Diabetic Ketoacidosis

Tiffany Berkshire, DO, MPH, MBA
Internal Medicine/Pediatrics
Epidemiology (DKA)

- 25-40% of newly diagnosed cases present in DKA
- 0.2 – 1% of DKA associated with *clinically apparent* cerebral edema
- *Clinically apparent* cerebral edema fatal in 40 – 90% of cases and majority of deaths in DKA attributable to cerebral edema

Case Scenario #1

- A 10 y/o male (~30 kg) presents to the ED with a one-day history of emesis and lethargy.
- Vitals show T 37°C, HR 110, RR 25 BP 99/65. Patient is lethargic, but oriented x 3. Exam reveals the odor of acetone on the breath, dry lips, but otherwise unremarkable.
- Labs: pH 7.05 PaCO₂ 20, PaO₂ 100, BE -20, Na⁺ 133, K⁺ 5.2, Cl⁻ 96 CO₂ 8. Urine shows 4+ glucose and large ketones.
Case Scenario #1

- What is your assessment?
- DKA exists when:
  - Venous pH < 7.3
  - Serum bicarbonate < 15 mEq/dL
  - Blood glucose > 300 mg/dL
  - Presence of ketonemia/ketonuria
- How much fluid would you administer as a bolus?
- Would you administer bicarbonate?
- How much insulin would you administer?
- What IVF would you start? At what rate?
Clinical Manifestations

- Keotacidosis is responsible for the initial presentation of 25 - 40% of children
  - early manifestations are mild and include vomiting, polyuria, and dehydration
  - More severe cases include Kussmaul respirations, odor of acetone on the breath
  - abdominal pain or rigidity may be present and mimic acute appendicitis or pancreatitis
  - cerebral obtundation and coma ultimately ensue
Pathophysiology

- With progressive insulin deficiency, excessive glucose production and impairment of utilization result in hyperglycemia, with glucosuria developing when the renal threshold of ~180 mg/dL is exceeded.
- The resultant osmotic diuresis produces polyuria, urinary losses of electrolytes, dehydration, and compensatory polydipsia.
Pathophysiology

- Electrolyte derangements
  - Metabolic acidosis and osmotic diuresis lead to total body hypokalemia (extracellular shift may lead to falsely elevated values)
  - Hypophosphatemia also results with osmotic diuresis
  - Pseudohyponatremia (hyperglycemia and hyperlipidemia result in falsely lowered plasma sodium)
    - \( (Na_{\text{actual}} = Na_{\text{measured}} + 1.6[(\text{glucose} - 100)/100]) \)
Pathophysiology - Electrolytes

- Sodium
  - Often Hyponatremic at presentation
    - urinary losses as diuresis occurs
    - water shifts from the ICF to the ECF during the hyperosmolality state
  - Hypernatremia
    - Indicates severe dehydration
    - Increases serum osmolality
Pathophysiology - Electrolytes

- **Potassium**
  - Total body deplete, elevated serum concentrations
    - Osmotic diuresis increases potassium loss
    - Elevated serum concentration is a result of metabolic acidosis
      - Hydrogen moves across the cell membrane in exchange for potassium

- **Chloride**
  - Elevated $\rightarrow$ leads to a secondary hyperchloremic metabolic acidosis
    - Cl- reserved in kidneys to use as an exchange ion for ketones
    - Large volumes of Normal Saline
Pathophysiology

- Hyperosmolality as a result of progressive hyperglycemia contributes to cerebral obtundation in DKA
- Serum osmolality:

\[
\text{Plasma osmolality (mOsm/kg)} = 2 \times [\text{serum (Na)}] + \frac{[\text{Glucose}]}{18} + \frac{[\text{BUN}]}{2.8}
\]
What is our patient’s Osmolality?

- Na 133, glucose 540, BUN 28
- Plasma Osmolality?
- Cerebral Osmolality?
Case Scenario #2

- 16 year old obese male presents with fever to 102, abscess on R thigh, feeling poorly for 2 weeks. Further history reveals, no emesis or diarrhea, but headaches and increased thirst.
- T 102, HR 92, BP 130/79, RR 22, sats 100%
- Erythematous, raised, R thigh abscess with fluctuance, very tired and ill appearing
- WBC 30K, Hgb 15, Platelets 425K
Case Scenario #2

- Assessment?
- Labs needed?
- Treatment?
Hyperglycemic Hyperosmolar Syndrome (HHS)

- Similar presentation to DKA
  - Elevated glucose
  - Dehydration
  - Hyperosmolar state
  - Altered mental status

- Pathophysiology of HHS
  - Hyperglycemia results from increased gluconeogenesis and increased glycogenolysis in the setting of impaired insulin secretion and impaired glucose utilization
  - Acidosis is prevented by the low levels of insulin produced
  - Occurs most often in the setting of an infection
## DKA vs. HHS

