Dysnatremias: All About the Salt?

Internal Medicine Resident Lecture

1/12/16

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Water or salt?

Dysnatremias

- In general, disorder of water balance, not sodium balance…
- **Volume status is tied to total body sodium content**
- **Sodium concentration (ie hypo or hypernatremia) determined by proportion of total body sodium to water**
- The kidneys regulate sodium and water balance **independently**

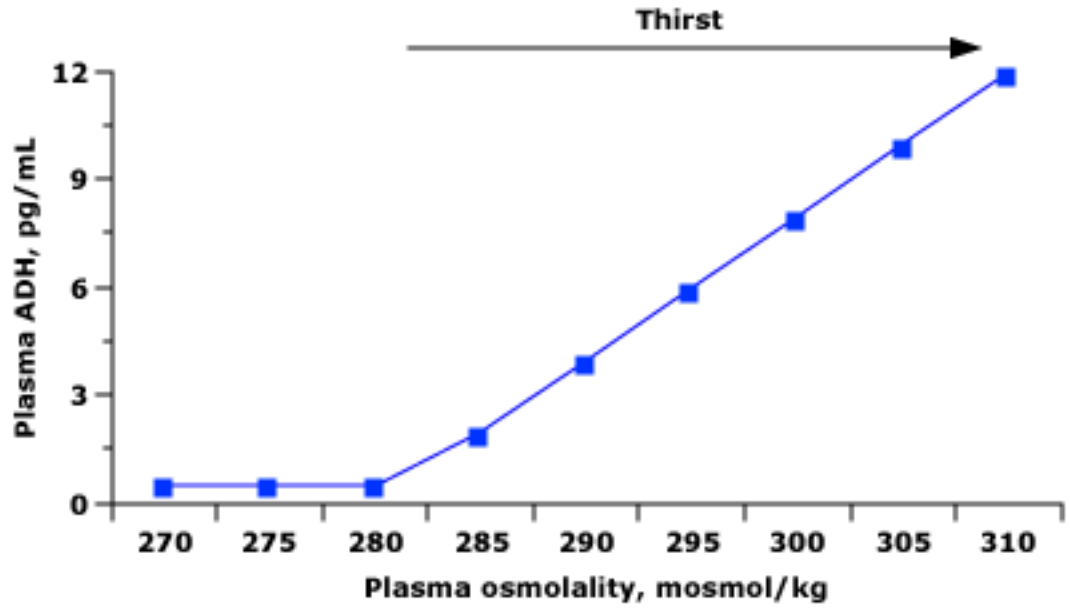
Physiology of water regulation

- You are in the desert w/ no access to water…
- What happens physiologically

Physiology of water regulation

- Insensible losses
  - **Skin**
    - 500cc (possibly more in hospitalized patients)
  - **Respiratory**
    - 400cc (more in hospitalized patients)
  - Stool
    - 200cc
- Urine losses
    - 500cc (electrolyte free water loss)

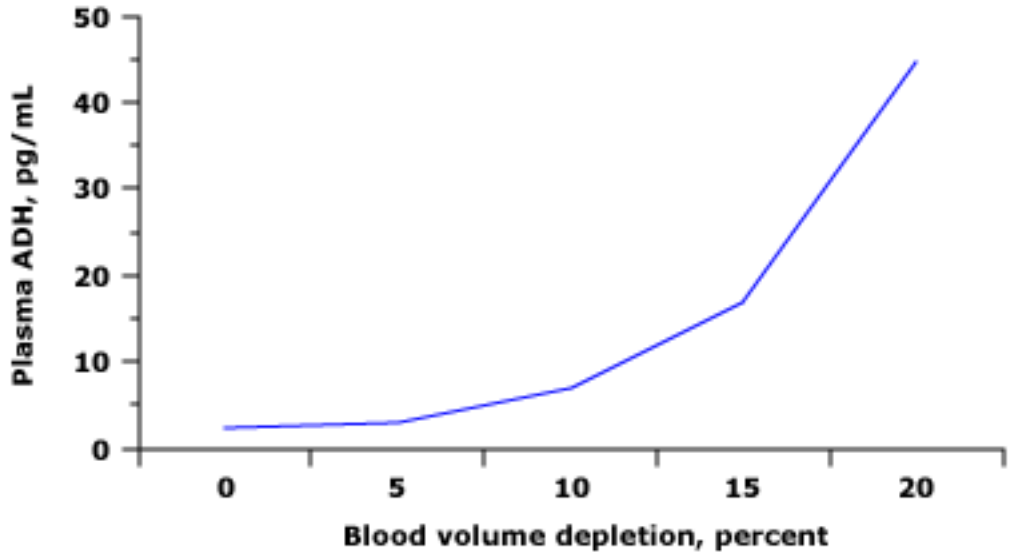
Osmotic regulation of ADH release and thirst



Relation between plasma antidiuretic hormone (ADH) concentration and plasma osmolality in normal humans in whom the plasma osmolality was changed by varying the state of hydration. The osmotic threshold for thirst is a few mosmol/kg higher than that for ADH.

