Diabetic Emergencies

DG van Zyl

3 Emergency Presentations
- Hypoglycaemia
- Diabetic keto-acidosis
- Hyperglycaemic hyperosmolar state

Hypoglycaemia

Normal Blood Glucose

3.9 – 5.8 mmol/l

Incidence
- Probably the most common endocrine emergency
- Frequently occurs in diabetic patients receiving insulin treatment with tight control
- In DCCT
  - 10-30% of type 1 diabetics per year
  - Of those, 10% required 3rd party intervention

Overview of Metabolic Pathways

Muscle
↑ Proteolysis → Alanine lactate → Glucose released in circulation

Liver
↑ Glycogenolysis → Glucose

Adipose tissue
↑ Lipolysis → Glycerol
## Hormonal Responses
- ↓ Insulin
- ↑ Glucagon
- ↑ Adrenalin
- ↑ Cortisol
- ↑ Growth hormone

## Hypoglycaemia – Causes (1)
- Drugs
  - Too much insulin
  - Too much Sulphonylurea
  - Alcohol
  - Too little food
  - Exercise
- Critical illnesses
  - Hepatic, renal, or cardiac failure
  - Sepsis (including malaria)
  - Autonomic neuropathy

## Hypoglycaemia – Causes (2)
- Hormone deficiency
  - Cortisol
  - Glucagon
  - Epinephrine
- Endogenous hyperinsulinism
- Insulinoma
- Functional cell disorders (nesidioblastosis)
- Noninsulinoma pancreatogenous hypoglycaemia
- Post gastric bypass hypoglycaemia

## Symptoms Consistent With Hypoglycaemia

### Neuroglycopenic responses
- Behavioral changes
- Confusion
- Fatigue
- Seizure
- Loss of consciousness
- Death

These responses are directly due to CNS glucose deprivation

### Autonomic response
- Adrenergic symptoms
  - Palpitations
  - Tremor
  - Anxiety
- Cholinergic symptoms
  - Sweating
  - Hunger
  - Paraesthesia

## Signs of hypoglycaemia
- Pallor
- Diaphoresis
- ↑ Heart rate
- ↑ Systolic blood pressure

## Diagnosis: **Whipple’s triad**
1. Symptoms consistent with hypoglycaemia.
2. A low plasma glucose concentration.
3. Relief symptoms after plasma glucose level is raised
Classification of Hypoglycaemic Disorders (1)
A) Symptomatic fasting hypoglycaemia with hyperinsulinism
1. Insulin reaction → insulin treated diabetes
2. Sulfonylurea overdose
3. Factitious hypoglycaemia
4. Autoimmune hypoglycaemia → Aβ to insulin
5. Pentamidine induced → Used for pneumocystis
6. Pancreatic β-cell tumours → insulinoma

Classification of Hypoglycaemic Disorders (2)
B) Symptomatic fasting hypoglycaemia without hyperinsulinism
1. Ethanol induced
2. Liver disease with low hepatic glucose output
3. Non-pancreatic tumours
   - Utilization of glucose by large tumours
   - Production of IGF-2 by tumour → insulin receptor

Classification of Hypoglycaemic Disorders (3)
C) Nonfasting hypoglycaemia
1. Postgastrectomy
   → Rapid gastric emptying ↑ vagal stimulation with ↑ in GIP release
2. Post gastric bypass
3. Late hypoglycaemia → Reactive hypoglycaemia
   - Occult diabetes
   - Delayed insulin release → Hyperglycaemia → Exaggerated / reactive insulin response

Insulinoma
- Insulin producing tumour of the pancreatic β-cell
  - 80% of these tumours are single and benign
  - 10% malignant
  - 10% multiple micro and macroadenomas
  - Inability of insulinoma cells to suppress insulin secretion during low glucose states
  - Leading to severe hypoglycaemia

Insulinoma: Diagnosis
- Blood glucose < 2.5mmol/L, with concommittant insulin level > 6μU/mL
- Confirm diagnosis with prolonged fast, up to 72 hours
  - P-glucose ↓
  - S- insulin and c-peptide ↑
- Localization can be problematic
  - Endoscopic ultrasonography / CT / MRI / Ocreotide scan
  - Selective angiography and venous sampling, with calcium stimulation
Insulinoma: Treatment

