Diabetic Emergencies: DKA, HHS, Hypoglycemia

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Objectives

• discuss the pathophysiologic processes of diabetic emergencies
• differentiate between the clinical presentation of the three types of diabetic emergencies
• describe evidence-based management strategies for diabetic emergencies

Diabetes mellitus

• a group of metabolic diseases characterized by hyperglycemia (confirmed by fasting serum glucose of greater than or equal to 126 mg/dL)
• results from defects in insulin section, insulin action, or both
• characterized by abnormalities in metabolism of carbohydrate, fat, protein and insulin

Type 1 diabetes

categorized by beta cell destruction, usually leading to absolute insulin deficiency

Type 2 diabetes

characterized by insulin resistance and a relative insulin deficiency

Diabetic ketoacidosis (DKA)

• A condition characterized by hyperglycemia, metabolic acidosis, and elevated serum ketones
  – ADA: hyperglycemia with serum glucose ≥ 250 mg/dL, a metabolic acidosis with HCO3 ≤ 18 mEq/L, an anion gap >10, and arterial pH ≤ 7.30 with moderate ketonemia or ketonuria
• The most serious metabolic disturbance of type 1 DM
DKA: Etiology

- Undiagnosed Type 1 diabetes mellitus: 20% of patients with DKA
  - most frequently adolescents

DKA: Etiology

- Causes in known Type 1
  - Illness or infection
    - 50% of patients with DKA have a concurrent illness, most likely an infection
  - Omission of exogenous insulin or inappropriate insulin dosing
  - Trauma
  - Surgery
  - Noncompliance: too many calories

DKA: Etiology

- Causes in patients with or without diabetes
  - Cushing's syndrome
  - Hyperthyroidism
  - Pancreatitis
  - Pregnancy
  - Drugs
    - Glucocorticoids (e.g., prednisone)
    - Thiazide diuretics (e.g., hydrochlorothiazide)
    - Phenytoin (Dilantin)
    - Sympathomimetics (e.g., epinephrine)
    - Diazoxide (Hyperstat)

DKA: Clinical presentation

- Tachycardia, orthostatic hypotension
- Polyuria, polydipsia, polyphagia
- Nausea, abdominal pain, vomiting, hypoactive bowel sounds
- Weakness, fatigue
- May have fever

DKA: Clinical presentation

- Clinical indications of dehydration
  - flushed, warm, dry skin
  - poor skin turgor
  - dry mucous membranes
  - sunken eyeballs
  - weight loss
  - decreased RAP, PAP, PAWP, CO/CI

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DKA: Clinical presentation

- Headache, visual disturbances
- Kussmaul’s ventilatory pattern, acetone (fruity) odor to breath
- Diminished deep tendon reflexes
- Lethargy progressing to coma

• Glucose: elevated 300-800 mg/dl; average 600 mg/dl
• Sodium: normal, elevated, or decreased depending on hydration status
• Potassium: elevated initially; decreases to normal or low as pH and dehydration is corrected

DKA: Clinical presentation

- Glucose: elevated 300-800 mg/dl; average 600 mg/dl
- Sodium: normal, elevated, or decreased depending on hydration status
- Potassium: elevated initially; decreases to normal or low as pH and dehydration is corrected

Potassium Shifts

- For every decrease in pH of 0.1, the serum potassium will increase by 0.5 mEq/L; for every increase in pH of 0.1, the serum potassium will decrease by 0.5 mEq/L
  - a patient is admitted with a serum glucose of 580 mg/dL, a pH of 7.0, and a serum potassium of 4.5
    - Should potassium be started now?
    - As the pH is correct, what will the potassium fall to?

DKA: Diagnostic

- Anion gap: elevated; >15

Anion gap

- \((Na + K) - (Cl + HCO_3)\)
- Normal: 5-15
  - if normal: metabolic acidosis due to bicarbonate loss
  - if increased: metabolic acidosis due to metabolic acid gain

DKA: Diagnostic

- Phosphorus: decreased
- Magnesium: elevated initially and then decreased
- Ketones: elevated; > 3 mOsm/liter
- BUN and creatinine elevated with BUN:creatinine ratio >10:1
- Serum osmolality: elevated; usually 295-330 mOsm/liter
- Lipids: may be elevated
DKA: Diagnostic

- Arterial blood gases: metabolic acidosis frequently with some degree of respiratory compensation
  - pH < 7.30
  - Bicarbonate < 15
  - PaCO2 < 35 mm/Hg
- Hematocrit: elevated
- WBC: elevated; unreliable indication of infection in DKA

- Urine: glucose and ketones: positive
- Electrocardiogram
  - May show changes associated with potassium levels
  - Sinus tachycardia is frequently seen

Assess high-risk patient; monitor:

- Vital signs hourly
- ECG monitoring
- Serum glucose hourly
- Urine output hourly
- Hemodynamic monitoring indicated especially for elderly patients or patients with cardiac history

REMEMBER:
PATIENTS WITH DKA DO NOT DIE OF HYPERGLYCEMIA!
THEY DIE OF HYPOVOLEMIC SHOCK
**Correction of fluid volume deficit**

- Establish IV access with at least one large (at least 18G) gauge catheter
- Normal (0.9%) saline for first 3-4 liters: rate at 200 ml-1 liter/hour (or 15-20 ml/kg) for first hour; then 300-500 ml/hour depending on cardiovascular status and volume deficit
  - if osmolality <320 mOsm/L: NS
  - if osmolality >320 mOsm/L: 1/2NS

**Correction of fluid volume deficit**

- Half-normal (0.45%) saline after first 3-4 liters
- Dextrose 5% is added when serum glucose is 250 mg/dl (D\textsubscript{5}NS or D\textsubscript{5}1/2NS)
- Dextrose 10% may be used if serum glucose falls to 150 mg/dl or less
- Total volume deficit usually 4-8 liters
- Colloids may be used initially if hypovolemic shock exists

**Normalize serum glucose level gradually**

- Regular insulin 0.1 units/kg IV bolus
- Regular insulin by IV infusion at 5-10 units/hour (or 0.1 unit/kg/hour)
  - Insulin is mixed in normal saline and the IV tubing is flushed with 50 ml of insulin solution to saturate binding sites on the IV tubing before administration

**Normalize serum glucose level gradually**

- Insulin drip is decreased to 2-3 units/hour when serum glucose is 250-300 mg/dl
- Subcutaneous regular insulin is usually started when serum glucose is <250 mg/dl; pH >7.2; bicarbonate >18
  - Insulin drip is usually discontinued 1-2 hours after subcutaneous insulin is started

**Normalize serum glucose level gradually**

- Serum glucose should drop by no more than 50-100 mg/dl/hour (or 10%/hour) to avoid hypoglycemia, hypokalemia, and cerebral edema

**Correct electrolyte imbalance**

- Total body potassium is low due to osmotic diuresis so potassium will decrease when pH and dehydration are corrected; potassium replacement is started when potassium level is at upper limit of normal
- Monitor hourly for first 4-6 hours
- Refractory hypokalemia suggests hypomagnesemia or hypocalcemia
Potassium Shifts

0.1 change in pH (from midline normal of 7.4) causes a change in the potassium level by ~0.5 mEq/L in the opposite direction.

Correct electrolyte imbalance

- Phosphorus levels are also frequently low
  - Replacement is indicated especially if patient is anemic, has HF, pneumonia or any other cause of hypoxia (remember that hypophosphatemia shifts the oxyhemoglobin curve to the left and impairs tissue oxygenation) or if serum phosphate level is <1 mg/dl

- Magnesium replacement may also be necessary: one to two grams of 10% solution if renal function adequate

Correct acid-base imbalance

- This is usually achieved by rehydration and insulin
- Sodium bicarbonate is indicated only if pH is 7.0 or less and should be discontinued as soon as pH is 7.2
- Note: some references say NEVER give sodium bicarbonate in DKA regardless of pH

Problems with bicarbonate

- may cause paradoxical CSF acidosis
- may shift the oxyhemoglobin dissociation curve to the left impairing oxygen delivery
- may cause cerebral edema
- may cause hypokalemia, hypocalcemia
Safety

- Prevent aspiration due to paralytic ileus commonly seen in DKA
  - Keep head of bed elevated 30 degrees
  - NG tube may be necessary
- Seizure precautions
- Monitor serum glucose and electrolytes carefully

Identification and treatment of cause

- Most commonly infection especially urinary tract infection; antibiotics as indicated
- Assess knowledge level related to self-care and provide teaching and counseling: be alert to possible drug therapy errors, noncompliance with diet, drug interactions

Monitor for complications

- Hypovolemic shock
- Dysrhythmias
- Thromboembolism
- Myocardial infarction
- Pulmonary edema
- Cerebral edema
- Seizures
- Coma
- Hypoglycemia
- Acute renal failure
- Electrolyte imbalances: potassium; sodium; phosphorus; magnesium

Diabetes Management

- Diet
- Exercise
- Weight normalization
- Drug therapy
  - insulin
  - oral agents

Hyperglycemic Hyperosmolar Syndrome (HHS)

- Severe hyperglycemia; absence of ketosis; profound dehydration; neurologic manifestations
- most common severe metabolic disturbance in type 2 DM