Data from Robertson GL, Aycinena P, Zerbe RL. Am J Med 1982; 72:339.

Hypovolemic stimulus to ADH release

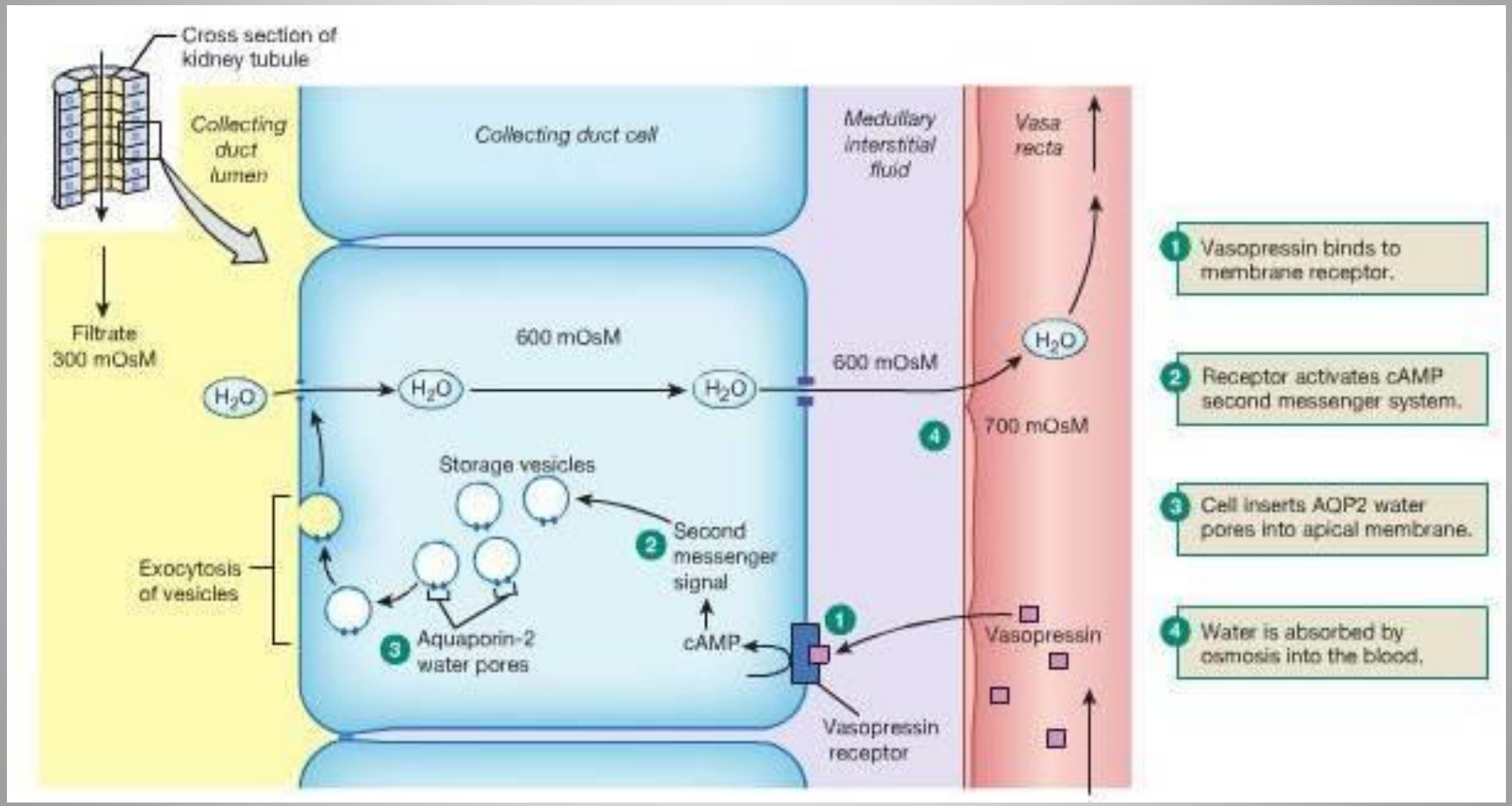


Relationship of plasma antidiuretic hormone (ADH) concentrations to isosmotic changes in blood volume in the rat. Much higher ADH levels can occur with hypovolemia than with hyperosmolality, although a relatively large fall in blood volume is required before this response is initiated.
Data from Dunn FL, Brennan TJ, Nelson AE, et al. J Clin Invest 1973; 52:3212.

