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Diabetic Ketoacidosis and Hyperosmolar Hyperglycemic State

Jennifer N. Thompson, MD
Project Hope
Objectives

DKA: Diabetic Ketoacidosis
HHS: Hyperosmolar Hyperglycemic State
   (HONKC – hyperosmolar nonketotic coma)

● What is the difference between DKA and HHS?
● How do I manage DKA and HHS?
● What complications should I look out for?
● What does the data say about cerebral edema?
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<td><strong>Relative</strong> insulin deficiency</td>
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<td>Mortality in admitted patients</td>
<td>1-4%</td>
<td>10% or more</td>
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Classic presentation of DKA

Age
- Young people, Type I DM

History
- Polydipsia, Polyuria, Fatigue
- Nausea/vomiting, diffuse abdominal pain.
- In severe cases – lethargy, confusion

Physical
- Ill appearance
- Signs of dehydration: Dry skin, dry mucous membranes, decreased skin turgor (skin tenting)
- Signs of acidosis:
  - Tachypnea → Kussmaul respirations
  - Characteristic acetone (ketotic) breath odor
Role of Insulin

- Required for transport of glucose into cells for use in making ATP
  - Muscle
  - Adipose
  - Liver

- Inhibits lipolysis

- Type I DM = inadequate insulin
Pathophysiology in DKA

Insulin

Counterregulatory hormones
- Glucagon
- Epinephrine
- Cortisol
- Growth Hormone

Gluconeogenesis
Glycogenolysis
Lipolysis
Ketogenesis
## Counterregulatory Hormones - DKA

<table>
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<tr>
<th>Hormone</th>
<th>Increases insulin resistance</th>
<th>Activates glycogenolysis and gluconeogenesis</th>
<th>Activates lipolysis</th>
<th>Inhibits insulin secretion</th>
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<tr>
<td>Epinephrine</td>
<td>X</td>
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No Lipolysis = No Ketoacidosis

Only a small amount of functional insulin required to suppress lipolysis
Underling stressors that tip the balance

- Newly diagnosed diabetics
- Missed insulin treatments
- Dehydration
- Underlying infection
- Other physiologic stressors:
  - Ex) Pulmonary embolism, Illicit drug use (sympathomimetics), Stroke, Acute Myocardial Infarction,
- Young type II diabetics with stressors

Pathophysiology

- Glucagon
- Epinephrine
- Cortisol
- Growth Hormone

- Gluconeogenesis
- Glycogenolysis
- Lipolysis
- Ketogenesis
Workup

Most important labs to diagnose DKA:
- Basic metabolic panel (glucose, anion gap, potassium)
- Arterial or venous blood gas to follow pH
- Urine dipstick for glucose and ketones (high sensitivity, high negative predictive value)

Additional tests:
- Serum ketones
- Magnesium, phosphorus
- EKG – if you suspect hyperkalemia, hypokalemia, arrhythmias

**Determine the underlying cause!**
Management

- Fluids
- Insulin
- Electrolyte repletion
- Find and treat any underlying cause!
Fluids

- Increases intravascular volume
  - Reverses dehydration
  - Restores perfusion to kidneys $\rightarrow$ ↑ GFR $\rightarrow$ urinate out excess glucose
  - Restores perfusion to periphery $\rightarrow$ ↑ uptake and use of glucose (when insulin present)

Take home message: Fluids hydrate patient AND reverse hyperglycemia
Fluids

Pediatrics

- Hypotension: treat with 20cc/kg NS boluses
- If no hypotension:
  - 10-20cc/kg NS bolus then 1.5 – 2x maintenance
    OR
  - Assume 10% dehydration and calculate fluid deficit plus maintenance
  - Replete deficit (plus maintenance) over 48-72hrs.
Insulin

- Allows glucose to enter and be used by cells
- Stops proteolysis and lipolysis
  - Stops Ketogenesis → Stops Acidosis
- Allows potassium to enter cells

Insulin goal: Treat the anion gap acidosis  
(not the hyperglycemia)

- Never stop the insulin before the anion gap is closed.
Insulin

- Dosing: 0.05 units/kg bolus then .05 units/kg/hr insulin drip. (Previously 0.1 units/kg/hr)

- Goal: Decrease glucose by <100 (5.5) per hour
  - Avoids sudden fluid shifts that may lead to cerebral edema

- Reason for IV insulin
  - Not affected by decreased peripheral circulation as with subcutaneous insulin
  - Smooth decline of glucose
  - Short half-life allows for more precise control of serum insulin concentration
Insulin

- If pt has an anion gap and your glucose is <250 (14), do you stop the insulin drip?

