INTERNÍ KLINIKA
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Acute diabetic complications
Diff.dg.of hypoglycaemia

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DIABETIC KETOACIDOSIS (DKA)

Diabetic ketoacidosis (DKA)

- A potentially life-threatening complication, typically in DM1 patients
- DKA results from an absolute shortage of insulin → burning fatty acids and production acidic ketone bodies → symptoms, complications
  - First described in 1886 and, until the introduction of insulin therapy in the 1920s, it was almost universally fatal
  - Still a mortality rate 3-4% (varies between centres)

DKA

- The first symptom of previously undiagnosed diabetes
- In known diabetics for a variety of reasons:
  - Poor compliance with insulin therapy
  - Intercurrent illness
  - Recreational drugs, eating disorder
  - 30-40% cases ???

The cardinal biochemical features

- Hyperketonaemia – glucose and ketones in urine; fingerprick blood ketones > 3 mmol/l
- Metabolic acidosis – pH < 7.3;
  bicarbonate < 15 mmol/l
- Hyperglycaemia > 11 mmol/l

Mechanism

- Absolute lack of insulin + corresponding excess of glucagon →
  - ↑ release of glucose by the liver (from glycogen through gluconeogenesis) + renal gluconeogenesis
  - ↑ Catabolic hormones, fatty acids → tissue insulin resistance
- Osmotic diuresis (glucose + Na, K)

⇒ Significant dehydratation

Mechanism (2)

- FFA (Free Fatty Acids) – the principal substrate for hepatic ketogenesis
- In DKA, the hormonal imbalance favours entry of FFA into mitochondria and the preferential formation of ketone bodies
  - Acetoacetate (acetone is formed by the spontaneous decarboxylation of acetoacetate, does not contribute to metabolic acidosis)
  - 3-hydroxybutyrate
    - An energy source for the brain

Mechanism (3)

- The body initially buffers this with the bicarbonate buffering system, but this is quickly overwhelmed

  $\rightarrow$ other mechanisms (hyperventilation) compensate

- Ketones participate as well in osmotic diuresis, further Na, K loss.

$\Rightarrow$ A total body water shortage of about 6 l (100 ml/kg) + substantial losses of Na, K, Cl, phosphate, Mg, Ca

Prevention

- „Sick day rules“

Signs and symptoms

- The symptoms usually evolve over the period of about 24 hours.
- Nausea, vomiting
- Pronounced thirst
- Excessive urine production
- Abdominal pain (particularly in the young)
- In severe DKA – Kussmaul respiration
  - Confusion, letargy, stupor, even coma

Physical examination

- Dehydratation
  - If profound → ↓ in the circulating blood volume → tachycardia, low blood pressure
- A ketotic odour – „fruity“, like the smell of pear drops
- ↑ respiratory rate (if Kussmaul respiration present)
- The abdomen may be tender
- (Non-specifially ↑ serum transaminases, creatine phosphokinase)

Initial management

DKA – stages of severity according to ADA (2006, for adults)

- Mild
  - pH: 7.25-7.3, serum bicarbonate 15-18 mmol/l,
    the patient is alert
- Moderate
  - pH: 7.0-7.25, serum bicarbonate 10-15 mmol/l, mild drowsiness
- Severe
  - pH below 7.0, bicarbonate below 10 mmol/l, stupor or coma may occur

Anion gap

- DKA usually presents with an anion gap acidosis (typically 25-35 mmol/l):

  sodium – (chloride+bicarbonate) > 15 mmol/l

Causes of anion gap acidosis

- Ketoacidosis
  - Diabetic
  - Alcoholic
- Lactic acidosis
- Chronic renal failure
- Drug toxicity
  - Methanol (metabolized to formic acid)
  - Ethylene glycol (to oxalic acid)
  - Severe salicylate poisoning

Management

The main aims in the treatment of DKA

replaicing the lost of fluids and electrolytes while suppressing hyperglycaemia and ketone production with insulin.

Management (2)

- Regular checking of many parameters
- ICU may be necessary
  - A urinary catheter if oliguric
  - A cardiac monitor if hyperkalaemia
  - A nasogastric tube if a reduced consciousness

Average electrolyte def.in adults with DKA

Electrolyte	Deficit (mmol)
Sodium	500
Chloride	350
Potassium	300 - 1000
Calcium	50 – 100
Phosphate	50 – 100
Magnesium	25 - 50

Acidosis + insulin deficiency + renal impairment → plasma potassium levels usually N/high at presentation

However – potassium concentration will fall during treatment (insulin → redistributing potassium into cells).

