Diabetic Ketoacidosis

October 2015

Michael T. McDermott MD
Director, Endocrinology and Diabetes Practice
University of Colorado Hospital

Case History
HPI: 24 yo man with recent 8 lb. weight loss, increased thirst and frequent urination
PMH: Negative        Meds: None
PE: BP 100/55  P 108  R 20  T 98.8
               Deep rapid (Kussmaul) 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. Sepsis
B. Dehydration
C. Pulmonary Embolus
D. Urinary Tract Infection
E. New Onset Type 1 Diabetes
Question 2
Besides insulin, what is the most important therapeutic intervention in DKA patients?

A. Antibiotics
B. Volume Repletion
C. Potassium Administration
D. Phosphate Administration
E. Bicarbonate Administration

Question 3
What is the most common reason that a patient fails to respond to treatment for DKA?

A. Use of SQ rather than IV insulin
B. Use of ½ NS rather than NS
C. Not treating the precipitating cause
D. Failure to give bicarbonate
E. Failure to give potassium

Diabetic Ketoacidosis
Clinical Setting
Type 1 DM (70-90%)
  • New Onset
  • Poor Compliance
  • Precipitating Event
Type 2 DM (10-30%)
  • Precipitating Event
Diabetic Ketoacidosis

Precipitating Events

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

Diabetic Ketoacidosis

Pathogenesis

Insulin Deficiency
Absolute
↑ Hormones
Relative
↓ Glucose Utilization
↑ Glycogenolysis

↑ Alkal Reserve
Hyperglycemia
Ketoacidosis
Dehydration
Hyponatremia

DKA → HHS

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

SGLT2 Inhibitors May Cause DKA

Taylor SL, J Clin Endocrinol Metab 2015; 100:2849-52
Diabetic Ketoacidosis
Water and Electrolyte Deficits

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

<table>
<thead>
<tr>
<th></th>
<th>DEKA</th>
<th>HIES</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>100 to 200</td>
</tr>
<tr>
<td>Na+ (mEq/L)</td>
<td>95 to 100</td>
<td>85 to 105</td>
</tr>
<tr>
<td>Cl- (mEq/L)</td>
<td>95 to 100</td>
<td>85 to 105</td>
</tr>
<tr>
<td>K+ (mEq/L)</td>
<td>2 to 8</td>
<td>4 to 2</td>
</tr>
<tr>
<td>PO4 (mEq/L)</td>
<td>1 to 7</td>
<td>2 to 7</td>
</tr>
<tr>
<td>HCO3- (mEq/L)</td>
<td>15 to 20</td>
<td>15 to 20</td>
</tr>
</tbody>
</table>

* Data are from Evers et al. (1994) and Kretser (1971).

Plasma Osmolality and Mental Status

**Useful Calculations**

**Serum Osmolality**

$$2 \times (\text{Na}^+) + \frac{\text{Glucose}}{18} + \frac{\text{BUN}}{2.8}$$

Normal Range: 285-295 mOsm/kg

**Anion Gap**

$$\text{Na}^+ - (\text{Cl}^- + \text{HCO}_3^-)$$

Normal Range: 7-13 mmol/L
**Diabetic Ketoacidosis**

**Diagnosis**
- Glucose ≥ 250 mg/dl
- HCO₃ ≤ 18 mEq/L
- pH ≤ 7.30*
- Anion Gap > 15
- Ketones Positive (Urine, Serum)

*Arterial pH best but venous pH OK

Wilson JF, Ann Intern Med 2010; ITCI-3, Jan 1

**Diabetic Ketoacidosis**

**Severity**

- **MILD**
  - Glucose: > 250 mg/dL
  - pH: 7.25-7.30
  - HCO₃: 15-18 mEq/L
  - Ketones: positive
  - Sensorium: alert

- **MODERATE**
  - Glucose: > 250 mg/dL
  - pH: 7.0-7.24
  - HCO₃: 10-14 mEq/L
  - Ketones: positive
  - Sensorium: alert/drowsy

- **SEVERE**
  - Glucose: > 250 mg/dL
  - pH: < 7.0
  - HCO₃: < 10 mEq/L
  - Ketones: positive
  - Sensorium: stupor/coma


**Diabetic Ketoacidosis**

**Treatment**

- **IV Fluids**
- **Insulin**
- **Potassium**
- **Bicarbonate?**
- **Treat Precipitating Cause**

Rehydrate: Monitor + Correct Hyponatremia

Correct Hyperglycemia

Prevent Hypokalemia

Correct Severe Acidosis (pH < 6.9)
**Diabetic Ketoacidosis**

**Treatment**

**IV Fluids**

- **1st Hour:** NS, 15–20 ml/kg/h (1.0–1.5 liters)
- **Maintenance:**
  - ½ NS, 250–500 ml/h if serum Na ↑ or Normal
  - NS, 250-500 ml/h if serum Na Low

