Current concepts in the management of diabetic emergencies

Acute Medicine

Monday 10 July 2017
Royal College of Physicians,

Barbara Philips
Reader in Intensive Care Medicine
St George’s University of London
What it used to be

- Diabetic Ketoacidosis –
  - Type 1,
  - Younger

- Hyperosmolar Non-ketotic coma (HONK)
  - Type 2
  - Older
  - Obesity
  - Co-morbidities
But hyperglycaemia emergencies ------
No longer DKA and HONK
more complex

- Better understanding

- Changing population
  - More type 2
  - Younger type 2
  - More obesity
DKA or HHS? - Spectrum
# Diabetic Ketoacidosis (DKA)

<table>
<thead>
<tr>
<th></th>
<th>DKA</th>
<th>DKA/HHS Mixed</th>
<th>HHS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Plasma Glucose (mmol/l)</strong></td>
<td>≥ 14.0 &lt; 33</td>
<td>≥ 33</td>
<td>≥ 33</td>
</tr>
<tr>
<td><strong>Arterial pH</strong></td>
<td>&lt; 7.3</td>
<td>&lt; 7.3</td>
<td>&gt; 7.3</td>
</tr>
<tr>
<td><strong>Serum bicarbonate (mmol/l)</strong></td>
<td>&lt; 18</td>
<td>&lt; 18</td>
<td>&gt; 15</td>
</tr>
<tr>
<td><strong>Plasma Ketones</strong></td>
<td>+++</td>
<td>+/-/+++</td>
<td>Negative</td>
</tr>
<tr>
<td><strong>Urine Ketones</strong></td>
<td>++/++++</td>
<td>++ +++</td>
<td>Negative</td>
</tr>
<tr>
<td><strong>Effective Serum Osmolality (mOsm/kg)</strong></td>
<td>variable</td>
<td>&gt;320</td>
<td>&gt; 320</td>
</tr>
<tr>
<td><strong>Anion Gap</strong></td>
<td>&gt; 10</td>
<td>&gt; 10</td>
<td>&lt;12</td>
</tr>
<tr>
<td><strong>Conscious level</strong></td>
<td>variable</td>
<td>confusion</td>
<td>depressed/coma</td>
</tr>
</tbody>
</table>
DKA

- Hospital admissions - constant (7,500 - 8,500 per year).

- Children, 40% new diagnosis present with DKA
  - younger age increases this risk.

- Women x2 more likely as men to be admitted

- Most have Type 1 DM

- Recurrent DKA accounts for 15% of cases
  - more common in patients who are socially deprived, poorly educated or those with learning difficulties
Management of Diabetic Ketoacidosis

Insulin

Suggested regimen
- NaCl 0.9% initially
- 11 in 1 hour
- 11 in 2 hours
- 11 in 4 hours
- 11 in 6 hours

This should be varied according to clinical need. Colloids may be used initially as required.

Severe dehydration
- Assess volume status of patient
- IV Fluids

Mild Dehydration
- In patients with less severe DKA, rehydration with NaCl 0.9% at 500 ml/h for 4 hours, followed by 250 ml/h for 4 hours, then fluids as required, may be sufficient.

Continuous infusion
- Soluble insulin 6–10 units
- (50 units of soluble insulin in 50 ml 0.9% NaCl to give 1 unit per ml)
- Begin infusion at 0.1 unit/kg/hr
- Aim to decrease glucose by 3–5 mmol/l/h
- If glucose does not decrease by 3 mmol/l, increase insulin by 0.1 unit/kg/hr, up to 3 units.
- Maintain insulin infusion at 0.1 unit/kg/hr until ketones are cleared.
- 5% glucose may be required as the hyperglycaemia is corrected.
- Aim to maintain glucose 8–11 mmol/l until DKA resolved.

Intravenous Bolus
- Soluble insulin 6–10 units

Potassium

Check K+ on admission
- Aim for K+ 4.5–5.5 mmol/l
- Withhold K+ if patient is anuric or if K+ > 5.5 mmol/l, continue to check every 2 hours

If K+ < 4 mmol/l, replace 40 mmol/l NaCl 0.9%
- 5 units/kg of body weight

Bicarbonate:
- No clear indication for using NaHCO3 to correct pH. May be used (100 ml 8.4% NaHCO3) if pH < 6.9 and impending respiratory or cardiac or respiratory collapse. Monitor potassium and calcium carefully. Replacement has not been shown to counter a benefit but may be indicated in severe respiratory hypophosphataemia (phosphate < 0.33 mmol/l) or in patients with anaemia, cardiac dysfunction or respiratory failure. Care must be taken to avoid hyperkalaemia.

