symptoms are particularly evident because the brain is dependent on a steady source of glucose for neural activity. Symptoms are varied, particularly in the neonate.

Hyperinsulinism, inborn errors of metabolism, endocrine disorders (including adrenal and pituitary dysfunction), ketotic hypoglycemia, and drugs and toxins – including exogenous administration of insulin – are the broad categories of conditions leading to hypoglycemia. An extensive endocrine and metabolic workup is necessary to establish the diagnosis. Propranolol and other β-blockers might mask the symptoms (tachycardia, sweating) of hypoglycemia. Laboratory tests, including cortisol, insulin, growth hormone, urine ketones, serum chemistry, and liver function tests, should be obtained during the hypoglycemic episode, if possible.

Once hypoglycemia has been confirmed, immediate treatment with IV glucose should be initiated. Administration of 2 to 4 mL/kg of 25% dextrose IV will provide 0.5 to 1 g/kg of glucose. This solution can be diluted 1:1 so that a 12.5% solution is injected into a peripheral vein or intraosseously. Because dextrose is fairly hyperosmolar, neonates should not be given more than 12.5% dextrose. A bolus of 10 mL/kg of 5% dextrose will provide 0.5 g/kg of glucose.

2. Hyperglycemia

A blood glucose level >150 mg/dL is considered hyperglycemia. This condition is not unusual in the critically ill child. It is the result of a stress response and the presence of high levels of circulating epinephrine and other anti-insulin stress hormones. Glucose levels should be monitored in the postresuscitation stabilization period.

B. Diabetic Ketoacidosis

Diabetic ketoacidosis (DKA), a diagnosis sometimes missed, can lead to cerebral edema with catastrophic neurologic outcomes. A newly diagnosed diabetic child (approximately 30% present in DKA) or a known insulin-dependent diabetic patient can present with this condition and requires prompt attention to fluid management and correction of the acidosis.

An intercurrent illness might trigger the episode of DKA. Patients present with headaches, emesis, abdominal pain, lethargy, and clinical signs of dehydration. There may be a history of weight loss, polydipsia, and polyuria. The abdominal pain and emesis might lead to a mistaken diagnosis of an intra-abdominal process or "surgical abdomen." If the dehydration is severe, evidence of hypovolemic shock may be seen at presentation. The classic clinical signs of rapid/Kussmaul respirations have been mistaken for asthma and respiratory distress. The presence of a fruity (ketotic) odor is helpful in making the diagnosis.

DKA is defined as a blood glucose concentration >200 mg/dL, with ketonemia/ketonuria, and a venous pH <7.3 or bicarbonate <15 mEq/L. The severity of DKA is categorized on the basis of the degree of acidosis (mild, venous pH <7.3 or bicarbonate <15 mEq/L; moderate, pH <7.2 or bicarbonate <10 mEq/L; severe, pH <7.1 or bicarbonate <5 mEq/L).

1. Initial Stabilization

Once initial laboratory studies confirm the diagnosis, the mainstay of therapy is the administration of insulin by continuous infusion and correction of the dehydration. If the history is suggestive of an infectious trigger, this should be investigated and appropriately treated.

An initial fluid bolus of 10 mL/kg of normal saline is administered, with an additional bolus given if the patient is hemodynamically unstable as a result of the dehydration. Only isotonic fluid should be administered during this initial fluid resuscitation phase. Lactated Ringer solution should be avoided if renal function is significantly impaired.

An insulin infusion—without a bolus of IV insulin—should be initiated at 0.05 to 0.1 U/kg/h. Subsequent IV fluids can be started using normal saline with 20 mEq/L of potassium chloride and 20 mEq/L of potassium phosphate (as long as urine output is adequate) at 1.5 to 2 times maintenance, for a total amount not to exceed 3,500 mL/m²/d. A dextrose solution (10% dextrose in normal saline with potassium chloride and potassium phosphate) can be added once the blood glucose level is below 300 mg/dL.

