Case C: A Patient with Acute Heart Failure and Hyponatremia

A Case-Based Approach to Hyponatremia: Applying the Expert Panel Recommendations to Clinical Practice

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Overview

• There are two indications for treating hyponatremia in patients with heart failure (HF):
  – Symptoms
  – Need to correct or avoid worsening hyponatremia when ongoing diuresis is needed in the setting of a falling or dangerously low serum sodium

• Aquaretic therapy may be of particular value when the need to treat hyponatremia coincides with the need for aggressive decongestion

• Current consensus recommendations as well as the American College of Cardiology (ACC)/American Heart Association (AHA) guidelines for treatment of hyponatremia in HF support this approach
Case - Clinical Presentation

- 71-year-old white male with a history of hypertension, diabetes, stage 3 chronic kidney disease, and chronic congestive HF (ejection fraction - 28%)
- Presents with 1 week of worsening shortness of breath and weight gain
- No prior coronary artery disease history, no chest pain or history of atrial fibrillation
- On chronic therapy with furosemide 80 mg/d, ACEI, carvedilol, and spironolactone
Case - Physical Exam

- Uncomfortable, appearing older than stated age, clearly breathless, and unable to speak in full sentences
- HR - 110 beats per minute (bpm), BP - 130/90 mmHg, RR - 24 breaths per minute
- Lungs with scattered rales
- Jugular venous pressure (JVP) > 16 cm, normal S1 and S2, prominent S3, 2-3/6 mitral insufficiency murmur
- 3+ edema, palpable liver edge
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Case - Initial Lab Exam

- ECG: Sinus tachycardia, no acute ST-T changes
- Chest x-ray: Moderate cardiomegaly, diffuse infiltrate consistent with pulmonary edema
- Electrolytes:
  - Serum $\left[ \text{Na}^+ \right]$ 128 mmol/L
  - Serum $\left[ \text{K}^+ \right]$ 4.6 mmol/L
- Renal function: Creatinine 1.8 mg/dL, BUN 36 mg/dL
- Blood gases (on 4l O$_2$): pO$_2$ 100 mmHg, pCO$_2$ 32 mmHg, pH 7.46
- Troponin: Borderline increased
What therapeutic options are available to treat hyponatremia in this patient?

1. Fluid restriction
2. Furosemide
3. Non-loop diuretic therapy
4. Vaptans
5. Hypertonic saline
2013 ACC/AHA Guidelines

“Fluid restriction (1.5 to 2 L/d) is reasonable in stage D, especially in patients with hyponatremia, to reduce congestive symptoms. (Level of Evidence: C)”

-2013 ACCF/AHA Guideline for the Management of Heart Failure

- Limited fluid intake (2 L/d) - adequate for most hospitalized patients with HF who respond to diuretics and do not have significant hyponatremia
- Strict fluid restriction – diuretic-resistant or hyponatremic
- Fluid restriction/sodium restriction – supplements volume management with diuretics
  – Difficult to achieve and maintain

Case - Initial Course

• Prescribed 80 mg IV furosemide in divided doses daily; 1000 cc fluid restriction
• Prior to admission medications: All continued
• Brisk initial urine output
• Patient improves with less dyspnea
Case - Hospital Day 2

- Patient remains dyspneic with minimal activity
- Vital signs:
  - HR - 96 bpm
  - BP - 120/70 mmHg
  - RR - 20 breaths per minute
- Input/output: Net 1 L diuresis
- Labs:
  - $[Na^+]$ 126 mmol/L
  - $[K^+]$ 4.2 mmol/L
  - Creatinine 2.0 mg/dL
  - BUN 38 mg/dL
- Medication: Furosemide dose doubled
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Case - Hospital Day 3

- Patient feels mildly improved
- Vital signs:
  - HR - 88 bpm
  - BP - 120/70 mmHg
  - RR - 16 breaths per minute
- Input/output: Net 1.5 L diuresis
- Exam shows persistent increase in JVP, continued 3+ edema
- Labs:
  - $[\text{Na}^+]$ 124 mmol/L
  - $[\text{K}^+]$ 4.0 mmol/L
  - Creatinine 2.2 mg/dL
  - BUN 44 mg/dL
- Metolazone 5.0 mg given prior to evening furosemide dose
Case - Hospital Day 4

- Patient reports little change in symptoms
- Vital signs:
  - HR - 92 bpm
  - BP - 124/76 mmHg
  - RR - 16 breaths per minute
- Exam: Persistent elevated JVP, 2+ edema
- Input/output: 0.75 L incremental diuresis prior 24 hours
- Labs:
  - Serum $[\text{Na}^+]$ 122 mmol/L
  - $[\text{K}^+]$ 3.8 mmol/L
  - Creatinine 2.6 mg/dL
  - BUN 50 mg/dL
Case - Therapeutic Options