HHS: Etiology

- Usually seen in patients over 60 years with glucose intolerance or type 2 DM
  - Frequently iatrogenic (e.g., enteral feedings, dialysis solution, corticosteroids)
- Acute illness or infection: UTI
- Trauma
- Surgery
- Pancreatitis
- Burns
- Hepatitis
HHS: Etiology

- Cushing’s syndrome
- Hyperthyroidism
- Renal disease: peritoneal dialysis; hemodialysis
- Hypertonic nutrition: enteral or parenteral
- Alcohol
- Drugs
  - Glucocorticoids (e.g., prednisone)
  - Thiazide diuretics (e.g., hydrochlorothiazide)
  - Loop diuretics (e.g., furosemide [Lasix])
  - Phenytoin (Dilantin)
  - Diazoxide (Hyperstat)
  - Immunosuppressive drugs
  - Beta-blockers (e.g., propranolol [Inderal])
  - Chlorpromazine (Thorazine)
  - Cimetidine (Tagamet)
  - Calcium channel blockers
  - Mannitol
  - Sympathomimetic drugs (e.g., epinephrine)

HHS: Clinical Presentation

- Tachycardia, orthostatic hypotension, decreased CVP, RAP, PAOP
- Tachypnea
- Polyuria, polydipsia
- Nausea, vomiting (no abdominal pain)
- Weakness, fatigue
- May have fever
- Clinical indications of dehydration: weight loss; flushed, warm, dry skin; poor skin turgor; hyperthermia
- Glucose 600-2000 mg/dl; average 1100 mg/dl
- Sodium: normal or elevated
- Potassium: decreased
- Phosphorus: decreased
- Magnesium: decreased
- BUN and creatinine: elevated with BUN:creatinine ratio >10:1
HHS: Clinical Presentation

• Serum osmolality elevated; >330; may be as high as 450 mOsm/liter

Serum osmolality

• \((2 \times \text{Na}) + \text{BUN} + \text{glucose}\)
  
  \[
  \begin{array}{ccc}
    2.6 & 18 \\
  \end{array}
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• Normal: 280-295 mOsm/liter

HHS: Diagnostics

• Arterial blood gases
  – Normal pH or only mildly acidotic
    • Acidosis if present is lactic acidosis related to hypoperfusion instead of ketoacidosis

• Hematocrit: elevated

• WBC: elevated

HHS: Diagnostics

• Urine
  – Glucose: positive
  – Ketones: negative

• Electrocardiogram
  – May show changes associated with potassium levels
  – May show sinus tachycardia

HHS Collaborative Management

Correct fluid volume deficit: as for DKA except:

• Normal (0.9%) saline for first liter if serum sodium normal or if serum osmolality is <320 mOsm/liter; half-normal (0.45%) saline if hypernatremic or serum osmolality is >320 mOsm/liter; half-normal (0.45%) saline is usually used after the first liter

  – Rate at 200 ml-1 liter/hour for first hour; then 300-500 ml/hour depending on cardiovascular status and volume deficit
Correct fluid volume deficit: as for DKA except:
• Colloids such as albumin or plasma protein fraction may be needed
• Total volume deficit usually 8-15 liters

Normalize serum glucose level gradually: as for DKA
• NOTE: Even though HHS causes higher serum glucose levels, smaller amounts of insulin are needed to normalize serum glucose
• IV insulin therapy may be discontinued when the serum glucose is 200-250 mg/dl

Correct electrolyte imbalance (as for DKA)
• treat hypokalemia (will not have potassium shift since not acidotic)

Identify and treat cause
• Most commonly infection; antibiotics as indicated

Monitor for complications (as for DKA)

<table>
<thead>
<tr>
<th>Indicator</th>
<th>DKA</th>
<th>HHS</th>
<th>Both</th>
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<tbody>
<tr>
<td>Serum glucose greater than 300 mg/dL</td>
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<tr>
<td>Kussmaul's respirations</td>
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<td>pH less than 7.3</td>
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<td>Positive serum and urine ketones</td>
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<td>Abdominal pain</td>
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<td>Dehydration</td>
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<td>Lethargy → coma</td>
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<tr>
<td>Serum glucose greater than 600 mg/dL</td>
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Hypoglycemia

decrease in the amount of glucose in the blood; serum glucose level of 70 mg/dl or less

Hypoglycemia: Etiology

- Insufficient nutrient intake
  - Missed or delayed meal
  - Nausea, vomiting
  - Interrupted tube feedings or parenteral nutrition
- Excessive insulin dose
  - Poor visual acuity causing dose inaccuracy
  - Change to human insulin
  - Injection in area of improved absorption
- Insufficient nutrient intake
  - Missed or delayed meal
  - Nausea, vomiting
  - Interrupted tube feedings or parenteral nutrition

