The Management of Diabetic Ketoacidosis in Adults

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What’s Going On Around the UK

- 96.5% of hospitals have published protocols for the treatment of DKA
  
  (n = 249 Hospital Trusts. Sampson et al Diab Med 2007;24(6):643)

- Approximately 35,000 bed days are taken up annually by DKA in English Trusts
  

- 36% of UK Trusts do not refer their DKA’s to the specialist diabetes team on the day of admission, 45.7% do not refer their HONK’s
  
  (n = 249 Hospital Trusts. Sampson et al Diab Med 2007;24(6):643)
How It’s Been Done So Far

- ABC

- Lots of normal saline

- Stat intravenous insulin followed by constant or variable rate intravenous insulin infusion

- A few other things (potassium, phosphate, ± bicarbonate, etc.)
What’s *Actually* Happening...

- Hopefully make the correct diagnosis
- Give a bit of, or too much, insulin; give (too much) fluid
- Criminally assault patient with arterial blood gas assessment, despite $O_2$ sats being 100%
- Put patient in a corner or on a non-medical ward...dependent on what bed manager says
What’s *Actually* Happening...

- Forget to repeat bloods, or forget to call lab for result
- Forget to review patient
- Correct potassium 4 hours after it falls
- Stop long-acting subcutaneous insulin to ensure delayed recovery
Confusion Reigned!

Variability in perioperative IV sliding scale insulin infusion rates by glycaemic thresholds in 30 UK Acute Trusts (Sampson/Walden 2010)
Confusion Reigned!

Joint British Diabetes Societies Inpatient Care Group

The Management of Diabetic Ketoacidosis in Adults

Launched at DUK Liverpool 2010
“Consensus of Worthy Opinion”

Writing Group
Mark W Savage (Chair of Sub Group)
Maggie Sinclair-Hammersley (Chair of JBDS IP Care Group)
Gerry Rayman
Hamish Courtney
Ketan Dhatariya
Philip Dyer
Julie Edge
Philip Evans
Michelle Greenwood
Girly Hallahan
Louise Hilton
Anne Kilvert
Alan Rees
and many others
Areas of Controversy

- Measurement of venous pH
- The use of bedside ketone monitors
- The use of crystalloid not colloid
- Cautious fluid replacement in the young
- The fluid of choice is 0.9% sodium chloride solution
Areas of Controversy

- Continued use of long acting $s/c$ analogues
- The use of a fixed rate of insulin based on weight
- No bolus dose of insulin
- No intravenous bicarbonate routinely
- No phosphate replacement routinely
Paradigm Changes in the New Document

- Using ketones as the basis for treatment and monitoring, not glucose or bicarbonate
- Abolish the use of the useless arterial blood gas measurement and use venous samples instead
- The early and mandatory involvement of the specialist diabetes team
Why The Changes?

- Realisation that the main problem in DKA is the “K and A”
  - Blood sugar may be normal or only slightly elevated (“Euglycaemic DKA”)

- Developments in last 10 years:
  - Venous pH is almost the same as arterial (0.02 pH units difference)
  - Bed side monitoring of pH; ketones; U&Es, bicarbonate and glucose available allowing measurement of essential metabolic parameters quickly
The Management of Diabetic Ketoacidosis in Adults

For young people under the age of 18 years use British Society of Paediatric Endocrinology and Diabetes (BSPED) guidelines: http://www.bsped.org.uk/professional/guidelines/docs/DKAGuideline.pdf

Diagnostic criteria: all three of the following must be present
- capillary blood glucose above 11 mmol/L
- capillary ketones above 3mmol/L or urine ketones +++ or more
- venous pH less than 7.3 and/or bicarbonate less than 15 mmol/L

BOX 1: Immediate management: time 0 to 60 minutes
(TI-0 at time intravenous fluids are commenced)

- Consider 0.9% saline solution (or large bore cannula via intravenous pump)
- Low dose 2 U/hr rate of insulin replacement
- Arrange for transfer to medical in 1 hour (or 1 hour after insulin replacement
- Monitor patient closely during this period

- Accurate patient
  - Respiratory rate, temperature, blood pressure, pulse, oxygen saturation
  - Pulse oximeter
  - Blood glucose
  - Capillary and bicarbonate
  - Sodium
  - Potassium

- Consider
  - Further investigations
    - WBC
    - U/C
    - Hb
    - Platelets
    - Plasma ketone
    - Leucocytes
    - Creatinine
  - Further investigations if indicated

