Management of a Patient With Diabetic Ketoacidosis in the Emergency Department

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Abstract: Diabetic ketoacidosis is a common problem among known and newly diagnosed diabetic children and adolescents for which they will often seek care in the emergency department (ED). Technological advances are leading to changes in outpatient management of diabetes. The ED physician needs to be aware of the new technologies in the care of diabetic children and comfortable managing patients using continuous subcutaneous insulin infusions. This article reviews the ED management of diabetic ketoacidosis and its associated complications, as well as the specific recommendations in caring for patients using the continuous subcutaneous insulin infusion, serum ketone monitoring, and continuous glucose monitoring.

Key Words: diabetes, diabetic ketoacidosis, continuous subcutaneous insulin infusion, cerebral edema, serum ketone monitoring

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TARGET AUDIENCE

The article is intended for physicians, nurse practitioners, physician assistants, and trainees who care for children in an emergency department (ED) setting.

LEARNING OBJECTIVES

After completion of this article, the readers should be able to:

1. Describe a framework for the management of patients in known or suspected diabetic ketoacidosis (DKA) in the ED.
2. Identify patients most at risk for the development of cerebral edema.
3. Understand continuous subcutaneous insulin infusions (CSIIs) and their use in the diabetic child in the ED.

An estimated 215,000 children and adolescents are living with diabetes mellitus in the United States today.[1] Each year, 15,600 children in the United States are newly diagnosed with type 1 diabetes.[1] Twenty-five percent to 40% of children will present in DKA at the time of their diagnosis.[2–4] There are more than 100,000 episodes of DKA in children and adolescents per year.[4] Of children that are already diagnosed with type 1 diabetes, they will have a yearly risk of DKA of 1% to 10%.[4] This accumulates health care costs of more than 2.5 billion dollars yearly for pediatric diabetes care.[4] Although DKA remains treatable, it is the leading cause of death in children with type 1 diabetes.[4] The vast majority of these deaths occur secondary to cerebral edema, which has up to a 25% mortality rate.[5] In light of the high prevalence of diabetes in children and adolescents and the acute presentation of both new-onset diabetes and DKA, it is clear that an emergency medicine physician needs to be well versed in acute management of diabetes and its complications, including the management of those using CSII.

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PATHOPHYSIOLOGY OF DKA

Diabetes ketoacidosis develops because of a deficiency in circulating insulin and the effects of the counterregulatory hormones epinephrine, glucagon, cortisol, and growth hormone.[6] An absolute insulin deficiency occurs in a previously undiagnosed diabetic, when children are not taking their prescribed insulin or when children or adolescents on an insulin pump have a pump malfunction. A relative deficiency in insulin occurs in times of the following stress to the body: with sepsis, trauma, febrile illness, or gastrointestinal illness causing vomiting and diarrhea.[7] The combination of low-serum insulin and high-counterregulatory hormones causes the liver and kidneys to release and make more glucose (via glycogenolysis and gluconeogenesis), impairs the body's use of glucose, and causes the liver to make more ketones. This hyperglycemia, hyperosmolality, ketogenesis, and increased lipolysis lead to ketonemia and acidosis. The hyperglycemia and hyperketonemia lead to osmotic diuresis, dehydration, and electrolyte loss, which continues the cycle whereby the counterregulatory hormones are further increased, worsening the insulin resistance, hyperglycemia, and hyperketonemia. Unless this cycle is interrupted, worsening dehydration and metabolic acidosis will occur. Patients in DKA suffer from dehydration, acidosis, and electrolyte abnormalities that all require correction.

CLINICAL PRESENTATION OF DKA

Depending on the duration of symptoms, children with DKA may be ill-appearing and unstable. They may present with polyuria, polydipsia, nausea, vomiting, and abdominal pain. They may be severely dehydrated, demonstrate significant tachypnea or Kussmaul respirations (deep fast breaths), have fruity-smelling breath, and have an altered level of alertness.

