Acute complications

(DIABETIC KETOACIDOSIS AND HYPEROSMOLAR HYPERGLYCAEMIC STATE)

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Comprehensive education course for Asian diabetes educators

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Objectives

After completing this module the participant will be able to

• Discuss the definition and incidence of diabetic ketoacidosis (DKA) and hyperosmolar hyperglycaemic syndrome (HHS)

• Discuss the signs and symptoms and treatment of DKA and HHS

• Discuss the importance of and strategies for the management of illness for people with diabetes
What is diabetes ketoacidosis (DKA)?

High blood glucose, ketones, acidosis and Dehydration

- Absolute or relative insulin deficiency
- Increase in counter-regulatory hormones (glucagon, catecholamines, cortisol, GH)
- Breakdown of fat and muscle
- Biochemical triad
  - Hyperglycaemia usually > 13.8 mmol/L (250 mg/dL)
  - Ketoacids — present
  - Metabolic acidosis — pH less than 7.3
DKA - Incidence

- Variable depending on country and environment
- Most common at onset in type 1 diabetes
- Recurrent episodes
- Can occur in type 2 diabetes (during the catabolic stress of acute illness)
- The most common cause of death in children or adolescent with type 1 diabetes
Acute complications

DKA - Precipitating factors

• Infection - most common
• New diagnosis of type 1 or type 2
• Discontinuation of or inadequate insulin
• Pancreatitis
• Myocardial infarction, stroke
• Medications such as corticosteroids, thiazides, sympathomimetic agents, pentamidine, antipsychotics and immune checkpoint inhibitors

American Diabetes Association 2009
DKA - Development

- Insulin Deficiency
  - Up
  - Lipolysis
    - Glycerol
    - Free fatty acids
  - Ketogenesis
    - Ketonemia
    - Ketonuria

- Glucose uptake
  - Down
  - Hyperglycaemia
    - Glucosuria
    - Osmotic diuresis
    - Urinary water losses

- Electrlyte depletion
- Dehydration
- Acidosis

(Adapted from Davidson 2001)
Ketones

- Used as fuel when calories are restricted
- Physiological ketosis when fasting or with prolonged exercise
- Insulin deficiency → lipolysis and ketone production → acidosis
  - Beta-hydroxybutyrate
  - Acetoacetate
  - Acetone
Ketones

- Beta-hydroxybutyrate predominant — not detected by nitroprusside reaction (which detects acetoacetate and acetone in a semiquantitative manner)

- Ketoacidosis may be present without detectable urinary ketones

- Blood ketone testing may enable early identification of DKA
Acute complications

DKA - Early clinical symptoms and signs

- Polyuria
- Polydipsia
- Polyphagia
- Tiredness
- Muscle cramps
- Flushed facial appearance
DKA - Later clinical symptoms and signs

- Weight loss
- Nausea and vomiting
- Abdominal pain
- Dehydration
- Acid-smelling breath
- Hypotension
- Tachycardia
- Shock
- Altered consciousness
- Coma
DKA – Investigations

Immediate for diagnosis
• Capillary blood glucose
• Urinary glucose and ketones

Urgent for assessment and treatment
• Blood glucose
• Blood gases
• Electrolytes, urea, creatinine
• WBC

Consider
• Cardiac monitor
• Blood culture, urine culture
• Chest X-ray
## DKA - Laboratory findings

