IX: Electrolytes. Sodium disorders

Dan Henry, MD
Clerkship Director
University of Connecticut School of Medicine

Specific Learning Objectives:

Knowledge
Subinterns should be able to describe:
a) The differentinal diagnosis of
Hyponatremia (congestive heart failure, cirrhosis, thiazide diuretics, SIADH, adrenal insufficiency, hypothyroidism, primary polydypsia)

Skills
Subinterns should demonstrate skill in:
a) Conduct a history:
   i. Obtain from patients and correctly interpret symptoms that could indicate an underlying electrolyte disorder, and they should be able to obtain and interpret the significance of the patient's medication history
b) Conduct a physical examination:
   i. Assess volume status, perform a mental status examination
c) Develop a management plan:
   i. Work through the differential diagnosis for hyponatremia in order to arrive at a specific diagnosis
   ii. Develop an efficient plan for using laboratory tests (including urine sodium to determine the cause of the hyponatremia)
   iii. Write orders for the correction of hyponatremia
d) Hyponatremia: prescribe the following interventions as appropriate with careful to avoid overcorrection:
   i. Fluid restriction
   ii. Volume repletion
   iii. Diuresis

Attitudes and professional behavior
Subinterns should demonstrate:
a) Motivation towards learning how to recognize and treat their patients' hyponatremia

1. In patients with hyponatremia they are classified as either hypovolemic, euvolemic, or hypervolemic. What are some of the causes for each of the classifications and under each of the classifications what is the mechanism to explain the U_{Na} & Uosm?

	Hypovolemic		**Euvolemic**	**Hypervolemic**
	Nonrenal	**Renal**	Syndrome of inappropriate ADH	Congestive heart failure
	Diarrhea Vomiting	Addison's Diuretic	- Lung disease Pneumonia - Small cell carcinoma - Brain Stroke Subdural Tumor - Hypothyroid - Compulsive water drinker[1]	Liver failure
U_{Na}	**< 20 mEq/L**	**> 20 mEq/L**	**> 20 mEq/L**	**< 20 mEq/L**
Uosm	**Increased**	**Increased**	**Increased**	**Increased**

[1]Compulsive water drinker may not have an elevated Uosm but still too high in the content of decreased P_{Na} & P_{osm}. The U_{Na} may not be that high since increased urine volume.

A. Hypovolemic

Nonrenal

1) U_{Na} – Example would be vomiting or diarrhea. The volume loss causes increased levels of catecholamines in response to decreased blood pressure. There is also activation of the renin angiotensin system causing increased angiotensin II and aldosterone. Increased proximal reabsorption of Na, is due to catecholamines and angiotensin II and aldosterone increased reabsorption in collecting duct.

   As a result the urinary sodium is usually <20mEq/L. Even though the urine is concentrated there is so little Na in the urine the concentration is low.

   U_{osm} – Due to the decreased volume this stimulates ADH. It is called non osmotic release of ADH.

2) Renal

   U_{Na} – Addisons disease causes decreased glucocorticords and mineralocorticoids. The loss of mineralocorticoids causes renal losses of sodium resulting in U_{Na} >20 mEq/L. The increased U_{Na} with diuretics is due to the action of diuretics.

   U_{osm} – Same as with nonrenal losses

B. Euvolemic

U_{Na} — The U_{Na} is high with euvolemic hyponatremia for two reasons:

- The patient is in sodium balance i.e. Na in = Na out i.e. total body sodium is normal.
- Concentrated urine due to increased ADH

U_{osm} — The increased U_{osm} is due to increased ADH release (inappropriate). The exception is compulsive water drinking where the U_{osm} may not be that elevated but too high to excrete the excess water intake.

C. Hypervolemic

U_{Na} — Both congestive heart failure and liver failure have decreased effective circulating volume leading to similar pathophysiology as hypovolemia to explain the decreased U_{Na}

U_{osm} — Due to decreased effective circulating volume this causes non osmotic realease of ADH.

CASE 1

SCENARIO: A 50-year-old man with congestive heart failure secondary to a myocardial infarction is admitted to the hospital with dyspnea on exertion, orthopnea, and paroxysmal nocturnal dyspnea. He was being treated with captopril (ACE inhibitor) and the loop diuretic furosemide, but ran out 1 week ago. On physical examination his blood pressure is 110/70 mm Hg, pulse is 110/min, and respirations 20/min. He has jugular venous distention, and rales are heard over the lower 1/2 of the lung fields. Heart sounds reveal a normal S1 and S2, and an S3 gallop at the apex. A grade II/VI holosystolic murmur is also heard at the apex, and radiating to the axilla. He has 2+ pitting edema in his legs. The following laboratory data are obtained.

Serum [Na+]	=	130 mEq/L	(nl = 135 – 145 mEq/L)
Serum [K+]	=	3.8 mEq/L	(nl = 3.5 – 5.0 mEq/L)
Serum [$C1^-$]	=	94 mEq/L	(nl = 95 – 105 mEq/L)
Serum [HCO_3]	=	25 mEq/L	(nl – 24 – 28 mEq/L)
Serum [BUN]	=	28 mg/dL	(nl = 7 – 18 mg/dL)
Serum [creat.]	=	1.1 mg/dL	(nl = 0.6 – 1.2 mg/dL)
Urine osm	=	600 mosm/L	
Urinary sodium	=	10 mEq/L	

1. What is the mechanism for the development of hyponatremia in this man, and how would you treat the hyponatremia?

The man developed hypervolemic hyponatremia where there is an increase in total body sodium but greater increase in total body H_20. In order to develop hyponatremia, water in is greater than water out.

$$\text{Urine volume (L)} = \frac{\text{mOsm excreted}}{U_{osm}\ \text{(mosm/L)}}$$

The mOsm are Na, K and their salts and urea.