Phosphate:
- Patients with DKA have a phosphate deficit. Replacement has not been shown to counter a benefit but may be indicated in severe hypophosphataemia (phosphate < 0.33 mmol/l) or in patients with anaemia, cardiac dysfunction or respiratory failure. Care must be taken to avoid hyperkalaemia.
Change in emphasis

- Routine used of ketometers
- **Ketones** end markers, not glucose

Joint British Diabetes Societies in-patient care group recommendations 2013:
Management of DKA

- **Key Features**
  - Reduction of blood ketone concentration by 0.5 mmol/h
  - Increase venous bicarbonate concentration by 3 mmol/L/h
  - Reduce capillary blood glucose by 3.0 mmol/L/h
  - No bolus dose of insulin
  - Maintain Potassium at 4.0 – 5.5 mmol/L

<table>
<thead>
<tr>
<th>WEIGHT in KG</th>
<th>INSULIN DOSE PER HOUR (Units)</th>
</tr>
</thead>
<tbody>
<tr>
<td>60-69</td>
<td>6</td>
</tr>
<tr>
<td>70-79</td>
<td>7</td>
</tr>
<tr>
<td>80-89</td>
<td>8</td>
</tr>
<tr>
<td>90-99</td>
<td>9</td>
</tr>
<tr>
<td>100-109</td>
<td>10</td>
</tr>
<tr>
<td>110-119</td>
<td>11</td>
</tr>
<tr>
<td>120-130</td>
<td>12</td>
</tr>
<tr>
<td>130-139</td>
<td>13</td>
</tr>
<tr>
<td>140-150</td>
<td>14</td>
</tr>
<tr>
<td>&gt;150</td>
<td>15 (any dose higher than this should be on the advice of the Diabetes Specialist Team)</td>
</tr>
</tbody>
</table>

Fixed rate insulin infusion (FRIII) based on 0.1units/kg/h
Continue patient’s normal subcutaneous insulin regimen
Increase the insulin infusion rate according to Ketone response or if no ketometer available, bicarbonate concentration.

*Joint British Diabetes Societies in-patient care group recommendations 2013:*
# Fluid management in DKA

<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

*Potassium chloride may be required if more than 1 litre of sodium chloride has been given already to resuscitate hypotensive patients

Caution in children and young adults
Death from DKA

• Mortality should be < 5%
  ▫ majority of deaths occur amongst the elderly or patients with significant co-morbidities and intercurrent illnesses.

• In children, DKA itself remains a common cause of death
  ▫ 0.15 – 0.3% of children with DKA dying
  ▫ Cerebral Oedema
## HHS and mixed presentations

<table>
<thead>
<tr>
<th></th>
<th>DKA</th>
<th>DKA/HHS Mixed</th>
<th>HHS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Plasma Glucose (mmol/l)</strong></td>
<td>≥ 14.0 &lt; 33</td>
<td></td>
<td>≥ 33</td>
</tr>
<tr>
<td><strong>Arterial pH</strong></td>
<td>&lt; 7.3</td>
<td>&lt; 7.3</td>
<td>&gt; 7.3</td>
</tr>
<tr>
<td><strong>Serum bicarbonate (mmol/l)</strong></td>
<td>&lt; 18</td>
<td>&lt; 18</td>
<td>&gt; 15</td>
</tr>
<tr>
<td><strong>Plasma Ketones</strong></td>
<td>+++</td>
<td>+/+++</td>
<td>Negative</td>
</tr>
<tr>
<td><strong>Urine Ketones</strong></td>
<td>++/+++</td>
<td>+++/+ +++</td>
<td>Negative</td>
</tr>
<tr>
<td><strong>Effective Serum Osmolality (mOsm/kg)</strong></td>
<td>variable</td>
<td>&gt;320</td>
<td>&gt; 320</td>
</tr>
<tr>
<td><strong>Anion Gap</strong></td>
<td>&gt; 10</td>
<td>&gt; 10</td>
<td>&lt;12</td>
</tr>
<tr>
<td><strong>Conscious level</strong></td>
<td>variable</td>
<td>confusion</td>
<td>depressed/coma</td>
</tr>
</tbody>
</table>
Hyperosmolar Hyperglycaemia Syndrome (HHS)

Definition and diagnosis

A precise definition of HHS does not exist and would be inappropriate, but there are characteristic features that differentiate it from other hyperglycaemic states such as DKA. These are:

- Hypovolaemia
- Marked hyperglycaemia (30 mmol/L or more) without significant hyperketonaemia (<3 mmol/L) or acidosis (pH>7.3, bicarbonate >15 mmol/L)
- Osmolality usually 320 mosmol/kg or more

N.B. A mixed picture of HHS and DKA may occur.
HHS or HHS with Ketones

- Type 2 patients
- Tend to be older but this trend is changing...
- Risk factors
  - Ethnicity – Black patients
  - Obesity
- HHS with Ketones not new....but increasing in frequency
  - idiopathic type 1 diabetes,
  - Flatbush diabetes,
  - atypical diabetes
  - ketosis-prone type 2 diabetes
- Co-morbidities
# Insulin and Time to Presentation

