypovolemic shock), then

- If Na<sup>+</sup> is normal or high, give 0.45% NaCl at 4–14 mL/kg/hr
- If Na<sup>+</sup> is low, give 0.9% NaCl at 4–14 mL/kg/hr

Add dextrose when glucose is < 250 mg/dL

Goal is to correct total body water deficit in the first 24 hr

### Insulin therapy

0.1 U/kg bolus followed by continuous infusion at 0.1 U/kg/hr

Goal is to decrease glucose by 50–75 mg/dL/hr

Continue insulin until pH, bicarbonate, and anion gap normalize

Overlap IV insulin with subcutaneous insulin for 1–2 hr after resolution of DKA

### Electrolyte repletion

Add 20–30 mEq potassium to each liter of IV fluid if potassium is < 5.3 mEq/L

Replace phosphate if phosphate is < 1 mg/dL

Give bicarbonate if pH is < 7.0

DKA = diabetic ketoacidosis; IV = intravenous.

DKA, bicarbonate levels will rise without supplementation. Several studies have shown no benefit to bicarbonate administration at a pH greater than 7.0.<sup>25,26</sup> However, no studies have addressed bicarbonate therapy in patients with a pH below 6.9. For pH levels between 6.9 and 7.0, the ADA recommends administration of 50 mmol of sodium bicarbonate in 200 mL of sterile water with 10 mEq of potassium chloride infused over 1 hour. For patients with a pH less than 6.9, the ADA recommends administering 100 mmol of sodium bicarbonate in 400 mL of sterile water with 20 mEq of potassium chloride infused over 2 hours. Venous pH and bicarbonate level should be measured every 2 hours, and treatment can be repeated every 2 hours as needed until the pH exceeds 7.0.<sup>4,5</sup>

### PREVENTION

Approximately 50% of hospitalizations for DKA are preventable.<sup>1</sup> Prevention begins with effective communication and patient education. Patients must be counseled on appropriate management of their diabetes, particularly during times of illness. One strategy is to encourage patient–provider communication in order to identify signs and symptoms of early DKA. Blood glucose and ketone monitoring are used to titrate insulin regimens during illness. In addition, patients must be educated about the deleterious effects of insulin deficiency.<sup>2–5,12</sup> Even when patients are ill and unable

**Table 3.** Complications of Treating Diabetic Ketoacidosis

Complication	Cause	Prevention/Comments
Hypoglycemia	Insulin administration	Check blood glucose every hr Low-dose insulin protocol
Hyperglycemia	Interruption of insulin coverage	Overlap insulin infusion and subcutaneous insulin once diabetic ketoacidosis resolves
Hypokalemia	Insulin administration Bicarbonate supplementation	Check potassium every 2–4 hr Supplement if potassium is < 5.3 mEq/L
Hyperchloremic acidosis	Intravenous NaCl fluids Urinary ketoacid loss	Resolves quickly Frequently clinically insignificant
Thromboembolism	Hypercoagulable state Severe dehydration	No data to support prophylactic anticoagulation
Fluid overload	Intravenous fluids	Monitor total body input and output
Cerebral edema	Unknown, possibly due to rapid correction of hyperosmolality	Check serum sodium every 2–4 hr Check serum osmolality every 2–4 hr Replace fluids gradually
Hypoxia/acute respiratory distress syndrome	Decreased osmotic pressure leads to increased lung water content	Add dextrose if glucose is < 250 mg/dl Avoid changing sodium at a rate > 1 mmol/hr Avoid changing osmolality at a rate > 3 mmol/hr

to tolerate oral intake, they still require basal insulin to prevent ketosis. Unfortunately, discontinuation of insulin for economic and psychiatric reasons is a common precipitant of DKA.<sup>4,5,14,15,27</sup> We must work to improve access to health care in populations at risk.

**CONCLUSION**

DKA is an endocrinologic emergency that carries a mortality rate of 2% to 10%.<sup>2</sup> Hyperglycemia, ketosis, and acidosis are the hallmark features of DKA. Management is directed at fluid resuscitation, restoration of insulin therapy, correction of metabolic acidosis and electrolyte abnormalities, and treatment of precipitating factors. Frequent monitoring is required to assess progress and avoid complications.<sup>1,2,4,5</sup> Patient education and patient–provider communication are essential for preventing DKA. **HP**

*Corresponding author: Sherita Hill Golden, MD, MHS, Johns Hopkins University School of Medicine, 2024 E. Monument Street, Suite 2-600, Baltimore, MD 21205; sahill@jhmi.edu.*