Diabetic ketoacidosis is diagnosed on the basis of the combination of hyperglycemia, acidosis, and ketosis or ketonemia. Laboratory parameters include the following:

1. Blood glucose more than 11 mmol/L (200 mg/dL)
2. Venous pH less than 7.3 or bicarbonate less than 15 mEq/L
3. Ketonemia more than 31 mg/dL (>0.3 mmol/L) or ketonuria more than 80 mg/dL

Diabetic ketoacidosis is considered severe if pH is less than 7.1 or bicarbonate is less than 5 and mild if pH is 7.2 to 7.3 and bicarbonate is 10 to 15.

Children at highest risk for developing DKA include those with previous episodes of DKA, a new diagnosis of diabetes, poor metabolic control, unstable social situations, noncompliance with insulin, psychiatric and eating disorders, limited access to medical care, as well as CSIIs.[8] Teenage females are also at higher

risk. Relative to adult diabetics, children with DKA less frequently have underlying infections precipitating their DKA, with an estimated 18% of DKA episodes occurring in the setting of viral infections and 13% in the setting of a bacterial infection.[9]

ED MANAGEMENT OF DKA

The goals of DKA management in the ED are to correct the hyperglycemia, dehydration, and electrolyte disturbances, while also avoiding the complications of DKA (Fig. 1). Any underlying precipitants to the development of DKA need to be identified as well. Patients with DKA should be managed carefully and systematically. Every patient should have a careful history taken and physical examination performed, including weight, with immediate attention to the child's hydration status and level of consciousness. The patient's airway and breathing should be assured, and the patient should be placed on a cardiorespiratory monitor. Special attention should be paid to signs of delayed capillary refill (beyond 3 seconds), poor skin turgor, and hyperpnea, because these signs are most accurate in predicting dehydration.[6,10] Most children in DKA have an estimated 5% to 10% fluid deficit.[6] Those children with weak or impalpable pulses, hypotension, or oliguria can be assumed to have more than 10% dehydration and require especially aggressive fluid resuscitation. Intravenous (IV) access should be efficiently obtained, preferably with a blood-drawing IV to facilitate frequent laboratory testing. Initial studies to be sent include serum glucose, electrolytes, blood urea nitrogen, creatinine, venous pH with P_{CO_2}, hemoglobin or hematocrit, hemoglobin A1C, urinalysis for ketones or serum β-hydroxybutyrate, and cultures, if there is a concern for underlying bacterial infection.

Three Key Components of DKA Therapy

1. Fluid Therapy

Normal Saline Resuscitation

- NS bolus 10-20 mL/kg
- Confer w/ ED Fellow/Attending before subsequent boluses

Two Bag System (IVF following the initial saline bolus)

Bag #1: NS, KCL, KAcetate

Bag #2: Same as bag#1 plus D_{10}

Bag #1
D_0 + electrolytes
Bag #2
D_{10} + electrolytes

D_5 = same rate each bag
$D_{7.5}$ = 25% D_0 bag, 75% D_{10} bag

Electrolytes

Patient's K mEq/L	mEq KCL/L	mEq KAcetate/L	mmol KPO_4/L*
< 4.0	30	30	0
4.0-5.4	20	20	0
5.5-6.0	10	10	0
> 6.0	0	0	0

*KPO4 has been removed from IV fluids due to shortage of product. Monitor phosphorus levels closely and consider replacement with IV potassium phosphate only when serum phosphorus levels are less than 2 mg/dL

$Na_{corrected} = Na_{measured} + 1.6 \times [\text{Serum glucose} - 100] / 100$

Dextrose

- Start dextrose when the patient's glucose is < 300 mg / dL
- Change dextrose delivered by changing flow rates of the two bags (total IVF rate remains the same)

Rate

Run IVF at 1 ½ maintenance rate based on patient weight

To calculate maintenance cc/hr, use patient's wght in kgs:

4 cc/kg for the first **10** kgs
+ **2** cc/kg for the next **10** kgs
+ **1** cc/kg for each kg over **20** kgs

Example: 25 kg
4 x 10 = 40
+ **2** x 10 = 20
+ **1** x 5 = 5
Maintenance rate is 65 cc/hr
1 ½ Maintenance is 98 cc/hr