Levels should be brought down by no more than 100 mg/dL (5.5 mmol/L) every hour. A more rapid decline might require the addition of dextrose to the IV fluid sooner, even if the serum level remains elevated above 300 mg/dL. Because insulin is responsible for correction of the acidosis, the insulin infusion should be maintained while adjusting the dextrose solution as required to effect an appropriate adjustment in blood glucose level.

Hourly monitoring of blood glucose and blood gases (every 2-4 hours), frequent monitoring of electrolytes (including sodium, potassium, calcium, magnesium, and phosphate), and cardiovascular ECG monitoring should be performed.

> !
>
> *Administration of sodium bicarbonate is not indicated unless severe acidosis, with resultant hemodynamic compromise or arrhythmias from hyperkalemia, is present. Sodium bicarbonate is potentially harmful as it causes significant osmolar shifts and potentially worsens cerebral edema.*
>
> !

2. Cerebral Edema

Most patients with DKA might have some degree of cerebral edema at presentation. The main risk factors for progression are administration of large quantities of hypotonic fluids, rapid hourly declines in blood glucose levels, and hyponatremia. The latter commonly occurs in DKA and is also a result of the hyperglycemia and hypertriglyceridemia (pseudohyponatremia).

$$Na^+ \text{ corrected} = Na^+ \text{ observed} + \{(\text{glucose in mg/dL} - 100/100) \times 1.6\}$$

If both hyperglycemia and hypertriglyceridemia are fully corrected, the sodium level can be predicted using the following formula:

$$\{\text{Reported sodium (mEq/L)}\}\ \{0.021[\text{triglycerides (g/dL)} + 0.994] + 0.016\ [\text{glucose (mg/dL)}]\}$$

PED Diabetic Ketoacidosis (DKA) Clinical Pathway

Initial Assessment

Clinical History and **Clinical Signs**

ABCs, vital signs, neurological exam (including GCS)

Assess **Cerebral Edema Risk Factors**

Initial Interventions

Establish vascular access (2 peripheral IVs)

Initial **Fluid Resuscitation** (10 ml/kg IV over 1 hour if not in shock)

Initial Lab Assessment (see EPIC order set)

Blood Glucose, UA, VBG, Serum Ketones, CBC, BMP, Beta-hydroxybutyrate (BHOB), Mg, Phos

Diagnosis

Hyperglycemia > 200 mg/dL **AND**

Venous pH < 7.3 or serum bicarbonate < 15 mmol/L **AND**

Ketonemia (blood ß-hydroxybuyrate ≥3 mmol/L) or moderate or large ketonuria (Note – do not need to delay management pending blood ß-hydroxybuyrate if other criteria met)

Management

Continue initial **Fluid Resuscitation**, then 1.5 X maintenance as outlined in sidebar

Electrolyte Assessment /Management

Discuss **Insulin** infusion with PICU attending – if no significant delay in transfer hold on starting insulin infusion until arrival in PICU; if delay start insulin infusion (see EPIC order set)

Monitoring

Vital signs and neurological exam (including mentation) every 15 min until stable

Serum pH, Blood glucose every 1 hour; BMP, UA for ketones every 2 hours

Begin dextrose infusion when the patient's glucose is < 300 mg/dL

Disposition

Consult Wolfson Children's Hospital (WCH) Pediatric Intensive Care Unit (PICU) for admission

904-202-5437

Request Kids Kare for transport

If not available, only transport via ALS unit

References

Clinical History

Polyuria, polydipsia, weight loss, fatigue, vomiting, confusion/AMS (especially in young patients)

Clinical Signs

Dehydration, Kussmaul breathing, smell of ketones, vomiting, lethargy/AMS, opportunistic infections

Cerebral Edema Risk Factors

Age < 3 years; prior history of DKA; pH < 7.0; failure of corrected Na to fall to normal range during treatment; administration of bicarbonate therapy; low initial $PaCO_2$ levels (11.3 ± 6.5 mm Hg); administration of insulin in first hour of fluid treatment; initial glucose > 1000 mg/dL

Fluid Resuscitation

Initial fluid bolus of 10 ml/kg IV over 1 hour (if not in shock)

