DKA, HHS, AND HYPOGLYCEMIA

Diabetes Strategies for the 21st Century
February 8, 2017
Katherine Lewis, MD, MSCR

DISCLOSURES

I have no conflicts of interest or other disclosures relevant to this presentation.
LEARNING OBJECTIVES

1. To describe the clinical findings, management, and complications of diabetic ketoacidosis (DKA)
2. To describe the clinical findings, management, and complications of hyperosmolar hyperglycemic state (HHS)
3. To recognize the similarities and differences between DKA and HHS
4. To define hypoglycemia and describe degrees of severity
5. To understand treatment and prevention of hypoglycemia in diabetes

CASE 1

- A 42 year old woman was transferred from another hospital with altered mental status and hyperglycemia.
- She had experienced a one-week history of flu-like symptoms associated with nausea and hematemesis.
- Her blood sugars on arrival was 1263 mg/dL.

Hyperglycemic Crisis: DKA vs. HHS

Leung, et al, 2014
CASE 1

Chemistry

160 122 60 723
3.9 14 2.4

- WBC's 19,000; + urine ketones
- ABG: pH 7.29, PCO2 36, PO2 76, HCO3 17
- Lipase 9,992 U/L, amylase 980 U/L, CK 1,039 U/L

Hyperglycemic Crisis: DKA vs. HHS

Leung, et al, 2014

DIABETIC KETOACIDOSIS (DKA)

- Uncontrolled hyperglycemia
- Metabolic acidosis
- Increased ketones

<table>
<thead>
<tr>
<th>Anion-gap acidosi</th>
<th>Mild DKA</th>
<th>Moderate DKA</th>
<th>Severe DKA</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH 7.25-7.30</td>
<td>pH 7.00-&lt;7.24</td>
<td>pH &lt;7.00</td>
<td></td>
</tr>
<tr>
<td>Bicarb &lt;15-18</td>
<td>Bicarb 10 to &lt;15</td>
<td>Bicarb &lt;10</td>
<td></td>
</tr>
<tr>
<td>Anion gap &gt;10</td>
<td>Anion gap &gt;12</td>
<td>Anion gap &gt;12</td>
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<table>
<thead>
<tr>
<th>Hyperglycemia</th>
<th>&gt;250</th>
<th>&gt;250</th>
<th>&gt;250</th>
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<table>
<thead>
<tr>
<th>Ketonemia/ketonuria</th>
<th>Present</th>
<th>Present</th>
<th>Present</th>
</tr>
</thead>
</table>

| Mental Status       | Alert     | Alert/drowsy | Stupor/coma |

Kitabchi, 2009
DIABETIC KETOACIDOSIS (DKA)

- 140,000 admissions for DKA in 2009 in the US
- 7.1 out of every 1000 diabetic patients were admitted with DKA in 2009 (22/1000 age-adjusted rate)


HYPEROSMOLAR HYPERGLYCEMIC STATE (HHS)

Previously known as:
- Hyperglycemic hyperosmolar nonketotic coma (HONK) or
- Hyperglycemic hyperosmolar nonketotic state (HNNK)

- Endogenous insulin is enough to prevent lipolysis and ketogenesis but inadequate to facilitate glucose utilization
- Dehydration >>> than in DKA
  - Total body water deficit usually 7-12 liters

Maletkovic, 2013; Gouveia, 2013; Pasquel 2014
PATHOGENESIS OF DKA AND HHS

- **Stress**
- **Infection**
- **Insufficient Insulin**
  - Absolute insulin deficiency
  - Relative insulin deficiency

Glucagon
Cortisol
Catecholamines
Growth hormone

Lipolysis
FFA's

Adipose tissue

Hyperketonemia

Ketone body production

Liver

Glycogenolysis

Gluconeogenesis

Glucosuria

Dehydration

Hyperosmolarity

Impaired renal function

HHS

PATHOGENESIS OF DKA

- **Stress**
- **Infection**
- **Insufficient Insulin**
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Glucagon
Cortisol
Catecholamines
Growth hormone

