MANAGEMENT OF DIABETIC KETOACIDOSIS (DKA)

Aetiology

- Complete or near complete lack of insulin, resulting in decreased peripheral glucose utilization and increased gluconeogenesis, lipolysis and ketogenesis
- Can also occur during severe physiologic stress – insulin requirements cannot be met by the diabetic pancreas
- Can occur in IDDM NIDDM or first manifestation of diabetes mellitus

Clinical Features

- Constitutional – malaise, weakness, myalgia
- Abdominal pain, nausea and vomiting
- Polyuria, polydipsia and loss of weight
- Signs of volume depletion and hypoperfusion +/- hypovolaemic shock
- Hyperventilation Kussmaul's breathing in severe acidosis), ketotic breath, pyrexia
- Pyrexia
- Delirium, reduced conscious level, coma
- Evidence of precipitating causes
    - Sepsis eg UTI, respiratory tract infection, bacterial meningitis, retropharyngeal abscess, hepatobiliary sepsis. Examine for sources of sepsis include "hidden" sites eg scalp, back, auditory meatus, perianal region
    - Noncompliance with diet or insulin therapy
    - Trauma
    - AMI
    - CVA
    - Pancreatitis
    - Drug or alcohol use

Laboratory Findings

- Hyperglycaemia (BSL >15mmol/L)
- Ketosis
    - Serum and urine detection uses nitroprusside reaction
    - Uurine ketones positive (+ or more). Standard dipsticks only detect acetoacetate and acetone. Cannot detect β-hydroxybutyrate
    - β-hydroxybutyrate:acetoacetate ratio is 3:1 in vivo. Ratio increase >3:1 during tissue hypoperfusion and hypoxia (acetoacetate → β-hydroxybutyrate) and decreases the apparent ketone detected, even though total ketones may be unchanged
- Metabolic acidosis (pH<7.3)
- High anion gap (25-35 mmol/L)
- Dehydration (urea:creatinine ratio increased)

- Renal impairment
  - Hypovolemia, pre-renal
  - Underlying DM nephropathy
  - Lab interference (Jaffe reaction) due to high circulating acetoacetate
- HypoK^+/hyperK^+
  - HyperK^+ initially, then hypoK^+ after insulin therapy
- HypoNa^+/hyperNa^+
  - Hyponatraemia may be real (dilutional from osmotic effect of hyperglycaemia initially)
  - Or expected as a result of hyperglycaemia (correction factor: ΔNa = - 0.016 x (glucose – 100)
- HypoPO_4, hypoMg^{++}
- Patients with chronic renal failure tend to have milder hyperglycaemia and dehydration, and more severe acidosis

Investigations
- CBC, U/Cr/Na/K/Cl/PO_4/MgGlucose, ABG, serum osmolality
- Urine for ketones may be negative initially in DKA (see above). Repeated hourly for 3 hours if diagnosis is strongly suspected
- Urine microscopy and culture
- Blood culture+/- lumbar puncture in a septic patient
- ECG
- CXR

Principles of Management
1. Aggressive fluid management
2. IV soluble insulin
3. Aggressive K replacement except in renal failure
4. Look for precipitating factors

Treatment
1. Fluid therapy
   - Aggressive fluid replacement about 2 L in 4 h, 1-2 L in the next 4 h; about 4-7 L in total within the first 24 h
   - NS is preferred because it helps to maintain intravascular volume and maintain peripheral perfusion and hence, clearance of ketones. It may also reduce risk of cerebral oedema when sugar is lowered
   - ½ NS is used if serum Na >150-155mmol/L
   - Change to D5% with additional NaCl when blood sugar is <14mmol/L
   - Avoid alternating NS with dextrose drip as this will cause fluctuations in blood sugar
   - CVP/PCWP monitoring in patient with history of heart failure or renal impairment

2. Insulin therapy
   - Continuous IV insulin infusion (CI) through a pump is preferred as it offers smooth control. A more gradual normalization in the first 12-24 h period is preferred to avoid cerebral oedema. Loading dose of IV insulin does not result in better clinical outcome
   - Dilute 50 U of soluble insulin in 50 ml of gelofusine in a syringe and deliver it by an infusion pump
   - The average initial CI rate is about 0.1U/kg/h. It should preferably not exceed 10U/h for patient weight >70kg
   - In severely insulin resistant cases eg morbid obesity, severe sepsis, high dose glucocorticoid treatment and TPN, a sliding scale with an initial rate of >10/h may be required
   - Blood sugar should be monitored at 2-h intervals. Depending on whether the blood sugar improves 4 h later, the sliding scale may be switched to one with a higher initial CI rates (eg scale 1 to scale 3)

BSL (mmol/L)	CI Scale 1 (U/h)	Scale 2	Scale 3	Scale 4	Scale 5	Scale 6	Scale 7
≥ 22	3.0	4.0	5.0	6.0	7.0	8.0	10.0
18 -	2.5	3.5	4.0	5.0	6.0	6.0	8.0
14 -	2.0	3.0	3.0	4.0	5.0	5.0	6.0
12 -	1.5	2.5	2.5	3.0	4.0	4.0	4.0
10 -	1.0	2.0	2.0	2.0	3.0	3.0	3.0
8 -	1.0	1.5	1.5	1.5	2.0	2.0	2.5
6 -	0.5	1.0	1.0	1.0	1.5	1.5	2.0
4 -	0.5	0.5	0.5	0.5	1.0	1.0	1.5
< 4	Stop iv insulin infusion and inform doctor						

3. Potassium replacement
   - Aggressive IV K^+ infusion should be given in initial phase because of the shift of K^+ with glucose into the intracellular compartment with hydration and insulin treatment
   - In presence of ECG changes of hypokalaemia, 30 mmol of K^+ diluted in 1 litre NS or ½ NS should be given over 1 h before laboratory confirmation is available. Checking of K^+ usually available in our ICU – use ABG machine
   - Replacement may be given according to the scale below:

K^+ level (mmol/L)	< 3.0	3 -	4 -	5 -	> 5.5
IV K^+ (mmol/h)	30	20	10	5	0

- Review K^+ infusion rate when blood sugar is normalizing (<14mmol/L). K^+ level should be measured every 4 h within the first 24 h

4. Bicarbonate/phosphate/magnesium
   - Most authors do not recommend bicarbonate or phosphate infusion in DKA
   - If measured phosphate or magnesium is low, replacement can be given
   - Mg^{++} may be considered if arrhythmias occur

5. Venous thromboembolism prophylaxis
   - Look under relevant chapter in the ICU manual

6. Termination of CI
   Continuous insulin infusion can be stopped when:
   - Blood sugar has been stabilized to ≤ 10 mmol/L on a steady insulin infusion rate for 12 h. The usual time frame is about 24-48 h of CI treatment
   - Urine ketones should be negative
   - Dehydration is almost corrected
   - Precipitating factor is under control. If patient is still acutely ill, insulin resistance will be high and rebound in blood sugar is likely