- Establish monitoring regimen
  - Hourly capillary blood glucose
  - Hourly electrolytes
  - Hourly capillary and bicarbonate and potassium
  - Continuous cardiac monitoring
  - Continuous pulse oximetry

- Action
  - Consider and prioritizing the cause and treat appropriately

HDU/Level 2 facility and/or insertion of central line may be required in following circumstances (request urgent senior review)
- Young people aged 18-25 years
- Diabetic
- Pregnant
- Recent history failure
- Other concomitant medications
- Sulfonylurea or biguanides
- Blood glucose above 6.5 mmol/L
- Venous bicarbonate below 5 mmol/L

BOX 2: Initial fluid replacement
Restoration of circulating volume is priority

<table>
<thead>
<tr>
<th>System</th>
<th>Initial amount</th>
<th>Additional amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>System</td>
<td>0.9% saline</td>
<td>1000-2000 mL</td>
</tr>
<tr>
<td>System</td>
<td>10 g sodium</td>
<td>10-20 g sodium</td>
</tr>
<tr>
<td>System</td>
<td>212 mL glucose</td>
<td>212 mL glucose</td>
</tr>
</tbody>
</table>

Potassium replacement
- Sodium 100 mmol/L
- Potassium 40 mmol/L
- Venous bicarbonate 5 mmol/L

BOX 3: 60 minutes to 6 hours

Aims of treatment:
- Rate of fall of ketones of at least 65 mmol/L in 2 hours
- Blood glucose fall 3 mmol/L per hour
- Monitor serum potassium in normal range
- Avoid hypoglycaemia
- Continue 6-10 U/hour replacement insulin therapy
- Continue 0.9% saline replacement
- Monitor and treat any complications
- If potassium is outside normal range, re-assess potassium replacement and check toxicity of diabetes after further 6 hours, intensive medical advice

BOX 5: 12 to 24 hours

- Insulin infusion rate may need review
- Assess ketones not falling by at least 1 mmol/L
- Assess bicarbonate not rising by at least 3 mmol/L
- Assess fall in pH falling by at least 0.1 mmol/L
- Continuous cardiac monitoring
- Continuous pulse oximetry

- Action
  - Monitor and treat any complications

- If patient is not in a Normal state, or if they are not improving

- If DKA not resolved review insulin infusion (see BOX 2)
- If DKA not resolved go to BOX 6

Additional measures
- Regular observations
- Check oxygen saturation
- Blood glucose
- Venous bicarbonate
- Body weight
- Urine output
- Serum ketones
- Nephrectomy
- Monitor and treat any complications

How is DKA Defined?

- Ketonaemia of $\geq 3$ mmol/L OR significant ketonuria ($>2+$ on dipstix)

  AND

- Blood glucose $>11.0$ mmol/L or known to have DM

  AND

- $\text{HCO}_3^- < 15$ mmol/L AND/OR venous pH $< 7.3$
Immediate Management: Time 0 to 60 Minutes

BOX 1: Immediate management: time 0 to 60 minutes
(T=0 at time intravenous fluids are commenced)

If intravenous access cannot be obtained request critical care support immediately

Action 1: Commence 0.9% sodium chloride solution (use large bore cannula) via infusion pump.
See Box 2 for rate of fluid replacement

Action 2: Commence a fixed rate intravenous insulin infusion (IVI).
(0.1 unit/kg/hr based on estimate of weight) 50 units human soluble insulin (Actrapid® or Humulin S®) made up to 50ml with 0.9% sodium chloride solution. If patient normally takes long acting insulin analogue (Lantus®, Levemir®) continue at usual dose and time.

Action 3: Assess patient
- Respiratory rate; temperature; blood pressure; pulse; oxygen saturation
- Glasgow Coma Scale
- Full clinical examination

Action 4: Further investigations
- Capillary and laboratory glucose
- Venous BG

Action 5: Establish monitoring regimen
- Hourly capillary blood glucose
- Hourly capillary ketone measurement if available
- Venous bicarbonate and potassium at 60 minutes, 2 hours and 2 hourly thereafter
- 4 hourly plasma electrolytes
- Continuous cardiac monitoring if required
- Continuous pulse oximetry if required

Action 6: Consider and precipitating causes and treat appropriately

Immediate Management: Time 0 to 60 Minutes

- **Action 1**: Commence 0.9% sodium chloride solution
- **Action 2**: Commence a fixed rate intravenous insulin infusion (IVII)
- **Action 3**: Assess patient (examination)
- **Action 4**: Investigations
- **Action 5**: Establish monitoring regime
- **Action 6**: Consider precipitating causes and treat appropriately
Consider Admission to Level 2 (HDU) Care