Lipolysis
FFA's

Adipose tissue

Hyperketonemia

Ketone body production

Liver

Glycogenolysis

Gluconeogenesis

Glucosuria

Dehydration

Hyperosmolarity

Impaired renal function

HHS

PATHOGENESIS OF HHS

Stress
Infection
(Insufficient Insulin)

Relative insulin deficiency

Proteolysis

Minimal ketones

Reduced glucose utilization

Hyperglycemia

Glucosuria

Dehydration

Hyperosmolarity

Impaired renal function

Liver

Glycogenolysis

Gluconeogenesis

Peripheral tissues

Glycogenolysis

Ketone body production

Gluconeogenesis

Hyperketonemia

DKA

HHS

Absolute insulin deficiency

Lipolysis

Adipose tissue

FFA’s

Glucagon

Cortisol

Catecholamines

Growth hormone

Adipose tissue

Glucosuria

Dehydration

Hyperosmolarity

Impaired renal function

HHS

PATHOGENESIS OF DKA AND HHS

DKA AND HHS

- Polyuria and polydipsia
- Nausea and vomiting
- Anorexia
- Fatigue/malaise

Maletkovic, 2013

DKA AND HHS

- Precipitating factors
  - Infection
  - Extreme physical stress
  - Missed or inadequate insulin therapy
  - Medications
    - Corticosteroids
    - Pentamidine
    - Terbutaline
    - Anti-psychotics
    - Cocaine
    - Religious fasting
    - Cannibas
    - DKA: SGLT2-inhibitors

Maletkovic, 2013; Galka, 2016; Goldenberg, 2016
**DKA VS. HHS**

<table>
<thead>
<tr>
<th>Timing</th>
<th>DKA</th>
<th>HHS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Develops over hours to days</td>
<td>Develops over days to weeks</td>
<td></td>
</tr>
<tr>
<td>Hyperventilation</td>
<td>+ (Kussmaul breathing)</td>
<td>-</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Mental status change</td>
<td>+/-</td>
<td>+</td>
</tr>
<tr>
<td>Dehydration</td>
<td>+</td>
<td>++</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Type 1 DM &gt;&gt; Type 2 DM</th>
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</thead>
</table>

**DKA**
- Anion-gap acidosis
- Hyperglycemia
- Ketosis
- Ketonuria
- Hyperkalemia

**HHS**
- Hyperglycemia
- High Osmolality
- Dehydration
- Altered Mental Status

Maletkovic, 2013

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**DKA VS. HHS**

<table>
<thead>
<tr>
<th>Anion-gap acidosis</th>
<th>pH &lt; 7.3</th>
<th>Bicarbonate &lt; 15</th>
<th>Anion gap &gt; 10</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Osmolality</td>
<td>&lt; 320</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>&gt; 250</td>
<td></td>
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</tr>
<tr>
<td>Ketonemia/ketonuria</td>
<td>Present</td>
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**DKA**
- Mortality 2% (5% in elderly)

**HHS**
- Mortality 20%

Kitabchi, 2009; Maletkovic, 2013
EVALUATION OF PATIENT WITH HYPERGLYCEMIC CRISIS

**Stabilize Patient**
- Secure airway, ensure adequate ventilation and oxygenation, obtain IV access, cardiac monitor, urinary catheter

**Physical Exam**
- Physical exam: mental status, respirations, fruity breath, signs of infection, signs of dehydration

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**Laboratory Evaluation**
- Glucose, metabolic panel, phosphate, magnesium, ABG
- CBC, serum ketones, urinalysis, cardiac enzymes, A1C, coagulation profile, urine pregnancy test
- Consider also urine and blood cultures, lumbar puncture, amylase and lipase depending on clinical presentation

**Other Studies and Imaging**
- EKG
- Chest radiograph,
- Additional imaging of chest, abdomen, brain

Maletkovic, 2013
INTERPRETATION OF LABS

• Calculating Anion Gap:
  - (Serum sodium) - (Chloride + bicarbonate)

• Sodium: osmotic forces drive water into vascular spaces
  - Corrected sodium: Add 1.6 mEq/L for every 100 points glucose is elevated
  - Some laboratories will reflect additional decreases in sodium measurement due to pseudohyponatremia from elevated lipids

