

Clinical Cases in Biochemistry: Electrolytes

Case number 1: Mr D, a 55-year-old diabetic arrived at A+E, in a severely inebriated state suffering from reduced consciousness.

Creatinine: 92 µmol/L (62 – 106),
Urea: 4,4 mmol/L (2.8 – 8.3),
Na: 143 mmol/L (136 – 146),
K: 4,1 mmol/L (3.5 – 4.5),
Cl: 96 mmol/L (98 – 107),
CO2 total: 10 mmol/L (24 – 32),
Anion gap: + 22 mmol/L (0 – 5),
Ethanol: 1.24 g/l.

The anion gap corresponds to non-quantified anions (phosphate and lactate). It is estimated using several formulae:
 Anion gap = (Na + K) – (CO2 level + proteins/4).

This patient appeared to present with metabolic acidosis (low CO2 level) and high anion gap. What could the aetiology be? What additional studies could be done?

DAs a first step, blood gas analysis is useful to confirm our hypothesis. Two hours following admission:

pH: 7.35 (7.35 – 7.45)
pCO2: 13.8 mm Hg (35 – 45)
pO2: 99,3 mm Hg (80 – 100)
HCO3-: 7.5 mmol/L (20 – 28)
Lactate: 3.8 mmol/L (0.5 – 2.2)
Glucose: 4.4 mmol/L (3.9 – 6.1).

This assessment confirms metabolic acidosis with efficient respiratory compensation due to hyperventilation: hypocapnia, pH normal.

What is the aetiology of the acidosis: diabetes? Negative, as blood sugar levels are normal. Lactic acid? Negative, lactate levels are slightly raised but this alone cannot explain the drop in bicarbonates. Related to kidney failure? Negative, as the creatinine level is normal.

What additional tests can be suggested?

Osmolality.

Measured osmolality: 360 mOsm/kg (295 – 305)

Calculated osmolality: 330 mOsm/L (295 – 305)

Osmolal gap (OG): 30 mOsm/kg (< 10).

Reminder about osmolality and the OG concept

Osmolarity = The sum of molar concentrations of osmotically active substances.

$c \text{ Osmo (calculated)} = (\text{Na} + \text{K}) \times 2 + (\text{urea} + \text{glucose})$.

Here $c \text{ Osmo} = 303 \text{ mOsm/L}$. N.B., you need to take into account blood ethanol levels: 1 g/L of ethanol is equivalent to 22 mOsm/L. From this $c \text{ Osmo} = 303 + (1.24 \times 22) = 330 \text{ mOsm/L}$.

$\text{OG} = m \text{ Osmo (measured)} - c \text{ Osmo}$

$\text{OG} = 360 - 330 = 30 \text{ mOsm/L}$.

m Osmo = osmolality measured by cryoscopy (measurement of the lowering of the freezing point) on an automated osmometer. In the case of an elevated OG, it could indicate a toxicological hypothesis (alcohol, glycols, acetone, salicylates etc.).

Our patient presented with metabolic acidosis, an elevated anion gap and an elevated OG. The pathologist called the accident and emergency doctor to discuss a toxicological hypothesis: from methanol? Ethylene glycol? Meanwhile, the condition of the patient worsened; the patient was transferred to intensive care. Toxicology investigations were delayed for 24 hours. The results were:

Methanol: 0.12 g/L (severe intoxication is from 0.1 g/L); Glycol Ethylene: None.

Methanol Poisoning: rare but serious

It is often accidental, secondary to the absorption of adulterated alcohol (e.g. home brewed alcohol). This is a cause to consider when faced with metabolic acidosis with a raised AG value, when accompanied with lactic acid levels that are normal or slightly raised and normal glucose and creatinine levels. In this case, you need to measure osmolality and calculate the OG.

The metabolism of methanol is toxically oxidative, with tropism of the nervous system and the optic nerve. The treatment relies on competitive inhibition of alcohol dehydrogenase to slow the metabolism of methanol and promote urinary and pulmonary elimination in its native form; to achieve this, ethanolismia must be maintained > 1 g/L. The alternative is to administer an antidote, 4-methyl pyrazole, however this is not necessarily available in an emergency.

In our case, the patient consultation did not contribute to the case (significant neurological symptoms and an uncooperative patient). It was not possible to ascertain any clinical ocular sign that are strongly indicative of methanol intoxication; the specific management of the intoxication was delayed for 24 hours and the patient was very weak (chronic alcohol intoxication). He died on Day 3.

Case number 2: Mr G., 61 years old, arrived at A+E suffering from episodes of confusion occurring over several weeks.

Creatinine : 84 µmol/L (62 – 106),
Urea : 4.5 mmol/L (2.8 – 8.3),
Na : 113 mmol/L (136 – 146),
K : 3.6 mmol/L (3.5 – 4.5).
Cl : 69 mmol/L (98 – 107),

Cl: 69 mmol/L (98 – 107),
 Total CO₂: 28 mmol/L (24 – 32),
 Anion gap: 0.9 mmol/L (0 – 5).
 Plasma appearance: normal.

What additional tests could be suggested to the doctor?

- A. Blood alcohol levels
- B. Blood osmolality
- C. Lipase
- D. Urinary electrolytes
- E. Glucose

Answer: B and E.

The results were:

- **Glucose:** 6.8 mmol/L (3.9 – 6.1),
- **Osmolality:** 245 mOsm/kg (295 – 305).