- Young people aged 18-25 years
- Elderly
- Pregnant
- Heart or kidney failure
- Other serious co-morbidities
- Severe DKA by following criteria
  - Blood ketones above 6 mmol/L
  - Venous bicarbonate below 5 mmol/L
  - Venous/arterial pH below 7.1
  - Hypokalaemia on admission (below 3.5mmol/L)
  - GCS less than 12
  - Oxygen saturation below 92% on air (Arterial blood gases required)
  - Systolic BP below 90 mmHg
  - Pulse over 100 or below 60 bpm
  - Anion gap above 16 \[ \text{Anion Gap} = (\text{Na}^+ + \text{K}^+) - (\text{Cl}^- + \text{HCO}_3^-) \]
Fluid Replacement

BOX 2: Initial fluid replacement

**Restoration of circulating volume is priority**

**Systolic BP (SBP) below 90mmHg**
Likely to be due to low circulating volume, but consider other causes such as heart failure, sepsis, etc.
- Give 500ml of 0.9% sodium chloride solution over 10-15 minutes. If SBP remains below 90mmHg repeat whilst requesting senior input. Most patients require between 500 to 1000ml given rapidly.
- Consider involving the ITU/critical care team.
- Once SBP above 90mmHg give 1000ml 0.9% sodium chloride over next 60 minutes. Addition of potassium likely to be required in this second litre of fluid

**Systolic BP on admission 90 mmHg and over**
- Give 1000ml 0.9% sodium chloride over first 60 minutes

**Potassium replacement**

<table>
<thead>
<tr>
<th>Potassium level (mmol/L)</th>
<th>Potassium replacement mmol/L of infusion solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 5.5</td>
<td>Nil</td>
</tr>
<tr>
<td>3.5-5.5</td>
<td>40 mmol/L</td>
</tr>
<tr>
<td>&lt; 3.5</td>
<td>senior review – additional potassium required</td>
</tr>
</tbody>
</table>

## Fluid Replacement

<table>
<thead>
<tr>
<th>Fluid</th>
<th>Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.9% sodium chloride 1L *</td>
<td>1000ml over 1st hour</td>
</tr>
<tr>
<td>0.9% sodium chloride 1L with potassium chloride</td>
<td>1000ml over next 2 hours</td>
</tr>
<tr>
<td>0.9% sodium chloride 1L with potassium chloride</td>
<td>1000ml over next 2 hours</td>
</tr>
<tr>
<td>0.9% sodium chloride 1L with potassium chloride</td>
<td>1000ml over next 4 hours</td>
</tr>
<tr>
<td>0.9% sodium chloride 1L with potassium chloride</td>
<td>1000ml over next 4 hours</td>
</tr>
<tr>
<td>0.9% sodium chloride 1L with potassium chloride</td>
<td>1000ml over next 6 hours</td>
</tr>
</tbody>
</table>

*Re-assessment of cardiovascular status at 12 hours is mandatory, further fluid may be required*

- Need to be adapted depending on age (young adults, elderly) and clinical circumstances
- Crystalloid not colloid
Fluid Replacement

- **Add** glucose 10% @125 mls/hr when blood glucose falls below 14 mmol/L
- Potassium supplements as required
- Bicarbonate not recommended
Insulin

- Commence fixed rate insulin infusion
  - 0.1 unit/kg/hr based on estimate of present weight
  - 50 units human soluble insulin made up to 50ml with 0.9% sodium chloride solution

- If the patient normally takes long acting a insulin analogue continue at usual dose and time
60 minutes to 6 hours

- **Aims of treatment**
  - Rate of fall of ketones at least 0.5mmol/L/hr
  - OR bicarbonate rise 3 mmol/L/hr with BG fall
  - Maintaining potassium in the normal range
  - Avoidance of hypoglycaemia

If ketones and BG not falling as expected, check equipment is working then increase insulin by 1 unit/hr hourly until targets achieved
60 minutes to 6 hours

Action 1: monitoring

- Clinical signs
- Hourly BG and ketones using meter
- Venous blood gases (pH, bicarbonate, potassium) at 60 minutes, 2 hours then 2 hourly
- If the K\(^+\) is outside normal range monitor hourly until in range

