

DIABETIC KETOACIDOSIS CLINICAL PATHWAY

EXECUTIVE SUMMARY

Physician Owner(s): Dr. Jason Burrows

Primary Objective

To create and implement an evidenced based pathway that guides treatment of diabetic ketoacidosis (DKA) from initial evaluation through transition to subcutaneous insulin.

Definitions

- 1) DKA is defined as the triad of blood glucose greater than 200 mg/dL, metabolic acidosis (defined as pH less than 7.3 or serum bicarbonate less than 15), and ketosis in the blood or urine.¹
 - a) Mild DKA is defined as pH of 7.2-7.3 or serum bicarbonate of 10-17.¹
 - b) Moderate DKA is defined as pH of 7.1-7.2 or serum bicarbonate of 5-10.¹
 - c) Severe DKA is defined as pH of less than 7.1 or serum bicarbonate less than 5.¹
 - i) DKA at any pH which is associated with mental status changes such as focal neurologic deficits, GCS less than 14, severe headache, or hypotension is also automatically classified as severe.
- 2) Successful treatment of DKA includes volume resuscitation and correction of ketoacidosis while also managing co-morbid diagnoses.
- 3) Cerebral edema is a rare but potentially catastrophic consequence of DKA accounting for 60-90% of all DKA deaths.^{2,3} Cerebral edema occurs in 0.39-1% of episodes of DKA with a mortality rate of 20-30% and similar rates of morbidity in survivors.^{1,2,3,4}

DKA pathophysiology

Diabetic ketoacidosis results from a complete or relative deficiency of insulin in comparison to counter-regulatory hormones including glucagon, epinephrine, growth hormone, and cortisol. Complete deficiency or circulating insulin occurs in new-onset type 1 diabetes mellitus as well as for those who did not take insulin. Alternately, during times of stress, such as illness or trauma, a relative insulin deficiency can occur due to elevations in counter-regulatory hormones. In the pathophysiologic state of DKA, the body rapidly undergoes glycogenolysis and gluconeogenesis in the liver while simultaneously having impaired peripheral glucose uptake and increasing peripheral lipolysis. DKA results in severe hyperglycemia, hyperosmolality, and ketone production causing osmotic diuresis, dehydration, ketoacidosis, and electrolyte derangements. Clinical signs and symptoms include nausea, vomiting, abdominal pain, tachypnea and/or deep breathing (Kussmaul respirations), changes in mental status from confusion to coma.¹

Recommendations/Goals

- 1) Maintain standard evaluation and treatment plan to provide evidence-based care with rapid initiation of fluid resuscitation and initiation of insulin as well as appropriate patient disposition.
- 2) Maintain transition to subcutaneous insulin guidelines to decrease delays in transition to SQ insulin.
- 3) Identify trends in 30-day readmission and devise system interventions to reduce repeat hospitalization for diabetes care.

Rationale

Safety: Will be improved by limiting practice variation and reducing gaps in management which increase the risk for harm.

Quality: Will be enhanced by reducing unnecessary patient transfers, shortening the duration of therapy on an insulin drip, and standardizing the transition to subcutaneous insulin.

Cost: Will be reduced by limiting redundant laboratory tests and total laboratory tests as well as decreasing the duration of therapy on an insulin drip.

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Engagement: The pathway is created and implemented with support of providers and staff across the institution who care for patients with DKA.

Satisfaction: We will improve satisfaction by providing high quality, evidenced based care as well as limiting frequency of new needle sticks for lab draws.

Implementation items

- 1) Diabetic Ketoacidosis Initial Evaluation Algorithm
- 2) Revised ED Epic DKA Order Set
- 3) Diabetic Ketoacidosis Inpatient Algorithm
- 4) Revised Inpatient Epic DKA Order Set
- 5) Creation of a DKA Transition Order set

Metric Plans

- 1) Maintain utilization of the DKA pathway/order set during the initial evaluation and medical management, goal >90% by April 2024. (Process Metric)
- 2) Increase percentage of patients that have insulin drip initiated in ≤ 150 minutes from arrival to Emergency Department for 90% of patients that present with DKA by April 2024. (Outcome Metric)
- 3) Reduce median time from first Beta-hydroxybutyrate BHB < 1 to transition to SQ insulin to less than 120 minutes by April 2024. (Outcome Metric)
- 4) Monitor readmissions within 30 days and 60 days for DKA until April 2024 to establish institutional baseline. (Balancing Metric)

DKA Pathway Committee Follow-up Plan

- 1) Meet biannually.
- 2) Review data for adherence to pathway, patient transfers, serum chloride, serum creatinine, and transitioning to SQ insulin.

