URINE ELECTROLYTES AND OSMOLALITY

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Urine electrolytes

- $\text{Na}^+$
- $\text{K}^+$
- $\text{Cl}^-$
- $\text{NH}_4^+$
- $\text{Mg}^{2+}$
- $\text{Ca}^{2+}$
- $\text{PO}_4^{2-}$
When are urine electrolytes indicated?

In the following clinical circumstances:
• Acute kidney injury
• Disorders of intravascular volume
• Hyponatremia
• Hypernatremia
• Polyuria
• Acid – base disorders
• Abnormalities of serum potassium concentration

Remember!
1. electrolyte and osmolality analysis should be done before institution of therapy
2. urine can be saved and analysed at a later time
Osmolality

Number of moles of solute per kg of solvent (water).

Urine osmolality can vary in healthy person from 80 - 1200 mOsm/kg H₂O.

Most important osmols in the urine are cations Na⁺, K⁺, NH₄⁺ with their corresponding anions and urea.

It can be calculated:

\[ U_{\text{osm}} = 2 \times (Na^+ + K^+ + NH_4^+) + (\text{urea}) + (\text{glucose}) \]

It is measured by an osmometer.

1. Freezing point osmometers
2. Vapor pressure osmometers
3. Membrane osmometers

\[ \text{Osmolality [mOsm/kg H}_2\text{O]} = \text{depression of freezing point [mK]} \div 1.858 \]
Antidiuretic hormone (ADH)

Nonosmotic influences:

- Drugs
- EFFECTIVE arterial volume
- Nausea
- Postoperative pain
- Pregnancy

High blood osmoticity
ADH action

distal tubule

urine

renal interstitium

ATP

cAMP

Protein kinase A

V₂ receptor
OSMOLALITY vs. SPECIFIC GRAVITY

• Osm: determines only number of particles
• SG: determines number of particles and their weight
• Usually they change in parallel
• SG of 1.020-1.030 → osmolality 800-1200 mOsm/kg H₂O
• SG of 1.005 → osmolality <100 mOsm/kg H₂O
• Disproportionate increase of SG if urine contains
  – glucose or proteins
  – radiocontrast material
Sodium excretion

• Filtered in the glomerulus (25.000 mmol/day)
• 1-3 % of this filtered load is excreted in the urine (FRACTIONAL EXCRETION)
• $\text{Na}^+$ determination in the urine is very suitable for differential diagnosis of AKI
• Any acute kidney injury causes $\text{Na}^+$ loss (↑ FE)
• In hypovolemia and hypoperfusion $\text{Na}^+$ is reabsorbed to a greater extent (↓ FE)
• Determination of 24-h $\text{Na}^+$ excretion is useful tool for determination of salt consumption (17 mmol $\text{Na}^+$ = 1 g salt)
Impact of hypovolemia on urine Na$^+$

- Hypovolemia
  - Renin
    - Angiotensin II
      - Aldosterone
        - Na$^+$ tubular reabsorption
          - Concentrated urine with low Na$^+$

  - ADH
Diagnosing the cause of AKI by urine Na⁺

Prerenal azotemia? or Acute tubular necrosis?

Urine Na⁺ < 20 mmol/L
↓
prerenal azotemia
(osmolality > 500 mOsm/kg)

Urine Na⁺ > 40 mmol/L
↓
acute tubular necrosis
(osmolality < 350 mOsm/kg)

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Diagnosing the cause of AKI by urine Na⁺

STATES WHEN URINE Na⁺ CAN BE MISLEADING

• Metabolic alkalosis with volume depletion (vomiting):
  Urine Na⁺ is not maximally reduced
  → obligate Na⁺ excretion with HCO₃⁻

  Urine Cl⁻ is more accurate in such conditions
  (Cl⁻ < 20 mmol/L).

• Prerenal azotemia in preexisting CKD
• Diuretic use
Fractional excretion of Na⁺

The most accurate test to distinguish prerenal AKI from ATN in oliguric AKI (24h urine < 400 ml)

**Definition:** % of filtered Na⁺ excreted in the urine

FE 1 % $\rightarrow$ 99 % of filtered Na⁺ reabsorbed, 1 % excreted in urine

\[
\text{FENa\%} = \frac{\text{urine Na}^+ \times \text{serum creatinine}}{\text{urine creatinine} \times \text{serum Na}^+} \times 100
\]

< 1%: prerenal AKI > 2 %: ATN
Pitfalls of FENa

It should allways be taken with caution. It is validated only in persons with oliguria. FENa in healthy person is allways <1%. Low in several renal conditions not associated with volume depletion:

- GN
- contrast AKI
- pigment nephropathy
- vascular diseases
- vasculitis
- liver disease

Some hypovolemic patients will not have low FENa. Value of excreted sodium is related to GFR: as GFR decreases- FENa increases.

Elderly pts and pts with CKD are not able to generate FENa <1%.
Hyponatremia

• The most abundant electrolyte disturbance, present in 15% to 30% of hospitalized patients

• Hyponatremia represents an excess of water relative to solute in the body.

