Diabetic Ketoacidosis and Hyperglycemic Hyperosmolar Syndrome

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Case History
HPI: 24 yo man with recent 8 lb. weight loss, increased thirst and frequent urination
PMH: Negative Meds: None
Smoke: 1 ppd EtOH: 1-2/day
PE: BP 100/55 P 108 R 20 T 98.8
Deep rapid breathing
Lab:
Glucose 714 CO2 14 Ph 7.03 Ketones +160
K 4.9 Na 132 Cl 100 Anion Gap 18
Creat 1.4 Phos 4.5

Question 1
What is the most likely precipitating cause for diabetic ketoacidosis in this patient?

A. Dehydration
B. Urinary Tract Infection
C. Pulmonary Embolus
D. Sepsis
E. New Onset Type 1 Diabetes
Question 2
Besides insulin, what is the most important therapeutic intervention in patients with diabetic ketoacidosis?
A. Potassium Administration
B. Bicarbonate Administration
C. Volume Repletion
D. Antibiotics
E. Phosphate Administration

Question 3
What is the most common reason that a patient fails to respond to treatment for diabetic ketoacidosis?
A. Use of SQ rather than IV insulin
B. Not identifying / treating precipitating cause
C. Use of ½ NS rather than NS
D. Failure to give bicarbonate
E. Failure to give potassium

Diabetic Ketoacidosis
Clinical Setting
Type 1 DM
- New Onset
- Poor Compliance
- Precipitating Factor
Type 2 DM with Acute Illness
- Precipitating Event
Diabetic Ketoacidosis
Precipitating Causes

- Infection
- Adrenal Crisis
- Acute Abdomen
- Ischemic Extremity
- Pulmonary Embolus
- Myocardial Infarction
- Cerebrovascular Event
- New Onset Type 1 Diabetes

DKA and HHS
Pathogenesis

- Insulin Deficiency
  - Absolute
  - Counterregulatory Hormones
  - Relative

- Lipolysis → Ketogenesis → Alkaline Reserve

- Glucose Utilization → Gluconeogenesis

- Ketogenesis

- Hyperglycemia → Dehydration

DKA

HHS

Kitabchi A, Diabetes Care 2009;32:1335-43

Diabetic Ketoacidosis
Deficits of Water and Electrolytes

Typical total body deficits of water and electrolytes in diabetic ketoacidosis and hyperosmolar hyperglycemic state*

<table>
<thead>
<tr>
<th></th>
<th>DKA</th>
<th>HHS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total water (L)</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>Water (mL/kg)</td>
<td>100</td>
<td>200-250</td>
</tr>
<tr>
<td>Na+ (mEq/l)</td>
<td>7-10</td>
<td>3-13</td>
</tr>
<tr>
<td>CI- (mEq/l)</td>
<td>3-5</td>
<td>5-15</td>
</tr>
<tr>
<td>K+ (mEq/l)</td>
<td>4-6</td>
<td>4-5</td>
</tr>
<tr>
<td>PCO2 (mmHg)</td>
<td>9-12</td>
<td>3-7</td>
</tr>
<tr>
<td>HCO3- + (mEq/l)</td>
<td>13-15</td>
<td>13-15</td>
</tr>
<tr>
<td>Cae+ (mEq/l)</td>
<td>1-2</td>
<td>1-2</td>
</tr>
</tbody>
</table>

* Data are from Szeto et al (1964) and Kovacs (1974).
* For patients of body weight.

Diabetic Ketoacidosis

Plasma Osmolality and Mental Status

- Glucose > 250 mg/dL
- HCO3 < 18 mEq/L
- pH < 7.30
- Anion Gap > 12
- Ketones Positive (Urine, Serum)

Diabetic Ketoacidosis

Severity Classification

- **DKA**
  - MILD
    - Glucose: > 250 mg/dL
    - HCO3: 15-18 mEq/L
    - Ketones: positive
    - Sensorium: alert
  - MODERATE
    - Glucose: > 250 mg/dL
    - HCO3: 10-14 mEq/L
    - Ketones: positive
    - Sensorium: alert/drowsy
  - SEVERE
    - Glucose: > 250 mg/dL
    - HCO3: < 10 mEq/L
    - Ketones: positive
    - Sensorium: stupor/coma