1. Continue to push doses of furosemide with or without additional non-loop diuretics
2. Discontinue diuretic, switch to ultrafiltration for decongestion
3. Add nitroglycerin or nesiritide
4. Add low-dose dopamine
5. Add dobutamine or milrinone
6. Add vaptan
No solid evidence base exists upon which to guide therapy for cardiorenal syndrome with hyponatremia

- Loop diuretics: Increasing conventional diuretics will likely continue to produce suboptimal decongestion while worsening renal function and hyponatremia
- Ultrafiltration: Has not been shown to be more effective than continued diuretic therapy in setting of cardiorenal syndrome, and since it removes isotonic fluid will not correct hyponatremia

Case - Therapeutic Options (Cont’d)

- Vasodilators and inotropes: No vasodilator or inotropic agent has improved outcomes in acute HF patients including those at risk for or who have developed cardiorenal syndrome with or without hyponatremia
  - Recent failures include: nesiritide\(^1,2\) (normal or low-dose, with or without bolus), adenosine antagonists, low-dose dopamine
  - Prior failures include other vasodilators, milrinone, and levosimendan

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Case - Therapeutic Options (Cont’d)

- Aquaretic therapy (vasopressin V2R antagonism)
  - Has been studied in both chronic and acute HF
  - Improves serum \([\text{Na}^+]\) in hypervolemic hyponatremia
  - Acutely produces incremental weight loss
  - Acutely improves signs/symptoms of congestion
  - Chronically does not improve morbidity and mortality in patients with HF, but does lead to persistent correction of hyponatremia and lower body weight while preserving renal function

V2R, vasopressin V2 receptor subtype.
Objective: Signs/symptoms in-hospital

Short-term Clinical Status Trial A

Short-term Clinical Status Trial B

Long-term Outcome Trial
Long-term drug administration

OBJECTIVE:
Morbidity / mortality

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Study A

Composite Change in Global Status and Body Weight (Day 7 or Discharge)

Study B

Based on rank-sum analysis.
All-Cause Mortality

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Body Weight and Serum Sodium

**Body Weight** (kg)

**Serum Na⁺ (mEq/L)** (baseline < 134 mEq/L)

Dyspnea in Hyponatremic Patients

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"In patients hospitalized with volume overload, including HF, who have persistent severe hyponatremia and are at risk for or having active cognitive symptoms despite water restriction and maximization of GDMT, vasopressin antagonists may be considered in the short term to improve serum sodium concentration in hypervolemic, hyponatremic states with either a V2 receptor selective or a nonselective vasopressin antagonist. (Level of Evidence: B)"

-2013 ACC/AHA Guideline for the Management of Heart Failure
### Case - Therapeutic Decision and Results

- Furosemide dose decreased to 40 mg bid, metolazone stopped

<table>
<thead>
<tr>
<th>Day</th>
<th>Treatment</th>
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<tbody>
<tr>
<td>Day 3</td>
<td>Tolvaptan 15 mg</td>
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<tr>
<td>Day 4</td>
<td>Tolvaptan increased to 30 mg</td>
</tr>
<tr>
<td>Days 4–7</td>
<td>Continued improvement in symptoms with resolution of edema</td>
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<td>Incremental 6-L net diuresis</td>
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<td></td>
<td>Labs: Serum [Na⁺] improved to 134 mmol/L, creatinine decreased to 2.0 mg/dL, BUN decreased to 38 mg/dL</td>
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<td>Day 8</td>
<td>Patient discharged</td>
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### Consensus Recommendations for Management of Hyponatremia in HF

<table>
<thead>
<tr>
<th>Condition</th>
<th>Recommended Therapy</th>
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<tbody>
<tr>
<td>Severely symptomatic patient with very low or rapidly falling serum $[\text{Na}^+]$</td>
<td>Hypertonic (3%) NaCl combined with loop diuretic to prevent fluid overload</td>
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<tr>
<td>Mild to moderate symptomatic hyponatremia</td>
<td>Initiate fluid restriction (1 L/d total)</td>
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<td>Administer furosemide if volume overload evident</td>
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<tr>
<td>Failure of serum $[\text{Na}^+]$ to correct</td>
<td>Lift fluid restriction</td>
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<td></td>
<td>Start vaptan therapy</td>
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### Consensus Recommendations for Management of Hyponatremia in HF

<table>
<thead>
<tr>
<th>Hyponatremia in HF is typically chronic</th>
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<tr>
<td>• Limits for rates of correction should be observed</td>
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<tr>
<th>Tolvaptan may be up-titrated from 15–30 mg/d to 60 mg/d</th>
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<th>Discontinuation of treatment</th>
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<tr>
<td>• Serum [Na⁺] has normalized</td>
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<tr>
<td>• Symptom improvement</td>
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<tr>
<td>• Serum [Na⁺] not compromising use of diuretic therapy</td>
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<th>Assessment of need for post-discharge therapy</th>
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<tr>
<td>• Will vary from patient to patient</td>
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<tr>
<td>• Interruption of therapy holiday may be helpful in assessing need for chronic therapy of hyponatremia – 2–4 weeks after initiation of therapy</td>
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