MIL

NHS
Oxford University Hospitals
NHS Foundation Trust

Volume 4, No. 9 **March 2019**

This Medicines Information Leaflet is produced locally to encourage safe prescribing that is cost effective to the NHS. Information will be given on quality improvement issues and the costs to hospital and community.

Guidelines for Management of Diabetic Ketoacidosis (DKA) in Adults

All patients with DKA must be referred to the Diabetes Specialist Team within 24hrs. Referrals will automatically be submitted once the PowerPlan is launched. Referrals can also be submitted manually via Requests & Prescribing on EPR.

Diabetic ketoacidosis (DKA) is an acute metabolic complication of diabetes caused by absolute or relative insulin deficiency. It occurs in patients with type 1 diabetes (T1DM), but can also occur in some patients with type 2 diabetes (T2DM), known as ketosis-prone type 2 diabetes. These patients are often of Afro-Caribbean or Hispanic origin. The most common causes are omission of insulin, underlying infection, and new onset diabetes. The mortality associated with DKA is estimated at 0.67%.

Fluid resuscitation is a critical part of treating DKA. Adults with DKA need an average of 6 litres of IV (intravenous) fluid. This Medicines Information Leaflet (MIL) summarises the Trust's guidelines for managing DKA in adults. Guidelines must be read in conjunction with the *Adult DKA Management Flowchart* on page 3 of this document.

Confirming Diagnosis
General Principles – all three must be present

- Glucose above 11 mmol/L or known diabetes
- Ketonaemia above 3mmol/L (see below for discussion of capillary ketone measurement)
- pH below 7.3 and/or Bicarbonate ($HCO3^-$) below 15 mmol/L

- All cases of suspected DKA referred to the Emergency Department (ED) or Acute General Medicine (AGM) should be accepted and assessed by the physician on-call. The patient should be transferred as soon as possible to the Emergency Assessment Unit (EAU) at the JR or at the Horton.
- In patients presenting with ketosis (ketone (β-OHB) levels above 3mmol/L), but without significant acidosis, treatment with variable rate intravenous insulin infusion (Variable-RIII) can prevent the onset of acidosis.
- Patients with DKA have severe metabolic derangement and require intensive bedside monitoring.
- Those with **Severe DKA** should be considered for management in an HDU/ICU environment. Markers for severe DKA include:
  - pH below 7.0
  - Ketones above 6mmol/L
  - HCO_3 below 5 mmol/L
  - Potassium below 3.5mmol/L
  - Glasgow Coma Score (GCS) below 12
  - SpO_2 below 92% (assuming normal baseline respiratory function)
  - Systolic blood pressure (SBP) below 90mmHg
  - Heart Rate above 100bpm or below 60 bpm
  - Anion gap above 16mmol/L (anion gap = $(Na^+ + K^+) – (Cl^- + HCO_3^-)$)
  - Difficult IV access

Euglycaemic DKA ("euDKA")

Ketonaemia and acidosis **CAN** occur with a normal blood glucose. This is called "euglycaemic DKA" and can occur in patients taking a SGLT2 inhibitor (ie dapagliflozin, canagliflozin or empagliflozin) whose type 2 diabetes decompensates due to an acute event such as infection, myocardial infarction, surgery.

- Check blood ketones in all unwell patients with diabetes on a SGLT2 inhibitor (ie dapagliflozin, canagliflozin or empagliflozin). If raised, check pH and call on call SpR.

Best Practice Tariff requires **early** Diabetes Specialist Team involvement. Therefore, all patients with DKA should be referred *within 24 hours*.

Referrals to the Diabetes Specialist Team will be automatically submitted once the PowerPlan is launched. Manual referrals can be submitted via Requests & Prescribing on EPR (Power Chart). For details of how to refer, please visit the Diabetes – Adult intranet site.

Oxford & Horton sites
Inpatient Diabetes Nursing Team:
Tel: 01865 (2)22866 – leave a message if out of hours

For advice please bleep:
JR: 4433, CH: 6762, NOC: 6761, HGH: 9912

For urgent out of hours review or advice please contact the on-call Diabetes/Endocrine SpR via OUH Switchboard

Emergency Treatment and Investigations

- **Airway:** If the patient is not maintaining their airway (GCS below 10) contact the ICU team (JR – Bleep 4138, Churchill Bleep 5505). Consider an NG tube in persistent vomiting or obtunded patients.
- **Breathing:** Monitor oxygen saturation and respiratory rate.
- **Circulation and blood pressure:** Insert two large bore cannulas, take blood, and start intravenous fluids. If severely fluid depleted, give 500 ml 0.9% sodium chloride by IV infusion over 15-20 minutes, and repeat if necessary. Otherwise, commence 0.9% sodium chloride 1 litre over 1 hour (see flowchart). Contact the ICU team if systolic BP below 90 mmHg, despite 3 boluses of 500ml of sodium chloride 0.9%.

