

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

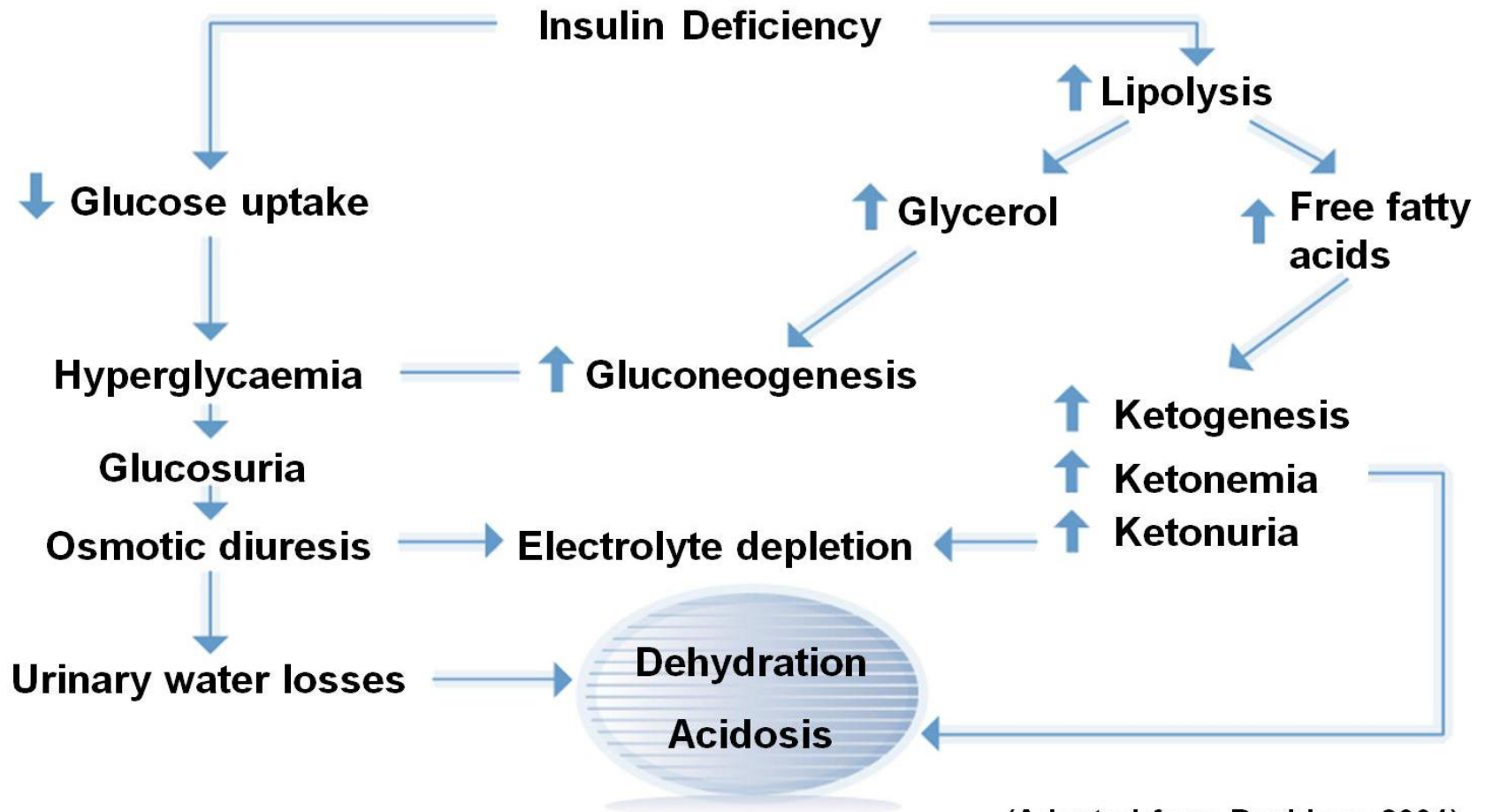
DKA - Incidence

- 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

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

DKA - Development



(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 semiquantative manner)
- Ketoacidosis may be present without detectable urinary ketones
- Blood ketone testing may enable early identification of DKA

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

Blood Glucose	>13.8 mmol/L (250mg/dL)
Ketones	Urine: moderate to large Blood: >3mmol/L
Osmolality	Increased – high blood glucose and urea/creatinine, dehydration
Electrolytes	Low/normal Na ⁺ and Cl ⁻ Low/normal/high K ⁺ (often misleading) Low HCO ₃ (normal 23-31)
Anion Gap	≥10 mild >12 moderate to severe
Blood Gases	pH ≤7.3, HCO ₃ ≤15 (mild) pH <7.0, HCO ₃ <10 (severe)

DKA - Management in adults (1 of 3)

IV fluids**Serum [K⁺]****Acidosis**

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)

DKA - Management in adults (2 of 3)

IV Fluids

Serum [K⁺]

Acidosis

Serum [K⁺]

- **If less than 3.3 mmol/L**
: give 40 mmol KCl (max 40mmol/h) and no insulin until [K⁺] > 3.3 mmol/L
- **If more than 3.3mmol/L but less than 5.0-5.5 mmol/L**
: give 10-40 mmol/L KCl (max 40mmol/h)
- Less aggressive KCl treatment with renal failure

DKA - Management in adults (3 of 3)

