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Hyponatremia

Made ridiculously simple

AHN

Agenda

- Definitions
- Mechanism of hyponatremia
- Significance of hyponatremia
- Approach to patients with hyponatremia
- Cases

Definition

- True vs pseudo hyponatremia
- Acute vs chronic hyponatremia
- Symptomatic vs Asymptomatic

Hyponatremia

- sNa < 135 mmol/L
- Most common electrolyte abnormality

Serum [Na+], mEq/L[3]		
<125	125–130	130–135
Severe hyponatremia	Moderate hyponatremia	Mild hyponatremia

Adrogue H, Madias NEJM 2000

Definitions

- **Pseudohyponatremia**: lab error in patients with extreme hyperlipidemia or hyperproteinemia.
- **Hyperosmolar hyponatremia**: elevated BG or administration of mannitol/sucrose. Decrease in sNa by 1.6 mmol/L for every 100 increase in pGlucose.

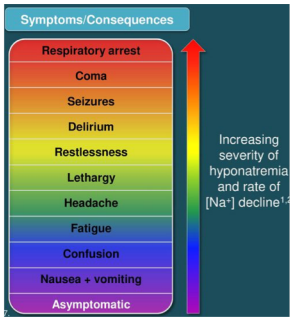
Spasovski et a Eur J Endoc 2014

Definitions

Acute (≤48 hours)	Chronic (>48 hours)
Symptoms include: • Cerebral edema • Seizures • Increased mortality risk[1]	Symptoms include: • Nausea/vomiting[1] • Confusion[1] • Neurologic dysfunction[1] • Gait disturbances[1] • Seizures (with very low serum [Na^+] levels)[2]
Rapid correction reverses cerebral edema without sequelae[1]	Rapid correction may cause brain dehydration and osmotic demyelination syndrome (ODS)[3]

Ghali Cardiology 2008
Verbalis J et al Am J Med 2013
Berl CJASN 2013

Symptoms and signs



Bagshaw S Can J Anesthesia 2009
Ghali Cardilogy 2008

Mechanism

Is hyponatremia a result of

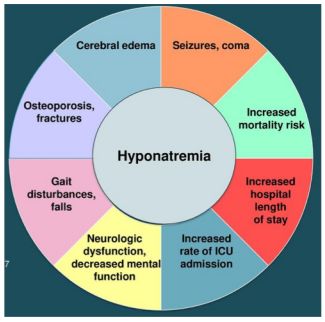
a) Too little sodium
b) Too much sodium
c) Too little water
d) Too much water

