Evaluation and Management of Diabetic Ketoacidosis

Clinical Practice Guideline

Approved by SSM Health Cardinal Glennon Clinical Practice Guidelines Committee March 28, 2024

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Evaluation and Management of Diabetic Ketoacidosis
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SSMHealth Cardinal Glennon
Access Center Transfer Line
888-229-2424

1. SSMHealth Cardinal Glennon CPG Home

2. Resources
a. ISPAD (International Society for Pediatric and Adolescent Diabetes) Clinical Practice Consensus Guidelines. *Pediatric Diabetes*. 2018; 19 (27): 155-177.
b. Kupperman N, et al. Clinical Trial of Infusion Rates in Pediatric Diabetic Ketoacidosis. *New Engl J Med*. 2018; 378(24): 2275-2287.

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DIABETIC KETOACIDOSIS (DKA) - DEFINITION AND CLINICAL SUSPICION

- Definition: Hyperglycemia, metabolic acidosis (pH < 7.30 and/or serum bicarbonate < 15), and ketonuria
- History: Polyuria, polydipsia, fatigue, anorexia or polyphagia, nocturnal enuresis, altered mental status, tachypnea
- Presumptive diagnosis: Based on history findings, hyperglycemia on glucometer, ketonuria on urine dipstick

- Evaluate ABC's, stabilize as appropriate
- Vital Signs
  - Temperature, Pulse, Respirations, Blood Pressure, O2 Saturation, Weight (kg), Height (cm), quick neuro exam
- Establish IV access, preferably two IV sites

ALTERED MENTAL STATUS OR OTHER CLINICAL CONCERN FOR CEREBRAL EDEMA

- Consider initiating treatment immediately, without delay for imaging
  - Hypertonic saline (3%) 5mL/kg over 10-15 minutes
- Elevate the head of bed, consider other supportive interventions such as mechanical hyperventilation
- Consider CT scan after treatment has been initiated and the patient stabilized

INITIAL FLUID RESUSCITATION

20mL/kg Normal Saline OR Lactated Ringers over 60 minutes (maximum 1000mL)

LABORATORY STUDIES

- Lytes + Creatinine + Magnesium + Phosphorus
- Venous blood gas
- Urinalysis

Is the patient currently at SSM Cardinal Glennon OR going to be admitted at local institution?

NO → **Call 888-229-2424 (SSM Health Cardinal Glennon Access Line) to Initiate Transfer**
Pediatric Endocrinology to be contacted by Access Center

DETERMINE AND DISCUSS
- Modality of transport and expected ETA
- Insulin drip: start prior to transport OR wait until arrival to CGCH
- Subsequent fluid hydration

YES

INSULIN DRIP (NOT BOLUS)
- Order STAT upon arrival to ED
- Concentration
  -> Standard: 1 Unit/mL (patients > 20 kg)
  -> Infant: 0.2 Unit/mL (patients ≤ 20kg)
- Infusion Rate: 0.1 Units/kg/hour
- For patients on insulin pump therapy, ensure insulin pump infusions are discontinued and the pump is disconnected from the patient
- If drip already initiated (at referring facility), verify correct rate (0.1 Units/kg/hour) and proceed to Disposition

TRANSFER FROM OUTSIDE HOSPITAL
- Determine how much fluid patient has already received
- Determine dose, timing, and delivery mode of all prior and ongoing insulin administration
- Perform bedside glucose testing upon arrival and repeat BMP, Phos
- Modify ongoing/subsequent fluids and labs on arrival based on findings

DISPOSITION
- Consult Pediatric Endocrinology Attending on-call after initial or repeat labs
- Admit to TCU or PICU
  - Findings indicating more severe illness and admission to the PICU to be considered:
    - pH < 7.10 for new onset or < 7.0 for known diabetic patients
    - Serum bicarbonate < 5
    - Glasgow Coma Scale (GCS) 12 or less
    - Serum Glucose > 1000
    - Potassium < 3.5
    - Corrected sodium > 155 (*see Box 1*)
    - Serum osmolarity > 320 (See Box 2 for calculation)
    - Patient age < 3 years (consider PICU for age 3-5)