IV Fluids**Serum [K⁺]****Acidosis**

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

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

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

	DKA			HHS
	Mild (plasma glucose >250 mg/dl)	Moderate (plasma glucose >250 mg/dl)	Severe (plasma glucose >250 mg/dl)	Plasma glucose >600 mg/dl
Arterial pH	7.25–7.30	7.00 to <7.24	<7.00	>7.30
Serum bicarbonate (mEq/l)	15–18	10 to <15	<10	>18
Urine ketone*	Positive	Positive	Positive	Small
Serum ketone*	Positive	Positive	Positive	Small
Effective serum osmolality†	Variable	Variable	Variable	>320 mOsm/kg
Anion gap‡	>10	>12	>12	Variable
Mental status	Alert	Alert/drowsy	Stupor/coma	Stupor/coma

*Nitroprusside reaction method. †Effective serum osmolality: $2[\text{measured Na}^+ (\text{mEq/l})] + \text{glucose (mg/dl)}/18$. ‡Anion gap: $(\text{Na}^+) - [(\text{Cl}^- + \text{HCO}_3^- (\text{mEq/l})]$.

HHS Incidence and features

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

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

Blood Glucose	>33 mmol/L (600 mg/dl)
Ketones	Urine: negative – small Blood: <0.6 mmol/L
Osmolality	>320 mOsm/kg - (raised Na, BG, urea)
Electrolytes	Raised Na, BG, urea creatinine
Anion Gap	Variable
Blood Gases	pH \geq 7.30 normal or raised HCO ₃

HHS - Treatment

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

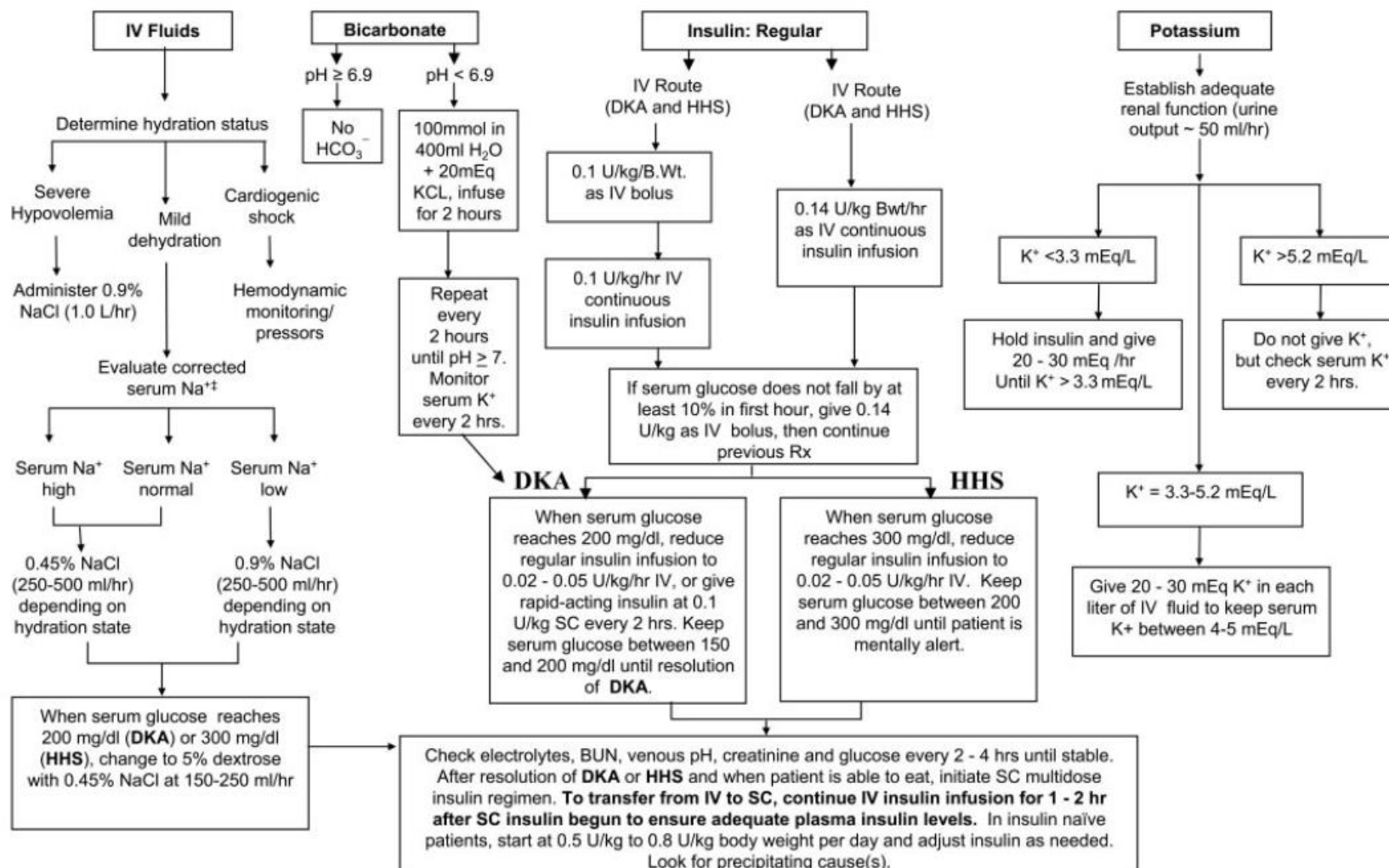
HHS - Complication

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

(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.[†]



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

Kitabchi AE, Guillermo E, Umpierrez GE, Fisher AI. Management of hyperglycemic crises in patients with diabetes. *Diabetes Care* 2009; 32: 1335-1343.

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

Treatment guideline for diabetes. *Korean Diabetes Association* 2015