- **HHS**
  - Glucose: > 600 mg/dL
  - pH: > 7.30
  - HCO3: > 18 mEq/L
  - Ketones: small
  - Sensorium: stupor/coma
**DKA and HHS**

**Treatment**

1. **IV Fluids**
   - Rehydrate: Monitor + Correct Hyponatremia
2. **Insulin**
   - Correct Hyperglycemia
3. **Potassium**
   - Prevent Hypokalemia
4. **Bicarbonate?**
   - Correct Severe Acidosis (pH < 6.9)

*In DKA, potassium phosphate may be considered in selected patients with serum phosphate < 1.0 mg/dL.*

Kitabchi A, Diabetes Care 2009;32:1335-43

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**Evidence Level:** Well conducted meta-analyses, systemic reviews of RCT’s, or RCT’s with low bias risk

Kitabchi A, Diabetes Care 2009;32:1335-43

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**DKA and HHS**

**Treatment**

1. **IV Fluids**
   - 1st Hour: NS (0.9%), 15–20 mL/kg/h or 1–1.5 Liters
   - Maintenance:
     - ½ NS (0.45%), 250–500 mL/h if serum Na↑ or Normal
     - NS (0.9%), 250–500 mL/h if serum Na Low
   - Change to D5 when glucose < 200 mg/dl in DKA and < 300 mg/dl in HHS

*Evidence Level: High quality meta-analyses, systemic reviews of RCT’s, or RCT’s with low bias risk*

Kitabchi A, Diabetes Care 2009;32:1335-43

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**DKA and HHS**

**Treatment**

1. **Insulin**
   - Infusion 0.14 U/kg/hr, OR Bolus 0.1 U/kg, then Infusion 0.1 U/kg/hr (Regular Insulin)
   - If BG not ↓ by 10% in the 1st hour, give 0.14 U/kg bolus and continue infusion at the previous rate
   - When BG < 200 (DKA) or < 300 (HHS), change fluid to D5 and ↓ rate to 0.02–0.05 U/kg/h

*Evidence Level: High quality meta-analyses, systemic reviews of RCT’s, or RCT’s with low bias risk*

Kitabchi A, Diabetes Care 2009;32:1335-43
**Hyperglycemic Emergencies**

**Evidence Based Management**

**Hyperglycemia / Ketonemia**

**Recommendation 4**

SQ insulin analogs may be used in the medical ward or emergency room in mild–moderate DKA.

Evidence Level: Well conducted meta-analyses, systemic reviews of RCT’s, or RCT’s with low bias risk

- Butkiewicz E, Diabetes Care 1995;18:1187–90

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**Diabetic Ketoacidosis**

**Insulin Given by Different Routes**

**Mild-Moderate DKA**

RCT: IV vs SQ vs IM Insulin

Conclusion: In Mild-Moderate DKA, Insulin May Be Given IV, SQ or IM

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**Hyperglycemic Emergencies**

**Evidence Based Management**

**Hyperglycemia / Ketonemia**

**Recommendation 6**

Some type 2 DM patients may be treated with oral anti-diabetic agents and lifestyle modification after recovery.

Evidence Level: Meta-analyses, systemic reviews of RCT’s, or RCT’s with high bias risk

- Della Manna T, Diabetes Care 2005;28:1856-61
Diabetic Ketoacidosis
Use of SQ Glargine During IV Insulin Infusion
RCT: IV Insulin vs IV Insulin + Glargine 0.25 U/Kg with 10 hours of IV Start

Open Bars (N=13)
No Glargine

Open Bars (N=12)
Glargine

Conclusion: In DKA, SQ Glargine Given with IV Insulin Reduces the Risk of Future Rebound Hyperglycemia without Increasing Hypoglycemia

DKA and HHS
Treatment
Potassium
- Replace after good urine output is verified and serum K is in normal range
- Give potassium replacement as 2/3 K Chloride and 1/3 K Phosphate