N.B. If blood glucose drops below 14mmol/L, then start a 10% glucose infusion at 125 mls/hr via a second line, ***concurrently*** with 0.9% Sodium Chloride**.** This maximises clearance of ketones.

- **Diagnosis** - Baseline investigations: urea, creatinine, venous glucose (note that point-of-care glucometers are unable to measure glucose levels above 27.8 mmol/L therefore VBG measurements are preferred), **venous** blood gas (including lactate), FBC, clotting and CRP. Anion gap should be calculated and recorded. An infection screen including urinalysis, blood and urine cultures and CXR should be considered. ECG should be recorded and consider measuring High Sensitivity Troponin.
- Measure capillary ketone levels using Freestyle Precision Pro™ meter (measures up to a level of 8mmol/L, see below).
- Bicarbonate therapy is rarely needed. Fluid and insulin therapy usually resolves the acidosis. If acidosis persists, discuss with the consultant physician or the Diabetes Registrar or Consultant.

Clinical Assessment

The following should be assessed/recorded:

- Degree of dehydration (using pulse/BP as a guide).
- Consciousness level (by documenting GCS).
- Evidence for any precipitating cause.
- Patient's usual medication, especially usual insulin regimen. Patient's weight (if unable to weigh, record the estimated weight used).

Please initiate fluid resuscitation as a priority whilst awaiting insulin infusion, but insulin infusion should also not be delayed.

Complete the VTE risk assessment on EPR to ensure appropriate VTE prevention and if indicated prescribe low molecular weight heparin (see MIL).

Monitoring

- Capillary glucose levels should be measured hourly.
- Capillary ketones should be measured hourly until less than 0.6 mmol/L.
- Serum potassium (K^+) and venous pH should be checked at 2, 4, 6, and 12 hours or until transfer to subcutaneous insulin.
- Fluid and insulin therapy should be adjusted according to the changes in ketone and blood glucose (BG) levels, using the flow chart (see below).
- Commence hourly neurological observations, if the patient is drowsy.

Insulin infusions

Fixed rate IV intravenous insulin infusion (Fixed-RIII) is recommended at a rate of 0.1 units/kg/ hour (See table on page 3).

- The initial Fixed-RIII dose should not exceed 15 units per hour (i.e. 15 ml/hour).
- However, if blood glucose and ketones do not fall by 3mmol/L/hr and 0.5 mmol/L/hr respectively, then the insulin infusion rate may exceed 15ml/hr. Please ensure that the pump and connections are working properly and that the correct infusion rate is running. Discuss these cases with the diabetes specialist registrar, and document the recommended regimen in the medical notes before altering the rate of infusion. Take all requests to confirm any aspect of the protocol seriously and clarify any concerns.
- Insulin administration must have an independent verification check and document (see OUH Medicines Policy). For the Fixed-RIII, this means the initial syringe and any rate changes.
- Record all IV insulin infusion rates in the relevant electronic monitoring section of the patient record (i.e. "titratable infusions" section of Interactive View on ePMA).

When prescribing in ePMA use the PowerPlan:

- Insulin – Adult management of diabetic ketoacidosis (DKA) PowerPlan

See LINK for further guidance on how to make amendments once a PowerPlan is launched

Reference

Joint British Diabetes Societies Inpatient Care Group. The Management of Diabetic Ketoacidosis in Adults; September 2013; available from http://www.diabetologists-abcd.org.uk/JBDS/JBDS_IP_DKA_Adults_Revised.pdf

Prepared by:

Drs: F Kavvoura, I Ramrachaya, G Thanabalasingham (Diabetes), J Edge (Paediatrics), T Frang, A Phelps (Geratology-AGM), Diabetes Inpatient Nurse Team, P Cawte-Dutheil (Pharmacy), Dr Clare Crowley (Medicines Safety Pharmacist), A Lumb (Diabetes & AGM Consultant) June 2015.
Revised: A Lumb, R Rea, G Tan, G Yebra, CCrowley
Review date: March 2022.

Adult Diabetes Ketoacidosis (DKA) Management Flowchart

All intravenous fluids must be given via a volumetric pump. All DKA patients should have two venflons sited. One should be purely for fluid and electrolyte replacement. Insulin and 10% glucose should be given through the second venflon, via a Y-connector with dual anti-reflux valves to stop the fluid going back up the line (NHS Code FKA322) and a syringe pump extension set with integral anti-syphon valve (NHS Code FKA040) to connect the insulin.

Insulin infusion and line must be changed every 24 hours (cannula in accordance to Trust guidance)

INTRAVENOUS FLUIDS

Treat dehydration with 6 litres of 0.9% sodium chloride in all patients.