• Serum Osmolality
  - \(2 \times \text{serum sodium} + \left(\frac{\text{glucose in mg/dL}}{18}\right) + \left(\frac{\text{BUN in mg/dL}}{2.8}\right)\)

Maletkovic, 2013

CASE 1

• Chemistry

<p>| | | | |</p>
<table>
<thead>
<tr>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>160</td>
<td>122</td>
<td>60</td>
<td>723</td>
</tr>
<tr>
<td>3.9</td>
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- Lipase 9,992 U/L, amylase 980 U/L, CK 1,039 U/L

Hyperglycemic Crisis: DKA vs. HHS
**INTERPRETATION OF LABS**

- **Calculating Anion Gap:**
  - (Serum sodium) - (Chloride + bicarbonate)

  **Case 1**
  
  \[160 - (122 + 14) = 160 - 136 = 24\]

Maletkovic, 2013

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**INTERPRETATION OF LABS**

- **Sodium:** osmotic forces drive water into vascular spaces
  - Corrected sodium: Add 1.6 mEq/L for every 100 points glucose is elevated

  **Case 1**
  
  Sodium 160 but glucose 723…
  
  \[
  \text{Step 1: } 723 - 100 = 623 \\
  \text{Step 2: } 623 \div 100 = 6.23 \\
  \text{Step 3: } 6.23 \times 1.6 = 10 \\
  \text{Step 4: } 160 + 10 = 170
  \]

Maletkovic, 2013
**INTERPRETATION OF LABS**

- **Serum Osmolality**
  - \((2 \times \text{serum sodium}) + \left(\frac{\text{glucose in mg/dL}}{18}\right) + \left(\frac{\text{BUN in mg/dL}}{2.8}\right)\)

  **Case 1**
  \((2 \times 160) + \left(\frac{723}{18}\right) + \left(\frac{60}{2.8}\right) = 320 + 40 + 21.4 = 381.4\)

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**CASE 1: DKA VERSUS HHS**

<table>
<thead>
<tr>
<th>DKA</th>
<th>HHS</th>
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<tbody>
<tr>
<td><strong>Anion-gap acidosis</strong></td>
<td>pH &lt; 7.3</td>
</tr>
<tr>
<td>Bicarbonate &lt; 15</td>
<td>pH &gt; 7.3</td>
</tr>
<tr>
<td>Anion gap &gt; 10</td>
<td>Bicarbonate &gt; 18</td>
</tr>
<tr>
<td>Osmolality</td>
<td>Anion-gap variable</td>
</tr>
<tr>
<td>&lt; 320</td>
<td>&gt; 320</td>
</tr>
<tr>
<td>&gt; 250</td>
<td>&gt; 600</td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>Rare</td>
</tr>
<tr>
<td>Ketonemia/ketonuria</td>
<td>Present</td>
</tr>
<tr>
<td>Mortality 2%</td>
<td>Mortality 20%</td>
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</table>

(Klabunde, 2009; Maletkovic, 2013)
TREATMENT OF DKA AND HHS

- Fluid replacement
  - Start normal saline at 10-20 ml/kg
  - Once euvoemia is achieved, may change to 1/2 NS for those with normal sodium or hyponatremia
    - In HHS, some experts recommend continuing isotonic saline unless osmolality is not falling despite adequate fluid resuscitation
  - Dextrose should be added at glucose of <250 mg/dL in DKA or <300 mg/dL in HHS

Maletkovic, 2013, Glaser 2005
Protocol for management of adult patients with DKA or HHS. DKA diagnostic criteria: IV Fluids

TREATMENT OF DKA AND HHS

- **Potassium**
  - Total body depletion of potassium due to urinary and gastrointestinal losses
    - Glucosuria may result in 70mEq/L loss of potassium
    - Shift of potassium out of cells from insulin deficiency, acidosis, and proteolysis will reverse with fluids and insulin
    - Start potassium supplementation at potassium of <5.3mEq/L.
**Protocol for management of adult patients with DKA or HHS: Potassium**