- Emergency hypoglycaemic treatment
- Surgical resection
- Medical therapy if patient inoperable
  - Diazoxide
  - Ocreotide
- 10% 20 year occurrence

Hypoglycaemia in Diabetes

- Mostly in diabetic patients on treatment attempting to reach normal or near normal blood glucose
- Most commonly in type 1 diabetic patients on Insulin, although it does occur in type 2 diabetic patients on insulin or sulphonylureas

Problem: Hypoglycaemia unawareness

Hypoglycaemic Unawareness

- Repeated episodes of hypoglycaemia → blunted response of the sympathetic nervous system to hypoglycaemia with absence of symptoms
- This can be improved by relaxing strict glucose control for a few weeks

Prevention

- Patient education
- Hypoglycaemia causes harm
- Carry glucose
- Diabetic card may help others to help them

Any person with diabetes treated with sulphonylureas or insulin who behaves oddly in any way whatsoever is hypoglycemic until proven otherwise

Emergency Treatment

Remember ABC’s in unconscious patients!

- A = Airway
- B = Breathing
- C = Circulation
- D = Drugs

Emergency treatment

1. Dextrose 50%: 50ml bolus – Orally/IV Followed by 10% glucose infusion
2. Glucagon: Especially useful if IV access is problematic 1 – 2 mg IV/IM/SC Ineffective during states of starvation
Diabetic keto-acidosis

**Background:**

- **Diabetic Ketoacidosis**
  - State of uncontrolled catabolism associated with insulin deficiency
  - Results from:
    - Grossly deficient insulin availability
    - Increase in counter regulatory hormones such as glucagon, cortisol, catecholamines and growth hormone

**Diagnostic Criteria**

- Blood glucose: > 13.9 mmol/l
- pH: < 7.3
- S Bicarbonate: < 15 mmol/l
- U Ketones: > 3+ (Nitroprusside reaction method)
- S Ketones: Positive at 1:2 dilutions
- S Osmol: Variable

**Diagnostic criteria for DKA**

<table>
<thead>
<tr>
<th></th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma glucose (mmol/L)</td>
<td>&gt;13.9</td>
<td>&gt;13.9</td>
<td>&gt;13.9</td>
</tr>
<tr>
<td>Arterial pH</td>
<td>7.25-7.30</td>
<td>7.00-7.24</td>
<td>&lt;7.00</td>
</tr>
<tr>
<td>Serum bicarbonate (mmol/L)</td>
<td>15-18</td>
<td>10-14</td>
<td>&lt;10</td>
</tr>
<tr>
<td>Urine ketones</td>
<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>Serum ketones</td>
<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>Anion gap</td>
<td>&gt;10</td>
<td>&gt;12</td>
<td>&gt;12</td>
</tr>
<tr>
<td>Alteration in sensorium</td>
<td>Alert</td>
<td>Alert/ Stupor/</td>
<td>Coma</td>
</tr>
</tbody>
</table>

**Pathogenesis: Alterations in metabolism**

Caused by:
- Ineffectiveness/ absence of insulin
- Elevations in glucagon, catecholamines & cortisol

Effects of insulin deficiency:
- Alterations in metabolism
  - Carbohydrates, proteins and lipids affected
  - Fluid and electrolytes
  - Hepatic gluconeogenesis, glycogenolysis, and lipolysis are affected
  - Fat, liver and muscle can survive without glucose
  - Brain must maintain use of glucose for starvation
Insulin

\[ \text{Insulin} \rightarrow \downarrow \text{Cell glucose uptake} \]
\[ \uparrow \text{Cell protein catabolism} \]
\[ \uparrow \text{Cell K release} \]
\[ \downarrow \text{Fatty acid oxidation} \]

Hyperglycemia

Glycosuria

Osmotic diuresis

Loss of H₂O, Na⁺, K⁺, PO₄

Typical Deficits

- Water: 6 L (100 ml/kg)
- Na⁺: 7 – 10 mmol/kg
- K⁺: 3 – 5 mmol/kg
- PO₄: ± 1 mmol/kg

Diabetic keto-acidosis

**Symptoms**
- Nausea / vomiting
- Thirst
- Polyuria
- Abdominal pain
- Shortness of breath

**Diabetic keto-acidosis**

**Signs**
- Lethargia / confusion / obtundation / coma
- Tachycardia / hypotension
- Dehydration / dry mucous membranes
- Tachypnoea / Kussmaul breathing
- Abdominal tenderness

**DKA**

With progressive dehydration, acidosis, hyperosmolality, and diminished cerebral oxygen utilization, consciousness becomes impaired, and the patient ultimately becomes comatose.