Physiology of water regulation

- Change in plasma osmolality (increase)
  - ADH
  - Thirst
  - Vasopressin receptor
    - V1
    - V2
  - Aquaporins
  - Water moves down concentration gradient

ADH physiology



Case 1

- 35 yr old man s/p motorcycle vs. auto seen in SICU. Has been in ICU for 3 weeks
  - Multiple trips to OR for orthopedic surgeries
  - Prolonged vent requirements
  - s/p VAP with sepsis
- Consulted for hypernatremia management

Case 1

- Receiving multiple drips and antibiotics mixed in saline.
- Receiving tube feeds. Surgical team added water flushes due to the hypernatremia at 100cc every 4 hours
- Exam sig for : On vent, normotensive and HDS, decreased breath sounds, anasarca. External fixators present on LLE
- Labs: Na 165 Cr 1.2 BUN 105

Case 1

What is your approach?

Case 1

- Problems:
  - Hypernatremia
    - Hypervolemic vs. euvolemic vs. hypovolemic
  - Azotemia
  - Hypervolemia
- Too much salt or too little water?

Case 1

- Water deficit calculation:
  - H2O def= TBW x (current Na/140 - 1)
  - TBW= 45-60% of lean body wt in kg
  - Data: current wt 110kg IBW 85kg
  - Recommendations?

Case 1

- Goal decrease in sodium
  - 10meq/L in 1st 24h max
  - 16-18meq/L in 1st 48h
- How much free water needed?
- How would you administer it?
- What monitoring is needed?

Case 1

- You decide about 3 L is needed
  - Water flushes increased to 125cc/hr
  - Call parameters given to RN
- Next AM you open chart
  - Serum sodium is 170
  - What happened?

Case 1

- You study I/O and med list a bit further…
  - Cardiology has started pt on lasix (polydoctoring)
  - Intake was 4L, output was 6.5L (drains, urine output, diarrhea from TF)
- Ongoing adjustment is needed to account for ongoing water losses. Impossible to quantify in most cases
- In general replacement rate will underestimate amount of water needed (ie will see undercorrection)

Hyponatremia

- Simply put, hyponatremia develops in 2 situations-
  - Water intake which overwhelms excretory capacity (rare, such as severe psychogenic polydypsia)
  - Intake of a water load which cannot be excreted due to low GFR or persistent effects of ADH

Hyponatremia

- Usually divided according to volume status
  - Hypovolemic hyponatremia
    - Total body water decreased
    - Volume (total body sodium) decreased more
  - Euvolemic hyponatremia
    - Total body water increased
    - Volume (total body sodium) no change
  - Hypervolemic hyponatremia
    - Total body water increased more
    - Volume (total body sodium) increased
- Best to think of volume status (sodium balance) and water balance (sodium concentration) completely separately

Hyponatremia

- My steps in evaluating hyponatremic disorders…
  - How much time do I have-- ie is pt symptomatic?
  - Hypo-osmolar? Rule out----
    - pseudohyponatremia (rare)
    - hypertonic hyponatremia
  - Volume status?
    - Signs of volume depletion?
    - Signs of volume excess?
    - If euvolemic, reason for SIADH?
  - Rule out thiazide diuretics, severe hypothyroidism, adrenal insufficiency
  - Rule out poor solute intake (“beer potomania” or “tea and toast diet”)
  - Working diagnosis
  - Treatment plan and monitoring frequency

Case 2

- 57 yo woman with PMH of hypothyroidism presents w/ a 1 week history of upper resp symptoms along w/ n/v. Very little intake other than trying to "hydrate." Brought to ER by family for progressive confusion. The time is noon.
- Exam: BP 100/54 HR 101, confused, no edema.
- Labs:
  - Na 118 K 3.4 BUN 5 Scr 0.4 Osm 250 BG 130 TSH wnl
  - Urine data Osm 141 Na 36 SG <1.005 (timing)

Case 2

- Hyponatremia
  - Type?
  - Symptomatic?

- Pt is bolused 2L NS in ED

Case 2

- You are consulted at 9pm by admitting hospitalist however RN “kindly” holds call till the next morning. Unit secretary calls in consult after case mgmt rounds
  - Time is 10am
  - Na is 140
  - Pt feels better, “back to normal”
  - RN states pt has put out “liters of urine” and asks if pt can be discharged today
- Are you concerned? What are the risks?