• Hyponatremia usually develops as a result of the action of ADH in the kidney to diminish free water excretion.

• Most common stimuli are nonosmotic: drugs, pain, nausea, decreased effective arterial volume, strenuous exercise ...

• Rarely develops as a consequence of
  • consuming very low quantities of solute or
  • polydipsia
Hyponatremia and antidiuretic hormone

Nonosmotic ADH production

- Drugs
- ↓ effective art. volume
- Nausea
- Postoperative pain
- Pregnancy

Physiological response in hyponatremia:

U-Osm < P-Osm

Serum [Na+] 135 mmol/L \(\rightarrow\) max. suppressed ADH \(\downarrow\)
urine osmolality < 100 mOsm/kg
Urine Na\(^+\) and osmolality in hyponatremia

<table>
<thead>
<tr>
<th>Condition</th>
<th>Urine sodium (mmol/L)</th>
<th>Urine osmolality (mOsm/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>True volume depletion</td>
<td>&lt; 20</td>
<td>&gt;300</td>
</tr>
<tr>
<td>Effective circulating volume depletion</td>
<td>&lt; 20</td>
<td>&gt;300</td>
</tr>
<tr>
<td>SIADH</td>
<td>&gt; 40 if consuming regular diet</td>
<td>&gt;100-150, not maximally dilute</td>
</tr>
<tr>
<td>Volume depletion and SIADH</td>
<td>Variable, may be &lt;20 until volume depletion corrected</td>
<td>&gt;300</td>
</tr>
<tr>
<td>Water intoxication</td>
<td>Variable, may be low due to dilute urine</td>
<td>&lt;100</td>
</tr>
<tr>
<td>Low solute intake (tea and toast)</td>
<td>May be &lt;20</td>
<td>Low (less than serum osmolality)</td>
</tr>
</tbody>
</table>

Urine chemistries in hypernatremia

- Deficit of free water relative to solute.
- Inadequate free water intake because of *impaired access, impaired thirst* (in elderly patients).
- Most adult patients with hypernatremia also have concurrent volume depletion.

<table>
<thead>
<tr>
<th>Reason</th>
<th>Urine osmolality (mOsm/kg)</th>
<th>Urine sodium (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water depletion</td>
<td>&gt;600-800</td>
<td>Variable</td>
</tr>
<tr>
<td>Water and volume depletion</td>
<td>&gt;600-800</td>
<td>&lt;20</td>
</tr>
<tr>
<td>Osmotic diuresis (hyperglycemia, manitol)</td>
<td>&gt;300</td>
<td>Variable</td>
</tr>
<tr>
<td>Diabetes insipidus (central or nephrogenic)</td>
<td>&lt;300 (&lt;100 in complete nephrogenic DI)</td>
<td>Variable (depends on intake)</td>
</tr>
<tr>
<td>Salt intoxication</td>
<td>&gt;600-800</td>
<td>&gt;20 (very high)</td>
</tr>
</tbody>
</table>

# Urine chemistry in polyuria

## Water diuresis:
- Polydipsia
- Diabetes insipidus

## Solute (osmotic) diuresis:
- I.v. NaCl
- Hyperalimentation
- Hyperglycemia
- High protein intake
- Recovery from AKI

## Table: Urine osmolality and sodium levels

<table>
<thead>
<tr>
<th></th>
<th>Urine osmolality (mOsm/kg)</th>
<th>Urine sodium (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water diuresis</td>
<td>&lt; 300</td>
<td>Low (total daily excretion matches intake)</td>
</tr>
<tr>
<td>Solute diuresis</td>
<td>Usually &gt; 300</td>
<td>Variable (high if sodium diuresis)</td>
</tr>
</tbody>
</table>

Diagnosing polyuria

Water restriction test:
1. At 8.00 a.m.:
   a) Empty bladder, record the volume, and send urine osmolality
   b) Take a serum osmolality
   c) Record the patient's weight.
2. Then for the next 8 hours check:
   Urine osmolality and weight every hour
   Serum osmolality every 2 hours
Stop the test if the patient's weight decreases by more than 3% of body weight (or by 4kg) or the serum osmolality rises >300 mOsm/kg/H₂O.
3. If the urine osmolality at 4 p.m. remains <600mOsm/kg proceed with the desmopressin test.
   a) Desmopressin (DDAVP) 20 µg intranasally or 2 µg intramuscularly
   b) Can eat and drink freely
   c) Hourly urine volumes and osmolality until 8.30 p.m.