**Laboratory findings:**

- Diagnosis dependent on
  - Hyperglycemia
  - Ketonuria
  - Acidosis
  - Leucocytosis is common
  - S- Amylase may be elevated
Differential diagnosis:
Differentiate from acidosis and coma due to other causes:
- hypoglycemia
- uremia
- gastroenteritis with metabolic acidosis
- lactic acidosis
- salicylate intoxication
- encephalitis

Precipitating factors
- Infection 40%
- Omission/inadequate insulin 25%
- Initial presentation of DM 15%
- Other medical/surgical illness (CVA / AMI / Pancreatitis / GIT Bleeds / Trauma) 15%
- Unknown 5%

Management goals
- High care / ICU
- Insulin
- Water and Sodium replacement
- Potassium replacement
- Correction of acidosis
- Phosphate and Magnesium replacement
- Monitoring
- Post hyperglycemic care

Insulin
Initial IV bolus of 0.15 U regular insulin per kg (± 10-12 U)
Continuous infusion of regular insulin 0.1 U/kg/h (5-8 U/h)

- 20 U Actrapid in 200 ml saline
- or
- 50 U Actrapid in 500 ml saline

Insulin Adjustment
THEN
Adjust insulin infusion rate based on blood glucose 2 hrly
- <5.6 mmol/l - ↓ by 10 ml/h and give 25 ml 5%DW
- 5.6 – 8.9 mmol/l - ↓ by 10 ml/h
- 9 – 12.2 mmol/l - no change
- 12.3 – 15.6 mmol/l - ↑ 10 ml/h
- >15.6 mmol/l - ↑ 10 ml/h and add 8 U Actrapid bolus
**Water and Sodium Replacement**

<table>
<thead>
<tr>
<th>S Na⁺ (mmol/l)</th>
<th>Infusion solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 165</td>
<td>2,5% DW</td>
</tr>
<tr>
<td>145 – 165</td>
<td>0,45% NaCl</td>
</tr>
<tr>
<td>&lt; 145</td>
<td>0,9% NaCl</td>
</tr>
</tbody>
</table>

- Fluid deficit = \[0.6 \times \text{kg} \times (\text{SNa}/140)\] – \[0.6 \times \text{kg}\]
- Average deficit for:
  - DKA is 4 – 6 L
  - HHS is 8 – 10 L

**Infusion rate**

1. **1st hour**: - 1 L
2. **2nd – 7th hour**: - 0,5L/h
3. **After 8th hour**: - 0,2 L/h

**Water and Sodium Replacement**

Infusion rate in patients with cardiac failure or older than 65 years according to CVP

<table>
<thead>
<tr>
<th>CVP (cm H₂O)</th>
<th>Infusion rate (l/h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 3</td>
<td>1</td>
</tr>
<tr>
<td>3 – 8</td>
<td>0,5 – 1</td>
</tr>
<tr>
<td>9 – 12</td>
<td>0,5</td>
</tr>
<tr>
<td>&gt;12</td>
<td>0,25</td>
</tr>
</tbody>
</table>

**Potassium**

<table>
<thead>
<tr>
<th>S-K⁺ (mmol/L)</th>
<th>Amount of K⁺ (mmol/h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;5.0 mmol/l</td>
<td>No K⁺, check K⁺ in 2h</td>
</tr>
<tr>
<td>3.0 – 5.0 mmol/l</td>
<td>Add 20 mmol in each litre of fluid administered</td>
</tr>
<tr>
<td>&lt; 3 mmol/l</td>
<td>Add 40 mmol/l to initial fluid, withhold insulin until K⁺ &gt; 3.0 mmol/l</td>
</tr>
</tbody>
</table>

