DIABETIC EMERGENCIES

Mervyn Singer
Bloomsbury Institute of Intensive Care Medicine
University College London, UK
DKA

- annual incidence (US): 4.6-8 episodes per 1000 diabetic pts
- “DKA” appears in 4-9% of all US discharge summaries of diabetics (†<5%)
- hyperosmolar, hyperglycaemic state “HHS” <1% († 15-30%)
- up to 20% of patients may present w/o past h/o diabetes
- degree of hyperglycaemia variable in DKA:
  - ... up to 15% may have normal/slightly elevated BS
- mental status relates to serum osmolality
This is what we’re advised to do in the UK ..

... but should we?
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 3 mmol/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**

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-5</td>
<td>1. Compress 0.9% sodium chloride solutions (use large bore central line) to infuse pump</td>
</tr>
<tr>
<td>10-15</td>
<td>2. Compress a fixed dose intravenous insulin infusion (IVI). Dose based on estimated weight of 50 units human soluble insulin (Actrapid or Humulin P) made up to 50ml with 0.9% sodium chloride solution. If patient normally takes long acting insulin analogue (Lantus, Laspine), continue at usual dose and time.</td>
</tr>
<tr>
<td>30-60</td>
<td>3. Assess patient — respiratory rate, temperature, blood pressure, pulse, oxygen saturation, GCS on coma scale or full clinical examination</td>
</tr>
<tr>
<td>60 ± 20</td>
<td>4. Further investigations — capillary and arterial blood gases, VBG</td>
</tr>
</tbody>
</table>

**BOX 2: Initial fluid replacement**

<table>
<thead>
<tr>
<th>Volume (ml)</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>500-1000</td>
<td>1. Give 500-1000 ml 0.9% sodium chloride solution over 15-30 minutes.</td>
</tr>
<tr>
<td>10-15</td>
<td>2. If MAP remains below 90 mmHg, repeat whilst maintaining urinary output. Most patients require between 500 to 1000 ml given rapidly.</td>
</tr>
</tbody>
</table>

**Potassium replacement**

<table>
<thead>
<tr>
<th>Level (mmol/L)</th>
<th>Potassium replacement mEq of infusion solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5-1.5</td>
<td>30 mEq/L followed by 20 mEq/L over 60 minutes</td>
</tr>
<tr>
<td>1.5-2.5</td>
<td>20 mEq/L over 60 minutes</td>
</tr>
<tr>
<td>2.5-3.5</td>
<td>10 mEq/L over 60 minutes</td>
</tr>
</tbody>
</table>

**BOX 3: 60 minutes to 6 hours**

<table>
<thead>
<tr>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Re-assess patient, monitor vital signs</td>
</tr>
<tr>
<td>2. Continuous fluid infusion as per pump</td>
</tr>
<tr>
<td>3. Assess response to treatment</td>
</tr>
</tbody>
</table>

**Additional measures**

- Regular observations and Early Warning Score (EWS)
- Fluid balance chart, minimum urine output 5 ml/kg/h
- Continuous ECG monitoring, potassium level and cardiac enzymes
- More fluid and electrolyte replacement if necessary
- Monitor arterial blood gases and repeat blood gas if bicarbonate remains less than 92%
- Hematocrit and platelet count
- Correct electrolyte abnormalities, if necessary

**BOX 4: 6 to 12 hours**

**Removal of edematous fluid at 12 hours, further fluid may be required.**

- Ensure clinical and biochemical parameters improving
- Patient not experiencing nausea, vomiting or abdominal pain
- Patient is able to tolerate oral fluids
- No paralyzing agents or ventilatory support
- Oxygen saturation of > 95%
- Lactate level of < 4 mmol/L

**Actions**

- Review biochemical and metabolic parameters
- At 6 hours check venous, bicarbonate, potassium, ketones and glucose
- Lactate level of < 4 mmol/L
- Patient able to tolerate oral fluids
- Oxygen saturation of > 95%

**Groups represented:**
- Association of British Clinical Diabetologists
- British Society for Endocrinology and Diabetes
- Association of Children’s Diabetes Clinicians
- Diabetes Parental Specialist Nurse (DPSN) Group
- Diabetes UK
- NHS Diabetes (England)
- Northern Ireland Diabetologists
- Society of Academic Medicine
- Welsh Endocrine and Diabetes Society
- Scottish Diabetes Group
**Recommendations**