<table>
<thead>
<tr>
<th></th>
<th>DKA</th>
<th>DKA/HHS Mixed</th>
<th>HHS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Plasma Glucose (mmol/l)</strong></td>
<td>≥ 14.0 &lt; 33</td>
<td>≥ 33</td>
<td>≥ 33</td>
</tr>
<tr>
<td><strong>Arterial pH</strong></td>
<td>&lt; 7.3</td>
<td>&lt; 7.3</td>
<td>&gt; 7.3</td>
</tr>
<tr>
<td><strong>Serum bicarbonate (mmol/l)</strong></td>
<td>&lt; 18</td>
<td>&lt; 18</td>
<td>&gt; 15</td>
</tr>
<tr>
<td><strong>Plasma Ketones</strong></td>
<td>+++</td>
<td>+/++</td>
<td>Negative</td>
</tr>
<tr>
<td><strong>Urine Ketones</strong></td>
<td>++/++++</td>
<td>++/++++</td>
<td>Negative</td>
</tr>
<tr>
<td><strong>Effective Serum Osmolality (mOsm/kg)</strong></td>
<td>variable</td>
<td>&gt; 320</td>
<td>&gt; 320</td>
</tr>
<tr>
<td><strong>Anion Gap</strong></td>
<td>&gt; 10</td>
<td>&gt; 10</td>
<td>&lt; 12</td>
</tr>
<tr>
<td><strong>Conscious level</strong></td>
<td>variable</td>
<td>confusion</td>
<td>depressed/coma</td>
</tr>
</tbody>
</table>
Insulin and Time to Presentation

1. Precipitating event / inadequate insulin intake
2. Failure of insulin production
3. Hyperglycaemia
4. Increased Ketones
5. Severe metabolic Acidosis / DKA
6. DKA
7. HHS
8. Peripheral insulin resistance
9. Gluconeogenesis
10. Increased:
    - Glucagon
    - Cortisol
    - Catecholamines
    - Growth hormone
11. Ketone production
12. Severe Dehydration
13. Electrolyte depletion
14. Hyperosmolality
15. Decreased glucose utilisation
16. Glycogenolysis
17. Proteolysis
18. Amino acids
19. Osmotic diuresis and natruresis
20. Glycosuria
21. Proteolysis
22. Peripheral tissues
23. Adipocytes
24. Lipolysis
25. Increased Ketones
26. Severe metabolic Acidosis / DKA
27. DKA
28. HHS
## Deficits in hyperglycaemic crises

<table>
<thead>
<tr>
<th>Deficits per kg body weight</th>
<th>DKA (Deficit for 70kg)</th>
<th>HHS (Deficit for 70kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water (ml/kg)</td>
<td>100 (7 l)</td>
<td>100 – 200 (7 – 14 l)</td>
</tr>
<tr>
<td>Na⁺ (mmol/kg)</td>
<td>7 – 10 (490 – 700)</td>
<td>5 – 13 (350 – 910)</td>
</tr>
<tr>
<td>K⁺ (mmol/kg)</td>
<td>3 – 5 (210 – 350)</td>
<td>4 – 6 (280 – 420)</td>
</tr>
<tr>
<td>Mg²⁺ (mmol/kg)</td>
<td>0.5 – 1 (35 – 70)</td>
<td>0.5 – 1 (35 – 70)</td>
</tr>
<tr>
<td>Ca²⁺ (mmol/kg)</td>
<td>0.5 – 1 (35 – 70)</td>
<td>0.5 – 1 (35 – 70)</td>
</tr>
<tr>
<td>PO₄²⁻ (mmol/kg)</td>
<td>0.5 – 1 (35 – 70)</td>
<td>0.5 – 1 (35 – 70)</td>
</tr>
</tbody>
</table>
Osmolality

- **Normal Osmolality**
  - 275–295 mosm/kg (mmol/kg)

- **Measured in the lab**
  - Takes time

- **Calculated**
  - $2\text{Na}^+ + \text{glucose} + \text{urea}$
  - $2(\text{Na}^+ + \text{K}^+) + \text{glucose} + \text{urea}$
  - $2(\text{Na}^+ + \text{K}^+) + \text{glucose}$
  - $2\text{Na}^+ + \text{glucose}$
HHS

- Sodium
  - Can be low, normal or high on presentation
  - But
    - Overall total body deficit of 5-13 mmol/kg
  - Regardless of serum sodium....these patients have a total body sodium deficit
Patient 35 yrs old, BMI > 35, African, not known to have diabetes mellitus