Following initial bolus, begin 1.5 times maintenance with NS

To calculate maintenance mL/hr, use patient's weight in kg:

- 4 mL/kg for the first 10 kg
- +2 mL/kg for the next 10 kg
- +1 mL/kg for each kg over 20 kg

Two-bag system: NS + D10NS = 1.5x maintenance. Titrate ratio of NS:D10NS based on blood glucose. Start with 100% NS then initiate D10NS when blood glucose < 300mg/dl

Electrolyte Assessment/Management

Sodium: $Na_{correct} = Na_{measured} + (1.6 \times [(Glucose - 100) / 100$

Potassium: Replacement based on initial serum K+

Serum K+	K+ in Fluids
> 5.5	None
4.0 – 5.5	20 mEq/L K-Acetate + 20mEq/L K-Phos
< 4.0	30 mEq/L K-Acetate + 30mEq/L K-Phos

Perform ECG if serum potassium < 2.5 or > 6.0

Insulin

Discuss insulin infusion with PICU attending prior to initiating: if no significant delay in transfer hold on starting insulin infusion until arrival in PICU; if delay start insulin infusion in ED (see EPIC order set).

Initiate **regular** insulin at rate of 0.1 u/kg/hr one hour AFTER the start of the fluid resuscitation.

Do not use insulin bolus (increases risk of cerebral edema).

Goal is to lower glucose by no more than 50 – 100 mg/dL every hour

APH Diabetic Ketoacidosis Management Protocol - Emergency Department

- Eligible Patients
  - Diagnosis of diabetic ketoacidosis
  - Needs admission to PICU or PSCU
- Initial management: no bicarbonate bolus, no insulin bolus, patient should have at least 2 PIVs or a CVL
  - Administer 10 cc/kg 0.9 % NS bolus (give over 1st hour of resuscitation)
    - Repeat 10 cc/kg 0.9% NS bolus over 2nd hour prn inadequate organ perfusion
  - LABS in ER (ON ARRIVAL):
    - Whole blood (AND Q1h while in the ER)
    - CBC
    - Beta-hydroxybutyrate
    - BMP
    - UA
- Insulin
  - Insulin gtt at 0.1 units/kg/hr
- Intravenous fluids
  - IVF rate in ml/hr = **2x Maintenance Rate**
    (or use actual fluid calculation: (84 ml/kg – bolus given) /23 hr + maintenance rate)
  - Potassium:
    - Default: include potassium if K < 5.5
    - If K ≥ 5.5, use two-bag system without potassium
    - If K < 4, use two-bag system with 60meq/L potassium (30 meq/L Kacetate + 30mmol/L KPhos)
    - If K < 3, hold insulin drip until IVF are started
  - Two-bag system: order both bags simultaneously STAT

	½ NS + 20meq/L K-acetate + 20mmol/L KPhos	D_{10} ½ NS + 20meq/L K-acetate + 20mmol/L KPhos
INITIAL BLOOD GLUCOSE <500		
Serum glucose	Percent of IVF	Percent of IVF
>350	100% = ____ mL /hr	0%
250-349	50%= ____ mL /hr	50%= ____ mL /hr
100-249	0%	100%= ____ mL /hr
< 100	Notify physician	
INITIAL BLOOD GLUCOSE ≥ 500		
Serum glucose	Percent of IVF	Percent of IVF
>500	100%=___ ml/hr	0%
400-499	75%=___ ml/hr	25%=___ml/hr
300-399	50%=___ml/hr	50%=___ml/hr
200-299	25%=___ml/hr	75%=___ml/hr
100-199	0%	100%=___ml/hr
<100	Notify physician	

*If blood glucose drops by more than 100 mg/dL in one hour contact physician

- NURSING
  - VS q30min
  - Neuro checks Q30min
  - Notify H.O. for vomiting, confusion, agitation, bradycardia, urinary incontinence, abnormal neurological exam, headache, or if BG drops by more than 100 mg/dL in 1 hr
  - RN and physician to assess adequacy of fluid resuscitation after 1st bolus of 10 cc/kg over 1 hr completed

Revision – 1/22/2014

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Managing Diabetic Ketoacidosis in Children

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0196-0644/$-see front matter
Copyright © 2021 by the American College of Emergency Physicians.
https://doi.org/10.1016/j.annemergmed.2021.02.028

Continuing Medical Education exam for this article is available at http://www.acep.org/ACEPeCME/.