The Diabetic Ketoacidosis Clinical Care Pathway

Clinical care guidelines:

Intended for patients:

- Known diabetes or new onset diabetes with clinical concerns for diabetic ketoacidosis

Excludes:

- Patients with corrected serum sodium less than 130 or greater than 150
- Patients with an initial serum glucose >1000
 - Consult Endocrinology for recommendations as these are concerning for possible hyperglycemic hyperosmolar syndrome
- Patients with hemodynamic instability
- Patients with concern for cerebral edema

Emergency Department

All patients with suspected or potential DKA are encouraged to first be assessed in the Emergency Department. Direct admissions to the floor are discouraged unless patient is being transported via CHMC critical care transport team and meets the Med/Surg admission criteria (see below).

Clinical Assessment



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- 1) Triage as minimum of level 2 and notify provider immediately.
- 2) Vital signs and neurologic checks q1H.
- 3) If patient uses an insulin pump, discontinue, and remove the device.

Initial Management and Laboratory Studies

- 1) Manage airway, breathing, circulation (ABC's) or comorbid problems as appropriate. Evaluate mental status by Glasgow Coma Scale (GCS).
 - a) If patient has hemodynamic instability or acute respiratory failure, manage off this pathway.
- 2) Obtain STAT EPOC on arrival to ED room.
- 3) If EPOC is consistent with DKA (pH < 7.3 and/or HCO₃ < 15) - obtain stat BMP, VBG, and serum beta-hydroxybutyrate with placement of PIVs. If possible, place 2nd PIV for future lab draws.
- 4) Evaluate for co-morbid diagnoses.
 - a) Consider additional studies such as lipase, CBC, blood culture, etc. based on clinical assessment.
- 5) Order and infuse 20ml/kg (up to 1L) lactated ringers bolus over 1 hour.
 - a) If patient is hypotensive or demonstrates signs of shock, additional fluid should be given to stabilize the patient's cardiovascular status as appropriate, and the patient should be managed off pathway.
- 6) Confirm DKA and determine severity based on initial BMP and VBG results as well as a positive serum beta-hydroxybutyrate.
 - a) **Calculate corrected sodium** = [serum sodium + (serum glucose – 100)/100 x 1.6]
 - i) If corrected sodium is less than 130 or greater than 150
 - (1) Patients should not be managed on this pathway if corrected serum sodium is less than 130 or greater than 150.
 - (2) Strongly consider discussing plan of care with accepting team and using two-bag fluids containing 154 mEq/L NaCl (0.9%)
- 7) Use the ED DKA order set for patients with corrected serum sodium of 130-150,
 - a) Insulin infusion at 0.1 units/kg/hr to start after completion of lactated ringers bolus.
 - b) If initial serum potassium 3.5-5.9 mEq/L, order standard DKA fluids
 - i) Standard "S" fluid bag: 115mEq/L sodium chloride with 20mEq/L potassium acetate and 20mEq/L potassium phosphate
 - ii) Standard "D" fluid bag: 10% dextrose with 115mEq/L sodium chloride and 20mEq/L potassium acetate and 20mEq/L potassium phosphate.
 - c) If initial serum potassium ≥ 6.0 mEq/L,
 - i) Substitute "S" fluid bag: lactated ringers
 - ii) Substitute "D" fluid bag: 5% dextrose with lactated ringers (D5 LR)
 - (1) Titration of fluid rates needs to take into account the lower dextrose concentration in D5+NS. These fluids should be used for initial management with custom IV fluids ordered if prolonged hyperkalemia is anticipated.
 - (2) *Addition of potassium and switch to standard "S" and "D" fluid bags should occur when patient demonstrates adequate urine output for age or the serum potassium normalizes. Typically, within the first 2-4 hours of fluid resuscitation.*
 - d) If initial serum potassium is < 3.5 mEq/L,

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- i) Begin potassium repletion during the first hour of fluid resuscitation and prior to starting the insulin infusion.
- ii) Start with standard two bag system and notify inpatient team about the low potassium value.
 - (1) Standard "S" fluid bag: 115mEq/L sodium chloride with 20mEq/L potassium acetate and 20mEq/L potassium phosphate
 - (2) Standard "D" fluid bag: 10% dextrose with 115mEq/L sodium chloride and 20mEq/L potassium acetate and 20mEq/L potassium phosphate.
- e) Order total fluid rate with sliding scale based on serum glucose values,
 - i) Patient < 30 kg at 1.5x maintenance
 - ii) Patient ≥ 30 kg at 2.0x maintenance.