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<thead>
<tr>
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<th>DKA</th>
<th>HHS</th>
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<tr>
<td>Glucose</td>
<td>&gt;250</td>
<td>&gt;600</td>
</tr>
<tr>
<td>pH</td>
<td>&lt;7.3</td>
<td>&gt;7.3</td>
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<tr>
<td>$\text{HCO}_3$</td>
<td>&lt;15</td>
<td>&gt;15</td>
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<tr>
<td>U Ketones</td>
<td>++++</td>
<td>+</td>
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<td>S Ketones</td>
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<td>&gt;320</td>
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<tr>
<td>Mental Status</td>
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</tbody>
</table>
Pathophysiology

- With progressive dehydration, acidosis, hyperosmolality, and diminished cerebral oxygen utilization, consciousness becomes impaired, and the patient ultimately becomes comatose
Treatment

- Intravascular volume expansion
  - dehydration is most commonly in the order of 10% - plan to correct over 48 hours
  - initial hydrating fluid should be isotonic saline
    - this alone will often slightly lower the blood glucose
    - rarely is more than 20 cc/kg fluid required to restore hemodynamics
- Treatment of electrolyte abnormalities
  - serum K$^+$ is often elevated, though total body K$^+$ is depleted
  - K$^+$ is started early as resolution of acidosis and the administration of insulin will cause a decrease in serum K$^+$
Treatment

- Potassium (give as Kphos, Kacetate, or KCl)
  - If K > 6 = No K initially
  - If K 5 – 6 = consider adding K+
  - If K < 5 = at least 40 mEq/L
  - Don’t forget “hyperkalemia associated with acidosis” and role of insulin
    - Hafeez W Contemp Pediatr. 2000 - modified
Treatment

- Insulin
  - continuous infusion of low-dose insulin IV (~ 0.1 U/kg/hr) is effective, simple, and physiologically sound
  - goal is to slowly decrease serum glucose (≤ 100 mg/dL/hr)
  - No evidence-based benefit for insulin bolus (but plenty of theoretical concern)
Treatment

- Dextrose
  - Dextrose is added to IVF when blood glucose is ~ 250 mg/dL or when glucose level falling faster than 100 mg/dL/hr
  - 2 bag system works great....
  - Avoid stopping or slowing insulin infusion, if possible
Treatment

- Alkali

**BICARBONATE IS ALMOST NEVER ADMINISTERED**
  - bicarbonate administration can lead to increased cerebral acidosis
    - $\text{HCO}_3^{-}$ combines with $\text{H}^+$ and dissociated to $\text{CO}_2$ and $\text{H}_2\text{O}$. Whereas bicarbonate passes the blood-brain barrier slowly, $\text{CO}_2$ diffuses freely, thereby exacerbating cerebral acidosis and ischemia
Case Scenario #3

- A 4 y/o female in the PICU is undergoing treatment for new onset IDDM and DKA. She is on an insulin infusion at 0.1 u/kg/hr, and fluids are running at 1.5 maintenance.

- Over the last hour, she has been complaining about increasing headache. She is now found to be unresponsive with bilateral fixed and dilated pupils, HR is 50 with BP 150/100.

- What is your next step in management?
Treatment pitfalls

- Cerebral edema is the major life-threatening complication seen in the treatment of children with DKA
  - usually develops several hours after the institution of therapy
  - Most commonly presents in children between 5 – 14 years
Treatment pitfalls

- Clinically evident cerebral edema – about 1%. However, increasing evidence suggests that subclinical cerebral edema occurs in the majority of patients treated with fluids and insulin for DKA
  - Glaser N J Pediatr. 2004
Treatment pitfalls

- Cerebral edema
  - manifestations include headache, alteration in level of consciousness, bradycardia, emesis, diminished responsiveness to painful stimuli, and unequal or fixed, dilated pupils
Treatment pitfalls

- Therapy of cerebral edema includes treatment aimed at lowering increased intracranial pressure (mannitol, hypertonic saline, hyperventilation, etc.)
Treatment pitfalls

- Traditional risk factors thought to be excessive use of fluids, use of bicarbonate, and large doses of insulin
  - (or just sicker patients?)
Treatment pitfalls

• More recently identified risk factors
  • Increased BUN at presentation (reflective of greater dehydration)
  • Profound neurologic depression at diagnosis of cerebral edema
  • Endotracheal intubation with hyperventilation (Marcin J Pediatr 2002)

• But ....
Other pitfalls

- Thrombosis associated with femoral venous catheterization in children with DKA (Gutierrez JA. Critical Care Medicine 2001)

- Hypoglycemic Reactions (Insulin Shock)
  - symptoms and signs include pallor, sweating, apprehension, trembling, tachycardia, hunger, drowsiness, mental confusion, seizures and coma
  - management includes administration (if conscious) of carbohydrate-containing snack or drink
  - glucagon 0.5 mg is administered to an unconscious or vomiting child
Suggested Reading


References

References

- Krane E. DKA and cerebral edema. Stanford, CA