Diabetic Ketoacidosis (DKA)

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Epidemiology

- Most common cause of DKA is new onset Type 1 diabetes mellitus (T1DM)
  - 25-40% of new diagnoses of T1DM present with DKA
- In diagnosed T1DM, the yearly risk of DKA is 1-10%
  - Causes include infection, inadequate insulin administration (accidental or as rebellious behavior), chronic disease, eating disorders
- Type 2 diabetes mellitus (T2DM) can also present in DKA and can co-exist with type 1
  - 10% of new diagnoses of T2DM present with DKA
- Other causes without diabetes: high dose corticosteroids, atypical antipsychotics, immunosuppressives, diazoxide overuse

Pathogenesis of DKA

- Inadequate insulin levels -> Increased counter-regulatory hormones (GH, glucagon, cortisol, catecholamines):
  - Absolute deficiency, such as in T1DM resulting in pancreatic B-cell failure
  - Relative deficiency, such as in infection, stress, inadequate insulin intake

- Results in hyperglycemia, hyperosmolality, ketosis, and acidosis
  - Increased gluconeogenesis + increased glycogenolysis + decreased glucose utilization + increased **lipolysis**

- A blood glucose of ~200mg/dL, exceeds renal capacity
  - Leads to glucosuria -> osmotic diuresis -> **dehydration** + electrolyte wasting

- Increased lipolysis -> Increased free fatty acids to liver -> **Ketogenesis**

Clinical presentation

- Classic signs: Polyuria, polydipsia, polyphagia, weight loss
- Additional Sx: vomiting, abdominal pain, dehydration, weakness, lethargy, tachypnea/Kussmaul respirations (deep fast breaths)
  - Associated abdominal pain may be severe enough to mimic an acute abdomen
  - Consider **pancreatitis** if focal TTP in epigastrum:
    - Insulin deficiency -> lipolysis and inhibition of lipoprotein lipase in peripheral tissues -> elevated triglycerides -> DKA-induced hypertriglyceridemic acute pancreatitis

- Severity of presentation can depend on the duration of symptoms

- Children appear to maintain their BP despite severe dehydration due to the increased plasma catecholamines and increased ADH
  - However, when these mechanisms are overwhelmed, the presentation can be more severe
  - **Severe presentation**: hypotension, shock, altered mental status

- Most feared DKA complication = cerebral edema

Cerebral Edema (CE)

- ~0.5% of DKA cases. Mortality ~30%
- Due to cerebral hypoperfusion, reperfusion and neuroinflammation
  - Pathogenesis incompletely understood
- Risk factors: <5yo, 1st DKA presentation, severe dehydration, longer duration of symptoms, bicarb therapy
  - Labs associated with development of cerebral edema
    - Elevated BUN, severe acidosis, severe hypocapnia, failure of corrected Na to rise with treatment

- DIAGNOSIS: 1 diagnostic criteria OR 2 major OR 1 major + 2 minor (92% sensitivity, 96% specificity - Muir 2004):
  - Diagnostic: abnormal motor/verbal response to pain; posturing; focal signs (CN palsy); abnormal respirations
  - Major: slowing of HR (>20 lower than normal); AMS or fluctuating level of consciousness; incontinence
  - Minor: headache; vomiting; lethargy; DBP >90

- Management:
  - Elevate HOB 30deg
  - Mannitol 1g/kg over 20min (can repeat Q1-2H) - diuretic
  - Alternatively may give Hypertonic saline (3%) 5ml/kg over 20min - volume expander
  - Give only as much fluid as needed to avoid hypotension, maintain cerebral perfusion
  - Intubate only if respiratory failure (associated with worse outcomes) - goal pCO_2 ~35
  - Give oxygen as needed to maintain normal O_2 sat

Cerebral Edema (CE) Key Literature

- Traditional cautious approach of fluids in DKA unlikely cause of brain injury (Kuppermann 2018)
- Brain CT does not enhance decision making of cerebral edema and delays treatment. Subclinical CE on CT is common, while severe CE may have normal CT (Soto-Rivera 2017)
- Bicarbonate has no benefit in DKA and increases risk of CE (Chua 2011)
- Intubation in DKA does not have any unique indications: if airway is not patent/protected or patient is failing to oxygenate/ventilate or is apneic, intubation is indicated (Chua 2011)
    - However, intubation of a DKA patient is high-risk as the patient is dependent on tachypnea-induced respiratory alkalosis compensation
    - Best intubator available, avoid prolonged apnea, match patient's pre-intubation pCO_2 in post-intubation phase

Initial DKA Diagnostic Tests

- ED Labs
- Serum glucose, electrolytes, BUN, Cr, venous pH with Hgb/Hct, Udip for ketones or serum B-hydroxybutyrate (BHOB), new onset diabetes labs
  - Include cultures if concern for underlying bacterial infection
  - Serum BHOB gives a more accurate assessment of acidosis (urine ketones lag slightly behind) but is expensive and does not typically change management plan if typical DKA labs are obtained