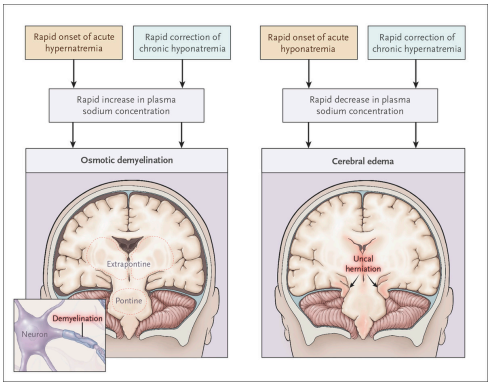
Google.com

Clinical Significance

- **Why should we care?**
- **Is acute symptomatic hyponatremia an emergency?**

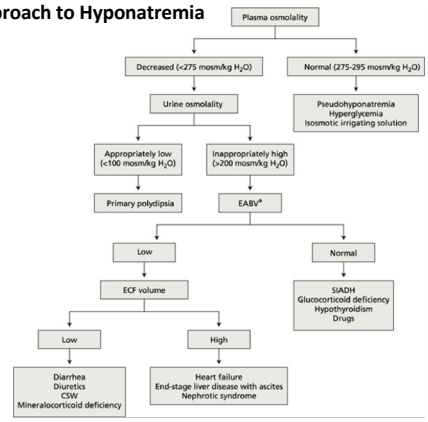
Consequences of Hyponatremia





Sterns R, NEJM 2015

My approach to Hyponatremia

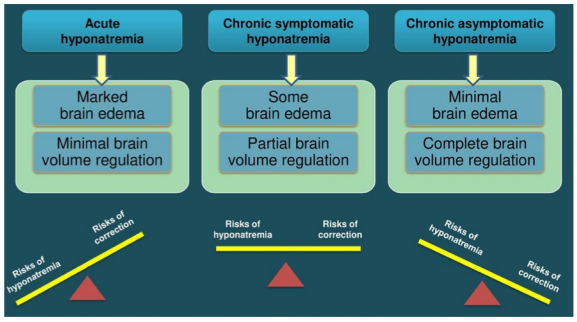


Management- Key points

- Assess the case: Acute vs Chronic, Symptomatic or not, mild-severe.
- Volume status
- Identify pts at risk for rapid correction and those at risk of ODS
- Avoidance of rapid correction
- Even modest improvement in sNa has survival benefit- do not ignore hyponatremia
- Monitor sNa levels and UOP frequently

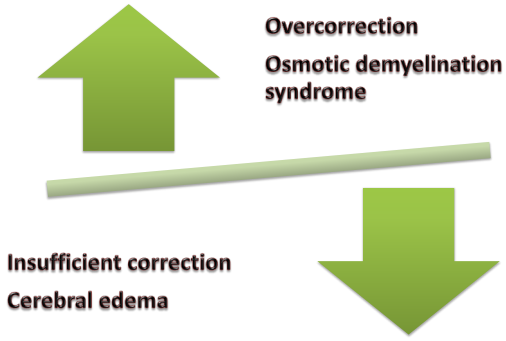
Adrogue NEJM 2000, Ellison et al NEJM 2007, Verbalis Am J Med 2007

Treatment challenges



Trends in endocrine metab textbook: Verbalis J 1992

Goals of Treatment



Cases of inadvertent overcorrection

- Hypovolemic cases
- Thiazide induced hyponatremia
- Adrenal insufficiency
- Drug and stress induced SIADH

Risk for ODS

- Chronic hyponatremia
- Severe Hyponatremia < 105
- Concomitant hypokalemia
- ETOH abuse and malnutrition
- Liver cirrhosis

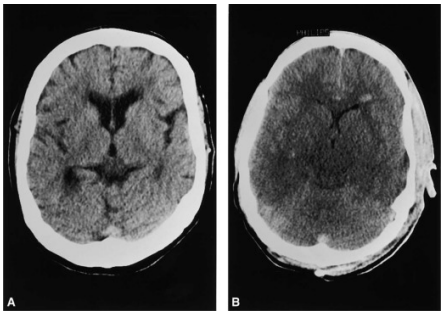
King J et al Am J Med Sci 2010
Berl T et al AJKD 2010

Goals of Correction

- First 24 hrs: 6 mmol/L no more than 8 mmol/L
- First 24 hrs: 12 mmol/L no more than 16 mmol/L
- Symptomatic patients: raise sNa by 4 points in 4 hours is enough to stop brain edema.
- Acute (<48 hrs) hyponatremia can be reversed.

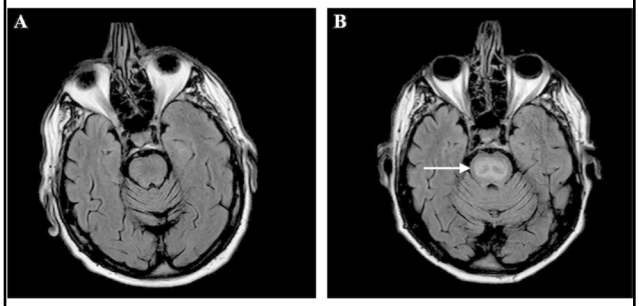
Sterns R CJASN 2018
Sterns R et al Curr Op Neph Hyp 2015