- In A&E
  - Confused (GCS 14/15)
  - Blood glucose 90 mmol/L
  - Sodium 115 mmol/L
  - Potassium 4.5 mmol/L
  - Osmolality 329 mosmol/L

- Young with 2+ Ketones in Urine..therefore assumed to be DKA!!!!!
Management in A&E

- Bolus of insulin bolus
- Infusion of Actrapid 6IU/h
- IL of rapid intravenous 0.9% NaCl
- 500mL/h 0.9% NaCl thereafter

- Blood glucose 20 mmol/L
- Serum sodium 145 mmol/L
- Osmolality 310 mosmol/L
- GCS 3/15

- Sudden Hypertension, bradycardia - death
Movement of Water

Dehydrated cell
Net movement of water out of cells down osmotic gradient
Glucose
H₂O
Na⁺
Insulin lack/resistance no uptake of glucose by cells
Na⁺ concentration diluted by movement of water
Build up of idiogenic osmoles within cells may include increased intracellular sodium

Hydrated cell/oedema
Net movement of water into cells down the osmotic gradient generated by idiogenic osmoles
Glucose
H₂O
Na⁺
Na⁺ concentration increased due to movement of water No change in total Na⁺

On administering insulin, glucose is rapidly taken up by cells and metabolised to glucose-6-phosphate
Na⁺ concentration increased due to movement of water No change in total Na⁺

In children with DKA

- Cerebral Oedema is the main cause of death
  - due to immature blood brain barrier (BBB)
  - Increased survival with incremental increases in Sodium
  - Unproven in adults
What Next?

BUT WHAT IF I DON'T WANT TO BE FUNDAMENTALLY TRANSFORMED...??

www.MATRICIDE.COM

CAGLE CARTOONS
The management of the hyperosmolar hyperglycaemic state (HHS) in adults with diabetes

Joint British Diabetes Societies Inpatient Care Group

August 2012
Patient 52, BMI 32 new onset DM

• Presentation
  ▫ GCS 13/15
  ▫ Na\(^+\) 124 mmol/L
  ▫ K\(^+\) 4.1 mmol/L
  ▫ Glucose 70 mmol/L
  ▫ Ketones +
  ▫ Osmolality – 326 mosmol/L
Management in A&E

- Resuscitation started, 0.9% NaCl and **no** insulin.
  - GCS 14/15
  - $\text{Na}^+ \ 155 \text{ mmol/L}$
  - Glucose 40 mmol/L
  - Osmolality – 350 mmol/L
Admit to HDU

- Calculate osmolality to monitor therapy

- An initial rise in Sodium is to expected.
  - THERE IS NO PLACE FOR HYPOTONIC FLUIDS TO CORRECT THE SODIUM
  - NaCl 0.9% will cause hyperchloremia, significance unknown

- 0.9% NaCl, maximum 3 – 6 litres in first 12 hours.
  - If anything err towards less...this took days to develop
Insulin therapy in HHS

- *Glucose levels should decrease at $\leq 5$ mmol/L/h*

  - NO INSULIN ........
  - Insulin is only indicated......if ketones persist or if correction of glucose with fluids alone stalls
  - Maintain blood glucose 10 – 15 mmol/L – Give 10% glucose to achieve this
  - Insulin at a maximum of 0.05U/kg/h when/if indicated
Management cont’d

• Allow the patient to drink free fluids when able
• Assessment of conscious level frequently
• Look for underlying precipitants
• Anticoagulation
• Feet
Thank you
RESULTS—A total of 279,937 patients experienced 302,095 hospitalizations for hyperglycemia, and 404,467 patients experienced 429,850 hospitalizations for hypoglycemia between 1999 and 2011. During this time, rates of admissions for hyperglycemia declined by 38.6% (from 114 to 70 admissions per 100,000 person-years), while admissions for hypoglycemia increased by 11.7% (from 94 to 105 admissions per 100,000 person-years). In analyses designed to account for changing diabetes mellitus prevalence, admissions for hyperglycemia and hypoglycemia declined by 55.2% and 9.5%, respectively. Trends were similar across age, sex, and racial subgroups, but hypoglycemia rates were 2-fold higher for older patients (≥75 years) when compared with younger patients (65–74 years), and admission rates for both hyperglycemia and hypoglycemia were 4-fold higher for black patients compared with white patients. The 30-day and 1-year mortality and 30-day readmission rates improved during the study period and were similar after an index hospitalization for either hyperglycemia or hypoglycemia (5.4%, 17.1%, and 15.3%, respectively, after hyperglycemia hospitalizations in 2010; 4.4%, 19.9%, and 16.3% after hypoglycemia hospitalizations).
Increased Mortality associated with Hypoglycaemia

- Type 1 and Type 2 diabetes
- Related to management of glycaemia
- Underlying cardiovascular disease
- Many episodes occur at night