Blood glucose	"S" bag rate - percent of total fluid rate	"D" bag rate - percent of total fluid rate	Final dextrose concentration
>300	100%	0%	D0%
250-299	75%	25%	D2.5%
200-249	50%	50%	D5%
150-199	25%	75%	D7.5%
<150	0%	100%	D10%

- 8) Repeat blood glucose hourly.
 - a) Goal is to decrease blood glucose by less than 100 mg/dL per hour.
- 9) After completion of fluid bolus, start insulin infusion and fluid infusion with combination of "S" and "D" fluids based on orders.
- 10) Page Pediatric Hospitalist or Intensivist for admission based on placement criteria below.
- 11) Repeat BMP +/- VBG every 2 hours while in the Emergency Department.

Patient Placement

Criteria for PICU admission – based on initial BMP and VBG lab value and current neurologic status.

- 1) Mild or Moderate DKA (pH < 7.3 or bicarbonate <15) and any of the following:
 - a) Significant headache
 - b) Mental status abnormalities or GCS < 14
 - c) Hemodynamic instability
 - d) Age < 24 months
- 2) Severe DKA (pH < 7.1 or bicarbonate < 5)
 - i) *Patients who are clinically stable with biochemically severe DKA should receive care in the ICU and monitoring for 12 hours or more before transfer to the floor.*
 - (1) *Note: ICU level care is the combined time patient is receiving DKA management including transport, ED, and PICU.*
 - (2) *If patient remains stable for 12 hours of ICU care with improving biochemical markers, transfer to the floor is encouraged to avoid delays in the transition to SQ insulin.*

*Strongly consider PICU admission for any patient less than 5 years of age or with corrected serum sodium less than 125 or greater than 160.

Transport Team

Initial assessment and continued management - Per transport team policy.

- 1) Confirm the diagnosis by reviewing the outside hospital's labs and repeat an EPOC lab on arrival.

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- 2) Review management including volume of fluid resuscitation given by the outside hospital.
- 3) Notify Medical Control provider (MCP) for management during transport.

Disposition – Med/Surg vs PICU

- 1) Per patient placement definition listed above as well as discussion with MCP and pediatric hospitalist on call.

Inpatient Med/Surg

Clinical Assessments

- 1) Perform admission evaluation including ABC's and neurologic assessment (GCS).
- 2) Repeat vital signs every 2 hours and neurologic checks with vitals while on an insulin drip.
- 3) If patient develops any of the following, escalate care based on clinical appropriateness, and follow recommendations for treatment outlined in the cerebral edema section below until Intensivist or transfer to the PICU is available.
 - a) Significant headache
 - b) Mental status abnormalities or GCS < 14
 - c) Focal neurologic deficits
 - d) Elevated blood pressure and bradycardia

Initial Management and Laboratory Studies

- 1) Review workup and treatment from Emergency Department or referring facility. Verify isotonic fluid bolus has been completed - 20ml/kg (up to 1L) Lactated Ringer over 1 hour.
 - a) *If patient is directly admitted via CHMC transport team, it is strongly encouraged that a licensed provider be present for bedside handoff when the patient arrives.*
- 2) **Calculate corrected sodium** = [serum sodium + (serum glucose – 100)/100 x 1.6]
 - a) If corrected sodium falling during fluid resuscitation,
 - i) Patients should not be managed on this pathway.
 - ii) Strongly consider using two-bag fluids containing 154 mEq/L NaCl (0.9%)
- 3) Continue or initiate insulin infusion and two bag system for rehydration,
 - a) Insulin infusion at 0.1 units/kg/hr
 - b) If most recent serum potassium is 3.5-5.9 mEq/L, order standard DKA fluids
 - i) Standard “S” fluid bag: 115mEq/L sodium chloride with 20mEq/L potassium acetate and 20mEq/L potassium phosphate
 - ii) Standard “D” fluid bag: 10% dextrose with 115mEq/L sodium chloride and 20mEq/L potassium acetate and 20mEq/L potassium phosphate
 - c) If most recent serum potassium ≥ 6.0 mEq/L,
 - i) Substitute “S” fluid bag: lactated ringers
 - ii) Substitute “D” fluid bag: 5% dextrose with lactated ringers
 - (1) Titration of fluid rates needs to take into account the lower dextrose concentration in D5 lactated ringers.
 - (2) If prolonged hyperkalemia is anticipated, order custom IV fluids without potassium to allow for increased dextrose concentration as well as to reduce chloride,
 - (a) Substitute “S” fluid bag: 115mEq/L sodium chloride
 - (b) Substitute “D” fluid bag: D10 + 115mEq/L sodium chloride

