Not All Osmoles Are Created Equal: 
A Case of Hyperosmolar Hypotonic Hyponatremia

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- Due to the potential danger of fluid shifts in the brain, the judicious correction of serum tonicity is fundamental to treating hypotonic hyponatremia.
- Hypotonic hyponatremia is usually marked by low serum osmolality, but exceptions arise when tonicity and osmolality differ. Understanding this distinction is key to the diagnosis and management of cases such as this one—a patient with profound hypotonic hyponatremia despite elevated serum osmolality.

Learning Objectives
1. Distinguish between osmolality and tonicity in a physiologic context.
2. Incorporate the recognition of ineffective osmoles into the clinical management of disorders of serum osmolality.

Case Presentation

History:
A 52-year-old woman presents for 1 week of generalized weakness, vomiting, and poor food intake.
She has a history of alcohol misuse disorder and multiple hospitalizations for severe hyponatremia. She is nonadherent to prescribed salt tablets. Reported ongoing alcohol intake is 6 beers per day.

Vital Signs:
T 99.6°F HR 116 bpm BP 149/83 mmHg RR 18 breaths/min O₂ sat 96% on room air

Notable Physical Exam Findings:
Alert & oriented, diffuse sacropenia, dry oral mucosa, regular tachycardia, non-focal neurologic exam.

Admission Labs:

<table>
<thead>
<tr>
<th>Component</th>
<th>Result</th>
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<tbody>
<tr>
<td>Osmolality</td>
<td>303 mOsm/kg</td>
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<tr>
<td>Osmolar gap</td>
<td>&gt;34 mOsm/kg</td>
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<tr>
<td>Serum protein &amp; lipids within normal limits.</td>
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Lactic acid 8.9 mmol/L
β-hydroxybutyrate 5.15 mmol/L
Ethanol 78 mg/dL

Osmolality: 303 mOsm/kg
Osmolar gap >30 mOsm/kg

Overnight treatment: 1 L NS, 250 mL 1/2NS; 2 mcg desmopressin (to prevent excessive aquarexia).

12 hours after admission: Na 119 mmol/L, serum osmolality 273 mOsm/kg (normal osmolal gap).
Lactic acid 1.6 mmol/L, β-hydroxybutyrate 1.46 mmol/L. No adverse clinical effects of precipitous drop in serum osmolality.

Day of discharge (hospital day 6): Na 131 mmol/L.

Discussion

Our patient’s hyperosmolar serum presented a diagnostic question: was her hyponatremia hypotonic, warranting tightly controlled correction? In order to assess her serum tonicity, her unmeasured osmols had to be characterized as effective or ineffective.

Serum Osmoles

- Effective
  - Na+, K+, glucose
- Ineffective
  - Urea, other organic solutes

Organic solutes present in lactic acidosis and ketoacidosis (particularly alcoholic) can constitute excess osmols.

- Lactic acidosis: small organic molecules released by ischemic tissues.
- Ketoacidosis: acetone & its metabolites.
- Because cell membranes are permeable to these organic molecules, they are ineffective osmoles.

Both lactic acidosis and alcoholic ketoacidosis were present in our patient to a high degree. Their associated occult organic solutes were the most likely unmeasured osmols in her case and are ineffective, making her hyperosmolar serum hypotonic.

Conclusion

Understanding ineffective osmoles as contributors to serum osmolality but not to tonicity and appreciating the scenarios in which they may be present allows the clinician to accurately assess serum tonicity across a range of osmolality. In this case, it allowed appropriate diagnosis and guideline-directed treatment of hypotonic hyponatremia despite the unexpected presence of hyperosmolality.

REFERENCES