- NO!
  - Add D5 when glucose <250 (14).
  - If glucose <150 (8.3), consider D10.

TAKE HOME POINT:

- Do not stop insulin until anion gap is closed.
- Main goal of insulin therapy is to fix the acidosis.
Transitioning to Subcutaneous Insulin

- ONLY after the Anion Gap is closed!
- OVERLAP IV and subcutaneous insulin administration
  - Give long-acting insulin dose (ex. lantus) at least 30 to 60 minutes prior to stopping insulin drip.
- Feed patient
Managing electrolytes

- Potassium
- Sodium
- Phosphorus
- Glucose
Electrolyte management
Potassium

Total Body Potassium depletion

- Acidosis $\rightarrow$ $K^+$ exits cells as $H^+$ enters to buffer
- Dehydration and volume depletion
  - Osmotic diuresis + $\uparrow$ aldosterone $\rightarrow$ loss of $K^+$

$\Rightarrow$ Although serum $K^+$ is usually normal or high, total body $K^+$ is low.
Electrolyte Management
Potassium

- With insulin therapy
  - $K^+$ moves into cells

- To avoid hypokalemia
  - Give oral and/or IV potassium to avoid hypokalemia when $K < 4.5$
  - Monitor $K^+$ levels and EKG
    - Low $K$ – Biphasic T, U-wave
    - High $K$ - tall peaked T, flat P waves, wide QRS
    - Cardiac dysrhythmia

- Monitor K+ levels and EKG
- With insulin therapy
  - K+ moves into cells

- To avoid hypokalemia
  - Give oral and/or IV potassium to avoid hypokalemia when K < 4.5
  - Monitor K+ levels and EKG
    - Low K – Biphasic T, U-wave
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    - Cardiac dysrhythmia
Pseudohyponatremia:
- For each 100mg/dl increase of glucose above 100, Na⁺ decreases by 1.6 mEq/L

- Corrected Na⁺ = measured Na +
  \[ 1.6 \text{ meq/L} \times \frac{(\text{glucose}-100)}{100} \]

- Example:
  \[ \text{Na⁺} = 125 \text{ meq/L and Glucose = 500 mg/dl} \]
  \[ 500 - 100 = 400 \]
  \[ 400/100 = 4 \]
  \[ 4 \times 1.6 = 6.4 \text{ meq/L} \]
  Corrected Na⁺ = 125 + 6.4 = 131.4 meq/L
Electrolyte Management
Phosphorus

Hypophosphatemia

- Occurs after aggressive hydration/treatment
- Monitor phosphorus and replete as needed to keep > 1
  - Total body phosphorus depleted
  - Mostly a theoretical problem
  - Potential complications: muscle weakness, myocardial dysfunction, CNS depression
Management review

- Rehydrate patient with IV fluids
- Continue insulin drip until anion gap is closed
- Until insulin drip is off:
  - Check glucose every hour. Avoid hypoglycemia.
  - Check electrolytes every 1-2hrs. Avoid hypokalemia.
- Replete potassium when K < 4.5 and patient making urine
ICU Monitoring

Careful nursing monitoring of the following:

- I/Os (input and urine output.)
- Urine dipstick with every void
  - resolution of ketonuria may lag behind clinical improvement
- Monitor for any signs of cerebral edema:
  - Change in mental status, severe headache
  - Sudden drop in heart rate
  - Neurologic deficits
DKA Complications

- Dehydration, shock, hypotension
- Hypokalemia/ hyperkalemia
- Hypoglycemia
- Aspiration pneumonia
- Sepsis
- Acute tubular necrosis
- Myocardial infarction
- Stroke
- Cerebral edema

* Death rate in U.S when managed in hospital setting
  = 1-4%
DKA Complications
Cerebral edema

- Clinical manifestations:
  - Altered mental status
  - Headache
  - Persistent vomiting
  - Sudden and persistent drop in heart rate
  - Seizure
  - Unequal or fixed, dilated pupils

