Diabetic Ketoacidosis (DKA)

Description

Life-threatening acute Cx of DM characterised by dehydration, hyperglycaemia, glycosuria, ketonaemia, ketonuria & acidosis. [Biochem: BSL>11, pH <7.3, HCO_3^-<15mmol/L, ketonuria/aemia].

Pathophysiology

- Inadequate insulin→progressive hyperglycaemia→'cellular starvation'→ ↑release of glucagon, catecholamines, cortisol and GH → glycogenolysis & gluconeogenesis, ↑BSL
- The stress response →proteolysis and lipolysis, forming free fatty acids, which are then converted to the ketoacids acetoacetate, beta-hydroxybutyrate and acetone.
- The high glucose levels cause a huge osmotic diuresis and gross dehydration which may reduce tissue perfusion and further derange metabolism by causing lactic acidosis

Epidemiology

1-5% T1DM (20% new). T2DM unusual (HONK more likely). Esp young adults or children. 2F:1M.

Precipitating conditions:

- Infection (19–56%) e.g. pneumonia, UTI
- Inadequate insulin/non-compliance (15–41%)
- Undiagnosed diabetes (10–22%)
- Other medical illness (10–12%) e.g. hypothyroidism, pancreatitis, inborn errors of metab
- Cardiovascular disease (3–6%) e.g. PE, stroke, MI
- Other physiological stress e.g. pregnancy, surgery
- Drugs e.g. corticosteroids, sympathomimetics, α- and β-blockers and diuretics
- Cause unknown (4–33%)

Presentation

History

- Insidious onset of ↑thirst (polydipsia), worsening polyuria, & weight loss. (Rarely ↑hunger)
- Nausea and vomiting are common ± non-specific abdominal pain
- Lassitude, weakness and fatiguability often occur
- Global cerebral symptoms such as confusion and disorientation may be present
- Note focal symptoms of infection, dyspnoea, chest pain, palpitations, abdominal pain, recent changes in medication, episodes of overdose/ingestion of poisons, and EtOH use
- If on insulin note regimen and compliance

Examination

- Check vitals (T,HR, BP, RR, SaO2, GCS)
- Signs of gross dehydration
- Ketotic foetor (pear drops or nail-polish remover)
- Respiratory compensation of acidosis can lead to tachypnoea or Kussmaul's respiration
- Assess mental status and orientation & neurology
- Examine the chest, abdomen, skin for signs of infective precipitant
- Check cardiovascular system for signs of cardiac failure, pericardial rub and murmurs

Differential Diagnosis

- Alcoholic ketoacidosis
- HONK
- Lactic acidosis
- Causes of metabolic acidosis, e.g. OD
- Acute pancreatitis
- Septicaemia without ketoacidosis
- Acute abdomen
- Ketoacidosis due to starvation

Investigations

Bloods: FBC, UEC, Glucose, ABG, anion gap, plasma osmolarity, Trop/CK, amylase, cultures. Note:

- Assay of blood ketones is more sensitive and specific but is not always available
- GAD, IAA, IA-2 autoantibodies if new T1DM suspected
- WCC, Trop/CK, amylase may all be ↑ by DKA itself rather than by a precipitant
- Na^+ may ↑(dehydration), normal or ↓(pseudohypoNa: Corr.Na=Na + (glu-5.5)/2.75)
  K^+ may ↑(acidosis), normal or occ. ↓, but overall there is depletion of body K^+;
  Cr & Ur rise with pre-renal RF; bicarbonate ↓.
- Plasma Osmolarity = 2([Na] + [K]) + [Ur] + [glucose]. >290mOsm/L in cases of DKA.
  Consider HONK if >320 mOsm/l and lack of ketonuria or glu>30mmol/L.
- Anion Gap = ([Na] + [K]) – ([Cl] + [HCO3]) >13 mEq/l in DKA

Urine: urinalysis for glycosuria and ketonuria. Send for M, C & S
Radiology: CXR (?pneumonia or cardiac failure), CT/MRI (if LOC, ?CVA), LP (if ?meningitis)
Other: ECG

Management

General:

- Triage to resuscitation/acute area. Attach continuous monitoring, weigh if possible
- ABCD. Give O_2, consider intubation and ventilation if ↓LOC
- Obtain large-bore peripheral IV access + sampling line or insert central venous catheter
- Consider urinary catheterisation ± NG

Intravenous fluid and electrolyte replacement:

- Adult: may be sig. dehydrated (10%) can give: 1L NS stat, q1h, q2h unless concern of CCF.
- Child: 10-20mL/kg if shocked, beware cerebral oedema. Maintenance+deficit over 48hrs.
- Give potassium replacement when K^+<5.5 and urine output established & chk UEC q2–4h

Insulin therapy:

- Initially 6U/hr (child: 0.05/kg/hr if<5y else 0.1U/kg/hr) short-acting soluble insulin
- In adults use a sliding scale for hourly insulin dose based. In children do not ↓insulin.