LAB AND CARE FREQUENCIES
- Hemoglobin A1c
- New onset patients
  - IA-2, GAD-65, Zinc transporter-8, and Insulin autoantibody
- Vital signs every 1 hour (PICU) or every 2 hours (TCU) for 24 hours
- Neuro checks every 1 hour (PICU) or every 2 hours (TCU) for 24 hours
- Bedside glucose every 1 hour
- Lytes and Serum Magnesium and Phosphate minimum every 4 hours
- BMP every 12 hours (can omit blood gas/GEM electrolytes at this time
- Serum potassium every 2 hours if initially abnormal (< 3.0 or > 5.5)
- Urine ketones every 8 hours
- Strict I/O's
- Keep patient NPO

SUBSEQUENT FLUID RESUSCITATION
- Total fluid rate should be 3L/m^2/day (2x maintenance fluid rate) for the first 24 hours
- Order 2 bags of fluid simultaneously
  - Bag #1: 1/2 Normal Saline OR Normal Saline, with potassium
  - Bag #2: D10 1/2 Normal Saline OR D10 Normal Saline, with potassium
- Potassium Content

Serum Potassium	Potassium-Acetate	Potassium-Phosphate	Total Potassium in Fluids (K-Acetate and K-Phos total)
3.0-4.0*	30 mEq/L	30 mEq/L	60 mEq/L
4.1-5.5	20 mEq/L	20 mEq/L	40 mEq/L
> 5.5**	None	None	None

* = Larger amounts may be needed if serum K is less than 3.0
**= Check potassium every 2 hours, once serum K is < 5.5, add 40mEq/L as above

- Sodium Content
  - Normal saline is recommended if corrected serum sodium is < 135 (see Box 1), if the child meets criteria for PICU admission, or if there is any concern for cerebral edema
  - If normal saline is started initially, maintain ongoing fluid resuscitation with normal saline until the initial bag is complete before switching to an alternative base solution

GLUCOSE TITRATION
- Titrate Dextrose-containing fluid contribution to fluid rate based on serum glucose. Suggested ratio:

Blood Glucose Level	% D10 Maintenance Fluid	% 1/2 NS or NS Maintenance Fluid
≥ 300	0%	100%
251-299	50%	50%
201-250	75%	25%
151-200	100%	0%

* = Fluid components may require individualization based on patient response, rate of glucose correction, and other patient factors

- Ensure dextrose content of fluids is maximized prior to decreasing the insulin drip rate (may require up to D12.5)
- Discuss dose and timing of administration of long-acting insulin with Pediatric Endocrinologist on-call
- Insulin drip may be reduced to 0.05-0.08 U/kg/hr to maintain blood glucose at 150-250 if acidosis is correcting and dextrose content of the fluids is maximized

Box 1: Corrected Serum Sodium
Below are minimum measured serum sodium levels corresponding to corrected value thresholds by glucose range:

Corrected Sodium of 155 or Higher Threshold

Glucose Range (mg/dL)	Measured Sodium (mEq/L)
200	153
201-300	152
301-400	150
401-500	148
501-600	147
601-700	144
701-800	142
801-900	141
901-1000	139

Corrected Sodium of 135 or Lower Threshold

Glucose Range (mg/dL)	Measured Sodium (mEq/L)
200	132
201-300	130
301-400	129
401-500	127
501-600	125
601-700	124
701-800	122
801-900	121
901-1000	119

Corrected Sodium = Measured Serum Sodium (in mEq/L) + (0.016 X (Serum glucose in mg/dL - 100))

Box 2: Serum Osmolarity

(Na x 2) + (Glucose/18) + (BUN/2.8)

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Transition to Subcutaneous Insulin in Patients with Diabetic Ketoacidosis (DKA)

READINESS TO TRANSITION TO SUBCUTANEOUS INSULIN

- **Bicarbonate > 18 OR Bicarbonate > 14 if chloride is above the upper limit of normal**
- **Patient is alert and ready to eat a meal**
- **Anion gap is < 16**

↓

Consult with the Pediatric Endocrinologist On-call prior to transition to subcutaneous insulin

↓

Insulin injection or insulin pump therapy being initiated?