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<table>
<thead>
<tr>
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<tbody>
<tr>
<td><strong>Blood Glucose</strong></td>
<td>&gt;13.8 mmol/L (250mg/dL)</td>
</tr>
<tr>
<td><strong>Ketones</strong></td>
<td>Urine: moderate to large</td>
</tr>
<tr>
<td></td>
<td>Blood: &gt;3mmol/L</td>
</tr>
<tr>
<td><strong>Osmolality</strong></td>
<td>Increased – high blood glucose and urea/creatinine, dehydration</td>
</tr>
<tr>
<td><strong>Electrolytes</strong></td>
<td>Low/normal Na+ and Cl-</td>
</tr>
<tr>
<td></td>
<td>Low/normal/high K+ (often misleading)</td>
</tr>
<tr>
<td></td>
<td>Low HCO₃ (normal 23-31)</td>
</tr>
<tr>
<td><strong>Anion Gap</strong></td>
<td>≥10 mild</td>
</tr>
<tr>
<td></td>
<td>&gt;12 moderate to severe</td>
</tr>
<tr>
<td><strong>Blood Gases</strong></td>
<td>pH ≤7.3, HCO₃ ≤15 (mild)</td>
</tr>
<tr>
<td></td>
<td>pH &lt;7.0, HCO₃ &lt;10 (severe)</td>
</tr>
</tbody>
</table>
Acute complications

DKA - Management in adults (1 of 3)

IV fluids

- Severe shock — treat with 0.9 NaCl 1-2 L/h to correct hypotension/shock (then treat as ‘mild to moderate’ after shock is corrected)

- Mild to moderate — treat with 0.9 NaCl 500 mL/h x 4 h, then 250 mL/h x 4 hours

(Canadian Diabetes Association, 2013)
Serum [K⁺]

- If less than 3.3 mmol/L
  : give 40 mmol KCl (max 40 mmol/h) and no insulin until [K⁺] > 3.3 mmol/L

- If more than 3.3 mmol/L but less than 5.0-5.5 mmol/L
  : give 10-40 mmol/L KCl (max 40 mmol/h)

- Less aggressive KCl treatment with renal failure

(Canadian Diabetes Association, 2013)
Acute complications

DKA - Management in adults (3 of 3)

<table>
<thead>
<tr>
<th>IV Fluids</th>
<th>Serum [K⁺]</th>
<th>Acidosis</th>
</tr>
</thead>
</table>

**Acidosis**

- If [K⁺] < 3.3 mmol/L
  
  : correct hypokalaemia before starting Insulin

- If [K⁺] > 3.3 mmol/L
  
  : administer IV short acting insulin 0.1U/kg/h

- Adjust rate of infusion to avoid hypokalaemia and Hypoglycaemia

- If pH < 7.0
  
  : give NaHCO₃ 1 ampoule/h until pH > 7.0

(Canadian Diabetes Association, 2013)
DKA - Complications

• Hypoglycaemia +/- hypokalaemia

• Acidosis not improving — possibly caused by continuing dehydration or infection such as TB or HIV

• Aspiration pneumonia related to vomiting and impaired consciousness

• Headache +/- falling level of awareness — consider cerebral edema and urgent treatment with Mannitol

(Canadian Diabetes Association, 2013)
DKA - Recovery

• Rapid improvement
• Continue IV insulin while ketosis present
• Oral intake when possible
• Rapid-acting insulin before discontinuing IV insulin
• Return to usual insulin regimen
• Consider drinks and food containing potassium
Acute complications

DKA – Recovery criteria

• Normalized glucose (<200 mg/dL) +
  • Serum bicarbonate ≥ 15 mEq/L
  • pH > 7.3
  • Anion gap ≤12 mEq/L
What is hyperosmolar hyperglycaemic syndrome (HHS)?

- Primarily in older people with/without history of type 2 diabetes
- Develops over weeks
- Always associated with severe dehydration and hyperosmolar state
- Ketosis may or may not be present
- Coma not always present
# Diagnostic criteria for DKA and HHS