[Ann Emerg Med. 2021;78:340-345.]

INTRODUCTION

Diabetic ketoacidosis is a life-threatening complication of childhood diabetes (mainly associated with type 1 or insulin-dependent diabetes).[1] Thirty percent of children with new-onset type 1 diabetes present with diabetic ketoacidosis, and an additional 6% to 8% develop diabetic ketoacidosis each year. [2,3] Presenting symptoms may be nonspecific, but laboratory findings of hyperglycemia and ketosis are diagnostic. Treatment involves administration of intravenous fluids and insulin. Children with diabetic ketoacidosis require serial laboratory studies for electrolyte derangements and close clinical monitoring for signs of cerebral edema, an uncommon but potentially fatal complication of pediatric diabetic ketoacidosis. For years, clinical guidelines for the treatment of diabetic ketoacidosis have recommended limited (if any) fluid resuscitation, isotonic fluids, and slow fluid rehydration rates in order to reduce the rate of cerebral edema.[4] A recently completed clinical trial explored the relationship between fluid replacement and cerebral injury and edema, and it provided new evidence to guide safe and effective fluid treatment for pediatric diabetic ketoacidosis.[5]

DIAGNOSIS

Clinical Presentation

Early signs and symptoms of diabetic ketoacidosis include polyuria, polydipsia, weight loss, and fatigue. These symptoms may be more difficult to recognize in younger children, particularly those who are preverbal or use diapers. A detailed history may elicit these signs and symptoms of diabetic ketoacidosis in children with new-onset diabetes and identify potential triggers, including nonadherence to insulin regimen (particularly among adolescents) or intercurrent illness.

If untreated, a child with diabetic ketoacidosis may develop abdominal pain, vomiting, and headache. Clinicians should maintain a high index of suspicion and low threshold for laboratory testing, even for children without known diabetes. Despite significant dehydration, many children with diabetic ketoacidosis present with normal blood pressure or, occasionally, hypertension.[6] Clinical signs (eg, pulse rate or peripheral perfusion) may be inaccurate for assessing the degree of dehydration in children with diabetic ketoacidosis.

As diabetic ketoacidosis progresses, respiratory compensation for the metabolic acidosis of diabetic ketoacidosis causes tachypnea and a deep and labored breathing pattern referred to as Kussmaul respirations. Changes in mental status, including drowsiness, irritability, lethargy, and confusion, may also occur.

Diabetic Ketoacidosis Definition

Based on recent international consensus, diabetic ketoacidosis is defined by hyperglycemia and metabolic acidosis with low serum bicarbonate level, high serum ketones level, or urinary ketones (Table 1).[7]

Laboratory Evaluation

Once a diagnosis of diabetic ketoacidosis is suspected, initial laboratory studies should include point-of-care glucose, venous blood gas, serum electrolyte levels (including magnesium and phosphorus), serum creatinine level, β-hydroxybutyrate level, and urinalysis and a pregnancy test in adolescent women (Table 2). Measured serum sodium level should be corrected for the presence of hyperglycemia with the following formula: corrected sodium=measured sodium+[1.6 (glucose−100)/100]. A complete blood count is frequently obtained to evaluate for an infectious trigger for diabetic ketoacidosis but may demonstrate a nonspecific leukocytosis.[8] In patients with abnormal serum potassium levels (either high or low), an electrocardiogram is indicated. Hemoglobin A1c provides a measure of glucose control over the previous several months.

Acute kidney injury is present in a substantial percentage of children with diabetic ketoacidosis. In a retrospective study of 165 and a prospective study of

Table 1. Diabetic ketoacidosis definition.

