

Diabetic Ketoacidosis

In children under 10 years of age, diabetic ketoacidosis causes 70% of diabetes-related deaths. The incidence of diabetes is 27.6 per 1,000. Diabetic ketoacidosis is easily defined by the triad of hyperglycemia, acidosis, and ketosis.

American Diabetes Association Guidelines for Hospital Admission of Patients with Diabetic ketoacidosis

Hyperglycemia (glucose > 250 mg/dL)

Arterial pH <7.35, or venous pH <7.30, or serum bicarbonate <15 mEq/L

Ketonuria, ketonemia, or both

I. Clinical Presentation

- A. Diabetes is newly diagnosed in 20% of cases of diabetic ketoacidosis. The remainder of cases occur in known diabetics in whom ketosis develops after a precipitating factor, such as infection or noncompliance with insulin therapy.
- B. **Symptoms of DKA:** Polyuria, polydipsia, fatigue, nausea, and vomiting developing over 1 to 2 days. Abdominal pain is prominent in 25%.
- C. **Physical Exam**
 1. Patients are typically flushed (despite hypotension) and tachycardiac. Tachypnea is common. Kussmaul's respiration, with deep breathing and air hunger, occurs when the serum pH is between 7.0 and 7.24.
 2. A fruity odor on the breath indicates the presence of acetone, a by-product of diabetic ketoacidosis.
 3. Fever is seldom present even though infection is common. Hypothermia may also occur.
 4. Eighty percent of patients with diabetic ketoacidosis have altered mental status. Most are awake but confused; 10% are comatose.
- D. **Laboratory Findings**
 1. Serum glucose level >250 mg/dL
 2. pH <7.35
 3. Bicarbonate level below normal with an elevated anion gap
 4. Presence of ketones in the serum

II. Differential Diagnosis

- A. Diabetic ketoacidosis must be differentiated from other causes of ketosis, acidosis, and

hyperglycemia.

B. Differential Diagnosis of Ketosis-Causing Conditions

1. Ketosis may result from alcoholic ketoacidosis or starvation.
2. The majority of patients with alcoholic ketoacidosis do not have diabetes, and the serum glucose level is not elevated. Alcoholic ketoacidosis occurs with heavy drinking and vomiting.
3. Starvation ketosis occurs after 24 hours without food and is not usually confused with diabetic ketoacidosis because glucose and serum pH are normal.

C. Differential Diagnosis of Acidosis-Causing Conditions

1. Metabolic acidoses are divided into increased anion gap (>14 mEq/L) and normal anion gap (anion gap is determined by subtracting the sum of chloride plus bicarbonate from sodium).
2. All ketoacidoses increase the anion gap (DKA, lactic acidosis, uremia, poisoning from salicylates or methanol).
3. Acidoses without an increased anion gap are associated with a normal glucose level and absent serum ketones. Non-anion gap acidoses are caused by renal or gastrointestinal electrolyte losses.

D. Hyperglycemia Caused by Hyperosmolar Nonketotic Coma

1. Hyperosmolar coma occurs in patients with type II diabetes, and it causes severe hyperglycemia. Patients are usually elderly and have a precipitating illness.
2. Serum glucose level is markedly elevated (>600 mg/dL), osmolarity is increased, and ketosis is minimal.

III. Treatment of Diabetic Ketoacidosis

A. Fluid Resuscitation

1. Fluid deficits average 5 L (50 to 100 mL/kg).
2. Give 1 liter of normal saline solution in the first hour and the second liter over the second and third hours. Thereafter, 1/2 normal saline solution should be infused at 250-500 mL/h.
3. Higher rates of fluid administration may be required in patients who are extremely dehydrated.
4. Lower rates are indicated for patients with chronic renal failure because they have not had major fluid losses.
5. When the glucose level reaches 250 mg/dL, 5% dextrose should be added to the replacement fluids to prevent hypoglycemia. If the glucose level declines rapidly, 10% dextrose should be used along with regular insulin IV infusion until ketosis resolves and

anion gap normalizes.

B. Insulin

1. An insulin 0.1 U/kg IV loading dose is followed by an infusion of 0.1 U/kg per hour. The biologic half life of IV insulin is less than 20 minutes, so an IV bolus without a follow-up infusion has a very short-lived effect, and serum glucose will rise rapidly if the insulin infusion is discontinued.
2. The insulin infusion should be adjusted so that rate of glucose decline does not exceed 100 mg/dL per hour. The insulin infusion should be continued until anion gap normalizes.
3. When the bicarbonate level is greater than 16 mEq/L and the anion gap is less than 16 mEq/L, the insulin infusion rate should be decreased by half. However, if the bicarbonate level is not rising and the anion gap is not falling after 2 hours of treatment, the insulin infusion rate may need to be doubled.