Osmotic demyelination syndrome

- Acute hyponatremia causes brain edema
- Adaptation begins immediately and is complete around 48hrs
  - Loss of water, sodium, intracellular potassium, organic solutes
- Rapid correction can result in ODS
  - Usually in pts w/ serum sodium <120 on presentation
  - At risk pts: cirrhosis, alcoholism, malnourished, OLTx
- Current rate of correction recommendations:
  - Less than 10-12 mEq/L in 1st 24h and 18mEq/L in 1st 48h

Case 2

- What are your recommendations???

Case 2

- Increase in Na ---
- Goal increase ---
- Therapy ---

Case 2

DDAVP Is Effective in Preventing and Reversing Inadvertent Overcorrection of Hyponatremia

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Background and objectives: Adherence to therapeutic guidelines for the treatment of hyponatremia becomes difficult when water diuresis emerges during therapy. The objective of this study was to assess the effectiveness and safety of desmopressin acetate as a therapeutic agent to avoid overcorrection of hyponatremia and to lower the plasma sodium concentration again after inadvertent overcorrection.

Design, setting, participants, & measurements: Retrospective chart review was conducted of all patients who were given desmopressin acetate during the treatment of hyponatremia during 6 yr in a 528-bed community teaching hospital.

Results: Six patients (group 1) were given desmopressin acetate after the 24-h limit of 12 mmol/L had already been reached or exceeded; correction was prevented from exceeding the 48-h limit of 18 mmol/L in five of the six. Fourteen patients (group 2) were given desmopressin acetate in anticipation of overcorrection after the plasma sodium concentration had increased by 1 to 12 mmol/L. In all 14 patients who were treated with desmopressin acetate as a preventive measure, correction was prevented from exceeding either the 24- or 48-h limits. After desmopressin acetate was administered, the plasma sodium concentration of 14 of the 20 patients fell by 2 to 9 mmol/L. In all six group 1 patients and in five of the group 2 patients, the plasma sodium concentration was actively lowered again by the concurrent administration of desmopressin acetate and 5% dextrose in water; no serious adverse consequences from this maneuver were observed.

Conclusion: Desmopressin acetate is effective in preventing and reversing inadvertent overcorrection of hyponatremia.

Clin J Am Soc Nephrol 3: 331-336, 2008. doi: 10.2215/CJN.03190807

Case 3

- 48 yo man with smoking history presents with confusion and drowsiness. Meds include combivent. BP 130/84 HR 70, JVP 4cm, clear lungs, no edema. CXR shows COPD changes. Family is concerned that he “drinks beer all day” and eats very little.
- Labs- Na 117 K 3.6 SOsm 258
  - Una 90 Uosm 662

Case 3

- Symptoms?
- Volume status?
- Differential diagnosis?
- What other labs or imaging would you order?
- Treatment options?

Table 2 Etiologies of dilutional (euvolemic and hypervolemic) hyponatremia

- Impaired Renal Free Water Excretion
  - Euvolemic
    - SIADH
      - Tumors
        - Pulmonary/mediastinal (bronchogenic carcinoma, mesothelioma, thymoma)
        - Nonchest (duodenal carcinoma, pancreatic carcinoma, ureteral/prostate carcinoma, uterine carcinoma, nasopharyngeal carcinoma, leukemia)
      - CNS disorders
        - Mass lesions (tumors, brain abscesses, subdural hematoma)
        - Inflammatory diseases (encephalitis, meningitis, systemic lupus, acute intermittent porphyria, multiple sclerosis)
        - Degenerative/demyelinative diseases (Guillain-Barré syndrome; spinal cord lesions)
        - Miscellaneous (subarachnoid hemorrhage, head trauma, acute psychosis, delirium tremens, pituitary stalk section, transphenoidal adenomectomy, hydrocephalus)
      - Drug induced
        - Stimulated AVP release (nicotine, phenothiazines, tricyclics)
        - Direct renal effects and/or potentiation of AVP antidiuretic effects (DDAVP, oxytocin, prostaglandin synthesis inhibitors)
        - Mixed or uncertain actions (ACE inhibitors, carbamazepine and oxcarbazepine, chlorpropamide, clofibrate; clozapine, cyclophosphamide, 3,4-methylenedioxymethamphetamine ["Ecstasy"], omeprazole; serotonin reuptake inhibitors, vincristine)
      - Pulmonary diseases
        - Infections (tuberculosis, acute bacterial and viral pneumonia, aspergillosis, empyema)
        - Mechanical/ventilatory (acute respiratory failure, COPD, positive pressure ventilation)
      - Other
        - AIDS and ARC
        - Prolonged strenuous exercise (marathon, triathalon, ultramarathon, hot-weather hiking)
        - Senile atrophy
        - Idiopathic
    - Glucocorticoid deficiency
    - Hypothyroidism
    - Decreased urinary solute excretion
      - Beer potomania
      - Very-low-protein diet