DKA and HHS
Treatment
Bicarbonate
- If pH ≤ 6.9, give 100 mmol Na bicarbonate in 400 ml sterile water with 20 meq KCl at a rate of 200 ml/h for 2 h until the venous pH is > 7.0
- Patients with pH > 6.9 do not require bicarbonate therapy

Evidence Level (1st): Expert opinion
Evidence Level (2nd): High quality meta-analyses, systemic reviews of RCT’s, or RCT’s with low bias risk
DKA and HHS
Treatment

Phosphate
- Not indicated in most DKA patients
- Add 20–30 meq/l K Phosphate to IV fluids if potential hypophosphatemic complications
- Monitor serum calcium level in patients receiving phosphate infusion

Evidence Level: High quality systematic reviews of case control or cohort studies


Hyperglycemic Emergencies
Evidence Based Management

Hypercoagulable State
Recommendation 1
Prophylactic heparin use may be beneficial in DKA. Full anticoagulation may be indicated if there are no contraindications in HHS.

Evidence Level: Expert opinion


Diabetic Ketoacidosis
Treatment Protocol

**Diabetic Ketoacidosis**

Resolution

- Glucose < 200 mg/dl
- HCO₃ > 18 mEq/L
- pH > 7.30
- Anion Gap ≤ 12
- Ketones Negative (Urine, Serum)

**Diabetic Ketoacidosis**

Ketone Response to Treatment

- Nitroprusside Measures Acetoacetate
- B Hydroxybutyrate Predominates
- Caveat: Measured Ketones Worsen Transiently Before Improving

**DKA / HHS Treatment Orders**

Use Them
Diabetic Ketoacidosis

Pitfalls

- Precipitating Cause: don't fail to treat
- Cerebral Edema: don’t correct BG too rapidly
- Relapse: don’t turn off the IV insulin too soon
- Relapse: remember to give SQ long acting insulin before you stop the IV insulin

DKA and HHS

Mortality Risk

Mortality
- DKA: < 5%
- HHS: ~15%

Adverse Prognostic Factors
- Coma
- Hypotension
- Age Extremes
Case History
He is given a 10 U insulin bolus and a 7 U/hr (0.1 U/kg/hr) infusion and NS with 40 mEq/L KCl at 250 cc/hr IV.

The DKA resolves after 6 liters of fluid and 74 U of insulin over 24 hrs.

During the next 24 hrs, he is kept on a low dose insulin infusion rate of 0.7 U/hr and is given a total of 15 U of short acting insulin to cover meals and hyperglycemia (24 hr insulin = 32 U).

24 Hour Insulin Requirement: 32 Units
What regimen would you start prior to discharge?

- **Glargine insulin**
  - Dose: ____________________
- **Detemir insulin**
  - Dose: ____________________
- **Lispro insulin**
  - Dose: ____________________
- **Aspart insulin**
  - Dose: ____________________
- **Glulisine insulin**
  - Dose: ____________________
- **NPH insulin**
  - Dose: ____________________
- **Regular insulin**
  - Dose: ____________________

24 Hour Insulin Requirement: 32 Units
What regimen would you start prior to discharge?

- **Glargine insulin**
  - Dose: 15 U or
- **Detemir insulin**
  - Dose: 15 U
- **Lispro insulin**
  - Dose: 5 U or
- **Aspart insulin**
  - Dose: 5 U or
- **Glulisine insulin**
  - Dose: 5 U

Uninsured and/or can’t afford insulin analogs:

- **NPH insulin**
  - Dose: 14 AM, 6 PM
- **Regular insulin**
  - Dose: 6 AM, 6 PM

Analog Insulin: Basal - 50% TDD; Boluses - 50% TDD
Human Insulin: AM – 2/3 TDD (2/3 N, 1/3 R); PM 1/3 TDD (1/2 N, 1/2 R)
**DKA and HHS**

**Summary**

- In DKA and HHS, Find Precipitating Cause
- Treat with Insulin, Volume Repletion, KCl
- Monitor Closely and Use a Flow Sheet
- Transition to SQ Insulin before DC IV Insulin
- Discharge Patient on Insulin
- Close Follow-up is Critical

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**Thank You**