<table>
<thead>
<tr>
<th></th>
<th>Polydypsia</th>
<th>Central DI</th>
<th>Nephrogenic DI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum osmolality</td>
<td>&lt;295</td>
<td>&gt;300</td>
<td>&gt;300</td>
</tr>
<tr>
<td>(mOsm/kg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urine osmolality</td>
<td>&gt;600</td>
<td>&lt;300</td>
<td>&lt;300</td>
</tr>
<tr>
<td>(mOsm/kg)</td>
<td>(400-600 if chronic)</td>
<td>Often &lt;200</td>
<td></td>
</tr>
<tr>
<td>Post DDAVP urine osmolality</td>
<td>No or mild response</td>
<td>&gt;400-600</td>
<td>No response</td>
</tr>
</tbody>
</table>
Acid-base disorders

Kidney role in maintaining acid-base balance:
- resorption or excretion $HCO_3^-$
- secretion of $H^+$
- production of $NH_3$

Most acid-base disorders can be diagnosed and treated without measurement of urine electrolytes.

Exceptions:

1. METABOLIC ALKALOSIS
Urine $Cl^-$ more useful than urine $Na^+$ to assess volume status.
$HCO_3^-$ excreted in urine and followed by $Na^+$.
Urine $Cl^- < 20$ mmol/L suggests volume depletion.

2. NON-ANION-GAP METABOLIC ACIDOSIS
Urine electrolyte measurement in non-anion-gap metabolic acidosis to distinguish between bicarbonate loss and impaired renal acid excretion.
Urine anion-gap

\[
\text{UAG} = (\text{urine Na}^+ + \text{urine K}^+) - (\text{urine Cl}^-)
\]

\[
\text{NH}_3 + \text{H}^+ \rightarrow \text{NH}_4^+
\]

\[
\uparrow \text{NH}_4^+ \rightarrow \uparrow \text{Cl}^-
\]

In steady state UAG is positive: with a mean 41 ± 9 mmol/L.

\[
\text{NH}_4^+ = 0.8 (\text{Cl}^- - \text{Na}^+ + \text{K}^+) \times V_u + 80
\]

In severe diarrhea with metabolic acidosis urine \( \text{NH}_3 \) will increase and be secreted with \( \text{Cl}^- \rightarrow \) negative urine anion gap

In type 4 and type 1 RTA \( \text{NH}_3 \) excretion is defective \( \rightarrow \) positive urine anion gap
Potassium disorders

- Daily $K^+$ dietary load is 80-120 mmol, excreted mainly in the urine.
- The amount of excreted $K^+$ arises from the tubular excretion in the distal and collecting tubule – effect of aldosterone.
- Daily $K^+$ excretion: 10 mmol - 400 mmol.
- The most important indication for determination of urine $K^+$ is differential diagnosis of hypokalemia.

<table>
<thead>
<tr>
<th>Hypokalemia, $U_{K^+} &lt; 10$ mmol/L</th>
<th>Hypokalemia, $U_{K^+} &gt; 30$ mmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduced potassium intake</td>
<td>Renal potassium loss</td>
</tr>
<tr>
<td>Extrarenal potassium loss</td>
<td></td>
</tr>
</tbody>
</table>
TRANSTUBULAR POTASSIUM GRADIENT

Potassium concentration in a urine spot is difficult to interpret without daily urine volume and urine concentration.

- to assess kidneys tendency to reabsorb or excrete potassium
- it is a surrogate measure of aldosterone effect

\[
\text{TTKG} = \frac{\text{urine } K^+ / \text{serum } K^+}{\text{urine osmolality} / \text{serum osmolality}}
\]

**High value:** kidney is excreting \(K^+\)
**Low values:** conservation of \(K^+\)

Urine must be isotonic or hypertonic to serum (300 mOsm/kg)
Urine Na\(^+\) concentration must be \(>25\) mmol/L
# TTG in hypokalemia and hyperkalemia

<table>
<thead>
<tr>
<th></th>
<th>Hypokalemia</th>
<th>Hyperkalemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transtubular potassium gradient</td>
<td>&lt; 2</td>
<td>&gt; 2</td>
</tr>
<tr>
<td>Cause</td>
<td>gastrointestinal loss</td>
<td>hyper-aldosteronism</td>
</tr>
<tr>
<td>Example</td>
<td>Diarrhea</td>
<td>Conn syndrome</td>
</tr>
</tbody>
</table>

Magnesium excretion

- Mg\(^{++}\) concentration in serum does not provide accurate information about the actual Mg\(^{++}\) content in the body.

- Renal Mg\(^{++}\) excretion is surprisingly accurate at regulating the total Mg\(^{++}\) content.

- In Mg\(^{++}\) deficiency excretion in the urine is reduced, therefore Mg\(^{++}\) excretion can be used for diagnosing of Mg\(^{++}\) deficiency, even though Mg\(^{++}\) concentration is normal.

<table>
<thead>
<tr>
<th>Hypomagnesemia, (U_{\text{Mg}^{++}} &lt; 0.5 \text{ mmol/L})</th>
<th>Hypomagnesemia, (U_{\text{Mg}^{++}} &gt; 1.5 \text{ mmol/L})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extrarenal magnesium loss</td>
<td>Renal magnesium loss</td>
</tr>
</tbody>
</table>

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Conclusion

Urinary electrolytes and osmolality are useful tool in many clinical situations, and they have to be used more often, to show their full value.