*Change to D5 when BG < 200 mg/dl (DKA) or < 300 mg/dl (HHS)*

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

Wilson JF, Ann Intern Med 2010; ITCI-3, Jan 1


---

**Insulin (Regular)**

- IV Bolus 0.1 U/kg, then Infusion 0.1 U/kg/hr
- If BG not ↓ by 10% in 1 hour, IV bolus 0.14 U/kg and continue infusion at the previous rate

*Decrease rate to 0.02-0.05 U/kg/hr when BG < 200 mg/dl (DKA) or < 300 mg/dl (HHS)*

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

Wilson JF, Ann Intern Med 2010; ITCI-3, Jan 1


---

**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*

Kitabchi A, JCEM 2008;93:1541-52
Diabetic Ketoacidosis

### Treatment

**SQ insulin analogs may be used in mild–moderate DKA in ED or inpatient**

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

---

### Diabetic Ketoacidosis

**IV Insulin + SQ Glargine**

RCT: IV Insulin vs IV Insulin + Glargine 0.25 U/Kg within 10 hours of IV Start

![Graph showing average glucose and percent rebound with Glargine and no Glargine](image)

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

University of Colorado DKA Study
Hsia E, J Clin Endocrinol Metab 2012;97:3132-7

---

### Diabetic Ketoacidosis

**Treatment**

**Potassium (check every 2 hours)**

- Serum K⁺ ≥ 5.2 meq/L: Don’t give K⁺
- Serum K⁺ 3.3-5.1 meq/L: Give K⁺ 20-30 meq/L
- Serum K⁺ < 3.3 meq/L initially: **Delay Insulin Rx.**
  
  Give K⁺ 20-30 meq/h until serum K⁺ ≥ 3.3 meq/L

Kitabchi A, Diabetes Care 2009;32:1335–43
Wilson JF, Ann Intern Med 2010; ITCI-3, Jan 1
**Diabetic Ketoacidosis**

**Treatment**

**Bicarbonate**

- pH ≤ 6.9: Na Bicarbonate, 2 amps (100 mmol) in 400 ml H2O with 20 meq KCl, at rate of 200 ml/h for 2 hr until the venous pH is > 7.0
- pH > 6.9: Na Bicarbonate therapy not required

Kitabchi A, Diabetes Care 2009;32:1335–43
Wilson JF, Ann Intern Med 2010; ITCI-3, Jan 1

**Phosphate**

- Not indicated in most DKA patients
- Potential hypophosphatemic complications:
  - Add 20–30 meq/l K Phosphate to IV fluids
  - Monitor serum calcium level

Kitabchi A, Diabetes Care 2009;32:1335–43
Wilson JF, Ann Intern Med 2010; ITCI-3, Jan 1

**Hypercoagulable State**

DKA: prophylactic heparin use may be beneficial
HHS: full anticoagulation if no contraindications

Kitabchi A, Diabetes Care 2009;32:1335–43
Wilson JF, Ann Intern Med 2010; ITCI-3, Jan 1
Diabetic Ketoacidosis

Resolution

- Glucose < 200 mg/dl
- HCO\(_3\) > 18 mEq/L
- pH > 7.30
- Anion Gap ≤ 13
- Ketones Negative (Urine, Serum)

Diabetic Ketoacidosis

Ketone Response to Treatment

Nitroprusside
Measures Acetoacetate

B Hydroxybutyrate
Predominates Early;
Converts to Acetoacetate
With Treatment

Caveat
Ketones Measured by
NP May Worsen
 transiently Before
Improving

Diabetic Ketoacidosis

Treatment Protocol – Use One

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

*Treatment Flowsheet – Use One*

- **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

**Diabetic Ketoacidosis**

*UCH Treatment Protocol – Use One*
**Diabetic Ketoacidosis**

**Mortality**
- DKA: ~ 4%
- HHS: ~ 15%

**Adverse Prognostic Factors**
- Coma
- Hypotension
- Age Extremes

---

**Case History**

He is given a 7 U (0.1 U/kg) insulin bolus and a 7 U/hr (0.1 U/kg/hr) insulin 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
- Detemir insulin
- Lispro insulin
- Aspart insulin
- Glulisine insulin
- NPH insulin
- Regular insulin

| Glargine = Lantus | Detemir = Levepin | Lispro = Humalog | Aspart = Novolog | Glulisine = Apidra |
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)

---

Diabetic Ketoacidosis
Summary

- 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
- Follow-up after Hospital Discharge

---

Thank You