- Mostly children

- High mortality rate
  - 1% of DKA pts, > 25% mortality rate

- High morbidity rate
  - High rate of neurologic complications

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DKA Complications
Cerebral edema

Risk Factors
- Age < 5 years
- More often seen in your sickest patients
  - (high BUN, low bicarb <15)
  - Fall in serum Na or lack of increase during treatment
- Rapid correction of hyperglycemia
  - Goal: decrease glucose <100 mg/dl (5.5) per hour
- Sodium bicarbonate administration
- Excessive fluids
DKA Complications
Cerebral Edema - treatment

- Mannitol 1mg/kg IV
- Reduce IV fluid rate (ex. 70% maintenance)
- Consider intubation
  - set the ventilator close to rate that patient was breathing beforehand
  - be cautious of over hyperventilation
    - Temporary measure
    - Keep pCO2 > 22mmHg
- May consider 3% hypertonic saline
  - but not enough data to truly recommend
#### Diabetic Ketoacidosis

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#### HHS - Hyperosmolar hyperglycemic state

(AKA HONKC = hyperosmolar nonketotic coma)

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#### Demographics

- **Mostly type I DM**
  - Children, young people
- **Mostly type II DM**
  - Elderly

#### Insulin activity

- **Absolute functional insulin deficiency**
- **Relative insulin deficiency**

#### Mortality in admitted patients

- 1-4%
- 10% or more
HHS
(Hyperosmolar Hyperglycemic State)

- Elderly and mentally or physically impaired patients
- Usually associated with underlying physiologic stressors
  - Ex. Infection, myocardial infarction, stroke.
- Slower onset (ex. 1 week vs. 1-2 days in DKA)
- Higher Mortality rate than DKA (>10%)
  - Older patients, more comorbidities

Presentation:
- Altered mental status (confusion, neurologic deficits)
- Signs of severe dehydration (tachycardia, hypotension, dry mucous membranes, skin tenting)
Insulin Deficiency

↓ Glucose uptake

↑ Proteolysis

↓ Lipolysis

Amino Acids

Glycerol

Free Fatty Acids

Gluconeogenesis

Glycogenolysis

Ketogenesis

Hyperglycemia

Osmotic diuresis

Dehydration

Acidosis

No Lipolysis = No Ketoacidosis

Only a small amount of functional insulin required to suppress lipolysis

Low catecholamine levels in elderly patients ➔ less insulin resistance
Therapy:
- Fluid repletion
  - Total fluid deficit ≈ 10 liters in adults
  - Normal saline 2-3 liters rapidly
  - Replete ½ in first 6 hours
- Insulin drip 0.05 units/kg/hr
  - Decrease glucose by approximately 50 mEQ/hr
- Check electrolytes q1-2hrs. Check glucose q1hr
  - Monitor potassium for hypokalemia/hyperkalemia
- Treat underlying precipitating illness

Potential complications are the same as DKA
Summary

- Pathophysiologic difference between DKA and HHS
  - DKA is a state of absolute functional insulin deficiency
  - Only in DKA: Lipolysis $\rightarrow$ ketogenesis $\rightarrow$ acidosis

- You are never specifically treating the glucose
  - In DKA – you are treating the underlying acidosis/ketogenesis (reflected by the anion gap)
  - In HHS – you are treating the underlying shock caused by poor tissue perfusion/severe dehydration
Summary (continued)

- Being too aggressive in management may cause more harm than good
- If you don’t pay attention to details, you will cause an iatrogenic death
  - Monitor electrolytes (especially potassium)
- Beware cerebral edema.
- Therapy for DKA and HHS is similar.
Thank you
Pathophysiology of diabetic ketoacidosis
β-cell destruction → Insulin Deficiency

- Decreased Glucose Utilization & Increased Production
- Glucagon
- Increased Ketogenesis, Gluconeogenesis, Glycogenolysis

Stress
- Epi, Cortisol
- GH

Adipocytes
- Increased Lipolysis

Amino Acids

Increased Protein Catabolism

Muscle

Liver

Polyuria
- Volume Depletion
- Ketonuria

Threshold 180 mg/dl

Hyperglycemia
- Ketoacidosis
- HyperTG
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