Insulin Injection

- **Provide long-acting insulin dose at least 2 hours prior to discontinuing insulin drip**

Insulin Pump

- **Make sure patient has pump supplies present and guardian will be at bedside to assist pump management**
- **Start pump basal rate at least 1 hour prior to discontinuation of insulin drip**

↓

Make sure insulin orders are entered for carbohydrate and correction dosing, and that insulin is on the floor

↓

Check pre-meal point-of-care blood glucose

↓

Allow the patient to eat

↓

After the patient has eaten, administer subcutaneous insulin dose by pump or injection for meal carbohydrates consumed and pre-meal correction

↓

Discontinue the insulin drip and dextrose-containing IV fluids; discuss the need to continue non-dextrose containing fluids with the Pediatric Endocrinology Attending

MANAGEMENT OF DIABETIC KETOACIDOSIS

Diabetic ketoacidosis (DKA), defined as the presence of ketonuria, metabolic acidosis (pH < 7.30 and/or serum HCO3 < 15), and hyperglycemia is a medical emergency. A presumptive diagnosis can usually be made at the bedside on the basis of history, glucometer check, and urine dipstick.

I. RESUSCITATION

VENOUS ACCESS

Establish venous access within 30 minutes of arrival. Having two IV sites, one for fluid/medication infusion and one for sampling, is ideal.

ADMISSION LABORATORY STUDIES

On arrival, send venous blood STAT for sodium, potassium, chloride, HCO3, BUN, creatinine, glucose, and pH. If infection is suspected (if fever is present), consider chest X-ray and cultures of blood and urine. A hemoglobin A1c and autoimmune antibody studies (IA-2, GAD-65, Zinc transporter 8, and Insulin autoantibody) should be sent in the new-onset child.

INITIAL FLUID RESUSCITATION

Once IV access is established, and while awaiting the results of the admission laboratory studies, administer normal saline (NS) or lactated ringer's (LR) 20 mL/kg IV over 60 minutes. If shock or hypotension persists, give additional boluses of 10-20 cc/kg; **however**, DKA brings most children to the hospital with only moderate dehydration (10% of usual body weight), so larger initial boluses are usually not needed. The composition of subsequent rehydration fluids can await the admission laboratory studies (see below).

INITIAL INSULIN INFUSION

Once the diagnosis is established and the blood glucose is known, start IV regular insulin at a rate of 0.1 Unit/kg/hour. If the patient is on insulin pump therapy, ensure the pump is disconnected prior to initiation of the insulin drip. A bolus dose of IV insulin is NOT RECOMMENDED. It is imperative that the physician check the insulin infusion once it is begun.

II. ADMISSION DISPOSITION

Admission to the Pediatric Intensive Care Unit (PICU) is recommended for any of the following:

- Altered mental status
- pH < 7.1 for new onset or pH < 7.0 for known diabetic patients
- Potassium < 3.5
- Age < 3 years (consider PICU admission for age 3-5)
- Serum glucose > 1000 mg/dL
- Corrected sodium > 155 mEq/L
    - Corrected Na = Serum Na + (0.016 x (Serum Glucose – 100))
- Serum osmolarity > 320
    - Serum Osmolarity = (Na x 2) + (Glucose/18) + (BUN/2.8)

Notify the Pediatric Endocrinologist on-call of all DKA admissions, even if they are being admitted to the PICU. Patients not admitted to the PICU are admitted at SSM Health Cardinal Glennon to the TCU under the Pediatric Endocrinology attending.