1. Measure venous rather than arterial bicarbonate and pH ± but be consistent
2. Blood ketone meters should be used for near patient testing
3. Crystalloid rather than colloid solutions are recommended for fluid resuscitation
4. Cautious fluid replacement in young adults
5. 0.9% sodium chloride solution is the recommended fluid of choice
6. Subcutaneous long-acting analogue insulin should be continued
7. Insulin should be administered at a fixed rate calculated on body weight
8. Do not use a priming dose (bolus) of insulin
9. Bicarbonate administration is not recommended routinely
10. Phosphate should not be supplemented routinely

..but why not everyone?
Mr F, 65 y.o. male
Multiple myeloma —> o/p high-dose steroid Rx

p/w: 1/52 h/o lethargy, polyuria, polydipsia

O/E: HR 102   BP 110/70
chest - clear
abdomen - soft
GCS 15
CASE REPORT

BM stix ‘unrecordable’  BS - not formally measured (!)
Na 143  K 5.5
Urea 16.5  Creatinine 142 (normal 2/52 prior)
Osmolality 386
Ketones ++
Arterial pH 7.23  PaCO₂ 2.7 kPa  BE -20  lactate 3.6 mmol/l
CASE REPORT

Treated as per DKA guidelines

- 7 litres of n-saline in 12 hours
- 0.1 Units insulin/kg/hr (= 8 U/hr)
- Potassium

Referred to ICU

- Na 168 (from 143)
- Cl 127 (from 98)
- Glucose 10 (from ‘unrecordable’)
- BE -2.2, lactate 2.4
- (Luckily) still cerebrating well, not in pulmonary oedema
• fluid (NaCl ± colloid)
• insulin
• potassium
• other (e.g. Mg, N-G tube)
FLUID - BY THE BOOK?

Action 2 – Restoration of circulating volume

Assess the severity of dehydration using pulse and blood pressure. As a guide 90mmHg may be used as a measure of hydration but take age, gender and concomitant medication into account.

Systolic BP (SBP) on admission below 90mmHg

Hypotension is likely to be due to low circulating volume, but consider other causes such as heart failure, sepsis, etc.

- Give 500 ml of 0.9% sodium chloride solution over 10-15 minutes. If SBP remains below 90mmHg this may be repeated whilst awaiting senior input. In practice most patients require between 500 to 1000 ml given rapidly.

<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 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 8 hours</td>
</tr>
</tbody>
</table>

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

- Once SBP above 90mmHg follow fluid replacement as below
DKA - FLUID MY WAY ...

In general, 5-10 l debt (Na debt 400-700 mmol)
- treat hypoperfusion .... but avoid drowning!

1 litre in 30 min, 1 litre in 1 h, 1 litre in 2 h, 1 litre in 4 hrs

Tailor requirements to individual need:
Signs of organ hypoperfusion?
Yes: colloid or crystalloid to restore normovolaemia
No: 0.9% NaCl or Hartmann's (may need 0.45% NaCl)
  150-200 ml/hr until fluid and Na replete,
  .. then 5% glucose
3. Colloid versus crystalloid?
Many guidelines suggest that in hypotensive patients initial fluid resuscitation should be with colloid. However, the hypotension results from a loss of electrolyte solution and it is more physiological to replace with crystalloid. Moreover, a recent Cochrane review did not support the use of colloid in preference to crystalloid fluid (Perel 2007).

4. Rate of fluid replacement?
There is concern that rapid fluid replacement may lead to cerebral oedema in children and young adults. National and international paediatric guidelines recommend cautious fluid replacement over 48 hours. Existing adult guidelines (ADA, ABCD, SIGN) all recommend rapid initial fluid replacement in the first few hours. No randomised controlled trials exist to guide decision making in this area. We therefore recommend cautious fluid replacement in small young adults who are not shocked at presentation.

Exercise caution in the following patients
- Young people aged 18-25 years
- Elderly
- Pregnant
- Heart or kidney failure
- Other serious co-morbidities

.. why not everyone??
<table>
<thead>
<tr>
<th>Infusion solution</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>0.9% sodium chloride</strong></td>
<td>• Decades of clinical experience</td>
<td>• Hyperchloremic metabolic acidosis which may cause renal arteriolar vasoconstriction leading to oliguria and a slowing of resolution of acidosis</td>
</tr>
<tr>
<td></td>
<td>• Readily available in clinical areas</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Commercially available ready mixed with potassium at required concentrations, 20mmol/L (0.15%) or 40mmol/L (0.3%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Supports safe practice with injectable potassium (NPSA compliant (NPSA alert 2002))</td>
<td></td>
</tr>
<tr>
<td><strong>Compound sodium</strong></td>
<td>• Balanced crystalloid with minimal tendency to hyperchloremic metabolic acidosis</td>
<td>• Insufficient potassium if used alone</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Not commercially available with adequate pre-mixed potassium. Potassium addition in general clinical areas is unsafe. (NPSA alert 2002)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Unfamiliar and not routinely kept on medical wards</td>
</tr>
</tbody>
</table>