In Shock (SBP below 90mmHg)

- Severely depleted – give 500ml of 0.9% sodium chloride IV over 15 to 20 minutes
- Repeat until SBP above 90mgHg (maximum of 3 boluses) – if SBP still below 90mmHg refer to ICU team
- **DO NOT** give potassium chloride in fluid boluses, in the first litre, or if serum potassium (K^+) over 5.5mol/L
- All subsequent fluid, for the next 24 hours, should contain potassium, unless urine output is below 30ml/hr or serum potassium remains in excess of 5.5mmol/l

Not Shocked (SBP over 90mgHg)

- Recommended fluid

0.9% Sodium chloride 1L	Over 1 hour
0.9% Sodium chloride 1L with potassium chloride	Over 2 hours
0.9% Sodium chloride 1L with potassium chloride	Over 2 hours
0.9% Sodium chloride 1L with potassium chloride	Over 4 hours
0.9% Sodium chloride 1L with potassium chloride	Over 4 hours
0.9% Sodium chloride 1L with potassium chloride	Over 6 hours

- Recommended potassium replacement in DKA

Potassium Level	Replacement/litre fluid
Over 5.5mmol/L	nil
3.5-5.5mmol/L	40mmol/L
Under 3.5mmol/L	More aggressive replacement method needed, seek advice from specialist.

- When BG drops to below 14 mmol/L commence 10% Glucose to run **concurrently** with 0.9% sodium chloride.

10% glucose **500ml**	Over 4 hours

If serum potassium exceeds 5.5mmol/L, omit potassium but repeat measurements hourly as glucose + insulin will cause serum potassium to fall and replacement is highly likely to be necessary.

INSULIN

Use fixed rate intravenous insulin infusion to clear ketones. Continue long acting basal insulin

Immediate

- **DO NOT** give a stat dose of insulin
- If the patient normally receives long acting insulin (i.e. Lantus/Abasaglar/Toujeo™ (glargine), Levemir™ (detemir) or Tresiba™ (degludec), **continue** at their usual dose (suspend other insulins and medicines for diabetes whilst on insulin infusion)
- Start IV human soluble insulin 50units in 50ml via pump (available as ready mixed syringe, to prevent need to mix Actrapid™ on the ward)
- Infuse IV insulin at fixed rate depending on weight (0.1 unit/kg/hour):

Weight (kg)	Infusion rate (unit/hour)
40 - 49	4
50 - 59	5
60 – 69	6
70 – 79	7
80 – 89	8
90 -99	9
100-109	10
110-119	11
120-129	12
130-139	13
140-150	14
Above 150	15

- Infusion rates above 15 units/hour should only be on the advice of the diabetes team

Hourly

- Review patient response to insulin infusion pump after 1 hour.
- If BG not dropping by 3mmol/L/hr and capillary ketones by 0.5mmol/L/hr, increase infusion rate by 1unit/hr* (i.e. 1ml per hour)
- Increase infusion rate hourly as necessary to achieve reduction in BG and capillary ketones
- Continue **Fixed-RIII** until ketones below 0.6mmol/L, venous pH above 7.3 and bicarbonate above 18mmol/L

When stable (ketones below 0.6, pH above 7.3)

- If patient is eating and drinking regularly change to S/C insulin regimen at the next meal
- Stop IV insulin infusion 1 hour later
- If not eating, change to Variable-RIII (see MIL)
- Do not restart Fixed-RIII, unless ketones above 3mmol/L. If ketones below 3 mmol/L, use Variable-RIII

MONITORING

Record IV insulin rate on electronic system. Ketones should fall by 0. 5mmol/L every hour*.

First 12 Hours

- Measure capillary glucose hourly while on IV insulin. Send venous sample to lab if out of range of bedside analysis.
- Measure ketones hourly until less than 0.6 mmol/L, then only if CBG above 12mmol/L.
- Venous blood gas for bicarbonate and potassium levels at 0, 2, and 6 hours, and then 6 hourly until pH is above 7.3.
- Monitor hourly urine output.
- Consider urinary catheter if no urine output at 4 hours.

12 to 24 Hours

Continue to measure capillary glucose and ketones as above.

Continue measuring K^+ 12 hourly aiming to keep K^+ at 4 – 5 mmol/L.

Note

- Bicarbonate is rarely, if ever, needed to correct the acidosis of DKA. Decision to administer should be made by a consultant or diabetes registrar and it should **never** be given if pH is over 7.0
- There is no evidence that bicarbonate therapy affects outcomes or improves metabolism

Abbreviations:

DKA - Diabetic Ketoacidosis
Fixed-RIII - fixed rate intravenous insulin infusion
Variable-RIII - variable rate intravenous insulin infusion
BG - blood glucose
K^+ - serum potassium
SBP - systolic blood pressure
S/C - subcutaneous
Glucose = Dextrose

**If ketones not falling as expected, check insulin infusion pump is working, check the following: cannula is patent, tubing and infusion equipment working appropriately, insulin and substrate infusions running at correct rate. If appropriate, check that the IV cannula is working with a sodium chloride 0.9% flush.*