**TREATMENT OF DKA AND HHS**

- **Insulin**
  - Start after initial fluid resuscitation; delay if potassium is <3.3 mEq/L
  - Initial insulin bolus does not offer significant benefit
  - Regular insulin via IV is preferred therapy (0.1 unit/kg/hr in DKA)
  - Delay or reduce insulin rate in HHS in favor of hydration to avoid rapid osmotic shifts
  - Intramuscular injection of rapid-acting analogues has been studied as well
  - Insulin should continue until resolution of anion gap in DKA, not resolution of hyperglycemia

Maletkovic, 2013; Glaser 2005
TREATMENT OF DKA AND HHS

**Bicarbonate**
- Administration is controversial and limited to severe acidosis
- Risks of hypokalemia, hypematremia, paradoxical CNS acidosis
- Children with DKA treated with bicarbonate were more likely to have cerebral edema

**Phosphate**
- Not clearly beneficial in all patients
- Risk of hypocalcemia

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Maletkovic, 2013; Glaser, 2005; Glaser, 2001
COMPLICATIONS OF DKA AND HHS

- Hypoglycemia
- Hypokalemia
- Thrombosis
- Cardiac arrhythmias
- Cerebral edema
- Pulmonary edema
- Renal failure
- Hypotension
- Intestinal necrosis
- Cerebral hemorrhage
- Pancreatitis

Maletkovic, 2013; Glasser 2009
COMPLICATIONS OF DKA AND/OR HHS

**DKA**
- Cerebral edema in children with DKA (0.3-1%) with mortality of 21-24% in those who develop cerebral edema and permanent neurologic morbidity in 21-26%
  - Prompt administration of mannitol (0.25-1g/kg) may be beneficial
  - Hypertonic saline (3%) has grown in favor but increased mortality over mannitol seen in retrospective analysis

**HHS**
- Malignant hyperthermia-like syndrome
- Hyperpyrexia and rhabdomyolysis


**CASE 1**
- CT scan confirmed pancreatitis
- Initial management performed with aggressive fluid resuscitation
- Blood pressure dropped to 91/54
- She was transferred to the ICU, intubated, and started on pressors
- Blood cultures grew staphylococcus
- She eventually recovered
  - Further history revealed a history of type 2 diabetes, treated with insulin and metformin
    - She had taken neither insulin nor metformin for several weeks prior to her admission

Leung, et al, 2014
PREVENTION OF DKA AND HHS

• Education regarding sick day management
  • Early contact with health care team
  • Education about importance of insulin during illness
  • Initiation of easily digestible liquid diet containing carbohydrates and salt when needed
  • Education of family members about sick day management
• Use of home ketone monitoring

Kitabchi, 2009; Lewis, 2013

PREVENTION OF DKA AND HHS

• Assess economic factors, social, and psychological factors
  • Lack of resources to afford insulin or regular diabetes care
  • Psychological reasons for missing insulin: depression, or other mood disorder:
    • 58% of patients with recurrent DKA at MUSC Children’s Hospital had psychological diagnosis (depression, ADHD, bipolar disorder)

Kitabchi, 2009; Lewis, 2013
LEARNING OBJECTIVES

1. To describe the clinical findings, management, and complications of diabetic ketoacidosis (DKA)
2. To describe the clinical findings, management, and complications of hyperosmolar hyperglycemic state (HHS)
3. To recognize the similarities and differences between DKA and HHS
4. To define hypoglycemia and describe degrees of severity
5. To understand treatment and prevention of hypoglycemia in diabetes

CASE 2

• A 12 year old girl with 4 year history of type 1 diabetes presents to the ER with altered mental status and hypoglycemia
  • Her parents found her unresponsive on the couch that evening
  • They gave her glucagon in route to the ER
  • Upon arrival to the ER, glucose was 29 and IV dextrose was given
  • However, patient remained confused, so endocrinology was contacted

How would you classify her hypoglycemia?
How would you treat her hypoglycemia?