Brain Edema



Gross et al Kidney Int 2001

Osmotic Demyelination Syndrome



Reijanders T et a Cureus 2020

Case 1

- An 80-y/o woman with h/o depression presents to ER with weakness and dizziness. She takes furosemide 20 mg qd for LE edema. She reports that her PCP prescribed hydrochlorothiazide for elevated BP 1 week ago. The patient denies fevers, chills, nausea, or vomiting
- BP is 100/60 mm lying down and 84/40 mm Hg sitting. Lungs are clear and there is no lower extremity edema
- Labs: serum osmolality of 260 mOsm/kg, serum Na of 125 mEq/L , serum K of 3.4 mEq/L Urine Na level of 50 mEq/L and urine osmolality of 200 mOsm/kg

Case 1

Which of the following is this patient's most likely diagnosis?

a) Adrenal insufficiency
b) Furosemide-induced hyponatremia
c) Hydrochlorothiazide-induced hyponatremia
d) Syndrome of inappropriate antidiuretic hormone (SIADH)
e) Thyroid disease

Case 1- discussion

- Thiazide-induced hyponatremia.
- Happens most in the elderly, low weight, frailty and beer drinkers.
- Usually occurs within 1 to 2 weeks of starting the drug.
- Diuretics can induce volume depletion and stimulate ADH release, which acts on the collecting duct to cause water reabsorption.
- Possible genetic factors
- Rx: d/c thiazide and may use normal saline.
- Pts are at risk of rapid correction after stopping the drug.
- Key is to monitor labs after starting the drug.

Case 2

- 72 y/o man who is a heavy smoker presents w cough/hemoptysis. Physical exam is only remarkable for nicotine stains on his fingers.
- (negative for edema, skin turgor is normal. MMM, clear lungs, no S3 or JVD)
- Takes No medications
- Chest x-ray reveals 4 cm RLL mass.

Labs: sNa 125 meq/L. K: 4.2 meq/L. sCr 1.1 mg/dl.

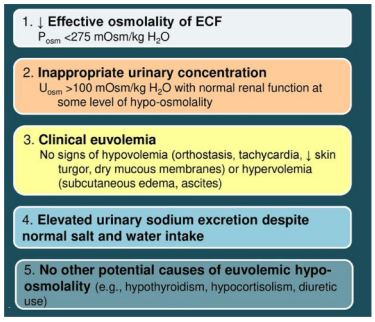
Case 2

- Serum Osmolality: 270 mOsom/L
- Urine Osom: 450 , Urine Na 50
- Too much ADH.
- Volume status: euvolemic.
- Kidney function is normal
- Check TSH and morning cortisol level
- Likely diagnosis is SIADH secondary to possible lung malignancy

SIADH

- Most common cause of hyponatremia
- Effective blood volume is normal therefore, UNa is usually >40, however Uosom is >200
- Should identify an underlying etiology
- Treat the underlying disorder