FIGURE 1. ED pathway for evaluation/treatment of children with known/suspected type 1 diabetes mellitus with DKA.[20]

TABLE 1. Fluid and Sodium Requirement Calculations

Calculating fluid requirements
Fluid requirement = deficit + maintenance fluid needs
Deficit = % dehydration × body weight (kg)
Calculate 48-hour maintenance needs
Deficit + 48-hour maintenance = total IVF for 48 h
From total IVF for 48 h, subtract any boluses given
Divide total by 48 to get hourly maintenance rate
Calculating corrected sodium
Corrected Na = measured Na + 1.6 × (serum glucose − 100)/100

IVF indicates intravenous fluids.

Children in DKA are depleted in sodium, potassium, and free water. Despite a total body potassium deficit of 3 to 6 mmol/kg, initial serum potassium levels may be normal or increased. There is also an initial pseudohyponatremia, which should correct as the glucose is corrected. Fluid resuscitation should begin immediately, with the goal to replace both water and salt losses (Table 1). Any fluids given at a previous facility should be taken into account when calculating fluid replacement. In the first hour of resuscitation, 10 to 20 mL/kg of 0.9% normal saline (NS) should be given. The remaining fluid deficit should be replaced during the next 48 hours, in the form of 0.45% NS or 0.9% NS with potassium phosphate, potassium chloride, or potassium acetate, as per the measured serum potassium and phosphate levels. Typically, 40 mEq/L of potassium should be added to the IV fluids after initial resuscitation, unless the serum potassium is elevated, with the amount of potassium replacement given adjusted per the potassium laboratory measurements. If there is concern for hyperkalemia or peaked T waves on the cardiac monitor, an electrocardiogram should be obtained immediately.

The sodium is expected to rise 0.5 to 1 mmol/h with improvement in the hyperglycemia. Careful attention should be given to the rate of rise of sodium because inadequate rise can be associated with the development of cerebral edema. A general rule of thumb for fluid replacement is that the IV fluids should run at a rate of 1.5 to 2 times the daily maintenance rate of fluids as based on weight. After the first hour of fluid resuscitation, insulin should be given to correct the insulin deficiency and stop the production of ketone bodies that are contributing to the acidosis. A continuous insulin infusion should be started using regular insulin at a rate of 0.1 U/kg per hour. This infusion should be continued beyond glucose normalization, until the ketosis and acidosis have both resolved. If an insulin infusion cannot be given, intramuscular or subcutaneous injections of rapid or short-acting insulin should be given every 1 to 2 hours. When the blood glucose level falls below 14 to 17 mmol/L (250–300 mg/dL), the insulin infusion should not be stopped but rather 10% dextrose should be added to the fluids to prevent hypoglycemia. Unless there is severe acidosis (pH < 6.9) or concern for cardiac dysfunction, bicarbonate should not be given in an attempt to reverse the acidosis. Bicarbonate administration has not been shown to improve outcomes in children with DKA, whereas some reports have linked its use to the development of cerebral edema. The combination of insulin and fluid resuscitation alone is adequate.[11]

Children in DKA should have strict monitoring while in the ED. This should include hourly intake and output, vital signs, mental status checks (Glasgow Coma Scale and pupil reactivity examination), and blood glucose.

Blood or urine ketones every 1 to 2 hours and a venous pH and serum electrolytes every 2 to 4 hours should also be obtained.

If the hyperglycemia, ketosis, and acidosis resolve and the child is tolerating oral intake, has normalization of vital signs, has a normal mental status, has family members who are well trained in diabetes sick day management, and has adequate outpatient follow-up, the child may be a candidate for discharge from the ED to home. In most cases, however, children in DKA will require admission to a pediatric unit comfortable in the care of diabetes. Pediatric diabetes specialists and nursing staff well trained in diabetes monitoring and management should be available. Facilities must exist for frequent laboratory testing. Those patients in DKA with altered mental status, hemodynamic instability, severe acidosis, or concern for cerebral edema should be admitted to a pediatric intensive care unit.