C. Potassium

1. The most common preventable cause of death in patients with DKA is hypokalemia. Deficits are caused by osmotic diuresis and cellular shifts. The typical deficit is between 300 and 600 mEq.
2. Replacement therapy with potassium chloride should be started when fluid therapy is started. In most patients, the initial rate of potassium replacement is 20 mEq/h, but hypokalemia requires more aggressive replacement (40 mEq/h).
3. All patients should receive potassium replacement, except for those with known chronic renal failure, no urine output, or an initial serum potassium level greater than 6.0 mEq/L.

D. Sodium

1. Patients with diabetic ketoacidosis sometimes have a low serum sodium level because the high level of glucose has a dilutional effect. For every 100 mg/dL that glucose is elevated, the sodium level should be assumed to be higher than the measured value by 1.6 mEq/L.
2. Frequently, patients have an initial serum sodium greater than 150 mEq/L, indicating severe dehydration. Initial rehydration fluid should consist of 1/2 normal saline.

E. Phosphate

1. Diabetic ketoacidosis depletes phosphate stores.
2. Serum phosphate level should be checked after 4 hours of treatment. If it is below 1.5 mg/dL, potassium phosphate or sodium phosphate should be added to the IV solution.

F. Bicarbonate

1. Bicarbonate therapy is not required unless the arterial pH value is 7.0 or lower. For a pH of less than 6.9, intravenous administration of 88 mEq/L of sodium bicarbonate is

recommended.

2. Bicarbonate administration may exacerbate hypokalemia and cause a paradoxical intracellular acidosis, a negative shift in the oxygen dissociation curve, and late alkalemia.

G. **Additional Therapies**

1. A nasogastric tube should be inserted in semiconscious patients to protect against aspiration.
2. Deep vein thrombosis prophylaxis should be provided for patients who are elderly, unconscious, or severely hyperosmolar; subcutaneous heparin, 5,000 U every 8 hours.

IV. **Monitoring of Therapy**

- A. The serum bicarbonate level and anion gap should be monitored to determine the effectiveness of insulin therapy.
- B. Follow-up evaluation of acidosis, not just of glucose level, is very important because in some patients glucose levels may normalize early in therapy, but the acidosis takes longer to resolve. Continued insulin infusion with a 10% glucose infusion may be needed to resolve the acidosis.
- C. **Glucose Levels:** Check glucose level at 1-2 hour intervals during IV insulin administration
- D. **Electrolyte Levels:** Assess q2h for first 6-8 hours, and then q4h
- E. Phosphorus and magnesium levels should be checked after about 4 hours of treatment, and replacement therapy should be started if they are significantly below normal.
- F. Testing for plasma and urine ketones is helpful in diagnosing diabetic ketoacidosis, but is not necessary during therapy.

V. **Determining the Underlying Cause**

- A. Infection is the underlying cause of diabetic ketoacidosis in about 50% of cases. Infection of the urinary tract, skin, sinuses, or teeth should be sought. Fever is unusual in diabetic ketoacidosis and indicates infection when present; an elevated white blood cell count is usually present whether or not there is infection.
- B. Physical examination, chest film, and urinalysis should be completed to exclude infection. If infection is suspected, antibiotics should be started empirically.
- C. Omission of insulin doses (common in adolescents) is often a precipitating factor.
- D. Myocardial infarction, ischemic stroke, and abdominal catastrophes may precipitate DKA.

VI. **Initiation of Subcutaneous Insulin**

- A. When the serum bicarbonate level is normal and the patient is ready to eat, subcutaneous insulin can be started.
- B. It is critical to overlap intravenous and subcutaneous administration of insulin to avoid

redevelopment of ketoacidosis. The intravenous infusion may be stopped 1 hour after the first subcutaneous injection of regular insulin.

C. **Estimation of Subcutaneous Insulin Requirements**

1. Multiply the final insulin infusion rate times 24 hours and divide the total into morning and evening doses.
2. Two thirds of the total dose is given in the morning, as two thirds NPH and one third regular insulin. The remaining one third of the total dose is given before supper as one half NPH and one half regular insulin.
3. Adjust subsequent doses according to the patient's blood glucose response.

VII. **Complications**

- A. Death from diabetic ketoacidosis can be caused by hypokalemia, hypoglycemia, untreated infection, aspiration, thromboembolism, cerebral edema, and myocardial infarction.
- B. Excessive use of normal saline solution can result in fluid overload and hypernatremia.
- C. Cerebral edema occurs in 1 of 200 patients with diabetic ketoacidosis, usually in those younger than age 20. It is manifested by abrupt worsening of the mental status. Patients should be treated aggressively with dexamethasone and mannitol. §