McAuley, 2000
HYPOGLYCEMIA

- Occurs in 35-42% of Type 1 diabetes patients
- Higher rates of severe hyperglycemia if longer duration of diabetes
  - >15 years vs. >5 years: rates of 46% vs. 22%
- Cause of significant loss of productivity and hospital stays

HYPOGLYCEMIA SYMPTOMS

<table>
<thead>
<tr>
<th>Adrenergic Symptoms</th>
<th>Neuroglycopenic Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pallor</td>
<td>Confusion</td>
</tr>
<tr>
<td>Diaphoresis</td>
<td>Slurred Speech</td>
</tr>
<tr>
<td>Shakiness</td>
<td>Irrational behavior</td>
</tr>
<tr>
<td>Hunger</td>
<td>Disorientation</td>
</tr>
<tr>
<td>Anxiety</td>
<td>Loss of consciousness</td>
</tr>
<tr>
<td>Irritability</td>
<td>Seizures</td>
</tr>
<tr>
<td>Headache</td>
<td>Pupillary Stuggishness</td>
</tr>
<tr>
<td>Dizziness</td>
<td>Decreased response to noxious stimuli</td>
</tr>
</tbody>
</table>

Cryer, 2009
Kalra, 2013
HYPOGLYCEMIA

Plasma glucose of $\leq 70$ mg/dL ($\leq 3.9$ mmol/L)

<table>
<thead>
<tr>
<th>Classification</th>
<th>Features</th>
<th>Glucose value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe hypoglycemia</td>
<td>An event requiring assistance of another person</td>
<td>Neurological recovery after glucose returns to normal</td>
</tr>
<tr>
<td>Documented symptomatic hypoglycemia</td>
<td>Typical symptoms of hypoglycemia              $\leq 70$ mg/dL</td>
<td></td>
</tr>
<tr>
<td>Asymptomatic hypoglycemia</td>
<td>No typical symptoms                           $\leq 70$ mg/dL</td>
<td></td>
</tr>
<tr>
<td>Probably symptomatic hypoglycemia</td>
<td>Typical symptoms                             Presumed to be $\leq 70$ mg/dL</td>
<td></td>
</tr>
<tr>
<td>Pseudo-hypoglycemia</td>
<td>Typical hypoglycemic symptoms                 Glucose $&gt;70$ mg/dl but approaching that level</td>
<td></td>
</tr>
</tbody>
</table>

Seaquist, 2013

HYPOGLYCEMIA TREATMENT

- **Mild to Moderate Hypoglycemia**
  - 15-20 g of carbohydrate in the form of glucose tablets (3-4), carb-containing beverages, etc.

- **Severe Hypoglycemia**
  - Glucagon 1 mg SQ or IM
  - Nausea and vomiting, hyperglycemia
  - IV Glucose 25g followed by glucose infusion

- Sulfonylurea overdose may lead to prolonged hypoglycemia

Cryer, 2009
CASE 2

- Glucose was rechecked and back down to 31
- Patient was given additional IV dextrose and transferred to tertiary care center for further evaluation and management

What are the potential causes of her hypoglycemia?

McAuley, 2000

CAUSES OF HYPOGLYCEMIA

<table>
<thead>
<tr>
<th>Too Much Insulin</th>
<th>Not Enough Glucose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incorrect amount of insulin</td>
<td>Inadequate carbohydrate intake or absorption</td>
</tr>
<tr>
<td>Increased insulin sensitivity</td>
<td>Decreased endogenous glucose production</td>
</tr>
<tr>
<td>Decreased insulin clearance</td>
<td>Increased utilization of carbohydrates and / or depletion of hepatic glycogen stores</td>
</tr>
<tr>
<td>Delayed gastric emptying: mismatch of timing of insulin and carbohydrate absorption</td>
<td></td>
</tr>
</tbody>
</table>

Kalra, 2013
HYPOGLYCEMIA RISK FACTORS

- Duration of diabetes and age
- C-peptide negativity
- History of severe hypoglycemia
- Impaired awareness of hypoglycemia
- Strict glycemic control
- Sleep/general anesthesia or other sedation
- Reduced oral intake; Emesis/vomiting
- Critical illness
- Unexpected travel after rapid-acting insulin

Kalra, 2013

HYPOGLYCEMIA RISK FACTORS

- Sudden reduction in corticosteroid dose
- Reduced IV dextrose administration
- Interruption of enteral feedings or TPN
- Drug dispensing error
- Renal and hepatic dysfunction
- Endocrine deficiencies
  - Hypothyroidism
  - Hypopituitarism
  - Primary adrenal insufficiency
  - Growth hormone deficiency