Criteria	Laboratory Test	Level
Hyperglycemia	Blood glucose	>200 mg/dL (11 mmol/L)
Metabolic acidosis	Venous pH	<7.3
	Serum bicarbonate	<15 mEq/L (15 mmol/L)
	Serum β-hydroxybutrate level	>30 mg/dL (3 mmol/L)
	Urine ketosis	
	Moderate to large	

1,359 diabetic ketoacidosis episodes, 64% and 43%, respectively, had acute kidney injury, and most received a diagnosis at presentation.[9,10] In both studies, acute kidney injury was associated with more severe dehydration and acidosis.

TREATMENT

The mainstays of diabetic ketoacidosis treatment are intravenous fluid resuscitation and insulin administration (Figure 1).

Fluid and Electrolyte Replacement

At the time of presentation, most children in diabetic ketoacidosis are typically 5% to 10% dehydrated. The goal is repletion of the patient's fluid deficit over the first 36 to 48 hours (Table 3). Initial fluid resuscitation with 10 mL/kg normal saline solution bolus is indicated. Patients with Glasgow Coma Scale scores of 14 or 15 who exhibit persistent tachycardia or signs of poor perfusion may safely receive an additional normal saline solution bolus immediately after completion of the first bolus.

After administration of the bolus(es), additional intravenous fluids should be provided to replete the remaining fluid deficit and provide ongoing maintenance. Table 3 demonstrates a range of fluid administration rates that can safely be used based on patient weight, estimated fluid deficit, and desired duration of repletion (typically 36 to 48 hours) but not patient age.[5] Intravenous fluids are continued until the acidosis has resolved and the patient is able to tolerate oral intake and is transitioned from intravenous to subcutaneous insulin. Fluid repletion and intravenous insulin will gradually correct the marked acidosis seen in children with diabetic ketoacidosis, and sodium bicarbonate should not be administered.[11]

Even when the serum potassium level is elevated, a child with diabetic ketoacidosis will have a total potassium deficit as the intracellular exchange of hydrogen ions for potassium leads to urinary potassium loss. Therefore, the addition of 40 mEq of potassium equivalent per liter of fluid (eg, 20 mEq potassium phosphate and 20 mEq potassium acetate or potassium chloride per liter) is typical when the serum potassium level drops below 5 mEq/L (5 mmol/L) and the patient has established urine output.

Children with diabetic ketoacidosis are frequently prevented from taking anything by mouth owing to nausea and the risk of worsening mental status with inability to protect an airway. However, in the appropriate clinical scenario, small amounts of water or ice chips can improve patient comfort.

Insulin Infusion

Insulin should be started after fluid resuscitation has been initiated and the diagnosis of diabetic ketoacidosis has been confirmed. In children with mild diabetic ketoacidosis who are able to tolerate oral fluids and nutrition, rapid-acting insulin may be given subcutaneously. However, for children with moderate to severe diabetic ketoacidosis (defined by pH<7.2), regular insulin should be delivered by continuous intravenous infusion (0.05 to 0.1 units/kg per hour).[7] Insulin boluses should be avoided. The insulin infusion should not be discontinued until the acidosis resolves.

Prevention of Hypoglycemia

During diabetic ketoacidosis treatment, the serum glucose level will decrease. When serum glucose levels drop below 300 mg/dL (16.7 mmol/L), dextrose should be added to the intravenous fluids without changing the insulin dosing. The "2-bag method" can be used to titrate patient blood glucose by varying the rates of 2 fluid types (1 with and 1 without dextrose) to keep the

Table 2. Other laboratory abnormalities associated with diabetic ketoacidosis.

