Diabetic Ketoacidosis

Definition / Supporting Information

Diabetic ketoacidosis (DKA) is the metabolic consequence of insulin deficiency, resulting in hyperglycaemia and acidosis.

- It is a medical emergency where early recognition and appropriate intervention are imperative

Essential History

Evaluation should progress only after the ABCs (airway, breathing, and circulation) of resuscitation have been addressed.

Ask about:

- Type 1 diabetes (T1D), particularly:
  - Poor glycaemic control (higher haemoglobin A_{1c} level)
  - High reported daily insulin doses
  - Omission of insulin
  - Previous episodes of DKA
  - Previous intensive treatment unit (ITU) admissions with DKA
  - Coexisting psychiatric disorders
  - Lower socioeconomic status
  - Family difficulties or social care / child protection concerns
  - Adolescent age
    - Especially girls
- Type 2 diabetes (T2D)
  - Although less commonly associated with DKA than T1D, patients with T2D may have DKA
- Other factors:
  - Illness
  - Trauma
  - Alcohol
  - Medications such as corticosteroids and thiazide diuretics
  - Pancreatitis
- Family history
  - Positive in most patients with T2D
  - Negative in most patients with T1D
- ‘Red Flag’ symptoms and signs (see below) - diabetic ketoacidosis may be the first presentation of new onset type 1 diabetes

‘Red Flag’ Symptoms and Signs

Ask about:

- Polyuria (especially nocturia)
  - Increase in the number of wet nappies
- Polydipsia
- Enuresis in previously continent children
- Fatigue
  - May be evident even before significant dehydration and acidosis
- Weight loss
  - Can be difficult to quantify unless a recent accurate weight is available
- Polyphagia may be evident early but is typically replaced with a loss of appetite as ketosis and metabolic acidosis worsen
- Abdominal pain
- Vomiting

Look for:

- Evidence of circulatory compromise (shock)
  - Tachycardia
  - Prolonged capillary refill time
  - Hypotension
- Signs of dehydration
  - Reduced skin turgor (intracellular and extracellular fluid loss)
  - Sunken eyes
  - Weight loss
- Kussmaul breathing
  - Rapid, deep respirations associated with metabolic acidosis
- Signs of neurological dysfunction
  - Confusion or altered consciousness
  - Headache
  - Signs of raised intracranial pressure
    - Irregular respirations
    - Elevated blood pressure
    - Bradycardia
  - Consider cerebral oedema in all patients with DKA who exhibit signs or symptoms of neurological compromise

Differential Diagnosis / Conditions

Coexisting illness should be considered if:

- Lactic acidosis or haemodynamic instability is present
  - Sepsis or poor perfusion may coexist with DKA
- Ketoacidosis does not improve or worsens with insulin administration

Investigations

Evaluation should progress only after the ABCs of resuscitation have been addressed. All patients with suspected DKA should be urgently referred to a specialist practitioner.

To be undertaken by non-specialist practitioners (eg, General Practitioner (GP) Team):

- Check capillary glucose
- Perform urinalysis for:
  - Glucose
  - Ketones
  - Blood
  - Protein
  - Leukocytes
  - Nitrites
- Refer to a specialist practitioner for further management

To be undertaken by specialist practitioners (eg, Paediatric Emergency Department / Paediatric Team(s)):

Diagnostic approach

- In most cases of DKA, blood glucose concentrations are raised; however, a blood glucose concentration < 11 mmol/L does not rule out DKA
- DKA must include two biochemical requirements for diagnosis of DKA [BSPED Guidelines; NICE guideline 18, section 1.4]):
  - Ketonaemia
    - Blood ketones (beta-hydroxybutyrate) > 3 mmol/L
  - Metabolic acidosis with a venous pH < 7.3 or bicarbonate level < 18 mmol/L

Laboratory assessments

- Serum sodium
  - Accurate assessment of sodium concentration is important to monitor during DKA management
    - Switching between 0.9% and 0.45% NaCl is no longer recommended [BSPED Guidelines; NICE guideline 18, section 1.4])

  - Note that there may be apparent hyponatraemia (pseudohyponatraemia) in the presence of marked hyperglycaemia
- Serum potassium
  - Must be monitored closely and replaced appropriately
  - Cardiac monitoring should be started in patients with elevated potassium concentrations, to determine whether cardiac abnormalities are present
  - At initial evaluation, serum potassium levels are typically normal or elevated because of acidaemia despite there being total body potassium loss
    - When treatment begins, serum potassium levels fall and may lead to hypokalaemia
  - Profound hyperkalaemia or hypokalaemia may lead to cardiac arrhythmias
- Serum phosphorus
  - Patients with DKA may have profound hypophosphatemia
    - May become apparent only during therapy
- Other laboratory tests
  - Urinary glucose and ketones
  - Cultures
    - If clinically indicated (eg, fever - not a sign of DKA)
    - Blood
    - Urine
  - Creatinine values
    - Typically elevated, consistent with a pre-renal state
  - Blood ketones
    - Near-patient testing of 3-hydroxybutyrate recommended (levels > 3 mmol/L are consistent with DKA)
  - Antibody levels against islet cell antigens and insulin
    - Frequently elevated at time of diagnosis
    - Not useful in diagnosis or management of DKA