- Criteria for diagnosis
  - Hyperglycemia: BG >200 mg/dL
  - Acidosis: Venous pH <7.3 or serum bicarb <15mEq/L
  - Ketosis: serum B-hydroxybutyrate ≥3mmol/L or ketonuria (moderate or severe)

- Severity
  - Mild: pH <7.3 or bicarb <15mEq/L
  - Moderate: pH <7.2 or bicarb <10mEq/L
  - Severe: pH <7.1 or bicarb <5mEq/L

- Lab interpretation
  - Pseudohyponatremia: dilutional effect of hyperglycemia causing an extracellular water shift
    - Corrected Na = measured Na + 1.6 ([plasma glucose – 100] / 100)
  - Leukocytosis is commonly seen
    - Does not necessarily indicate infection
  - Normal/Increased serum K, but usually an overall total body K deficit due to vomiting and osmotic diuresis
    - K appears normal due to extracellular K shift

New Onset Diabetes Labs

- Hb A1c
- Insulin level
- C-peptide
- TSH, T4, anti-TPO
- TTG Ab + total IgA (Celiac panel)
- Islet cell antibody, insulin antibody, glutamic acid decarboxylase antibody (Diabetes autoimmune test group, if available)

- Remember that new presentation can be as mild as vague weakness, dizziness/fall, or abdominal pain. Utility of POC glucose as first test

DKA: ED Management

- Goal = correct dehydration, correct acidosis, and reverse ketosis. Patients are at least 5% fluid down

1. NS bolus 10cc/kg over 30min:
   - 20cc/kg if early signs of shock: tachycardic with prolonged capillary refill
   - Push/pull multiple boluses if hypovolemic shock with escalation to inotropes
   - It is normal for acidosis to slightly worsen after initial resuscitation (due to reperfusion)

2. Confirm and act on serum potassium level:
   - < 3: hold insulin, give KCl 20mEq/h until >3.3 then add +40mEq/L in IV fluids. Obtain ECG (hypokalemia = U wave, flattened T waves, PR prolonged, ST depression)
   - 3-4: add 40 mEq KCl per L of IV fluids
   - 4-5: add 20 mEq KCl per L of IV fluids
   - >5: no KCl supplementation needed. Obtain ECG (hyperkalemia = peaked T waves, PR prolongation, QRS widening)

3. Begin insulin drip at 0.1U/kg/h*
   - Insulin rate 0.05U/kg/h has been found to be non-inferior (except in severe DKA) and may even be safer in young kids < 5yo (Nallasamy 2014)
   - Goal glucose decrease rate: 100/hr

4. Electrolytes and maintenance fluids
   - Stagger VBG and BMP Q4H so a lab is done every 2H
   - BG check and Neurochecks Q1H
   - Given degree of dehydration, may run at 1.5x maintenance rate
   - Typically NS + 20-40mEq KCl (based on serum K level), some use K-Ac and K-Phos in place of KCl
   - Add D5 when/if BG level <250

- DKA admissions will often dispo to the PICU due to the initial need for frequent lab draws (Q2H) and neurochecks (Q1H)

- Discharge from ED is possible if initially mild and hyperglycemia, ketosis, and acidosis resolve, patient tolerates PO, has normal mental status, and has adequate family support and outpatient follow-up

Continuous insulin infusions (CSII)

- Also known as insulin pumps: small computerized devices that deliver short acting insulin continuously through a small catheter placed under the skin

- Because pts receiving CSII are not receiving other long acting basal insulin, if the pump malfunctions, then DKA can develop in <12hrs
  - Pump mechanism malfunction, **kink in tubing***, air bubble in tubing, subcutaneous scarring/lipohypertrophy preventing insulin absorption
  - Always examine insulin pump site and apparatus. Kinking is very common!

- If a patient on CSII presents in DKA, it is usually recommended for the pump to be discontinued and all insulin given IV or IM
- DKA management proceeds in the same manner as non-CSII users

Hyperglycemic Hyperosmolar State

- BG > 600
- pH > 7.3
- Bicarb > 15
- Small ketonuria
- Serum Osm >320 (normal 275-295)
  - Serum Osm = 2Na + BUN/2.8 + BG/18
- Management: Usually discharged after IV fluid rehydration and glucose improvement/correction in ED unless remain ill-appearing and/or cannot tolerate PO

PIR CME Questions (August 2019)

1. A 16-year-old girl with type 1 diabetes mellitus (T1DM) is seen in the clinic for recurrent episodes of diabetic ketoacidosis (DKA). She is 5 ft 6 in (168 cm) tall and weighs 100 lb (45.4 kg). She is a well-adjusted honor roll student, and her teachers say she is a very pleasant person and gets along very well with her peers. Which of the following is most likely to be associated with her recurrent episodes of DKA?