**Correction of Acidosis**

- Only in DKA if pH < 7.0
- If pH 6.9–7
  - Bicarbonate 50 mmol in 200 ml
  - 0.45% saline over 1h
- If pH < 6.9
  - Bicarbonate 100 mmol in 200 ml
  - 0.45% saline over 1h
- Repeat 2 hrly till pH >7.0

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Phosphate and Magnesium

- If s-PO₄<sub>-</sub> < 0.5 mmol/l
  - Oral phosphate solution 15 ml 8 hrly
- If s-Mg<sup>++</sup> < 0.6 mmol/l
  - Infuse 20 – 40 mmol MgSO₄ over 8h

Monitoring of serum parameters

- Capillary blood glucose:
  → 1 hly, till BG<14 mmol/l, then 2 hourly
- Na⁺, K⁺, urea, pH, u ketones:
  → 2 hly for first 12 hrs, then 4 hourly
- PO₄<sub>-</sub>, Mg<sup>++</sup>:
  → 6 – 12 hly
- U- output, BP and heart rate:
  → 4 hly for at least the first 12 hrs
- CVP:
  → 1hrly for first 12 hrs

Other:

- Urine MCS
- Blood cultures if pyrexial
- CXR
- ECG
- NG tube if comatose
- Subcut heparin
- U - catheter

Treatment after blood glucose decreased below 14 mmol/l

- Continue with Insulin infusion until ketone free
- Change IV fluids to 5% Dextrose, rate as above

Resolution of DKA:

- With correct regimen, DKA usually is usually fully corrected in 36 to 48 hours
- Criteria for resolution:
  - serum bicarbonate > 18 mmol/L
  - venous pH > 7.30
  - glucose level <11 mmol/l

American Diabetic Association

As Soon As Ketone Free

- Injection of subcutaneous insulin
  - 0.6 – 0.7 U/kg/day (for new diabetic patient)
- Previous insulin regimen for previously diagnosed diabetic patients
- Monitor blood glucose 4 hly
- Patient must be able to eat
Complications of DKA

- Cerebral edema
- ARDS
- Thrombo-embolic events due to hypercoagulable state
- Hypokalaemia
- Myocardial infarction
- Acute gastric dilatation
- Late hypoglycemia
- Erosive gastritis
- Hypophosphatemia
- Mucor mycosis

Prognosis

- DKA accounts for 14% of all hospital admissions for diabetes and for 16% of diabetic related fatalities
- Overall mortality is about 2%

Beware:
Patients with DKA and pneumonia are unable to compensate for metabolic acidosis and are at high risk of dying – admit to ICU

Hyperglycaemic Hyperosmolar State (HHS)

Previously: Hyperosmolar Non-Ketotic Coma (HONC)

Diagnostic Criteria

- Blood glucose > 33 mmol/L
- Osmolarity > 320 mOsmol/L
- Arterial pH > 7.3
- $\text{S} \text{ bicarbonate} > 15 \text{ mmol/L}$
- Urinary Ketones <2+

Pathophysiology

- Concomitant disease
- Osmotic diuresis and shift with intracellular dehydration
- Exact reason for not developing ketosis is not known

Precipitating Factors

- Preceding illness that result in several days of dehydration
- Oral hydration is usually impaired by concurrent illness or chronic co morbidity (dementia, immobility, vomiting)
- Pneumonia and UTI is the most common concurrent illness
Treatment

- Treatment is the same as for DKA although fluid resuscitation should be more aggressive

- First hour: 1.5 L of 0.9% saline
- h 2 and 3: 1L of 0.9% saline
- h 4 onwards: 0.5 – 0.75L of 0.45% saline

Complications

- Same as for DKA
- A wide variety of neurological complications may be present, this can be focal or global

Prognosis

- Mortality of HHS is high even in the best hands between 10 and 20%
- Early recognition and aggressive therapy is essential
- Do not neglect the precipitating illness

Conclusion

- All acute diabetes complications are potentially lethal and the urgency of treatment should not be underestimated
- All patients should know about these complications and should be instructed to seek help early

Thank you