Imaging

- Central nervous system (CNS) imaging should be ordered promptly if symptoms of increased intracranial pressure are encountered at any time during the treatment of DKA

Treatment Approach

See Diabetes (type 1 and type 2) in children and young people: diagnosis and management [BSPED Guidelines; NICE guideline 18, section 1.4]

To be undertaken by non-specialist practitioners (eg, GP Team):

- Give 100% oxygen via facemask
- Identify and address any problems with ABC
- Urgently refer (arrange emergency transfer) any child with suspected DKA to specialist practitioners (eg, Paediatric Emergency Department / Paediatric Team(s)) for ongoing management
- Notify the receiving team if there are concerns about the possibility of increased intracranial pressure due to cerebral oedema (for example if there is altered / fluctuating level of consciousness or headache)

To be undertaken by specialist practitioners (eg, Paediatric Emergency Department / Paediatric Team(s)):

- Treatment approach depends on severity of DKA
  - Children and young people with a pH of > 7.1 have mild or moderate DKA
  - Children and young people with a pH of < 7.1 have SEVERE DKA
  - Mild DKA
    - Patients with established diabetes can be managed in the outpatient setting following specialist assessment if they can maintain oral intake
  - Moderate to severe DKA
    - Medical emergency requiring meticulous attention
- Principles of managing DKA
  - Obtain an accurate weight - ideally the child should be weighed. If this is not possible because of the clinical condition, a recent clinic weight can be used as a guideline or the weight can be estimated using the appropriate centile chart
  - Fluid and electrolyte replacement
  - Mandatory insulin administration
  - Correction of metabolic disturbances
  - Prevention of potential complications
  - Treatment of concomitant conditions

Fluid replacement

- Treat DKA with oral fluids and subcutaneous (SC) insulin **only** if the child or young person is alert, not nauseated or vomiting, and not clinically dehydrated
  - Ensure the child or young person is recovering by monitoring resolution of ketonaemia and acidosis

- Treat DKA with intravenous fluids and intravenous insulin if the child or young person is not alert, is nauseated or vomiting or is clinically dehydrated
  - Do not give oral fluids to a child or young person who is receiving intravenous fluids for DKA unless ketosis is resolving, they are alert, and they are not nauseated or vomiting.
- Initial fluid bolus
  - Do not give an intravenous fluid bolus to children and young people with mild or moderate DKA (indicated by a blood pH of 7.1 or above).
  - Do not routinely give an intravenous fluid bolus to a child or young person with severe DKA (indicated by a blood pH below 7.1)
  - Only if shocked (poor peripheral pulses, poor capillary filling with tachycardia, and / or hypotension) give 10 ml/kg 0.9% sodium chloride as a bolus
    - **DO NOT** give a second bolus without first discussing with the responsible senior paediatrician
      - Boluses given up to 20 ml/kg are no longer subtracted from the fluid calculation for subsequent fluid management
    - Very cautious additional fluid resuscitation may be required in some patients
  - Beware of possible cerebral oedema
- Ongoing fluid management
  - Aggressive fluid resuscitation is rarely required
    - When necessary, the aim is to restore circulating fluid volume
      - Rehydration should take place over 48 hours
      - Less aggressive rates of fluid replacement have been associated with more rapid correction of acidosis
      - Gradual rehydration may reduce the risk of cerebral oedema compared with more aggressive fluid administration
  - Fluid therapy (even before insulin) will reduce the blood glucose concentration
  - Calculating maintenance fluid required
    - For children and young people with DKA the following ‘reduced volume’ rules are used:
      - If they weigh < 10 kg give 2 ml/kg/hour
      - If they weigh 10–40 kg give 1 ml/kg/hour
      - If they weigh > 40 kg give a fixed 40 ml/hour
  - Calculating the degree of dehydration (fluid deficit)
    - Patients with mild to moderate DKA (pH 7.1 or above) are generally considered to be 5% dehydrated
    - Patients with severe DKA (pH below 7.1) are generally considered to be 10% dehydrated