Laboratory Study	Expected Result	Reason
Glucose	↑	Elevated despite intracellular depletion
Sodium	↓	Hyperglycemia decreases measured serum sodium
Potassium	↑ or normal	Serum potassium increases owing to displacement from intracellular space despite total body depletion
Phosphate	↑ or normal	Serum phosphate initially increases owing to displacement from intracellular space despite total body depletion
Anion gap	↑	Elevated because of ketosis and lactic acidosis

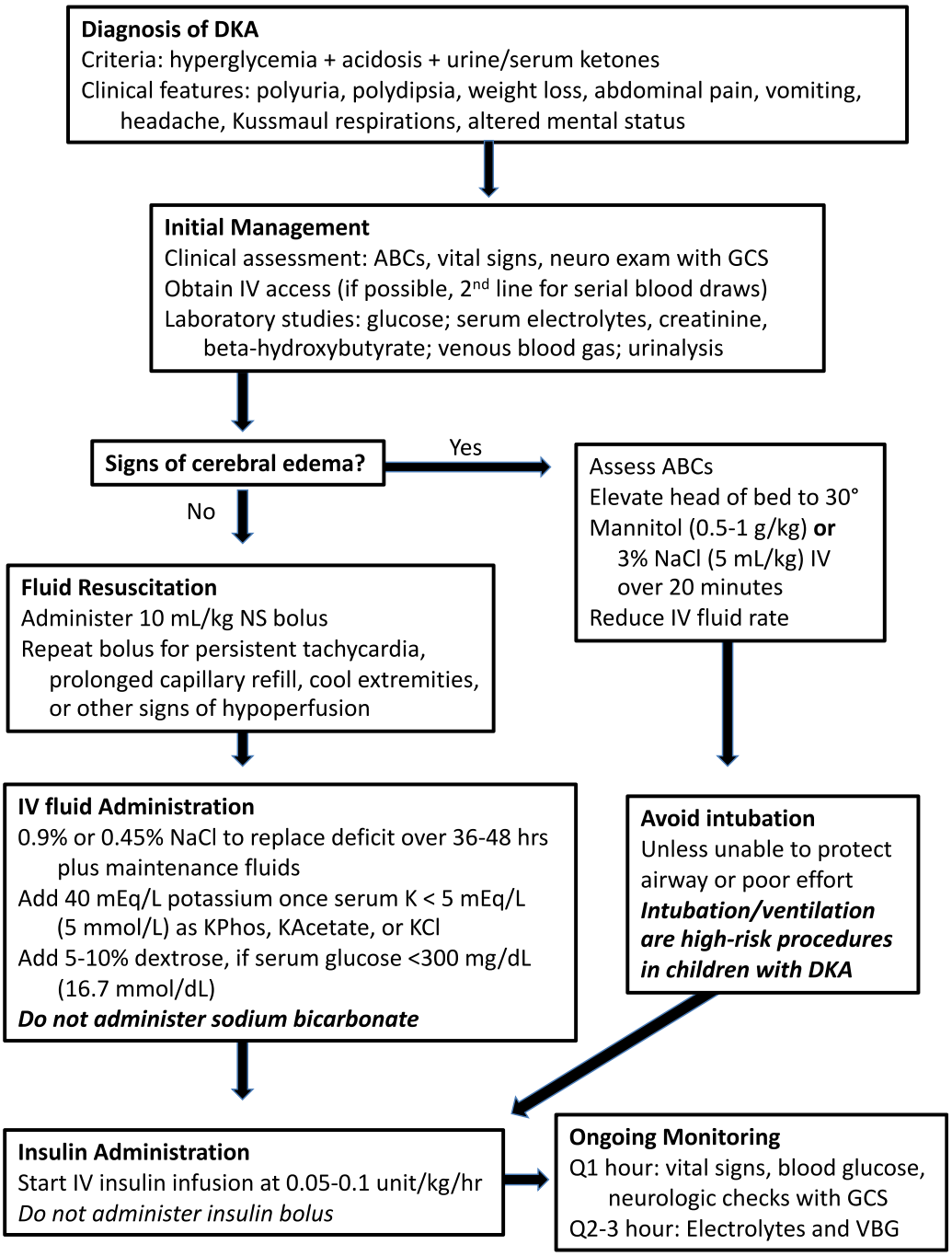

Figure 1. Diabetic ketoacidosis clinical algorithm. Concept adapted from Translating Emergency Knowledge for Kids Pediatric Diabetic Ketoacidosis Pediatric Package Algorithm. Visit www.trekk.ca/ for the complete algorithm. *ABC*, airway, breathing, circulation; *DKA*, diabetic ketoacidosis; *GCS*, Glasgow Coma Scale; *K*, potassium; *KAcetate*, potassium acetate; *KCl*, potassium chloride; *NaCl*, sodium chloride; *NS*, normal saline solution; *VBG*, venous blood gas.