<table>
<thead>
<tr>
<th></th>
<th>DKA</th>
<th>HHS</th>
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<tbody>
<tr>
<td><strong>Arterial pH</strong></td>
<td>Moderate (plasma glucose &gt;250 mg/dl)</td>
<td>Severe (plasma glucose &gt;250 mg/dl)</td>
</tr>
<tr>
<td></td>
<td>7.00 to &lt;7.24</td>
<td>&lt;7.00</td>
</tr>
<tr>
<td><strong>Serum bicarbonate (mEq/l)</strong></td>
<td>10 to &lt;15</td>
<td>&gt;18</td>
</tr>
<tr>
<td>Urine ketone*</td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>Serum ketone*</td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td><strong>Effective serum osmolality†</strong></td>
<td>Variable</td>
<td>Variable</td>
</tr>
<tr>
<td>Anion gap‡</td>
<td>&gt;12</td>
<td>&gt;12</td>
</tr>
<tr>
<td>Mental status</td>
<td>Alert/drowsy</td>
<td>Stupor/coma</td>
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</table>

*Nitroprusside reaction method. †Effective serum osmolality: 2[measured Na⁺ (mEq/l)] + glucose (mg/dl)/18. ‡Anion gap: (Na⁺) – [(Cl⁻ + HCO₃⁻) (mEq/l)].
HHS Incidence and features

- 5-20% mortality rate
- Can occur in type 1 diabetes and younger people

American Diabetes Association 2009
HHS - Prevention

- Early treatment of infection
- Early recognition of signs and symptoms of diabetes
- Maintain adequate hydration
- Assess/Recognize declining mental status
- Monitor glycaemia post major medical event
HHS – Key features

- Marked hyperglycaemia
- Hyperosmolarity
- Absence of severe ketosis
- Altered mental awareness
Precipitating factors

- Infection — most common
- New diagnosis of type 2
- Discontinuation of or inadequate insulin
- Pancreatitis
- Myocardial infarction, stroke
- Medications such as corticosteroids, thiazides, sympathomimetic agents and pentamidine
HHS - Signs and symptoms

- Initially polyuria and polydipsia
- Altered mental status
- Profound dehydration
- Precipitating factors
## HHS- Biochemical findings

<table>
<thead>
<tr>
<th>Blood Glucose</th>
<th>&gt;33 mmol/L (600 mg/dl)</th>
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<tbody>
<tr>
<td>Ketones</td>
<td>Urine: negative – small Blood: &lt;0.6 mmol/L</td>
</tr>
<tr>
<td>Osmolality</td>
<td>&gt;320 mOsm/kg - (raised Na, BG, urea)</td>
</tr>
<tr>
<td>Electrolytes</td>
<td>Raised Na, BG, urea creatinine</td>
</tr>
<tr>
<td>Anion Gap</td>
<td>Variable</td>
</tr>
<tr>
<td>Blood Gases</td>
<td>pH ≥7.30 normal or raised HCO₃⁻</td>
</tr>
</tbody>
</table>
# HHS - Treatment

<table>
<thead>
<tr>
<th>Rehydration</th>
<th>Caution!</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal saline 1 litre per hour initially</td>
</tr>
<tr>
<td></td>
<td>Consider ½ strength normal saline</td>
</tr>
<tr>
<td><strong>Potassium</strong></td>
<td>Only if hypokalaemic and renal function adequate – give before insulin</td>
</tr>
<tr>
<td><strong>Insulin</strong></td>
<td>May be needed as slow infusion</td>
</tr>
<tr>
<td></td>
<td>0.1 unit/kg/hour to be increased with care if BG is slow to fall</td>
</tr>
<tr>
<td><strong>Monitoring</strong></td>
<td>BG, BP, neurological function hourly until stable</td>
</tr>
<tr>
<td></td>
<td>Electrolytes 2-hourly</td>
</tr>
<tr>
<td></td>
<td>Cardiac or CVP monitoring</td>
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</table>
# HHS - Complication