        - Any fluid deficit should be replaced evenly over the first 48 hours.
    - The total fluid calculation for the subsequent 48 hours is the sum of the maintenance fluids and the fluid deficit
        - If more than 20 ml/kg of fluid boluses have already been given then subtract any additional bolus volumes from the total fluid calculation for the 48-hour period
            - If 30 ml/kg boluses were given then subtract 10 ml/kg from the total fluid calculation
    - Rate of fluid administration should rarely exceed 1.5–2 times that of maintenance fluids
        - Urinary losses are not added to the calculated fluid requirement
            - If a large diuresis continues for several hours after starting treatment discuss with the responsible senior paediatrician
    - Consider transition to oral intake after ketosis is resolving and the patient is not nauseous or vomiting
        - If oral fluids are given before the 48 hour rehydration period is completed, the IV infusion needs to be reduced to take in to account the oral intake.
- Content of IV fluid:
    - 0.9 % sodium chloride with potassium chloride at 40 mmol/L should be started immediately with rehydration fluid unless they have renal failure (e.g. anuria is suspected)
    - Change fluids to 0.9% sodium chloride with 5% dextrose and 40 mmol/L potassium chloride when blood glucose level falls below 14 mmol/L
        - Higher rates of dextrose infusion (e.g. 10% glucose containing fluids) may be required to prevent hypoglycaemia while ketoacidosis is resolving and should be implemented if glucose falls below 6 mmol/L

Electrolytes

- Sodium
    - Sodium depletion is addressed with isotonic solutions suggested for initial fluid management
    - Corrected sodium levels should rise as blood glucose levels fall during treatment
    - Corrected sodium can be calculated to account for hypoglycaemia by:
        - Corrected sodium [mmol/L] = measured sodium [mmol/L] + 0.4* (measured glucose [mmol/L] – 5.5)
    - Sodium concentrations should be monitored closely
        - Failure of the corrected sodium concentration to increase during treatment of DKA may be associated with higher risk of cerebral oedema and should be discussed with the responsible senior paediatrician

  - If the child is becoming hypernatraemic it is generally not an immediate problem, as it will be protective against cerebral oedema but the responsible senior paediatrician should be informed
- Potassium
  - Before insulin therapy, potassium concentrations may be elevated, normal, or low, depending on:
    - Severity of DKA
    - Duration of DKA
    - Gastrointestinal losses caused by vomiting
  - After initiation of insulin therapy, potassium concentrations invariably decline as acidosis resolves, and may become normal or low
  - Potassium should be replaced after:
    - Initial isotonic fluid bolus has been given, unless anuria suspected
  - Dosing:
    - Add 40 mmol/L potassium chloride to rehydration fluids
  - Potassium levels should be monitored closely and therapy adjusted according to individual patient needs
    - IV fluids containing more than 40 mmol/L potassium require a central venous line and monitoring on a paediatric intensive care unit
- Phosphorus
  - Phosphate concentrations may vary before initiation of insulin therapy and may be very low during the treatment of DKA
    - This is not clinically significant and no treatment is required
- Bicarbonate
  - Use of bicarbonate in patients with DKA is not routinely recommended because:
    - Ketoacidosis can be completely corrected by the administration of IV fluids and insulin
    - Bicarbonate will add sodium that may not be required
    - Bicarbonate therapy may cause paradoxical CNS acidosis
    - Bicarbonate therapy has been associated with an increased risk of cerebral oedema
  - Despite the above concerns, some patients may benefit from cautious alkali administration after seeking specialist advice:
    - Patients with cardiovascular dysfunction caused by severe acidosis and/or hyperkalaemia

Ongoing monitoring of glucose and electrolytes

- Frequent monitoring of the patient's response to therapy is imperative to assess whether change in treatment is required

- This should include:
  - Hourly measurement of blood glucose
  - Measurement of electrolytes, bicarbonate, ketones, and pH every 2–4 hours
- The frequency of monitoring can be reduced (from every 2 hours in severe DKA) to every 4 hours when improvement in ketoacidosis has been established

Insulin therapy

- Insulin infusion should be started 1 to 2 hours after starting fluid replacement therapy (ie, after the patient has received initial volume expansion)
  - Cerebral oedema is more likely to occur if insulin is started early
- IV soluable insulin is the preferred route of administration for regular insulin
- Dosing
  - Initial infusion rate:
    - 0.05–0.1 unit/kg per hour of IV regular insulin
    - A constant insulin infusion rate should be used
    - The rate of insulin infusion may need to be increased in some children if ketoacidosis does not improve or worsens
      - Do not give boluses of intravenous insulin
    - Metabolic acidosis often corrects many hours after euglycaemia has been restored
  - Blood glucose concentration:
    - Should not be used alone to determine when to discontinue or decrease rate of infusion
      - If a child or young person with DKA is using insulin pump therapy, disconnect the pump when starting intravenous insulin therapy
      - In discussion with a diabetes specialist, consider continuing subcutaneous basal insulin in a child or young person who was using a basal insulin before the onset of DKA
- SC insulin delivery
  - Consider converting to SC insulin when:
    - Blood ketone level is < 1.0 mmol/L (urinary ketones may still be present)
    - Serum bicarbonate level is > 18 mmol/L (or pH > 7.3)
    - The patient is alert, they can begin oral intake without nausea or vomiting
  -