However, there is no evidence that the hyperchloremic acidosis causes significant morbidity or prolongs length of stay.
INSULIN TREATMENT: WHAT THE GUIDELINES SUGGEST

Rationale for Best Practice - The New Paradigm

Ketones and Acidosis

Until recently, management of DKA has focussed on lowering the elevated blood glucose with fluids and insulin, using arterial pH and serum bicarbonate to assess metabolic improvement.

This strategy recognised that blood glucose is only a surrogate for the underlying metabolic abnormality. Recent developments now allow us to focus on the underlying metabolic abnormality (ketonaemia) which simplifies treatment of those who present with modest elevation of blood glucose but with acidosis secondary to ketonaemia ‘euglycaemic diabetic ketoacidosis’.

portable ketone meters now also allow bedside measurement of blood ketones (3-beta-hydroxybutyrate). This is an important advance in the management of DKA (Sheikh-Ali 2008, Bektas 2004, Khan 2004, Wallace 2004, Vaneli 2003, Naunheim 2006). The resolution of DKA depends upon the suppression of ketonaemia, therefore measurement of blood ketones now represents best practice in monitoring the response to treatment (Wiggam 1997).
INSULIN TREATMENT: WHAT THE GUIDELINES SUGGEST

60 minutes to 6 hours

- Infuse at a fixed rate of 0.1 unit/kg/hr
- Achieve a rate of fall of ketones of at least 0.5 mmol/L/hr
- In the absence of ketone measurement, bicarbonate should rise by 3 mmol/L/hr and blood glucose should fall by 3 mmol/L/hr
- Continue fixed rate IV until ketones less than 0.3 mmol/L, venous pH over 7.3 and/or venous bicarbonate over 18 mmol/L. (See section C)
- If glucose falls below 14 mmol/L commence 10% glucose given at 125 mls/hour alongside the 0.9% sodium chloride solution.
INSULIN TREATMENT: MY LUDDITE WAY

- i/v infusion
- short-acting insulin 2-5 U/hr (e.g. actrapid)

Aim:
Reduce blood glucose by 2-4 mmol/hr
Continue insulin, even after normoglycaemia (10 mmol/l) achieved
Change fluid to 5% glucose - by now 100 ml/hr total usually OK ..
- encourage eating
Look at ketone clearance
.. but wait until any RCT data are available showing benefit!
**POTASSIUM TREATMENT**

... debt 250-700 mmol

**Aim:**

- maintain normokalaemia
- levels often high initially but can fall rapidly with Rx
- Rx: 10 - 40 mmol/hr
- check blood levels 2 hrly initially - don’t rely on ECG
seek precipitating cause - e.g. sepsis
bicarbonate - no place, even if pH < 7.0
? magnesium - MgSO$_4$ 20-80 mmol/day
phosphate - no place
N-G tube - if obtunded
monitor regularly:
  BM hrly
  BS, U&E, Ca, Mg 2-hrly initially
  Blood gases 2-4 hrly
  Cardiac output - if unstable/cardiac history
OTHER HYPERGLYCAEMIC EMERGENCIES

“hyperglycaemic hyperosmolar state” (HHS)

Formerly known as...

★ hyperglycaemic hyperosmolar non-ketotic coma
★ hyperglycaemic hyperosmolar non-ketotic state

Reflects altered sensoria may be present without coma
- may have variable degrees of ketosis
HYPERGLYCAEMIC HYPEROSMOLAR STATE (HHS)

Particular aspects:

• more common in elderly, non-insulin dependent
• fluid depletion, coma and † greater
• ketoacidosis less than DKA
• coma, obtundation...often persists for 3-7 days post Rx
• commonest causes of †: thromboembolism, infection
HYPERGLYCAEMIC HYPEROSMOLAR STATE (HHS) - TREATMENT

As for DKA but:

• slower rate of volume depletion (2-3 days)
• more sensitive to insulin - halve dose
• Na often >160 mmol/l with Rx - despite 0.45% NaCl
  ... however, usually falls after 2-3 days
• fully heparinize
• may not need insulin long-term
QUESTIONS??