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- (3) *Addition of potassium and switch to standard “S” and “D” fluid bags should occur when patient demonstrates adequate urine output for age, or the serum potassium normalizes. Typically within the first 2 hours of fluid resuscitation.*
- d) If serum potassium is < 3.5 mEq/L and patient is not close to transitioning to sub-cutaneous insulin,
- i) Consider potassium repletion.
 - ii) Consider increasing potassium in two bag system, order custom IV fluids
 - (1) Substitute “S” fluid bag: 115mEq/L sodium chloride with 30mEq/L potassium acetate and 30mEq/L potassium phosphate
 - (2) Substitute “D” fluid bag: 10% dextrose with 115mEq/L sodium chloride and 30mEq/L potassium acetate and 30mEq/L potassium phosphate.
- e) Order total fluid rate with sliding scale based on serum glucose values,
- i) **Patient < 30 kg at 1.5x maintenance**
 - ii) **Patient ≥ 30 kg at 2.0x maintenance**
 - (1) Alternatively, fluid needs can be calculated using the equation,
 - i. $[(\text{Daily maintenance needs} + \text{estimated } 5\% \text{ dehydration}) - \text{initial bolus volume}] / 24 \text{ hours}^1$

Blood glucose	“S” bag rate – percent of total fluid rate	“D” bag rate - percent of total fluid rate	Final dextrose concentration
>300	100%	0%	D0%
250-299	75%	25%	D2.5%
200-249	50%	50%	D5%
150-199	25%	75%	D7.5%
<150	0%	100%	D10%

- 4) Repeat blood glucose hourly and adjust fluids based on table – goal is to decrease blood glucose by less than 100 mg/dL per hour.
- a) If blood glucose is falling >100 mg/dL per hour increase “D” bag rate by one additional step from what the table indicates.
 - b) If blood glucose < 100, increase “D” bag dextrose concentration to D12.5% and pause the insulin drip and repeat blood glucose every 15 minutes until blood glucose is > 120 mg/dL then resume the insulin drip.
 - c) Do not decrease the insulin infusion rate unless unable to maintain blood glucose > 100 mg/dL on D12.5% fluids or serum glucose is falling > 100mg/dL despite increasing the dextrose infusion.
 - i) **Note: an insulin rate less than 0.05 U/kg/hr will fail to correct diabetic ketoacidosis.**
- 5) Repeat BMP every 2 hours for two checks then, if improving, every 4 hours with serum beta-hydroxybutyrate until discontinuation of the insulin drip.
- a) Calculate corrected sodium $[\text{serum sodium} + (\text{serum glucose} - 100) \times 1.6]$ with each electrolyte result.
 - i) During early fluid resuscitation if corrected serum sodium falls or fails to correct to normal, strongly consider changing fluid resuscitation to 154mEq/L NS containing fluids.
 - b) If serum potassium falls to < 3.5 and patient is not close to transitioning to SQ insulin, consider

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- i) Changing to substitute “D” and “S” bag fluids to include 30 mEq/L potassium phosphorus and 30 mEq/L potassium acetate.
 - ii) If failing to improve, further treatment can include decreasing the insulin infusion rate and/or administering potassium repletion (oral vs IV depending on the ability to tolerate).
(1) Note: an insulin rate less than 0.05 U/kg/hr will fail to correct diabetic ketoacidosis
- 6) Recommend obtaining serum magnesium and phosphorus levels every 8 hours if initial values are normal. If initial values are abnormal or the patient has more severe illness, consider obtaining every 4 hours with routine labs.¹
- a) Treatment of hypophosphatemia is not indicated unless severe and/or chronic.
- 7) Treatment of hypomagnesemia is deferred to the licensed provider. Strongly consider replacement if severe hypomagnesemia is present.
- 8) Long-acting subcutaneous insulin may be given per provider discretion while a patient is on an insulin drip for DKA management.