**REFERENCES**

- Kearney T, Dang C. Diabetic and endocrine emergencies. *Postgrad Med J* 2007;83:79–86.
- Delaney MF, Zisman A, Ketylle WM. Diabetic ketoacidosis and hyperglycemic hyperosmolar nonketotic syndrome. *Endocrinol Metab Clin North Am* 2000;29:683–705, v.
- Eledrisi MS, Alshanti MS, Shah MF, et al. Overview of the diagnosis and management of diabetic ketoacidosis. *Am J Med Sci* 2006;331:243–51.
- Kitabchi AE, Umpierrez GE, Murphy MB, et al; American Diabetes Association. Hyperglycemic crises in diabetes. *Diabetes Care* 2004;27 Suppl 1: S94–102.
- Kitabchi AE, Umpierrez GE, Murphy MB, Kreisberg RA. Hyperglycemic crises in adult patients with diabetes: a consensus statement from the American

- Diabetes Association. *Diabetes Care* 2006;29:2739–48.
- Magee MF, Bhatt BA. Management of decompensated diabetes. Diabetic ketoacidosis and hyperglycemic hyperosmolar syndrome. *Crit Care Clin* 2001;17:75–106.
- Umpierrez GE, Smiley D, Kitabchi AE. Narrative review: ketosis-prone type 2 diabetes mellitus. *Ann Intern Med* 2006;144:350–7.
- Balasubramanyam A, Zern JW, Hyman DJ, Pavlik V. New profiles of diabetic ketoacidosis: type 1 vs type 2 diabetes and the effect of ethnicity. *Arch Intern Med* 1999;159:2317–22.
- Singh RK, Perros P, Frier BM. Hospital management of diabetic ketoacidosis: are clinical guidelines implemented effectively? *Diabet Med* 1997;14:482–6.
- Sola E, Garzon S, Garcia-Torres S, et al. Management of diabetic ketoacidosis in a teaching hospital. *Acta Diabetol* 2006;43:127–30.
- Umpierrez GE, Khajavi M, Kitabchi AE. Review: diabetic ketoacidosis and hyperglycemic hyperosmolar nonketotic syndrome. *Am J Med Sci* 1996; 311:225–33.
- Kitabchi AE, Wall BM. Management of diabetic ketoacidosis. *Am Fam Physician* 1999;60:455–64.
- Hillman K. Fluid resuscitation in diabetic emergencies—a reappraisal. *Intensive Care Med* 1987;13:4–8.
- Musey VC, Lee JK, Crawford R, et al. Diabetes in urban African-Americans. I. Cessation of insulin therapy is the major precipitating cause of diabetic ketoacidosis. *Diabetes Care* 1995;18:483–9.
- Umpierrez GE, Kelly JP, Navarrete JE, et al. Hyperglycemic crises in urban blacks. *Arch Intern Med* 1997;157:669–75.
- Savage MW, Kilvert A. ABCD guidelines for the management of hyperglycemic emergencies in adults. *Pract Diab Int* 2006;23:227–31.
- Meneilly GS, Tessier D. Diabetes in elderly adults. *J Gerontol A Biol Sci Med Sci* 2001;56:M5–13.
- Fisher JN, Shahshahani MN, Kitabchi AE. Diabetic ketoacidosis: low-dose insulin therapy by various routes. *N Engl J Med* 1977;297:238–41.
- Kitabchi AE, Ayyagari V, Guerra SM. The efficacy of low-dose versus conventional therapy of insulin for treatment of diabetic ketoacidosis. *Ann Intern Med* 1976;84:633–8.
- Wagner A, Risse A, Brill HL, et al. Therapy of severe diabetic ketoacidosis. Zero-mortality under very-low-dose insulin application. *Diabetes Care* 1999;22: 674–7.
- Clement S, Braithwaite SS, Magee MF, et al. Management of diabetes and hyperglycemia in hospitals [published errata appear in *Diabetes Care* 2004;27:856 and 2004;27:1255]. *Diabetes Care* 2004;27:553–91.
- Kreisberg RA. Diabetic ketoacidosis: new concepts and trends in pathogenesis and treatment. *Ann Intern Med* 1978;88:681–95.
- Barsotti MM. Potassium phosphate and potassium chloride in the treatment of DKA [letter]. *Diabetes Care* 1980;3:569.
- Fisher JN, Kitabchi AE. A randomized study of phosphate therapy in the

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- treatment of diabetic ketoacidosis. *J Clin Endocrinol Metab* 1983;57:177–80.
25. Morris LR, Murphy MB, Kitabchi AE. Bicarbonate therapy in severe diabetic ketoacidosis. *Ann Intern Med* 1986;105:836–40.
26. Lever E, Jaspan JB. Sodium bicarbonate therapy in severe diabetic ketoacidosis. *Am J Med* 1983;75:263–8.
27. Maldonado MR, Chong ER, Oehl MA, Balasubramanyam A. Economic impact of diabetic ketoacidosis in a multiethnic indigent population: analysis of costs based on the precipitating cause. *Diabetes Care* 2003;26:1265–9.

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