Diabetic Emergencies: Ketoacidosis and the Hyperglycemic Hyperosmolar State

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Objectives

• Describe the epidemiology of diabetic ketoacidosis (DKA) and the hyperglycemic hyperosmolar state (HHS)

• Differentiate between DKA and HHS

• List factors that may precipitate DKA and HHS

• Identify the metabolic derangements observed in DKA and HHS

• Describe the treatment of DKA and HHS as it relates to their pathophysiology
Agenda

• Introduction
  – Epidemiology and Statistics
  – Basic concept review

• Pathophysiology and clinical features of DKA and HHS

• Management of DKA and HHS

• Transitioning care for DKA and HHS patients
Introduction: Epidemiology and Statistics

• DKA is more common in younger patients with Type 1 DM

• HHS is more common in older adults with Type 2 DM

• In experienced centers, mortality is rare in DKA (~5%)

• Mortality rates from HHS are less clear, but higher (10% +)
Introduction: Healthcare Burden

• ~115,000 U.S. hospital discharges for DKA in 2003
  – 62,000 in 1980

• Average cost = $13000/hospitalization

• Treatment of DKA accounts for 1 out of every 4 dollars spent on Type 1 DM
Basic Concept Review

• Difference between Type 1 and Type 2 DM

• Effects of hyperglycemia
  – Glycosuria
  – Osmotic draw of water into vasculature

• Insulin deficiency

• The role of glucagon
Insulin Deficiency or Resistance

- Decreased Glucose Uptake
- Insulin deficiency or resistance
- Increased delivery of glucose precursors to liver
- Unsuppressed Glucagon Release*

* It takes less insulin to suppress glucagon than it does to transport glucose into cells
The Role of Glucagon

- Increased glucose production
- Glucagon
- Disinhibits ketogenesis
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The Pathogenesis of DKA and HHS

1. Insulin deficiency or resistance
2. Decrease glucose uptake and utilization
3. Enhanced glucagon release
4. Glycosuria
5. +/- Ketoacid formation
6. Hyperglycemia
7. Dehydration and electrolyte derangements
8. Increased Plasma osmolality
9. DKA and HHS
Reduction in the net effective action of insulin coupled with a concomitant elevation of counterregulatory hormones

**DKA**
- Usually due to insulin deficiency seen in Type 1 DM
- Predominant feature is development of acidosis secondary to production of ketoacids
  - More profound acidosis
  - Less profound hyperglycemia

**HHS**
- Occurs with lesser degrees of insulin deficiency as seen in Type 2 DM
- Predominant features are profound hyperglycemia and hyperosmolality
  - Ketoacid production less pronounced
  - Acidosis less severe
  - More profound fluid and electrolyte abnormalities
Absolute Insulin Deficiency

↑ Lipolysis

↑ FFA to liver

↑ Ketogenesis

↓ Alkali reserve

↑ Ketoadidosis

Triacylglycerol

Hyperlipidemia

Counterregulatory Hormones

↓ Protein synthesis

↑ Proteolysis

↑ Gluconeogenic substrates

↓ Glucose utilization

↑ Gluconeogenesis

↑ Glycogenolysis

Hyperglycemia

Glycosuria (osmotic diuresis)

Loss of water and electrolytes

Dehydration

Decreased fluid intake

Hyperosmolarity

HHS

DKA
Precipitating Factors of DKA and HHS

• Infection

• Non-compliance to diabetic treatment

• Underlying medical illness

• Medications

• Cocaine and Alcohol

• Undiagnosed diabetes
## Clinical Presentation of DKA

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Signs</th>
</tr>
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<tbody>
<tr>
<td>Nausea and Vomiting (50-80%)</td>
<td>Tachycardia</td>
</tr>
<tr>
<td>Thirst and Polyuria</td>
<td>Hypotension</td>
</tr>
<tr>
<td>Weakness and Anorexia</td>
<td>Dehydration</td>
</tr>
<tr>
<td>Abdominal Pain (30%)</td>
<td>Warm, Dry Skin</td>
</tr>
<tr>
<td>Visual Disturbances</td>
<td>SOB/Hyperventilation (Kussmaul’s)</td>
</tr>
<tr>
<td>Somnolence</td>
<td>Impaired consciousness or coma</td>
</tr>
<tr>
<td>Coffee-ground emesis (25% of vomiting patients)</td>
<td>Weight loss</td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td></td>
</tr>
<tr>
<td>Presence of ketones in urine</td>
<td></td>
</tr>
<tr>
<td>Fruity breath (like nailpolish remover)</td>
<td></td>
</tr>
<tr>
<td>Normal body temperature despite infection</td>
<td></td>
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</tbody>
</table>
Clinical Presentation of HHS

• Similar to DKA with the following possible exceptions:
  – Symptoms develop over longer period of time
  – Polyuria, polydipsia, weight loss
  – Altered mental status and coma more common due to higher osmolality
  – More significant volume depletion
  – Serum sodium is frequently abnormally high
  – Metabolic acidosis is seldom present
# Laboratory Findings