Initial fluid replacement

Fluid	Rate (ml/hr)	Time (hrs)
0.9% NaCl	1000	1
0.9% NaCl + KCl	500	2
0.9% NaCl + KCl	500	2
0.9% NaCl + KCl	250	4
0.9% NaCl + KCl	250	4
0.9% NaCl + KCl	250	4
0.9% NaCl + KCl	125	8
Total	7 l	25

Insulin

Guidelines bias but

1. The potassium level must be known.
2. Start with fluids and after 1 hr insulin to reduce the risk of cerebral oedema
3. 0.1 IU/kg bolus (6 IU/hr and later switch to 3 IU/hr)
4. Bellow 14 mmol/l (glycaemia) start glucose/K/insulin infusion
5. Transfer to insulin s.c.

Varia

- The most dangerous complication of DKA is cerebral oedema.
- Bicarbonate???
- During treatment of DKA - ↑ 3-hydroxybutyrate → acetoacetate (cave nitroprusside-based urine tests)
- Re-education, specific groups – eldery patient, adolescents…

HYPEROSMOLAR HYPERGLYCAEMIC SYNDROME

HHState (ADA)

- DM2, much less common than DKA, a much higher mortality rate

- Hyperglycaemia, often > 50 mmol/l
- Profound dehydratation (serum osmolarity > 350 mOsmol/l)+ pre-renal uremia
- ↓ Consciousness

- Lipolysis suppressed
- HHS usually precipitated by acute illness…
- The absence of vomiting
- Neurological signs, including focal signs

- Total body sodium reduced, plasma concentration at presentation N/low/high

- Isotonic saline is preferred.
- Thromboembolic complications, subsequent antidiabetic treatment

LACTIC ACIDOSIS

- Lactate > 5 mmol/l + serum pH < 7.35

- Raised lactate levels are indicative of tissue hypoxia, hypoperfusion and possible damage.

- If the oxygen supply inadequate, the mitochondria are unable to continue ATP synthesis at a rate sufficient to supply the cell with reguired ATP → glycolysis is increased to provide additional ATP, and the excess pyruvate

  → lactate

- But binding protons resulting from ATP hydrolysis → proton concentration rises and causes an acidosis

- Lactate is a good marker of hypoxia, but itself is not the cause of the low pH

Signs

- Deep and rapid breathing
- Vomiting
- Abdominal pain

The Cohen-Woods classification

- Type A: decreased perfusion or oxygenation
- Type B:
  - B1 – underlying diseases (sometimes causing type A)
  - B2 – medication/intoxication
  - B3 – inborn error of metabolism

- Hyperlactataemia in DKA (10-15%)

- Biguanides
  - Phenformin

- The generally poor prognosis (an exception after generalized epileptic convulsions) due to usually serious cause of MA

- Bicarbonate ???

HYPOGLYCAEMIA

Causes

- In DM patients
  - Insulin
  - Insulin secretagogues

Symptoms and signs

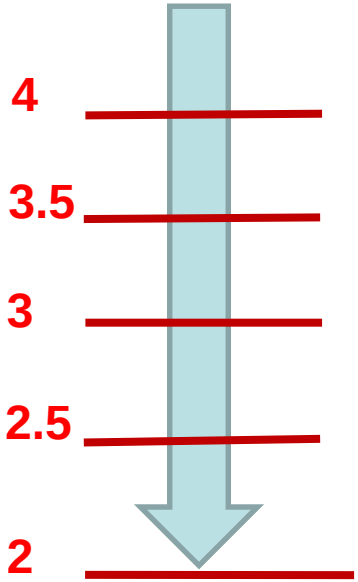
- Autonomic (adrenergic): tremor, sweating, anxiety…
  - Earlier than the level at which cerebral function becomes impaired
- Neuroglycopenia (below 2.7 mmol/l)
- Non-specific: hunger, weakness, blurred vision

Clinically hypogl.may be graded:

- Grade 1 – Biochemically confirmed but the absence of symptoms
- Grade 2 – Mild symptomatic – succesfully treated by the patient
- Grade 3 – Severe – asssistance required
- Grade 4 – very severe → coma/convulsions

Hierarchy of hormonal response to acute hypoglycaemia

Blood glucose (mmol/l)



↓Insulin
↑Glucagon, Adrenaline. Growth hormone, Cortisol

Warning symptoms
↓ Cognitive function
↑ Brain blood flow

EEG changes
Coma/convulsions

Tresholds ← factors
such as antecedent hypogl.

- Failure of counter-regulatory hormone responses predisposes to severe recurrent hypoglycaemia.

- Hypoglycaemia unawareness
  - Long-standing DM1
  - Who attempt to maintain glucose levels close to normal range.

  - **Alcohol!!!**
  - Beta-blockers

- Driving
- Nocturnal hypoglycaemia
  - „Dead in bed syndrome“

CGM (Continuous Glucose Monitoring)

Treatment and prevetion

- Grade 1 – 2 : 15-20 g of carbs (glucose bonbons etc.)
- Grade 3 – 4
  - Glucagen Hypokit