III. STABILIZATION

IV FLUIDS

Our DKA protocol utilizes a two-bag fluid system in addition to the insulin infusion. One bag will be 1/2 Normal Saline OR Normal Saline (NS), with potassium added according to the initial serum potassium level (see Table 1 below). The second bag will be D10 1/2 Normal Saline OR D10 Normal Saline, with potassium added according to the initial serum potassium level (see Table 1 below). Selection of appropriate sodium content (1/2 Normal saline or Normal saline) should be determined by the initial corrected sodium and clinical context of the patient (see section on 'Sodium' below).

Infusion Rate

The post-resuscitation fluids should run at 3 liters/m^2/24hr (Two times Maintenance Rate) for the first 24 hours. The patient should be NPO (oral swabs with water may be considered to help with dry mouth if patient has a normal mental status). The total fluid rate should remain the same, with only the component of dextrose content titrated as below.

Potassium

Ordered as equal parts K-acetate and K-phosphate, with total potassium in the IV fluids based on serum potassium level (see Table 1)

Table 1: Potassium recommendations for IV fluids based on initial serum potassium level

Serum Potassium	Potassium-Acetate	Potassium-Phosphate	Total Potassium in fluids (K-Acetate and K-Phos total)
3.0-4.0*	30 mEq/L	30 mEq/L	60 mEq/L
4.1-5.5	20 mEq/L	20 mEq/L	40 mEq/L
> 5.5**	None	None	None

* = Larger amounts may be needed if potassium level is less than 3.0

** = Check the serum potassium every 2 hours if no potassium is added to the IV fluids initially; once serum K is below 5.5, add potassium per Table 1.

Sodium

Normal Saline and D10 Normal Saline are recommended for the initial IV fluids if the corrected serum sodium is less than 135, if the child meets criteria for PICU admission, or if there is any clinical concern for cerebral edema. For all other children, 1/2 Normal Saline and D10 1/2 Normal Saline are recommended.

The 2018 PECARN FLUID Study found no significant differences in morbidity between use of 1/2 Normal Saline or Normal Saline. However, hyperchloremic acidosis was more common in the NS group, making it more difficulty to determine when DKA had resolved.

GLUCOSE TITRATION/INSULIN INFUSION

If blood glucose if over 300, all non-dextrose containing fluids are started. Once glucose is < 300, a combination of dextrose and non-dextrose containing fluids should be started (see Table 2 below). As treatment proceeds, the goal is to maintain blood glucose between 150-250. The preference is to maintain insulin infusion rate while increasing or decreasing IV dextrose rate to attain target glucose (see Table 2 below). This preference is based on the principle that persistent acidosis requires a high (0.1 Unit/kg/hour) rate of insulin infusion to suppress ketone production.

In some instances where blood glucose is < 150 despite being on all dextrose-containing fluids, a higher fluid rate of 3.5 L/m^2/day or the use of D12.5 1/2 Normal Saline or D12.5 Normal saline may be needed to maintain blood glucoses in target range and allow for continued insulin drip rates at 0.1 U/kg/hr.

If acidosis is resolving (HCO3 > 14, venous pH > 7.25), reduction of the insulin infusion to 0.05-0.08 Unit/kg/hour can be considered if blood glucose is < 150 on all dextrose-containing fluids.

Table 2: Suggested* Ratio of D10 and saline maintenance fluid based on blood glucose level

Blood Glucose Level	% D10 Maintenance Fluid	% 1/2 NS or NS Maintenance Fluid
≥ 300	0%	100%
251-299	50%	50%
201-250	75%	25%
151-200	100%	0%

* = Fluid components may require individualization based on patient response, rate of glucose correction, and other patient factors

If the patient is on an insulin pump, remove the pump from the patient when starting the insulin drip. If patient is on multiple daily injections of insulin (or will not be resuming pump therapy once off insulin infusion), contact the pediatric endocrinologist on call to discuss timing and dose of long-acting insulin administration during the correction of DKA. In general, we prefer to give long-acting insulin at the same time it is administered at home while hospitalized.