COMPLICATIONS

There are multiple complications of DKA. Patients may experience hypoglycemia, hypokalemia, and hyperkalemia or inadequate rehydration while undergoing treatment for DKA.[6] A small percentage (0.5%–1%) of children in DKA will develop cerebral edema, the major cause of morbidity and mortality from DKA in childhood and adolescence.[2] Of these children with DKA-related cerebral edema, 20% to 25% will die.

Signs of cerebral edema include headache, lethargy, irritability, restlessness, change in mental status, decrease in heart rate, elevation of blood pressure or widening of pulse pressure, or the development of focal neurologic findings (Table 2).

Children younger than 5 years, with newly diagnosed diabetes and with severe acidosis at presentation, are at highest risk for cerebral edema. Although some children will present with cerebral edema before any treatment, some studies report higher risk for this complication for those with a slow increase in serum sodium during rehydration, receiving a large volume of fluids initially or given any bicarbonate.[12]

Early recognition of cerebral edema by the emergency medicine provider is crucial. If concern for cerebral edema exists, the IV fluid resuscitation rate should be decreased by 33%. Either mannitol or hypertonic (3%) saline should be given in an effort to decrease intracranial pressure (Table 2). The patient should be placed with the head of the bed up. If signs of respiratory failure of lack of airway protective reflexes exist, intubation should be

TABLE 2. Cerebral Edema Key Points

Signs and symptoms of cerebral edema
Altered mental status
Headache
Lethargy
Restlessness, irritability, agitation
Focal neurologic findings
Decrease in heart rate
Elevation in blood pressure
Decreased oxygen saturation
Management of cerebral edema
Decrease IVF rate by 1/3
Mannitol 0.5–1 mg/kg IV, can be repeated if needed within 30–120 min
If mannitol not available, give hypertonic (3%) saline, 5–10 mL/kg for 30 min
Head of bed elevated to 30 degrees
Endotracheal intubation if signs of respiratory failure

IVF indicates intravenous fluids.

performed. A head computed tomography scan should be performed only after stabilization of the patient. All pediatric patients with cerebral edema should be managed in a pediatric intensive care unit with the consult of a pediatric endocrinologist.

THE CHILD ON A CONTINUOUS INSULIN INFUSION

Continuous subcutaneous insulin infusions are small computerized devices that deliver insulin into the subcutaneous tissues via a thin flexible catheter inserted 6 to 8 mm under the skin. Continuous subcutaneous insulin infusions have become an accepted standard of care for children and adolescents with type 1 diabetes. An estimated 30% of US children younger than 6 years CSIIs and increasing numbers of children of all ages are delivering their insulin via the CSII. There are numerous indications for use of CSII as follows:

1. Recurrent severe hypoglycemia
2. Wide blood glucose fluctuations
3. Dawn phenomenon
4. Infants/neonates
5. Needle phobia
6. Competitive athletes
7. Those who desire more flexibility in lifestyle

Continuous subcutaneous insulin infusion is thought to be the most physiologic and precise method of insulin delivery.[13–16] Patients using CSII have been found to have better glycemic control and lower hemoglobin A1C levels. Because of the ability to precisely adjust insulin delivery relative to carbohydrate intake and activity levels, children using an insulin pump have fewer episodes of exercise-related hypoglycemia. Overall, they report an improved quality of life, with greater flexibility, and a greater sense of control over their diabetes. Children will receive a continuous "basal" insulin delivery that accounts for 30% to 40% of their total daily insulin dose, while also receiving mealtime "boluses" making up the remaining 60% of their total daily insulin dose.[16,17] Patients using CSII are required to check their blood glucose at least 4 times daily and must continue to perform carbohydrate counting to determine the "bolus" dose of insulin to be released around mealtime. Patients using CSII have a finite insulin "depot" of only rapid-acting or regular insulin and are therefore prone to the rapid development of DKA should the pump malfunction.[18] In the setting of a pump malfunction, DKA may develop in less than 12 hours.[18] Pump malfunction can include problems with the physical pump, as well as kinking in the tubing, air bubbles in the tubing (causing inconsistent insulin delivery), or subcutaneous tissue scarring preventing absorption of insulin. Patients using insulin pumps are also susceptible to skin infections at the catheter insertion site.