    A. Fear of weight gain.
    B. Inadequately prescribed dosing of insulin.
    C. Low socioeconomic status.
    D. Misunderstanding insulin administration instructions.
    E. Underlying immune disorder predisposing to infection.

2. A 3-year-old girl with new-onset T1DM is admitted to the hospital with a diagnosis of DKA. On initial evaluation in the emergency department she was assessed to be severely dehydrated. Her parents report that she has been ill for a week. Laboratory studies show mild acidosis, high urine specific gravity, glucosuria, and ketonuria. Which of the following factors is least likely to place this patient at risk for cerebral edema?

    A. Age of 3 years.
    B. Mild acidosis.
    C. New onset of T1DM.
    D. Prolonged nature of her illness.
    E. Severe dehydration.

3. A 10-year-old girl with no significant medical history is brought to the emergency department because of vomiting, abdominal pain, polyuria, polydipsia, dehydration, and weight loss. She is diagnosed as having DKA. In addition to blood glucose, blood ketone, and serum electrolyte levels, which of the following laboratory studies is not recommended as part of the initial routine evaluation of this patient?

    A. Erythrocyte sedimentation rate.
    B. Glutamic acid decarboxylase antibody level.
    C. Hemoglobin A1c level.
    D. Islet cell antibody.
    E. Thyroperoxidase antibodies.

PIR CME Questions

4. A 15-year-old boy, with a history of vomiting and 10% dehydration is brought to the emergency department by ambulance after his parents called 911 when they noticed that he has been progressively becoming more "lethargic" for the past few hours. On arrival at the emergency department he is noted to have clinical signs of dehydration. He is sleepy but arousable and responds to painful stimuli. His initial laboratory evaluation is significant for a blood glucose level of 250 mg/dL (13.9 mmol/L) with serum pH 7.05 and a bicarbonate level of 4 mEq/L (4 mmol/L). A normal saline bolus is started, and a computed tomographic scan of the brain is ordered. Which of the following is the most likely finding to be seen on computed tomographic scan in this patient?

    A. Brain atrophy.
    B. Dural thrombosis.
    C. Effacement of cerebral sulci consistent with cerebral edema.
    D. Intraparenchymal hemorrhage.
    E. Ischemic stroke.

5. A 14-year-old girl with known T1DM has been noncompliant with her insulin dosing regimen. She is brought to the emergency department in DKA. Bicarbonate therapy should most likely be considered in which of the following clinical and laboratory findings?

    A. Serum pH 7.2, potassium level of 5 mEq/L (5 mmol/L), and normal cardiac output.
    B. Serum pH 7.0, potassium level of 6 mEq/L (6 mmol/L), and decreased cardiac output.
    C. Serum pH 6.7, potassium level of 7 mEq/L (7 mmol/L), and decreased cardiac output.
    D. Serum pH 7.1, potassium level of 4.5 mEq/L (4.5 mmol/L), and normal cardiac output.
    E. Serum pH 7.0, potassium level of 6 mEq/L (6 mmol/L), and normal cardiac output.

PEC CME Questions

1. Children at highest risk of diabetic ketoacidosis include
   a. Young children
   b. High school athletes
   c. Those using CSIIs
   d. Those using long-acting insulin
   e. Those with celiac disease

2. Initial studies to be sent for the patient in suspected DKA include all of the following except
   a. Serum glucose
   b. Electrolytes
   c. Urine or serum ketones
   d. Thyroid function tests
   e. Venous blood gas

3. Indications for admission to the pediatric intensive care unit include
   a. Bicarbonate less than 12
   b. Multiple previous episodes of DKA
   c. Cerebral edema
   d. Patient using CSII
   e. Child younger than 5 years

4. When in suspected or known DKA, patients using CSII should
   a. Increase their basal rate of insulin
   b. Switch their pump site
   c. Stop using the pump and use subcutaneous injections
   d. A, B, and C
   e. B and C

5. Benefits to home serum ketone testing include
   a. Less invasive for the patient
   b. Less expensive for the patient
   c. Results more indicative of current level of ketosis
   d. A and B
   e. A, B, and C

Answers

- PIR Questions
- 1) A
- 2) B
- 3) A
- 4) C
- 5) C

- PEC CME Questions
- 1) C
- 2) D
- 3) C
- 4) E
- 5) C

Further Reading

- *Cashen, K., Petersen, T.* (2019). **Diabetic Ketoacidosis** Pediatrics in Review 40(8), 412-420. https://dx.doi.org/10.1542/pir.2018-0231
- *Lavoie, M.* (2015). **Management of a Patient With Diabetic Ketoacidosis in the Emergency Department** Pediatric Emergency Care 31(5), 376-380. https://dx.doi.org/10.1097/pec.0000000000000429