THERAPEUTIC MONITORING

Admit to TCU or PICU
Vital Signs and Neuro Checks every 1 hour (PICU) or every 2 hours (TCU)
Hourly bedside glucose
Blood gas + GEM electrolytes every 4 hours
Magnesium and Phosphorus levels every 4 hours
BMP every 12 hours (can moit blood gas/GEM electrolytes at these times)
Serum K every 1-2 hours if abnormal
Urine ketones every 8 hours
Strict intake and urine output monitoring (Foley usually not needed)

IV. GOALS

- **CORRECT DEHYDRATION OVER 24 TO 36 HOURS**

- **MAINTAIN BLOOD GLUCOSE 150-250 ONCE STABILIZED**

- **ANTICIPATE (AND CORRECT, IF NECESSARY) MAJOR COMPLICATIONS**
    - Hypoglycemia
    - Hypo- or hyperkalemia
    - Pneumothorax/pneumomediastinum
    - Persistent acidosis (HCO3 < 10 after 12 hours)*
    - Cerebral edema**
    - Acute kidney injury

*** Persistent acidosis**

This is usually due to errors in carrying out standard treatment. The physician should check the insulin infusion, and re-order new solution to the bedside, if necessary. Alternative causes of persistent acidosis may include severe DKA or dehydration at presentation, infections, and pancreatitis.

****Cerebral edema**

Cerebral edema is the most common cause of death in DKA, usually occurring 8-12 hours into therapy, with little warning. The first signs are the complaint of headache and sudden decline in mental status (level of arousability and orientation). Part of the "neuro-check", therefore, should include arousing and talking to the patient, since bradycardia, hypertension, blown pupil, and decorticate posturing are late findings.

If a patient exhibits any signs of cerebral edema, the following actions should be performed immediately:

- Treat with hypertonic saline (3%) 5mL/kg IV over 10-15 minutes
- Elevation of the head of the bed
- Decrease IV fluid rate to maintenance
- Transition maintenance fluids to Normal Saline (if not already on normal saline)
- Transfer to the PICU (if not already admitted to the PICU)
- Other supportive measures such as mechanical hyperventilation

While CT scan of the head can demonstrate the presence of cerebral edema, TREATMENT WITH HYPERTONIC SALINE AND CLINICAL STABILIZATION SHOULD OCCUR PRIOR TO TAKING THE PATIENT FOR ANY IMAGING STUDIES.

The cause of cerebral edema is controversial, but the risk may be increased by excessive fluid administration, rapid changes in serum osmolarity, and bicarbonate administration. Demographic risk factors associated with increased risk for cerebral edema include severe DKA (pH < 7.1, bicarb < 5), new onset diabetes, and younger age (< 5 years). All three variables are important in deciding disposition to the PICU vs TCU

V. TRANSITIONING TO SUBCUTANEOUS INSULIN

Patients are ready to transition off insulin infusion when they meet the following criteria:

- Bicarbonate is > 18 OR Bicarbonate > 14 if chloride level is above upper limit of normal
- Patient is alert and ready to eat a meal
- Anion gap is < 16
- If patient is on insulin injections, the patient has received their long-acting insulin dose at least 2 hours prior to time of discontinuing the insulin drip
- If patient is on an insulin pump, patient has pump supplies present and guardian will be at bedside to assist in pump management. Pump should be started at least 1 hour prior to discontinuation of insulin drip

After the above criteria are met, the patient may be transitioned to subcutaneous insulin per pediatric endocrinology-approved regimen at the following meal-time. Below is a general protocol for transition from insulin drip to subcutaneous insulin. Please note, there may be variations based on individual patients or clinical situations, and always consult with the pediatric endocrinologist prior to the transition.

- Make sure insulin orders are entered for carbohydrate and correction dosing, and that insulin is on the floor. If not, call the pharmacy to expedite getting insulin to the floor
- Check pre-meal blood glucose
- Allow the patient to eat
- After the patient has finished eating, give subcutaneous insulin dose via insulin pump or injection for carbohydrates eaten and pre-meal correction.
- After carbohydrate/correction dose is given, discontinue insulin drip and dextrose-containing IV fluids. Discuss need to continue non-dextrose containing IV fluids with the pediatric endocrinology attending

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