In strictest practice, families and patients are taught that if they have 2 elevated blood glucose in a row that does not correct with a bolus dose of insulin from their pump, they should change the infusion site while also administering insulin via separate injection. When a child with a CSII has ketosis, ketonuria, or DKA, they should also change the pump site, while also switching to subcutaneous insulin injections altogether. It is important that the ED provider is aware of the method and schedule of a child's insulin delivery. If a child is on an insulin pump and presents with DKA, the pump should be discontinued and all insulin should be given IV or IM until ketones have cleared. After stopping the child's insulin pump, the ED provider will then treat the child in DKA in the same manner as all other patients in DKA. When hyperglycemia and acidosis have resolved, the patient can transition back to their CSII. Patients with CSII who have altered mental status, are critically ill, or are thought to be at risk for suicide should also have their pump disconnected and their blood glucose managed via insulin injections.

SERUM KETONE TESTING AND CONTINUOUS BLOOD GLUCOSE MONITORING

In addition to CSII, many children and families are also managing their diabetes using serum ketone testing and continuous blood glucose monitoring. Blood ketone testing is available for home use in the same method as home glucose testing—using capillary blood samples from a finger stick and blood ketone strips that detect levels of 3 hydroxybutyrate. Patients check serum ketones at the same time they would typically check urine ketones, when ill, when not tolerating oral intake, or when hyperglycemic. Although more expensive and more invasive than urine ketone testing, blood ketone testing has several advantages. Blood ketone testing gives an indication of a patient's ketone level at that very instant, whereas urine ketone testing can be inaccurate depending on when the bladder was last emptied. If a patient has not emptied his bladder in several hours, the ketone level is indicative of past ketonuria, but not necessarily the extent of ketosis at that exact time. For patients on CSII in particular, blood ketone testing can more readily detect lack of insulin such as occurs with pump malfunctions. In dehydrated patients who cannot easily void, blood ketone testing allows a method to check ketones without waiting for a patient to be rehydrated enough to urinate. Finally, because urine ketones can persist after resolution of DKA, patients checking urine ketones may give themselves excess insulin, leading to subsequent hypoglycemia. This does not occur when testing serum ketones.

Although there was initial concern that capillary ketone testing would be seen as too invasive by families and not incorporated into their diabetes management, the opposite has been found. When comparing children using blood ketone monitoring versus urine ketone monitoring during times of illness, 90% of patients using blood ketone monitoring checked for ketones, whereas only 60% of patients using urine monitoring checked for ketones.[4] Home blood ketone testing is recommended when possible. By allowing patients to more readily identify ketosis, it has been found to lead to 40% fewer ED visits and 60% fewer hospitalizations than when using urine ketone monitoring.[4] Because resolution of ketonemia is a more accurate marker of DKA resolution, it is also increasingly the practice in the ED care of children in DKA to monitor serum ketones.

Patients using CSII are also increasingly turning to continuous glucose monitoring to allow for even stricter glycemic control. Continuous glucose monitors require the patient to wear a subcutaneous glucose sensor. This sensor is connected to a wireless transmitter that sends the glucose readings to a receiver nearby, that then displays the glucose readings. The receiver can be programmed to give auditory or vibratory alerts if the glucose level is outside previously specified thresholds or if it is rising or falling rapidly. When worn consistently, continuous glucose monitoring has been shown to improve glycemic control.[19] For patients on CSII, continuous glucose monitoring can provide further information regarding glucose patterns to further optimize glycemic control.

SUMMARY

Children with diabetes will often present to the ED in diabetic ketoacidosis and will require urgent goal-directed care. The aim of the emergency medicine physician is to recognize the

presence of DKA and work to correct the dehydration, hyperglycemia, and acidosis that exist. This should be done systematically, with extra care taken in patients using CSIIs as they can more rapidly develop DKA. Special attention should be made to recognizing and treating cerebral edema early.

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