serum glucose level between 150 and 250 mg/dL (8.3 to 13.9 mmol/L) (Figure 2).[12] Alternatively, clinicians can steadily increase the dextrose content of the fluid by switching the amount of dextrose as the patient's serum glucose level falls. If serum glucose level continues to decrease despite administration of fluids containing 10% dextrose, the dose of the insulin infusion may be decreased to 0.05 units/kg per hour.

Airway Management

Intubation should be avoided in children with diabetic ketoacidosis except when a child has inadequate respiratory

Table 3. Fluid deficit by patient weight with range of appropriate fluid administration rates (after initial boluses).

Weight (kg)	Estimated Deficit (5%-10% Dehydration)	Replacement of Estimated Deficit + Maintenance = Initial Fluid Rate (mL/hour)*
10	500-1,000 mL	48-78
20	1,000-2,000 mL	77-135
30	1,500-3,000 mL	95-183
40	2,000-4,000 mL	113-230
50	2,500-5,000 mL	132-278
60	3,000-6,000 mL	150-325
70	3,500-7,000 mL	168-373

*Range based on estimated deficit and desired replacement rate over 36 to 48 hours with slower rates for smaller estimated fluid deficits or longer durations of therapy.

effort or an inability to adequately protect the airway. Assuming control of ventilation runs the risk of blunting compensatory respiratory alkalosis to correct for the metabolic acidosis. If intubation is required, hyperventilation beyond this compensatory level has been associated with worse clinical outcomes and should also be avoided.[13]

Patient Monitoring

Close monitoring of mental status with hourly measurements of the patient's Glasgow Coma Scale score is essential for rapid identification of neurologic deterioration. Regular laboratory studies include hourly serum glucose level as well as venous blood gas and serum electrolyte levels every 2 to 3 hours. The placement of a second peripheral intravenous line for serial laboratory draws avoids additional needlesticks. Central venous catheter placement is associated with an increased risk of deep venous thrombosis in pediatric diabetic ketoacidosis and should be avoided.[14,15]

Disposition and Transfer Considerations

Disposition of patients with diabetic ketoacidosis depends on the severity of the disease and the resources available. Patients with established diabetes and mild diabetic ketoacidosis (pH 7.2 to 7.3) are candidates for potential discharge home after emergency department treatment. To be safely managed as outpatients, children need to demonstrate improvement with regard to laboratory abnormalities and the ability to tolerate oral fluids with adequate resources for home monitoring and close follow-up. Otherwise, children require hospitalization in a center that can provide close clinical and laboratory monitoring until diabetic ketoacidosis resolves.

Owing to the need for hourly glucose testing, close neurologic monitoring, and frequent laboratory studies, many children with diabetic ketoacidosis are managed in intensive care units. Patients with severe diabetic ketoacidosis (pH<7.1), altered mental status, young age, or severe electrolyte abnormalities always require intensive care. When transferring a child with diabetic ketoacidosis, the use of a critical care transport team should be considered in all cases and is necessary for children with altered mental status or prolonged transport time when monitoring of blood glucose or titration of intravenous fluids may be necessary en route.

CEREBRAL EDEMA

Although <1% of pediatric episodes of diabetic ketoacidosis are associated with the development of clinically overt cerebral edema with altered mental status, subclinical cerebral edema occurs more frequently and may be associated with long-term neurocognitive deficits.[16] Although some children present for care with existing signs of cerebral injury or edema, most cases develop within 12 to 24 hours of treatment initiation.[11,16] The diagnosis of cerebral edema is made clinically based on neurologic abnormalities, vital sign changes, and symptoms of increased intracranial pressure.[17] Cranial computed tomography is not required for diagnosis and should not delay treatment with hyperosmolar therapy (mannitol or hypertonic saline solution).[18]

Prevention

Historically, cerebral edema in children with diabetic ketoacidosis was assumed to be caused by osmotic shifts from rapid correction of dehydration or electrolyte abnormalities. In recognition of this potential association, pediatric diabetic ketoacidosis treatment protocols have limited the rate and volume of intravenous fluid administration. However, a decade of high-quality evidence has challenged these assumptions.