A normal person excreting 600 mOsm (amount depends on dietary Na, K, and protein) can if necessary have a urine volume as high as 12 L if they can lower their Uosm to 50 mOsm/L, i.e. no ADH. They would need to drink more than 12 L before they would develop hyponatremia. In general, hyponatremia develops when there is either appropriate ADH release in a state of decreased ECV (true volume depletion or CHF) or inappropriate ADH release. In this patient with CHF, his urine volume is decreased due to

Decrease in Na excretion
– Increased catecholamines $\rightarrow$ increased proximal Na reabsorption
– Activation of renin angiotension system where angiotension II increases proximal Na reabsorption and aldosterone increases Na reabsorption in the collecting duct

Increase in U_{osm} – His U_{osm} is increased due to non osmotic release of ADH due to decreased effective circulating volume leading to concentrated urine
Treatment – Na restrict, H_20 restrict, diurese

2. The man is started again on furosemide, and urine output increases 300 cc/hr. What is the mechanism by which furosemide causes this increase in urine output?

$$\text{Urine V} = \frac{\text{mOsm excreted}}{U_{osm}}$$

Mosm excreted increases due to increased Na and K excretion with an anion
Uosm decreases to 300 mOsm/L from 600 mOsm/L since furosemide abolishes the counter-current system

The effect of both, leads to increased urine volume

3. After receiving furosemide, his urinary sodium is 40 mEq/L and urinary K is 25 mEq/L. For every liter he excretes with those urinary electrolytes, how much will be free water?

The electrolyte free water equation is:

$$\textbf{Urine Volume (V)} = \frac{(U_{Na} + U_k)\ V}{P_{Na}} + CH_20$$

The classic free water equation is:

$$V = \frac{Uosm \ X \ V}{Posm} + CH_20$$

$$CH_20 = V \ X \ (1 - Uosm/Posm)$$

This is not used clinically since the mOsm excreted includes Na + salts, K + salts and urea. What is important clinically is the electrolyte free water equation. The electrolytes include Na and K. Following is the rational.

$$Plasma\ Na = \frac{Total\ body\ (Na + K)}{Total\ body\ water}$$

The reason is that osmolality inside the cell (predominantly due to K) is the same as outside the cell (predominantly due to Na). A decrease in intracellular K would decrease intracellular osmolality and shift water outside the cell decreasing plasma sodium. The electrolyte free water excretion shown below is more important clinically since it eliminates the contribution of urea.

Electrolyte free water excretion:

The electrolyte free water equation is:

$$\text{Urine Volume (V)} = \frac{(U_{Na} + Uk)\ V}{P_{Na}} + CH_20$$

$$C_{H20} = V\left(1 - \frac{(U_{Na} + U_K)}{P_{Na}}\right)$$

In this patient the free water excretion in 1 liter is

$$CH_2O = 1\ L\left[(1 - \frac{(40\ mEq/L + 25\ mEq/L)}{130\ mEq/L}\right] = 0.5\ L$$

As a result the furosemide increases free water loss

CASE 2

SCENARIO: A 46 year old man with a history of AIDS due to intravenous drug use is seen because of a severe headache for 3 days. He was diagnosed 5 years ago and was on HAART treatment but was poorly compliant and it was discontinued one year ago. His most recent CD_4 is 50/mm^3 and viral load 50,000 copies/ml. He has no complications and takes TMP/SMX for PCP prophylais. Three days ago he began having severe headaches. The headache is constant and located in the occipital area and he rates it an 8 on a 10 point scale. Two days ago he noticed decreased ability to write due to right hand weakness. No visual problems or other neurological symptoms. Yesterday he vomited once and has had decreased food intake. Blood pressure is 100/60 mmHg, pulse is 100/min, respirations are 20/min temperature is 38°. Neurological exam reveals decreased hand grip and decreased flexion of right wrist. There is no edema.

The following laboratory are

Serum [Na+]	=	125 mEq/L	(nl = 135 – 145 mEq/L)
Serum [K+]	=	3.8 mEq/L	(nl = 3.5 – 5.0 mEq/L)
Serum [CI-+]	=	90 mEq/L	(nl = 95 – 105 mEq/L)
Serum [HCO_3+]	=	25 mEq/L	(nl = 24 – 28 mEq/L)
Serum [Cv]	=	1.0 mg/dL	(nl = 0.6 – 1.2 mq/dL)
Serum [BUN]	=	8 mg/dL	(nl = 7 – 18 mq/dL)
Urine sodium	=	60 mEq/L	
Urine osmolality	=	400 mOsm/L	

CT scan shows a ring enhancing lesion one in the left parietal area.

1) What is the most likely cause of the hyponatremia?

This patient most likely has SIADH secondary to the lesion in the brain (toxoplasmosis versus lymphoma). The urinary sodium is the key factor to make the diagnosis of SIADH. From the history of decreased intake and one episode of vomiting he could have been volume depleted but his urinary sodium should have been decreased. With SIADH the patient is in sodium balance so that his sodium excretion is equal to sodium intake. The hyponatremia develops since the inappropriate secretion of ADH decreases urine volume so the patient develops positive water balance resulting in hyponatremia.

2) What is the treatment?

Since his mental status is intact and no seizures the treatment is water restriction. The rise in sodium is usually very slow since difficult to develop negative water balance when urine output may only be one liter/day.

References

General overviews:

Electrolyte Free Water Excretion

Rose BD. New approaches to disturbance in the plasma sodium concentration. Am J Med 1986; 81:1033

Hyponatremia

Adroque HJ, Madias NE. Hyponatremia. NEJM 2000, 342(21): 1581-9.