Mr G therefore had a severe hyponatremia with hypo-osmolality ("true" hyponatremia). He presented with logical neurological clinical symptoms related to cerebral oedema (intracellular hyperhydration): disorientation and disturbed vigilance etc. The other associated clinical symptoms were nausea, vomiting, muscle weakness and headaches etc. A urinary electrolyte profile was carried out. This test is essential for a frequently complex aetiological diagnosis. Clinical severity is related to how quickly hyponatremia sets in rather than the concentration of Na⁺ (in cases of slow installation, the correction will also be slow).

What additional tests can be suggested to the doctor?

- A. Blood alcohol levels
- B. Blood osmolality
- C. Lipase
- D. Urinary electrolytes
- E. Glucose

Answer: B and E.

The results were:

- **Glucose:** 42.0 mmol/L (3.9 – 6.1),
- **Osmolality:** 293 mosm/kg (295 – 305).

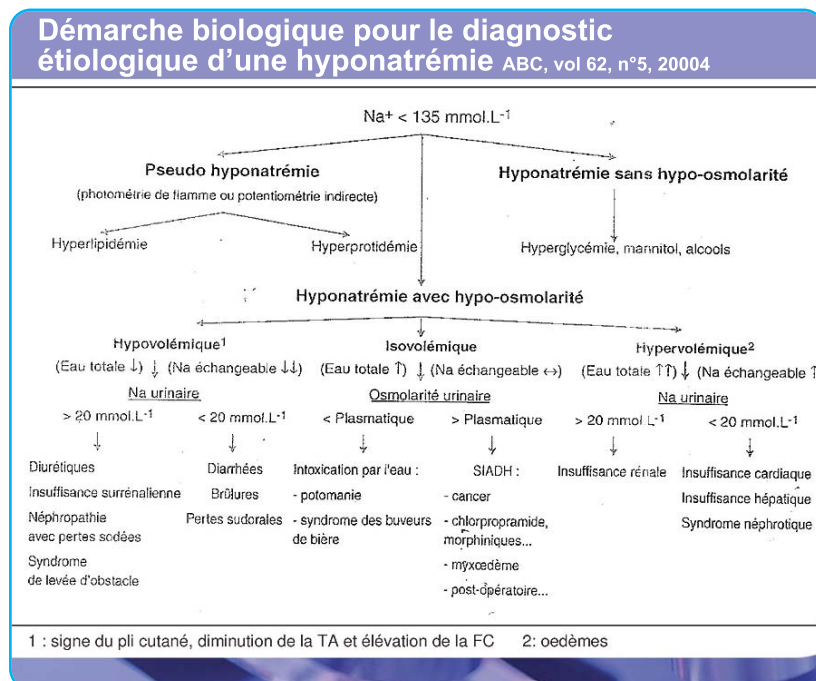
Mr D had hyponatremia without hypo-osmolality ("false" or pseudohyponatremia). It was not an electrolyte problem per se, but diabetic decompensation during infection .

On Day 1, the assessment of Mr D was as follows:

- **Na:** 136 mmol/L (136 – 146),
- **Glucose:** 6.7 mmol/L (3.9 – 6.1),
- **Osmolality:** 292 mOsm/kg (295 – 305).

The administration of Actrapid® insulin permitted correction of the hyponatremia at the same time as the hyperglycaemia. In cases of significant hyperglycaemia, the Katz formula can be useful to correct the levels of sodium in the blood:

Corrected Na = Na measured + (glucose in mmol/L x 0.3).
 In this case, Na concentration = 119 + (42 x 0.3) = 132 mmol/L.



Diagnostic tree when faced with hyponatremia:

Case number 3: Mr D, 44 years old, came to A+E experiencing episodes of confusion.

Creatinine: 79 µmol/L (62 – 106),
 Urea: 6.4 mmol/L (2.8 – 8.3),
Na: 119 mmol/L (136 – 146),
 K: 3.9 mmol/L (3.5 – 4.5),
 Cl: 74 mmol/L (98 – 107),
 Total CO₂: 31 mmol/L (24 – 32),
 Proteins: 70 g/L (63 – 83)
 Anion Gap: 0.9 mmol/L (0 – 5).

Case number 4: Mrs G., 23 years old, in the early stages of pregnancy, referred by her G.P to the Emergency Department for abdominal pains and fever.

Creatinine: 55 µmol/L (44 – 80),
 Urea: 2.3 mmol/L (2.8 – 8.3),
Na: 114 mmol/L (136 – 146),
 K: 3,2 mmol/L (3.5 – 4.5),
 Cl: 83 mmol/L (98 – 107),
 Total CO₂: 20 mmol/L (24 – 32),
 Proteins: 60 g/L (63 – 83),
 AG: 0,4 mmol/L (0 – 5),
 CRP : 142 mg/L (< 5).

What additional tests could be suggested to the doctor?

- A. Procalcitonin
- B. Blood osmolality
- C. HCG
- D. Lipase
- E. Glucose

Answer: B and E.

- **Glucose:** 7.3 mmol/L (3.9 – 6.1),
- **Osmolality:** 238 mOsm/kg (295 – 305).

This is a case of a severe hyponatremia with hypo-osmolality. Is this consistent with the clinical elements? The pathologist telephoned the ward: the patient came in for pyelonephritis and was not showing any neurological symptoms. As she was in pain, she received a perfusion of Perfalgan®. In this case, the cause was haemodilution in the perfusion liquid (relatively frequent in a hospital environment etc.).

PLEASE NOTE: All cases of hyponatremia are different! The clinical context and a thorough history and examination by the clinician are fundamental.

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