First, a 10-center case control study of 61 cases (children with diabetic ketoacidosis associated with

Figure 2. Two-bag fluid system. One bag contains 0.9% or 0.45% saline solution with 10% dextrose, and the other bag contains 0.9% or 0.45% saline solution without dextrose. To prevent hypoglycemia, an infusion of the dextrose-containing fluid is initiated when serum glucose level drops below 300 mg/dL (16.7 mmol/L) and increased to keep serum glucose levels between 150 and 250 mg/dL (8.3 to 13.9 mmol/L). The rate of the nondextrose-containing fluid is decreased accordingly to maintain a constant total fluid infusion rate.

cerebral edema) and 355 selected controls (children with diabetic ketoacidosis without cerebral edema) investigated treatment-related risk factors of cerebral edema.[11] After adjusting for diabetic ketoacidosis severity and degree of dehydration, the rate of fluid administration was not associated with cerebral edema. The only modifiable factor associated with cerebral edema identified after adjustment for diabetic ketoacidosis severity was the administration of sodium bicarbonate, which should be avoided.

Following this observation, Pediatric Emergency Care Applied Research Network investigators completed a 13-center randomized clinical trial of children younger than 18 years to compare the safety of 4 diabetic ketoacidosis fluid rehydration protocols.[5] After the initial 0.9% sodium chloride fluid bolus, children were randomized to either faster or slower fluid administration rate (0.9% or 0.45% sodium chloride fluids) for subsequent rehydration. In this study of nearly 1,400 children with diabetic ketoacidosis, rates of acute neurologic deterioration as well as short- and longer-term neurocognitive outcomes were similar between treatment groups, suggesting that neither the rate of fluid administration nor the sodium content within the ranges studied caused the brain injury.[5]

Based on the findings of this high-quality clinical trial, clinicians should use hydration status to guide the fluid resuscitation of children with diabetic ketoacidosis. Specifically, restricting fluid administration because of concerns about causing cerebral edema appears unfounded in children with initial Glasgow Coma Scale scores of 14 or 15.

Treatment

Once recognized, cerebral edema should be treated rapidly. Precautions for increased intracranial pressure, including elevation of the head of the bed, should be instituted. Either intravenous mannitol (0.5 to 1 mg/kg) or hypertonic 3% saline solution (5 mL/kg) can be rapidly administered, although hypertonic saline solution is being used increasingly as a first-line therapy.[19] One small study found an association between hypertonic saline solution and mortality, but this was likely owing to unmeasured confounding.[20] We believe that clinicians should not hesitate to use this therapy to treat cerebral edema in children.

In conclusion, children with diabetic ketoacidosis, particularly those with previously undiagnosed diabetes, may present with nonspecific symptoms. Early recognition with appropriate laboratory screening can identify children with diabetic ketoacidosis and drive appropriate therapy. Fluid hydration coupled with continuous insulin infusion is the cornerstone of therapy. Frequent clinical and laboratory monitoring is essential for clinicians to recognize and address complications, including cerebral edema. In contrast with prior teachings, intravenous fluid administration can be liberalized to appropriately treat dehydration associated with diabetic ketoacidosis in patients without evidence of cerebral edema prior to treatment.

Supervising editor: Steven M. Green, MD. Specific detailed information about possible conflict of interest for individual editors is available at https://www.annemergmed.com/editors.

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Authorship: All authors attest to meeting the four ICMJE.org authorship criteria: (1) Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND (2) Drafting the work or revising it critically for important intellectual content; AND (3) Final approval of the version to be published; AND (4) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Funding and support: The authors report this article did not receive any outside funding or support.

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