<table>
<thead>
<tr>
<th>Complication</th>
<th>Prevention</th>
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<tbody>
<tr>
<td>Hypoglycaemia</td>
<td>Prevent by adding glucose infusion when glucose &lt;14 mmol/L (250 mg/dL)</td>
</tr>
<tr>
<td>Hypokalaemia</td>
<td>Early potassium replacement and monitoring</td>
</tr>
<tr>
<td>Fluid Overload</td>
<td>Careful clinical monitoring and central line as needed</td>
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<tr>
<td>Vomiting/aspiration</td>
<td>NG tube, position patient on side</td>
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<tr>
<td>Cerebral Oedema</td>
<td>Avoid fast blood glucose falls (should be &lt;4 mmol/L (72 mg/dL) per hour; aggressive Mannitol treatment if any early signs of cerebral oedema</td>
</tr>
</tbody>
</table>

(Kitabchi, Guillermo, Umpierrez, Fisher, 2009)
Complete initial evaluation. Check capillary glucose and serum/urine ketones to confirm hyperglycemia and ketonemia/ketonuria. Obtain blood for metabolic profile. Start IV fluids: 1.0 L of 0.9% NaCl per hour. \(^1\)

**Acute complications**

**IV Fluids**
- Determine hydration status
  - Severe Hypovolemia
  - Mild dehydration
- Administer 0.9% NaCl (1.0 L/hr)
- Evaluate corrected serum Na\(^+\)
  - Serum Na\(^+\) high
  - Serum Na\(^+\) normal
  - Serum Na\(^+\) low
- 0.45% NaCl (250-500 ml/hr) depending on hydration state
- 0.9% NaCl (250-500 ml/hr) depending on hydration state

**Bicarbonate**
- pH \(\geq 6.9\)
- pH < 6.9
- No HCO\(_3\)\(^-\)
- Cardiogenic shock

**Insulin: Regular**
- IV Route (DKA and HHS)
  - 0.1 U/kg/B.Wt. as IV bolus
  - 0.1 U/kg/hr IV continuous insulin infusion
- IV Route (DKA and HHS)
  - 0.14 U/kg Sbw/hr as IV continuous insulin infusion
  - If serum glucose does not fall by at least 10% in first hour, give 0.14 U/kg as IV bolus, then continue previous Rx

**DKA**
- When serum glucose reaches 200 mg/dl (DKA) or 300 mg/dl (HHS), change to 5% dextrose with 0.45% NaCl at 150-250 ml/hr

**HHS**
- When serum glucose reaches 300 mg/dl, reduce regular insulin infusion to 0.02 - 0.05 U/kg/hr IV, or give rapid-acting insulin at 0.1 U/kg SC every 2 hrs. Keep serum glucose between 150 and 200 mg/dl until patient is mentally alert.

**Potassium**
- Establish adequate renal function (urine output - 50 ml/hr)
  - K\(^+\) < 3.3 mEq/L
    - Hold insulin and give 20 - 30 mEq/hr Until K\(^+\) > 3.3 mEq/L
  - K\(^+\) > 5.2 mEq/L
    - Do not give K\(^+\), but check serum K\(^+\) every 2 hrs.

Check electrolytes, BUN, venous pH, creatinine and glucose every 2 - 4 hrs until stable. After resolution of DKA or HHS and when patient is able to eat, initiate SC multidose insulin regimen. To transfer from IV to SC, continue IV insulin infusion for 1 - 2 hr after SC insulin begun to ensure adequate plasma insulin levels. In insulin naïve patients, start at 0.5 U/kg to 0.8 U/kg body weight per day and adjust insulin as needed. Look for precipitating cause(s).

(American Diabetes Association, 2009)
DKA and HHS- Prevention is key

Educating the person and family is key

- Check for ketones when blood glucose over 14mmol/L (252mg/dL)
- Stay hydrated
- Monitor blood glucose levels
- When to seek medical help identify and treat underlying cause

Can be prevented by

- Better public awareness
- Improved access to medical care
References


Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Hyperglycemic Emergencies in Adults. *Canadian Diabetes Association 2018*

Treatment guideline for diabetes. *Korean Diabetes Association 2015*