Disorders of water

Detlef Bockenhauer

Great Ormond Street Hospital for Children

NHS

NHS Trust

European Reference Network
for rare or low prevalence complex diseases

Network
Kidney Diseases (ERKNet)

UCL
How do we measure water?
How do we measure water?

- Not directly!
- Reflected best in Na concentration
- Water overload $\Rightarrow$ Hyponatraemia
- Water deficiency $\Rightarrow$ Hypernatraemia
- Dysnatraemia: is it salt? Or water?
True or false?

• The kidneys are to provide electrolyte homeostasis. Therefore, in hyponatraemia, the kidneys should preserve sodium (minimise renal sodium losses).
True or false?

• The urine sodium concentration can help distinguish between renal (cerebral/pulmonary) salt wasting and SIADH.
Hyponatraemia
Why is the sodium low?

• Too little salt
  – Weight should be decreased
  – Signs of dehydration/volume depletion

• Too much water
  – Weight should be stable or increased
  – Patient is eu- or hypervolaemic
case 1

- 6-months old boy with astrocytoma
- Receives vincristine and carboplatin
- 10 days later presents for routine follow-up
- Examination: well perfused, wt: 4.7 kg (+0.2 kg), BP: 82 mmHg

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<th>plasma</th>
<th>urine</th>
<th>unit</th>
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Is this salt wasting? Or water excess?

- Do we need to prescribe salt?
- Or do we need to restrict/eliminate water?
Clinical euvolemic or edematous
Increased body weight
Too much water

\[ U_{\text{Na}} \text{ high } \]
\[ U_{\text{osm}} < 100 \]

\[ U_{\text{Na}} \text{ Low } \]
\[ U_{\text{osm}} > P_{\text{osm}} \]

\[ U_{\text{Na}} \text{ High } \]
\[ U_{\text{osm}} = P_{\text{osm}} \]

\[ U_{\text{Na}} \text{ High } \]
\[ U_{\text{osm}} > 100 \]

Water overload

Heart failure
Nephrosis
Cirrhosis
Enteropathy
Low albumin

Diuretics
Intrinsic renal disease
PKD

SIADH
## Further course

<table>
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### Further course

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Key message

Sodium is reabsorbed to preserve intravascular volume and in response to renal perfusion.

Kidney does not sense or detect serum sodium concentration.
Case 2

- 3-months old infant referred for persistent hypertension
- Referred by endocrinology as BP>100 mmHg despite treatment with 4 antihypertensive drugs (amlodipine, propranolol, furosemide, captopril)
- Ongoing salt supplementation (7.5 mmol/kg/d) for hyponatraemia since birth
History

• Initial presentation in neonatal period with hyponatraemia and hypoglycaemia
• Brain MRI – Small anterior pituitary and ectopic posterior pituitary
• Diagnosis of panhypopituitarism
• Commenced cortisone, thyroxine and growth hormone
• Salt supplementation with subsequent hypertension
Hyponatraemia: The first critical decision

Too little salt?  Too much water?

How to decide ???
At admission (age 3 months)

- Well perfused, no oedema
- BP: 104 mmHg systolic

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<td><strong>Plasma</strong></td>
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<tr>
<td>Sodium (mmol/l)</td>
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<td><strong>Urine</strong></td>
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<td>Osmolality</td>
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Is this salt wasting? 
Or water excess?

• Do we need to prescribe salt?
• Or do we need to restrict/eliminate water?

Too little salt?  
Too much water?
Clinical euvolemic or edematous
Increased body weight
Too much water

\[ U_{Na} \text{ high} \quad U_{osm} < 100 \]

\[ U_{Na} \text{ Low} \quad U_{osm} > P_{osm} \]

\[ U_{Na} \text{ High} \quad U_{osm} = P_{osm} \]

\[ U_{Na} \text{ High} \quad U_{osm} > 100 \]

Water overload

Heart failure
Nephrosis
Cirrhosis
Enteropathy
Low albumin

Diuretics
Intrinsic renal disease
PKD

SIADH
### Admission to renal ward

- **Step 1:** Stop Sodium supplements
- **Step 2:** Fluid restriction

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<td><strong>Sodium suppl (mmol/kg/d)</strong></td>
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<td><strong>Weight (g)</strong></td>
<td>4500</td>
<td>4490</td>
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</table>

### Plasma

- Sodium (mmol/l) 130, 131
- Osmolality (mOsm/kg) 267, 268

### Urine

- Sodium (mmol/l) 99, 135
- Osmolality (mOsm/kg) 391, 579

BP normalised
All anti-hypertensives stopped
Fluid restriction in SIADH

- Often unsuccessful, as patients also have increased thirst
- Difficult in infants, as fluid and caloric input is coupled
Tolvaptan – Vasopressin 2 antagonist
Course in hospital-2

