

Diabetic ketoacidosis

Definition of diabetic ketoacidosis (DKA):

- A complication of diabetes mellitus (DM) caused by absolute or relative insulin deficiency
- It is diagnosed based on:
 - Hyperglycaemia >11 mM or known diabetes
 - Ketonaemia >3 mM or ketonuria >2+
 - Acidosis pH <7.3 and/or bicarbonate <15 mM
- Mostly occurs in patients with type 1 DM. However, it occurs in patients with type 2 DM, although they are much more likely to suffer with the related condition hyperglycaemic hyperosmolar state (HHS)

Epidemiology of DKA:

- Annual incidence of 1-5% amongst patients with type 1 DM
- More common in women than men

Aetiology of DKA:

- Lack of compliance with insulin therapy
- Acute illness (e.g. infection, MI, trauma)

Pathophysiology of DKA:

- Insulin deficiency renders cells unable to take up and metabolise glucose
- Glucose remains trapped in the blood from where it is filtered by the kidneys in concentrations that exceed renal reabsorption capacity
- Glycosuria causes a profound osmotic diuresis leading to severe dehydration
- Unable to rely on carbohydrate metabolism, cells switch to fat metabolism and oxidise fatty acids to release acetyl coenzyme A (CoA) in concentrations that saturate the Krebs's cycle
- Excess acetyl CoA is converted to the ketone bodies acetone, acetoacetate and beta-hydroxybutyrate, which are released into the blood causing a raised anion gap metabolic acidosis
- DKA mostly occurs in type 1 DM and is rare in type 2 DM because there is usually adequate levels of insulin to prevent ketogenesis

History in DKA:

- Polyuria
- Polydipsia
- Light-headedness
- Nausea and vomiting
- Abdominal pain
- Dyspnoea
- Drowsiness
- Loss of consciousness
- Lack of compliance with insulin therapy
- Symptoms of the precipitant

Examination in DKA:

- Airway
 - May be compromised by reduced conscious level

- Breathing
 - Kussmaul's breathing
 - Hyperventilation to compensate for metabolic acidosis manifesting as 'air hunger'
 - Acetone-smelling breath
- Circulation
 - Cold, pale peripheries
 - Prolonged capillary refill times (CRT >2 s)
 - Decreased skin turgor
 - Reduced jugular venous pressure (JVP)
 - Sunken eyes
 - Dry lips, mouth and tongue
 - Tachycardia
 - Postural hypotension
 - Absolute hypotension
 - Cardiac arrhythmias precipitated by electrolyte disturbances
- Disability
 - Confusion
 - Reduced conscious level
- Exposure
 - Signs of the precipitant

Differential diagnosis of DKA

- Hyperglycaemic hyperosmolar state (HHS)
- Any cause of an acute abdomen (including medical causes) if presenting with abdominal pain
- Other cause of raised anion gap metabolic acidosis
 - Alcohol
 - 'MUDPILES': Methanol, uraemia, [DKA], paraldehyde, isoniazid, lactate, ethylene glycol, salicylates
 - Carbon monoxide/cyanide

Investigation of DKA:

- Capillary blood glucose
- Capillary blood ketones
- Venous blood gas (VBG)
 - There is no need for an ABG unless you are concerned about gas exchange; a VBG provides the relevant other values accurately (i.e. pH, bicarbonate, K⁺, lactate).
- Bloods
 - Full blood count (FBC)
 - Urea & electrolytes (U&Es)
- Blood cultures
- Electrocardiogram (ECG)
- Urinalysis
- Chest radiograph (CXR)

Initial management of DKA:

- Assess the patient from an ABCDE perspective
- Maintain a patent airway: use manoeuvres, adjuncts, supraglottic or definitive airways as indicated and suction any sputum or secretions
- Deliver high flow oxygen 15L/min via reservoir mask and titrate to achieve oxygen saturations (S_pO_2) 94-98% or 88-92% if known to have COPD
- Attach monitoring
 - Pulse oximetry
 - Non-invasive blood pressure
 - Three-lead cardiac monitoring
- Request 12 lead ECG and portable CXR
- Obtain intravenous (IV) access and take bloods
- Fluid resuscitation
 - If systolic blood pressure (SBP) <90 mmHg, give 0.9% saline 500 ml IV stat and repeat as necessary until SBP >90 mmHg
 - If SBP >90 mmHg, give
 - 0.9% saline 1 L IV over 1 hour
 - 0.9% saline 1 L IV over 2 hours
 - 0.9% saline 1 L IV over 2 hours
 - 0.9% saline 1 L IV over 4 hours
 - 0.9% saline 1 L IV over 4 hours
 - 0.9% saline 1 L IV over 6 hours
- Fixed rate insulin IV infusion
 - Ask the nursing staff to draw up 50 units of actrapid in 50 ml of 0.9% saline (1 unit/ml) and run at 0.1 unit/kg/hour (i.e. 7 units/hour for a 70 kg individual)
 - Ketone levels should fall by 0.5 mM/hour; if this is not the case, increase the infusion rate by 0.1 unit/hour increments until this target rate is achieved
 - Rates adequate to switch off ketogenesis will usually render individuals hypoglycaemic so commence glucose 10% IV at 125 ml/hour once glucose <14 mM
 - Continue any long-acting insulin therapy at the usual dose and timing
- Potassium replacement
 - Although potassium levels may be high on arrival, they will fall rapidly once the fixed rate insulin IV infusion commences. The supplementation suggested below should be added to the resuscitation fluid.
 - Potassium >5.5 mM requires no supplementation
 - Potassium 3.5-5.5 mM requires supplementation of replacement fluid with potassium chloride (KCl) 40 mM
 - Potassium <3.5 mM requires supplementation of replacement fluid with KCl 60-80 mM and high dependency unit (HDU) care
- Anticoagulation
 - DKA is a hypercoagulable state so consider enoxaparin 1.5 mg/kg subcutaneously (SC)
- Monitoring
 - Blood glucose and ketones should be checked hourly
 - VBG should be repeated at 1 hour, and 2 hourly thereafter
 - Aim for a urine output of >0.5 ml/kg/hour; insert a urethral catheter if necessary

Further management of DKA:

- Identify and treat the underlying cause
- Identify and treat any complications
- Consider critical care referral for those with markers of severity
 - Clinical features
 - Hypoxia
 - Hypotension
 - Reduced conscious level
 - Age >65 years
 - Significant cardiac or renal co-morbidities
 - Biochemical features
 - pH <7.1
 - Bicarbonate <5 mM
 - Ketonaemia >6 mM
 - Serum osmolality >320 mOsm/L
 - Potassium < 3.5 mM on admission

Complications of DKA:

- Hyperkalaemia
- Hypokalaemia
- Hypoglycaemia from fixed rate insulin IV infusion without glucose supplementation
- Cerebral oedema
- Pulmonary oedema
- Death

Common questions concerning DKA:

- List the three criteria for diagnosing DKA
 - Hyperglycaemia >11 mM or known diabetes
 - Ketonaemia >3 mM or ketonuria >2+
 - Acidosis pH <7.3 and/or bicarbonate <15 mM
- Outline the mechanism of profound dehydration in DKA
 - Insulin deficiency renders cells unable to take up and metabolise glucose
 - Glucose remains trapped in the blood from where it is filtered by the kidneys in concentrations that exceed renal reabsorption capacity
 - Glycosuria causes a profound osmotic diuresis leading to severe dehydration
- Outline the mechanism of ketogenesis in DKA
 - Unable to rely on carbohydrate metabolism, cells switch to fat metabolism and oxidise fatty acids to release acetyl coenzyme A (CoA) in concentrations that saturate the Krebs cycle
 - Excess acetyl CoA is converted to the ketone bodies acetone, acetoacetate and beta-hydroxybutyrate, which are released into the blood causing a raised anion gap metabolic acidosis
- Explain the mechanism of Kussmaul's breathing in DKA
 - Hyperventilation creates a respiratory alkalosis to compensate for the metabolic acidosis
- List other causes of a raised anion gap metabolic acidosis
 - Carbon monoxide/cyanide
 - Alcohol
 - Toluene
 - Methanol
 - Uraemia

- Paraldehyde
- Isoniazid
- Lactate
- Ethylene glycol
- Salicylates
- List the three main components in the management of DKA
 - Fluid resuscitation
 - Fixed rate insulin IV infusion
 - Potassium replacement
- Outline the fluid resuscitation regime in DKA
 - 0.9% saline 1 L IV over 1 hour
 - 0.9% saline 1 L IV over 2 hours
 - 0.9% saline 1 L IV over 2 hours
 - 0.9% saline 1 L IV over 4 hours
 - 0.9% saline 1 L IV over 4 hours
 - 0.9% saline 1 L IV over 6 hours
- At what rate would you commence the fixed rate insulin IV infusion
 - 1 unit/kg/hour
- What action would you take once blood glucose became <14 mM
 - Commence glucose 10% IV at 125 ml/hour
- At what level would you add potassium supplementation to fluid resuscitation?
 - Potassium <5.5 mM