Transition to subcutaneous insulin

- 1) Patient is ready to transition when one of the following scenarios have been met,
 - a) Serum $\text{HCO}_3^- > 15$ and serum beta-hydroxybutyrate ≤ 1 mmol/L **AND** able to tolerate oral intake.
(a) OR
 - b) Serum $\text{HCO}_3^- > 17$ with normal anion gap **AND** able to tolerate oral intake.
- 2) Utilize the DKA transition order set to standardize insulin drip transition,
 - a) Place order “Discontinue insulin drip”
 - b) Allow patient to order meal and calculate carbohydrates.
 - c) Once food has arrived and immediately prior to eating,
 - i) Check blood glucose.
 - ii) Give long acting and short acting insulin OR, if patient has insulin pump, patient or family to insert new pump site per Children’s policy and restart insulin pump, including basal rate and giving a bolus for food and/or blood sugar.
(1) If patient < 5 years old or concerns about nausea, consider post-meal dosing of short acting insulin.
 - iii) Allow patient to eat meal.
 - iv) Turn off the insulin drip and IV fluids 30 minutes after subcutaneous insulin given or restarting the insulin pump.
(1) If blood glucose < 100, consider continuing “D” bag for 15 minutes after discontinuation of insulin infusion.
 - v) If patient is able to tolerate oral intake, we suggest setting an oral fluid goal over continuation of IV fluids for rehydration.
(1) Continue IV fluids based on patient hydration status and tolerance of oral intake.

Discharge Criteria

- 1) Reason for DKA identified and addressed as well as successfully transitioned to sub-cutaneous insulin regimen.

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- 2) Patient and/or caregiver has demonstrated ability to complete diabetes education, perform self-monitoring of blood glucose, independently calculate insulin doses, administer insulin, identify and treat hypoglycemia and ketonuria.
- 3) Completion of behavioral health consult to identify and address any contributing psychosocial factors.
- 4) Appointments with Endocrine and PCP (if needed) scheduled.
- 5) All diabetes supplies and prescriptions filled as needed.

Cerebral Edema

Cerebral edema accounts for the majority of morbidity and mortality associated with pediatric type 1 diabetes mellitus. Cerebral edema typically develops within the first 12 hours of treatment although it can be present at presentation to the hospital or develop greater than 12 hours into treatment. The exact mechanism is not understood and may include cytotoxic edema, vasogenic edema, and/or osmotic edema from fluid therapy. Risk factors for cerebral edema include age less than 5, new onset diabetes, and severe acidosis. **Modifiable risks** include rapid drop in blood sugar caused by insulin bolus, initiation of insulin drip before the one-hour fluid resuscitation is completed, rapid or aggressive fluid bolus(es), or bicarbonate bolus.^{1,2,3,4}

Clinical findings concerning for cerebral edema

- 1) Headache and/or vomiting
 - a) Specifically, if these first occur or worsen during the treatment of DKA.
- 2) Irritability, lethargy, or change in mental status
- 3) Elevated blood pressure and decreased heart rate
- 4) Incontinence
- 5) Pupillary reflex changes or cranial nerve palsy
- 6) Abnormal respiratory pattern or decreased oxygen desaturation
- 7) Decorticate or decerebrate posturing

Treatment of Cerebral Edema in DKA

- 1) Activate Code
- 2) Evaluate and manage airway, breathing, and circulation
- 3) Elevated head of bed to 30 degrees
- 4) Decrease IV fluid rate by one third while maintaining adequate circulation
- 5) Obtain rapid bedside blood glucose
- 6) Give Mannitol 0.5-1.0 g/kg IV over 20 minutes by PIV or 3% hypertonic saline 5mL/kg (preferably by central line) followed by continuous 3% saline infusion.⁵
- 7) After patient has been stabilized, obtain CT head to assess for cerebral edema vs alternate diagnoses such as venous sinus thrombosis or intracranial hemorrhage.
- 8) Neurosurgery consult for possible placement of ICP monitoring device

Pathway Development Team

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Literature

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