- **Step 3:** treatment with tolvaptan

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**Plasma**

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<td>130</td>
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<td>267</td>
<td>268</td>
<td>288</td>
<td>314</td>
<td>265</td>
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**Urine**

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<tr>
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<td>99</td>
<td>135</td>
<td>9</td>
<td>&lt;5</td>
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<td>Osmolality (mOsm/kg)</td>
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<td>391</td>
<td>579</td>
<td>49</td>
<td>80</td>
<td>415</td>
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Hyponatraemia-case 3

- 11-months old girl referred for assessment of hyponatraemia, first noted incidentally during investigations for viral illness and confirmed several times subsequently

- Examination: well perfused, BP: 90 mmHg

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<td>osmolalaty</td>
<td>249</td>
<td>252</td>
<td>mOsmol/kg</td>
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Diagnosis?

• Too much water?
• Too little salt?
Clinical euvolemic or edematous
Increased body weight
Too much water

- $U_{\text{Na}}$ high
  - $U_{\text{osm}} < 100$
  - Water overload

- $U_{\text{Na}}$ Low
  - $U_{\text{osm}} > P_{\text{osm}}$
  - Heart failure
  - Nephrosis
  - Cirrhosis
  - Enteropathy
  - Low albumin

- $U_{\text{Na}}$ High
  - $U_{\text{osm}} = P_{\text{osm}}$
  - Diuretics
  - Intrinsic renal disease
  - PKD

- $U_{\text{Na}}$ High
  - $U_{\text{osm}} > 100$
  - SIADH
Family History

• Mother and maternal grandmother were known to have had hyponatraemia. Maternal uncle has developmental delay and recurrent hyponatraemia (often with seizures)

• Mum and grandmother “don’t drink”
Diagnosis?

- Nephrogenic Syndrome of inappropriate antidiuresis
- X-linked inherited
- Gain-of-function in AVPR2: R137C/L
- Females usually less affected
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<td>1</td>
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<tr>
<td>P-Na [mmol/l]</td>
<td>146</td>
<td>126</td>
<td>145</td>
<td>141</td>
<td>14</td>
<td>120</td>
<td>14</td>
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<tr>
<td>P-Osm [mosmol/kg]</td>
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<td>ND</td>
<td>295</td>
<td>300</td>
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<td>P-Creatinine [mg/dl]</td>
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Treatment

• Intuitive by patients!
• ?Increased osmotic load during infancy (urea)
Hypernatraemia
Why is the sodium high?

• Too little water
  – Weight should be decreased
  – Signs of dehydration/volume depletion

• Too much salt
  – Weight should be stable or increased
  – Patient is eu- or hypervolaemic
Case 1

- 18-months old boy presents with recurrent vomiting and ?mild developmental delay.
- Previously presented multiple times to GP and A&E with vomiting, thought to be reflux, but reassured due to good urine output: wets nappies 8-10 times per day
- Seen by private GI and scoped: nl
- Examination: well, wt: 9.8 kg (2nd %ile), height 80 cm (25th %ile)
Laboratory Investigations

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<td>osmolality</td>
<td>328</td>
<td>78</td>
<td>mOsmol/kg</td>
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</table>
Further course

• DDAVP test: no response => Dx of NDI
• Brain MRI scheduled because of developmental delay
• Patient fastened prior and scan delayed: Laboratory investigation at the time: Na 179 mmol/l
• What is the appropriate treatment?
Treatment and further course

• Received 3 bolus of 20 ml/kg of 0.9% saline
• Subsequent plasma Na: 198 mmol/l
• Patient becomes unresponsive and needs intubation and ventilation
• MRI brain c/w myelinolysis
• Once extubated, he has severe paralysis, but subsequent partial recovery: able to walk again after 2 weeks
Tonicity balance

Na: $154 \times 0.6 = 92$ mmol

H$_2$O: 0.6 litre

Na: $+89$ mmol

H$_2$O: $\pm 0$

Na: $5 \times 0.6 = 3$ mmol

H$_2$O: 0.6 litre
Key messages Hyponatraemia

- Hyponatraemia is usually due to an excess in water, not a deficiency in sodium
- Kidneys do not sense or detect serum sodium
- Sodium is reabsorbed to preserve intravascular volume and in response to renal perfusion
- There is no biochemical test to distinguish salt wasting from water excess. This can only be done by clinical parameters!
Key messages Hypernatraemia

- Hypernatraemia is usually a deficiency in water, not an excess of sodium
- Beware of a dehydrated patient with ”good” urine output!
- Do not give salt to a patient with NDI!
- Sometimes, we have to use our brain, instead of following protocols
- A tonicity balance can help to understand dysnatraemias
True or false?

• The kidneys are to provide electrolyte homeostasis. Therefore, in hyponatraemia, the kidneys should preserve sodium (minimise renal sodium losses).

False
The urine sodium concentration can help distinguish between renal (cerebral/pulmonary) salt wasting and SIADH.

False