Making the case for SIADH



Janicic N, Verbalis J Endocin Met Clin N Am 2003

Causes of SIADH

Malignant diseases	Pulmonary disorders	Disorders of the central nervous system	Drugs	Other causes
Carcinoma	Infections	Infection	Drugs that stimulate release of AVP or enhance its action	Hereditary (gain-of-function mutations in the vasopressin V2 receptor)
Lung	Bacterial pneumonia	Encephalitis	Chlorpropramide	Transient or endurance exercise
Small-cell	Viral pneumonia	Meningitis	SSRIs	General anesthesia
Mesothelioma	Pulmonary abscess	Brain abscess	Tricyclic antidepressants	Nausea
Oropharynx	Tuberculosis	Rocky Mountain spotted fever	Clofibrate	Pain
Gastrointestinal tract	Aspergillosis	AIDS	Carbamazepine	Stress
Stomach	Asthma	Bleeding and masses	Vincristine	
Duodenum	Cystic fibrosis	Subdural hematoma	Nicotine	
Pancreas	Respiratory failure associated with positive-pressure breathing	Subarachnoid hemorrhage	Narcotics	
Genitourinary tract		Cerebrovascular accident	Antipsychotic drugs	
Ureter		Brain tumors	Ifosfamide	
Bladder		Head trauma	Cyclophosphamide	
Prostate		Hydrocephalus	Nonsteroidal antiinflammatory drugs	
Endometrium		Cavernous sinus thrombosis	(3,4-methylenedioxymeth amphetamine (MDMA ('ecstasy')	
Endocrine		Other	AVP analogues	
Thymoma		Multiple sclerosis	Desmopressin	
Lymphomas		Guillain–Barré syndrome	Oxytocin	
Sarcomas		Shy–Drager syndrome	Vasopressin	
Ewing's sarcoma		Delirium tremens		
		Acute intermittent porphyria		

AVP, arginine vasopressin; SSRI, selective serotonin reuptake inhibitor. Adapted from [1].

Ellison, Berl, SIADH, NEJM 2007

Case 2-Treatment

- Chronic, asymptomatic mild-moderate hyponatremia.
- Options for treatment:
  - Fluids restriction
  - Salt Tablets
  - Urea
  - Vasopressin V2 receptor antagonists (Vaptan)

Treatment of SIADH

- Fluids restriction:
  - Should be done right. Ideally 500 cc less than urinary volume.
  - Would most likely not work if Urine Osom is > 500 mOsom/kg and/or if sNa < Una +UK
- NaCl+ loop diuretics
  - Loop diuretics eliminate medullary gradient allowing lytes-free water excretion. NaCl usually 3 gr/day promotes water clearance.
  - Long term effect/tolerability is unknown
  - Frequent adjustments may be necessary

Verbalis J et al A J Med 2013

Treatment of SIADH

- Vasopressin Receptor Antagonist
  - tolvaptan (PO) and conivaptan (IV)
  - Effective, Aquaretics and Backed by RCT
  - Should be initiated as inpatients. 10-60 mg tabs
  - Patients should be alert and have access to water
  - Careful monitoring of serum sodium levels
  - Limit use to 30 days
  - Avoid in liver disease

Berl T, NEJM 2015

Treatment

- Urea:
  - Promotes free water diuresis
    - By decreasing Urinary Na and K concentration
  - Still not widely available and used
  - Concerns about palatability, now flavored
- Do Not use: demeclocycline

Soupart et al CJASN 2013
Sterns R et al Kid Int 2015

Case 3

- You were asked to see 72 y/o woman with h/o HTN, Depression and CAD who is POD#2 THA. She is delirious.
- Inpatient meds: ketolorac IV, HCTZ/Losartan, flouxetine, metoprolol, D5W/0.45 NS at 75 cc/hr.
- Exam: VSS. Lethargy. No JVD, no S3, no edema
- Labs: sNa 115 mmol/L. sK 3.2 meq/L. sCr 1.0 mg/dl.
- Labs pre op: sNa 136, sK 3.9, Cr 0.9

Case 3- approach

- Serum Osm: 252
- Urine Osm: 550, Urine Na: 54
- High ADH state due to stress, pain after surgery, nausea. Being on NSAID, SSRI while receiving hypotonic fluids
- Rx: D/C Ketolorac, SSRI and IVF.
- 3% saline 100 cc x 1
- Monitor UOP, sNa q 3-4 hrs.

Take home messages

- Hyponatremia is serious and common dyselectrolytemia
- Assessment and risk stratification of patients is essential
- Insufficient and overcorrection both can lead to irreversible neurological damage
- Frequent monitoring of sNa and UOP is essential during inpt treatment of hyponatremia
- Avoid hypotonic fluids post operatively
- Involve Nephrology consultants early on in the treatment of severe hyponatremia
- Check BMP 1-2 weeks after initiating thiazide in elderly patients