  - IV insulin infusion should continue for 30 minutes after the first SC injection of a rapid-acting insulin analogue
    - For a child who is using insulin pump therapy, restart the pump at least 60 minutes before stopping intravenous insulin
    - Change the insulin cartridge and infusion set, as well as inserting the cannula into a new subcutaneous site
  - For a child with previous diagnosis of diabetes, home insulin regimen may serve as a guide in choosing:
    - Initial SC insulin doses
    - Type of programme to use (split-mixed versus multiple daily injection)
  - Child with newly diagnosed diabetes
    - 0.5–1.0 units/kg per day in divided doses
  - Adjust dose on the basis of:
    - Meal plan
    - Level of activity
    - Pubertal status (insulin requirement is increased during puberty)

Assessment and management of cerebral oedema associated with DKA

- Assessment
  - Immediately assess children and young people with DKA for suspected cerebral oedema if they have any of these early manifestations:
    - Headache
    - Agitation or irritability
    - Unexpected fall in heart rate
    - Increased blood pressure.
- Immediate treatment for cerebral oedema is required if the patient develops any of the following signs:
  - Deterioration in level of consciousness
  - Abnormalities of breathing pattern, for example respiratory pauses
  - Oculomotor palsies
  - Abnormal posturing
  - Pupillary inequality or dilatation
- Management of cerebral oedema
  - Reduce rate of fluid administration to ½ maintenance rates
  - Use what is most readily available of
    - IV mannitol (20% 0.5–1 g/kg over 10–15 minutes) may be given and repeated after 2 hours if clinically indicated or
    - IV hypertonic (2.7% or 3% 2.5–5 ml/kg over 10–15 minutes) sodium chloride

- After starting treatment for cerebral oedema with mannitol or hypertonic sodium chlori
- If intubation is required, hyperventilation should be avoided, as this has been associated with worse outcomes

When to Refer

Refer to a paediatric specialist:

- All patients with suspected DKA, for treatment and admission

Escalate care to a paediatric intensive care unit or high-dependency unit team if:

- Severe acidosis pH < 7.1 with marked hyperventilation
- Severe dehydration with shock
- Reduced consciousness with risk of aspiration from vomiting
- Very young (< 2 years)
- Staffing levels on the wards are insufficient to allow adequate monitoring

'Safety Netting' Advice

- Parents are less likely to recognise symptoms of hyperglycaemia and DKA in children aged < 2 years
  - This may delay the diagnosis of diabetes
  - More children in this age group have DKA at initial diagnosis compared with older children
  - After a child or young person with known diabetes has recovered from an episode of DKA, discuss with them and their family members or carers (if appropriate) the factors that may have led to the episode
- Most children with established diabetes develop DKA because of omission of insulin
  1. Think about the possibility of non-adherence to therapy in known diabetic patients
  - Omission of insulin may arise because of a failure to recognise the need for
  2. This common mistake can be prevented by providing adequate education to the patient and family
  3. Consider devising a joint care plan with written information on what to do in case of intercurrent illness

Patient / Carer Information

Please note: whilst these resources have been developed to a high standard they may not be specific to children.

- Diabetic ketoacidosis (Web page), the NHS website

Resources

National Clinical Guidance

Diabetes (type 1 and type 2) in children and young people: diagnosis and management (Web page), NICE clinical guideline NG18, National Institute for Health and Care Excellence.

Management of diabetes (PDF), SIGN clinical guideline 116, Scottish Intercollegiate Guidelines Network.

Suggested Resources

Please note: these resources include links to external websites. These resources may not have national accreditation and therefore PCO UK cannot guarantee the accuracy of the content.

Diabetes – type 1, Scenario: Management – children and young people (Web page), NICE clinical knowledge summary, National Institute for Health and Care Excellence

BSPED Recommended DKA Guidelines 2015 (update) (Guideline), British Society of Paediatric Endocrinology and Diabetes

ISPAD Clinical Practice Consensus Guidelines 2014 (Guideline), International Society for Paediatric and Adolescent Diabetes

Dunger DB, Sperling MA, Acerini CL, et al.; European Society for Paediatric Endocrinology/Lawson Wilkins Pediatric Endocrine Society. European Society for Paediatric Endocrinology/Lawson Wilkins Pediatric Endocrine Society consensus statement on diabetic ketoacidosis in children and adolescents. Pediatrics 2004;113:e133–e140 [PubMed]

Dehydration (Web page - log-in requires), Spotting the Sick Child

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