Case 3

Table 2. Diagnosis of SIAD.*

Essential features

Decreased effective osmolality (<275 mOsm/kg of water)

Urinary osmolality >100 mOsm/kg of water during hypotonicity

Clinical euvolemia

- No clinical signs of volume depletion of extracellular fluid
  - No orthostasis, tachycardia, decreased skin turgor, or dry mucous membranes
- No clinical signs of excessive volume of extracellular fluid
  - No edema or ascites

Urinary sodium >40 mmol/liter with normal dietary salt intake

Normal thyroid and adrenal function

No recent use of diuretic agents

Supplemental features

Plasma uric acid <4 mg/dl

Blood urea nitrogen <10 mg/dl

Fractional sodium excretion >1%; fractional urea excretion >55%

Failure to correct hyponatremia after 0.9% saline infusion

Correction of hyponatremia through fluid restriction

Abnormal result on test of water load (<80% excretion of 20 ml of water per kilogram of body weight over a period of 4 hours), or inadequate urinary dilution (<100 mOsm/kg of water)

Elevated plasma AVP levels, despite the presence of hypotonicity and clinical euvolemia

Case 3

- How would you treat?
  - A. 3% saline
  - B. Fluid restriction
  - C. Salt tabs and lasix
  - D. Tolvaptan

Case 3

- 3% saline
  - Rate

Table 4. Formulas for Calculating Initial Saline Infusion Rates.*

Source	Step 1	Step 2	Example of Rate (ml/hr)
Traditional[1]	$\text{Na required} = \text{TBW} \times ([\text{Na}]_2 - [\text{Na}]_1)$	$\text{Volume (liter)} = \frac{\text{Na required (mmol)}}{513\ \text{mmol/liter}}$	82
Adrogué and Madias[1]	$\Delta[\text{Na}]_s\ \text{(with 1 liter)} = \frac{[\text{Na}]_{inf} - [\text{Na}]_1}{\text{TBW} + 1}$	$\text{Volume (liter)} = \frac{\text{Desired } \Delta[\text{Na}]_s}{\Delta[\text{Na}]_s\text{(with 1 liter)}}$	107

  - To raise serum Na by 10 meq/L over 24h assuming pt is 70kg, TBW=42L
  - Na needed is 420meq. Volume needed is around 800cc of 3% or a STARTING rate of 33cc/hr.
  - I would stop when pts symptoms ceased or when sodium >124
  - Close monitoring is essential

Case 4

- 58 yo woman with a history of ischemic cardiomyopathy admitted with pulmonary edema. Meds include metoprolol, spironolactone, furosemide, lisinopril.
- Exam- BP 97/54 HR 85, alert and oriented, JVP 9cm, lungs w/ diffuse crackles, 1+ LE edema
- Labs- Na 121 K 3.5 BUN 45 Scr 1.1
  - Urine data- UNa 15 UCl <5 Uosm 210 (6hrs after last diuretic dose)

Case 4

- Symptoms?
- Volume?
- Workup?
- Treatment options?

Vasopressin receptor antagonists

Table 3. Vasopressin-Receptor Antagonists.*

Drug	Dose of Drug	Vasopressin Receptor	Route of Administration	Urinary Volume	Urinary Osmolality	Sodium Excretion over 24 hr
Conivaptan (Vaprisol, Astellas Pharma)†	20–40 mg daily	V_{1A} and V_2	Intravenous	Increased	Decreased	No change
Tolvaptan (Otsuka)	15–60 mg daily	V_2	Oral	Increased	Decreased	No change
Lixivaptan (CardioKine)	100–200 mg	V_2	Oral	Increased	Decreased	No change with low dose; increased with high dose
Satavaptan (Sanofi-Aventis)	12.5–50 mg	V_2	Oral	Increased	Decreased	No change

- Advantages
  - Addresses underlying issue
  - Efficacy
  - Allows less strict fluid restriction
- Disadvantages
  - Hospitalization
  - Cost
  - Rapid correction
  - Thirst
  - Black Box Warnings

Questions?