<table>
<thead>
<tr>
<th>DKA</th>
<th>HHS</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 250, Generally &lt; 800</td>
<td>Blood Glucose</td>
</tr>
<tr>
<td>&lt;7.00 - 7.3</td>
<td>pH</td>
</tr>
<tr>
<td>&lt;10 – 18</td>
<td>Serum Bicarbonate</td>
</tr>
<tr>
<td>Positive</td>
<td>Urine Ketones</td>
</tr>
<tr>
<td>Positive</td>
<td>Serum Ketones</td>
</tr>
<tr>
<td>&gt; 10 (mild), usually &gt;12</td>
<td>Anion Gap</td>
</tr>
<tr>
<td>~ 6 liters</td>
<td>Total Water Deficit</td>
</tr>
<tr>
<td>Variable</td>
<td>Serum Osmolality</td>
</tr>
<tr>
<td>Variable</td>
<td>Mental Status</td>
</tr>
<tr>
<td>(stupor in severe DKA)</td>
<td></td>
</tr>
</tbody>
</table>
Electrolyte Disturbances in DKA and HHS

• Serum sodium is usually low because of the osmotic flux of water from intracellular to extracellular spaces in the presence of hyperglycemia
  – Increased sodium in the presence of hyperglycemia usually indicates profound water losses

• Elevations in serum potassium are caused by insulin deficiency, hypertonicity, and acidemia
  – Low potassium on admission reflects severe depletion and requires vigorous replacement and cardiac monitoring
Effects of DKA/HHS on Sodium & Potassium

- Extracellular
- Intracellular

- NA
- Water
- Glucose

- K
- Water
- Glucose
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True or False

• In DKA, the blood glucose is usually higher than in HHS
  – False

• Patients with HHS more commonly present with altered mental status than patients with DKA
  – True

• Patients with type 2 DM are more likely to present with DKA than with HHS
  – False

• The 2 most common precipitating factors in the development of DKA or HHS are inadequate insulin therapy and infection
  – True
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Management of DKA and HHS

- Correct dehydration
- Correct Hyperglycemia and Acidosis
- Correct Electrolyte Disturbances
- Identify and treat precipitating event

Frequent Patient Monitoring
Management of DKA

Complete initial evaluation. Start IV fluids: 1 L of 0.9% NaCl per hour. (Initially 15-20 ml/kg/hr)

- **IV Fluids**
  - Determine hydration status
  - Hypovolemic Shock
  - Mild Hypotension
  - Cardiogenic Shock

- **Insulin**
  - IV Route
    - Insulin: Regular 0.15 unit/kg as IV bolus
  - Subcut/IM Route
    - Insulin: Regular 0.4 unit/kg ½ IV bolus, ½ IM or Subcut

- **Potassium**
  - Serum K⁺ ≤ 3.3 mEq/L
    - Hold insulin and give 40 mEq K⁺ over 4 hrs (2/3 KCl and 1/3 KPO₄) until K⁺ is 3.3 mEq/L
  - pH < 6.9
    - Dilute 150 mEq of NaHCO₃ in 1 L D₃W and infuse at 200 ml/hr.
  - pH 6.9-7.0
    - Dilute 100 mEq of NaHCO₃ in 1 L of D₃W and infuse at 200 ml/hr.
  - pH > 7.0
    - No HCO₃

- **Assess need for Bicarbonate**

- **Evaluate corrected serum Na⁺**
  - Serum Na⁺ Normal
  - Serum Na⁺ Low
    - 0.45% NaCl (4-14 ml/kg/hr) depending on hydration state

- **When serum glucose reaches 250 mg/dL**
  - Change to 5% dextrose with 0.45% NaCl at 150-250 ml/hr with adequate insulin (0.05-0.1 unit/kg/hr IV infusion or 5-10 unit Subcut every 2 hrs) to keep the serum glucose between 150-200 mg/dl until metabolic control is achieved.

- **Check Clini Chem every 2-4 hrs until stable. Look for precipitating causes. After resolution of DKA, follow blood glucose (BG) every 4 hrs and give sliding scale regular insulin Subcut in 5 unit increments for every 50 mg/dl increase in BG above 150 mg/dl for up to 20 units for BG of ≥ 300 mg/dl.**
Goals of Management

Management of DKA and HHS

- Correct dehydration
  - Expansion of intravascular and extravascular volume and restore renal perfusion

- Correct Hyperglycemia and Acidosis
  - Glucose < 200
  - Bicarbonate ≥ 18
  - Venous pH > 7.3

- Correct Electrolyte Disturbances
  - Avoid Hypokalemia (keep K+ between 4-5)
  - Prevent cardiac complications and respiratory weakness
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Transition to Non-emergent Care

- Ensure treatment precipitating event
- Transition to subcutaneous insulin
- Patient education
  - Understanding Diabetes
  - Sick day management
- Improving access to medical care
Transition to Subcutaneous Insulin

• Calculate total insulin requirement over 24 hours
• Multiply by 0.8 to determine total daily dose (TDD) of SC insulin
• Give 50% of TDD as basal insulin dose
  – long acting analogue (glargine/detemir/NPH)
• Split remaining 50% into 3 doses of prandial insulin to be given before meals
• Calculate correction factor based on TDD
  – use rule of 1800 (for rapid acting analogues-lispro, aspart, etc.)
  – Use rule of 1500 for regular insulin
Patient Education

- Consider patient’s state of mind
  - Be compassionate
  - Help answer questions about hospital course
  - Use event as opportunity to motivate/educate

- Specific counseling should include
  - Blood glucose monitoring
  - Injecting insulin doses
  - Sick day management
    - When to contact HCP
    - BG goals and use of supplemental insulin during illness
    - Means to suppress fever and treat infection
    - Initiation of easily digestable liquid diet containing carbs and salt
  - Signs, symptoms, and management of hypoglycemia
  - Medical Alert Bracelet
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