Kalra, 2013
HYPOGLYCEMIA OUTCOMES

- Functional brain failure reversed by correction of glucose levels
- Prolonged hypoglycemia can cause brain death
- Glucose reperfusion in rat studies suggest that extreme hyperglycemia after hypoglycemia may contribute to neuronal death
- Long term cognitive effects seen in children (< 5, particularly vulnerable)
- Increased dementia, cerebral ataxia, cognitive problems in elderly


HYPOGLYCEMIA OUTCOMES

- Hypoglycemia may lead to sudden cardiac death from arrhythmia
- “Dead in bed” syndrome: death in young Type 1 patients likely due to prolonged QT and arrhythmia (Accounts for 5-6% of deaths in this demographic)
- Increase mortality in ACCORD (Action to Control Cardiovascular Risk in Diabetes) study in intensive group (goal a1C <6.5%) and 3 fold higher incidence of hypoglycemia

HYPOGLYCEMIA AND ALCOHOL

- Alcohol impairs endogenous glucose release
- Alcohol may also...
  - Blunt ability of patient to respond appropriately to early symptoms of hypoglycemia
  - Impair counter-regulatory response
  - May enhance cognitive deficits caused by hypoglycemia
- Hypoglycemic symptoms may be mistaken by others as intoxication
- May cause delayed hypoglycemia with increased risk lasting also long as 24 hour after ingestion

Choudhary, 2011; Richardson, 2005

HYPOGLYCEMIA AND ALCOHOL

- Advise to patients:
  - Don't include alcohol in their carb coverage/carb counting;
  - Eat with ingestion of alcohol
  - Be prepared to monitor frequently
  - Target blood sugar of 100-140 before bed

Choudhary, 2011; Richardson, 2005
HYPOGLYCEMIA UNAWARENESS

- Loss of adrenergic symptoms prior to onset of neuroglycopenic symptoms
- Hypoglycemia-associated autonomic failure (HAAF):
  - Defective counter-regulatory decrease in insulin and increase in glucagon and attenuated epinephrine release
  - May be reversed at least partially by avoidance of hypoglycemia, is maintained by recurrent hypoglycemia
  - 25-fold increased risk of severe hypoglycemia during intensive diabetes management

Sequist 2013; Moheet 2013

DRIVING SAFETY

- Patients with diabetes demonstrate a 12-19% increased risk of motor vehicle accident
- Main factor: hypoglycemia
  - Peripheral neuropathy and visual impairment should also be considered
- Prospective multi-center study:
  - 185 (41%) participants reported 503 episodes of moderate hypoglycemia
  - 23 (5%) participants reported 31 episodes of severe hypoglycemia while driving

Lorber, 2013; Cox 2013
**DRIVING SAFETY**

**Patient counseling:**
- Be prepared: meter, source of quick-acting sugar, snacks providing complex carbohydrate in the vehicle.
- Start out right: Blood sugar target before driving: 100 or greater.
- Stop vehicle with any symptoms of low blood sugar: Measure and treat.
- Wait: do not resume driving until cognition and blood sugar have recovered (20-30 minutes).
- Check again: recheck blood sugars periodically if driving for extended period of time.

*Loiber, 2013; Choudhary, 2011*

**HYPOGLYCEMIA PREVENTION**

- Monitoring and goal setting
  - Glucose self-monitoring, A1C goals, use of CGM
- Patient education
  - How to prevent and treat hypoglycemia
- Dietary intervention and counseling
  - Regular eating patterns, alcohol intake
- Exercise counseling
  - Monitoring, use of carbohydrate intake around exercise, reduced insulin dosing around exercise

*Seaquist, 2013; Cryer, 2009; Choudhary, 2011*
HYPOGLYCEMIA PREVENTION

- Medication adjustment
  - Evaluate regimen, consider agents without hypoglycemic potential if appropriate
- Evaluation for additional underlying causes
  - Kidney impairment or liver disease
  - Endocrine deficiencies
  - Celiac disease; malabsorption
  - Insulin binding antibodies

Seaquist, 2013; Cryer, 2009; Choudhary, 2011

CASE 2

- Insulin regimen? Recent A1C? Past hospitalizations?
- Past history of hypoglycemia?
- Last dose of insulin and most recent carbohydrate intake?
- Any recent illnesses, increased activity, or new symptoms?
- Any ingestions?
CASE 2