Hypoglycemia: Etiology

- Sulfonylurea therapy
  - Renal insufficiency potentiates effects
  - Hepatic insufficiency delays metabolism and excretion and impairs gluconeogenesis and glycogenolysis
  - Potentiated by salicylates, sulfonamides, phenylbutazone, alpha-glucosidase inhibitors (e.g., acarbose [Precose], miglitol [Glyset])

Hypoglycemia: Etiology

- Drugs
  - Ethanol
  - Quinidine
  - Disopyramide
  - Alpha-blockers
  - Salicylates
  - Haloperidol
  - Trimethoprim-sulfamethoxazole

Hypoglycemia: Etiology

- Inadequate production of glucose
  - Strenuous physical exercise or stress with inadequate adjustment of food intake and/or insulin dosage
  - Excessive alcohol intake ingested without adequate food intake
  - Glucagon deficiency

Hypoglycemia: Etiology

- Post-gastrectomy
- Pancreatic islet cell tumor (insulinoma)
- Adrenal insufficiency
- Severe liver disease
- Pregnancy
- Tumors
  - Beta cell tumors (i.e., insulinoma)
  - Nonbeta cell tumors
    - Malignant: sarcoma, mesothelioma, hepatomas, lymphoma, leukemia, adrenal carcinoma
    - Benign: carcinoid and carcinoidlike tumors, pheochromocytoma
Sliding Scale Insulin

“SSI therapy has been in existence since 1934. Despite an abundance of evidence demonstrating no significant benefit and increased episodes of hypoglycemia, SSI remains a mainstay of glycemic control in many hospitals. A Medline search of 52 trials from 1966 to 2003 found that no clinical trials showed benefit from SSI. A prospective cohort study determined that SSI did not control hyperglycemia and resulted in more frequent episodes of hypoglycemia. SSI does not consider weight, nutritional status, insulin sensitivity, or need for basal insulin. Insulin stacking may occur with SSI being given every 6 hours. A result of insulin stacking is a high risk of hypoglycemia, and the risk increases with high doses of SSI.”


Clinical presentation

Beta-blockers

Nocturnal hypoglycemia

- Restless sleep
- Nightmares
- Early morning headache
Hypoglycemia
Collaborative Management

Assess high-risk patient; monitor:
- Serum glucose by laboratory or bedside glucose monitoring device
- Neurologic assessment

Anticipate times when the patient is most likely to exhibit hypoglycemia
- Be aware of peak times for administered insulin therapy
- Be aware of missed or late meals or snacks which predispose the patient to hypoglycemia
- Be aware of excessive exertion which may predispose the patient to hypoglycemia

Restore normal serum glucose level
- Stat serum glucose level
- Administer 10-15 grams of carbohydrates for conscious patients

10-15 grams of CHO
- 4 ounces of apple or orange juice
- 4 ounces of cola or other carbonated beverage
- 8 ounces of skim or 2% milk
- 4 cubes or 2 packets sugar
- 3 glucose tablets
- 2 ounces of corn syrup, honey, or grape jelly
- 5 life savers or jelly beans
- 10 gumdrops
- 1/2 cup regular gelatin dessert
- 2 squares graham crackers
- 2 ounces cake decorating icing

Restore normal serum glucose level
- Parenteral glucose IV for patients unable to swallow
  - Usually 50 ml of 50% dextrose given over 3-5 minutes but may also be calculated as (100 – serum glucose) x 0.3 = Number of ml of D_{50}W
  - Thiamine 100 mg IV is recommended prior to dextrose administration especially in alcoholics to prevent Wernicke's encephalopathy
  - Infusion of 5% dextrose
**Restore normal serum glucose level**

- Glucagon 0.5 - 1 mg IM may be given to unconscious patients if unable to gain IV access
- Repeat serum glucose 15-30 minutes after treatment and q15 minutes until serum glucose is ≥ 80 mg/dL x 2 consecutively
- Give longer acting carbohydrate source (milk, cheese, crackers) or regularly scheduled meal to avoid recurrence

**Prevent injury**

Seizure precautions

**Identify and treat cause of hypoglycemia**

**Monitor for complications**

- Myocardial ischemia or infarction
- Seizures
- Coma
- Irreversible neurologic damage

**Somogyi**

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**References**

References


Which laboratory values would differentiate diabetic ketoacidosis (DKA) from a hyperosmolar hyperglycemic state (HHS)?

- a. Serum glucose of 600 mg/dL
- b. Serum potassium of 4 mEq/L
- c. Positive serum ketones
- d. Serum osmolality of 320 mOsm/L

A 55-year-old man has been prescribed acarbose (Precose) to control his type 2 diabetes mellitus. When you teach him about the drug, which of the following would you tell him to use for hypoglycemia?

- a. Orange juice
- b. Fresh fruit
- c. Cheese and crackers
- d. Glucose tablets