Action 2: fluid replacement

- 0.9% sodium chloride with potassium chloride
  - 1L in 2 hours
  - 1L in 2 hours
  - 1L in 4 hours
- Add 10% glucose 125 ml2/hr if BG falls below 14 mmol/L
60 minutes to 6 hours

Action 3: Assess response to treatment

- Check equipment and/or adjust insulin if targets not achieved

- Consider additional measures e.g. catheter, NG tube, thromboprophylaxis
6 to 12 hours

- **Aims**
  - Ensure clinical and biochemical parameters improving
  - Continue fluid replacement
  - Avoid hypoglycaemia
  - Assess for complications e.g. fluid overload, cerebral oedema
6 to 12 hours

- Check venous pH, bicarbonate and potassium at 6 hours
- Request senior advice if DKA not resolving
- Continue fluid replacement with addition of 10% glucose 125 mls/hour when BG falls below 14 mmol/L
- Reassess cardiovascular status at 12 hours – adjust rate of fluid as necessary
- Continue fixed rate insulin infusion until ketones cleared (<0.3 mmol/L) or pH over 7.3
- Ensure a referral has been made to the diabetes team
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- venous pH less than 7.3 and/or bicarbonate less than 15 mmol/L

BOX 1: Immediate management: time 0 to 60 minutes

Intravenous access cannot be obtained request critical care support immediately

- Action 1: 2-hour standard insulin infusion pump
- Action 2: 2-hour standard insulin infusion pump

BOX 3: 60 minutes to 6 hours

Aims of treatment
- Goal of IV fluids
- Goal of potassium replacement
- Goal of insulin infusion

Action 1: IV access
- Goal of fluid replacement
- Goal of potassium replacement
- Goal of insulin infusion

BOX 4: 6 to 12 hours

Aims of treatment
- Goal of fluid replacement
- Goal of potassium replacement
- Goal of insulin infusion

Action 2: Review biochemical and metabolic parameters
- Insulin therapy
- Fluid therapy
- Potassium therapy

BOX 5: 12 to 24 HOURS

Aims of treatment
- Goal of fluid replacement
- Goal of potassium replacement
- Goal of insulin infusion

Action 3: Review biochemical and metabolic parameters
- Insulin therapy
- Fluid therapy
- Potassium therapy

BOX 6: Resolution of DKA

Expectation: Patient should be eating and drinking within normal limits after fluid therapy has been given.

Transfer to subacute insulin

Counseling and education about insulin and dietary management.

Groups represented: Association of British Clinical Diabetologists; British Society for Endocrinology and Diabetes and Association of Children's Diabetes Clinicians; Diabetes Inpatient Specialist Nurse (DSN) Group; Diabetes UK; NHS Diabetes (England); Northern Ireland Diabetologics; Society of Acute Medicine; Welsh Endocrine and Diabetes Society.
12 to 24 hours

Expectation is that ketonaemia and acidosis will have resolved by 24 hours

Aim:

- Ensure clinical and biochemical improvement
- Continue IV fluid if not eating and drinking
- Change to variable rate insulin infusion if acidosis resolved but not eating
- Transfer to subcutaneous insulin once eating and drinking (Box 6)
BOX 6: Resolution of DKA

Expectation: Patient should be eating and drinking and back on normal insulin.
If DKA not resolved identify and treat the reasons for failure to respond. 
This situation is unusual and requires senior and specialist input.

Transfer to subcutaneous insulin
Convert to subcutaneous regime when biochemically stable (capillary ketones less than 0.3, pH over 7.3) and the patient is ready and able to eat.
Do not discontinue intravenous insulin infusion until 30 minutes after subcutaneous short acting insulin has been given
Conversion to subcutaneous insulin should be managed by the Specialist Diabetes Team. If the team is not available use local guidelines. If the patient is newly diagnosed it is essential they are seen by a member of the specialist team prior to discharge
Arrange follow up with specialist team
Summary of Recommendations

- Treat patients in designated areas with trained staff
- Involve the diabetes team as early as possible
- Use bedside monitoring (with QC and laboratory checks) to allow regular assessment
- Monitor response to treatment by blood ketone measurement (may require change in Trust policy)
- Use fixed rate insulin until blood ketones cleared/acidosis resolved
- Audit outcomes and adherence to guidelines
Where to Find This Document


- It’s the document labelled “Joint British Diabetes Societies Inpatient Care Group: The Management of Diabetic Ketoacidosis in Adults (PDF 2MB) - order reference: Diabetes 123”

Thank you for your attention