BSL (mmol/l)	**Insulin infusion rate** (U/hr=ml/hr for 50U fast-acting soluble insulin in 50ml 0.9%NaCl)
≥17	6
11–16.9	4
9–10.9	3
7–8.9	2
4–6.9	1
<3.9	Discontinue and repeat glucose estimation in 30 mins.

- Hourly BSL. Aim is to reduce plasma glucose by 3–5 mmol/hr after initial fluid bolus.
- When BSL<15mmol/l add 5%D (child: 0.45% NaCl+5%D) so BSL 8-12 til pH/ketone norm

Further measures:

- HCO_3 in rare cases (pH≤6.9) - 0.15 x wt x base deficit mmol (give over 1 hr & reassess)
- DKA leads to phosphate depletion but this rarely causes significant clinical problems.
- Any precipitating illness should be managed optimally as per current guidance

Progression:

- When eating dbl infusion rate while eating +1hr (meals) or +30min (snacks)
- If stable (pH>7.3, BSL<12, HCO_3>15, no ketonuria) & eating – convert to an sc insulin regime and wean off infusion 90min after sc dose.
- Give this dose before breakfast, lunch, dinner & about half this dose at midnight
- Dietician, education, blood testing, and conversion to home insulin regime

Complications

- Cerebral oedema commoner in children (~1%). Mortality 20–90%. Presents in first 24h with headache, behavioural changes and urinary incontinence → abrupt neurological deterioration and coma. Mx: Mannitol 0.5-1g/kg IV over 20mins or 5-10ml/kg of 3% saline, reduce rate of fluid administration, elevate head of bed, call ICU.
- Pulmonary oedema due to overzealous fluid replacement or as a spontaneous phenomenon
- Iatrogenic hypoglycaemia, hypokalaemia
- Cardiac dysrhythmia due to electrolyte disturbance (particularly K+) or acidosis
- Venous thromboembolism
- Diabetic retinopathic changes may be seen prior to or after therapy for DKA
- Hypophosphataemia
- Adult respiratory distress syndrome

Prognosis

- Txf to ICU - age<5, pH<7.2, Na^+>150, BSL>50, CNS depression
- Prognosis worsens with age and the severity of the underlying precipitating pathology (particularly MI, sepsis and pneumonia)
- Coma at presentation, hypothermia or persistent oliguria are poor prognostic indicators
- Overall mortality rates vary from 1–10% (less in children) depending expertise of Mx
- There has been a marked ↓mortality in expert centres over the last 20 years.

Prevention

- Education programs for diabetic patients & carers
- Improved awareness of the management of diabetes and intercurrent illness, and the presentation and early management of DKA, in the medical/allied healthcare professions

Alcoholic Ketoacidosis

Pathophysiology

Complex. Chronic EtOH consumption with NADH/NAD ratio & malnourished (↓glycogen stores). ↑lipolysis→FFA & ketoacids esp. β-hydroxybutyrate. Vomiting & dehydration exacerbate issue.

Epidemiology

Usually acute high use of EtOH in heavy alcohol abuser

Presentation

History: Nausea & vomiting. Anorexia. Mild abdominal pain.
Exam: ↑HR, ↑RR, signs of dehydration or chronic EtOH abuse, mildly tender abdo

Investigations

Bloods: FBC, UEC, BSL (↓, normal), ABG (met.acidosis±met.alkalosis [vom]), AG (↑), amylase, LFT, cultures. Nitroprusside assay of bld ketones may be -ve as doesn't detect hydroxybutyrate.
Urine: urinalysis for glycosuria and ketonuria. Send for M, C & S
Radiology: CXR (?pneumonia or cardiac failure), CT/MRI (if LOC, ?CVA), LP (if ?meningitis)
Other: ECG

Management

General: ABCD as necessary. Obtain IV access
Fluids: 5% dextrose in 0.9% saline.
Other: Thiamine. Correction of other metabolic/electrolyte/vitamin derangements.
Treat underlying conditions. Manage alcohol withdrawal or other complications.