- Patient’s mother was a nurse who took meticulous records about her carbohydrate intake, blood sugar, and insulin doses
- Patient’s parents were responsible for her insulin dosing
  - Glargine 16 units daily and Aspart 1/15g for TDD of 30 units (0.6 units per kg/day)
- Over the last 6 months, she has frequent episodes of severe hypoglycemia requiring glucagon
  - Mother called in numbers to diabetic nurse practitioner who reduced insulin doses on multiple occasions due to the severe hypoglycemia
  - She also had an elevated A1C of 9% and admission for DKA during this time
- Patient denies any ingestions
  - She had been over to her grandmother’s house (next door) prior to this episode but family denies use of insulin at grandmother’s house

CASE 2:

- Patient has not had nausea, vomiting, diarrhea, weight loss, or anorexia. She has no lightheadedness and growth chart shows normal growth. She has no headaches or visual changes
- Her exam shows Tanner III breast development, no thyromegaly, no hyperpigmentation or hypopigmentation
- Patient’s glucoses stabilized and she was taken of IVFs
- Her blood sugars were running high on her home regimen, so the doses were increased
CASE 2:

- Patient was asked privately to demonstrate how much Glargine insulin her mom usually gave her by pointing out level on insulin syringe: this matched her home doses.
- An insulin and C-peptide were requested to be run on the blood sample drawn during hypoglycemia at the outside hospital:
  - Insulin 180 µUnits/ml
  - C-peptide <0.1 ng/ml

Based upon this new information, what is the cause of this patient’s hypoglycemia?

A. Insulinoma  
B. Sulfonylurea poisoning  
C. Adrenal insufficiency  
D. Insulin overdose
Based upon this new information, what is the cause of this patient's hypoglycemia?

A. Insulinoma
B. Sulfonylurea poisoning
C. Adrenal insufficiency
D. Insulin overdose

CASE 2

• Parents returned to the hospital with insulin and supplies they found at grandmother's house hidden under the bathroom sink
• Patient admitted to giving extra insulin in order to be able to have extra “treats” to treat lows
• She had also hidden an extra Aspart pen in her purse after telling her parents that she needed to restock the insulin at school
• Patient had prior history of lying about low blood sugars in order to get food
• She was discharged home in the care of her parents and did not have further severe hypoglycemia episodes
RELATED CASES

- Admission for severe hypoglycemia in patient in elderly gentleman on insulin pump
  - Patient's pump history records large night-time boluses that he did not recall
- Admission for severe hypoglycemia in patient with diet-controlled type 2 diabetes
  - Evaluation showed elevated insulin and C-peptide; + sulfonylurea screening
  - Patient mistakenly took sulfonylurea (had been prescribed in past) instead of pain medication post-operatively
  - No further episodes
- Admission for severe hypoglycemia in patient without diabetes
  - Elevated insulin and C-peptide; + sulfonylurea
  - Pharmacy had dispensed sulfonylurea instead of ditropan
  - No further episodes
- Recurrent severe hypoglycemia in adolescent on insulin pump for type 1 diabetes
  - Bolus history unrevealing
  - “Priming” history on pump scrutinized—priming with site connected as a way to manipulate insulin
- Unexplained fasting hypoglycemia of 40 on meter download in patient with type 1 diabetes being seen for the first time as an outpatient; all other morning values at target or above target
  - After counseling patient about effect of alcohol on blood sugars, he refers back to meter download and reports—“Yeah, I was drinking the night before that.”

CONCLUSIONS

- Acute diabetes complications associated with hyperglycemia include diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS)
- DKA and HHS have some unique characteristics and treatment approaches
- Patients may have a mixed picture of DKA and HHS
- Hypoglycemia is common in diabetes and can result in significant morbidity as well as mortality
- Prevention of acute diabetes complications requires adequate patient education, assessment of patient risk, an individualized treatment approach, and sometimes some very careful investigation
REFERENCES

- Centers for Disease Control and Prevention. National Hospital Discharge Survey. Available at: www.cdc.gov/nchs/nhds.htm