

Hyponatremia

Brief Review and Update

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Hyponatremia

Classification

Hypovolemic

- Renal
- Extra-renal

Euvolemic (SIADH)

Hypervolemic

- Renal
- Extra-renal

Excess Water Ingestion

- Primary polydipsia
- Fresh water drowning

Hyponatremia

Classification

Hypovolemic

- Renal: diuretics, CSW, aldo def
- Extra-renal: GI loss, 3rd space, sweat loss

Euvolemic (SIADH)

Hypervolemic

- Renal: ARF and ESRD
- Extra-renal: heart failure, cirrhosis, nephrotic

Excess Water Ingestion

- Primary polydipsia
- Fresh water drowning

Euvolemic Hyponatremia

SIADH

- Tumors: pulmonary and extra-pulmonary
- CNS disease
- Medications
- Pulmonary disease
- Glucocorticoid deficiency
- Myxedema
- Beer potomania
- Misc: AIDS, EAH, senile atrophy, idiopathic

AVP release despite hyponatremia

Control of AVP Secretion

- Osmolar
 - Osmoreceptor
- Non-osmolar/hemodynamic
 - Baroreceptors
 - Pressure/volume

Body chooses volume over composition

Brain Adaptation to Hyponatremia

- Acute: increase in brain water-cerebral edema
- Chronic: brain water slightly increased because of extrusion of organic osmoles
- Therapeutic implications
 - Rapid correction of acute hyponatremia(48h)
 - Slow correction of chronic hyponatremia
 - Osmotic demyelination syndrome (CPM)

Diagnosis

- Assess volume status
- Verify hyponatremia with plasma S.G.
- Measure U osmolality
- Measure U Na⁺
- Remember
 - U osm increased in hypoV, euV and hyperV hyponatremia
 - U Na⁺ increased in only euV except when ARF, ESRD, diuretics, aldo deficiency

Treatment

- Acute requires rapid correction
- Chronic
 - Water restriction
 - Drugs: cause NDI...demeclocycline, lithium
 - Osmotic solutes:urea
 - “Vaptans”: AVP Rc antagonists

Vaptans

- AVP Rc antagonists
 - G-protein coupled Rc
 - V1a: vasoconstriction, inotropic, platelet aggregation
 - V1b: pituitary ACTH secretion
 - V2: renal collecting tubules/ducts and endothelium
 - Metabolized by CYP3A4
 - Conavaptan (Vaprisol): parenteral
 - Tolvaptan (Samska): oral

Things to know about vaptans-1

- Use in euvolemic/hypervolemic hypoNa⁺
- Contraindicated in hypoV hypoNa⁺
- Tolvaptan: V2:V1a=29
- Metabolized by CYP3A4: other drugs?
- Heart failure decreases clearance
- Avoid in pregnant women
- Promotes slow aquaresis
- No OSDS
- AEs: Thirst 8-16%; dry mouth 4-13%

Things to know about vaptans-2

- Hyponatremia develops in 5%
- Correction rate > 12 mmol/L/24h-3%
 - If rate of correction too rapid use water or DDAVP
- Not studied in acute hyponatremia
 - aquaresis delayed 1-2 h
- Not studied in patients with $sNa < 115$ mmol/L
- Role in hyponatremia due to over treated DI?
- No reduction in M/M with long term use in heart failure

Exercise associated hyponatremia “EAH”

- May be severe: cerebral edema, noncardiac PE
- H₂O excess; impaired renal H₂O excretion
- Observational study: JCEM 2008;93:2072-78
 - 56 km ultramarathon
 - n=82
 - Measurements: plasma Na, AVP
 - Ad-lib H₂O
- Results
 - pNa unchanged but pvolume ↓8.5%
 - pAVP ↑3.9x
- Take home message:
 - Nonosmolar AVP release may contribute to hyponatremia if water in >out
 - Recommend: limit water to 400-800 ml/h; drink only when thirsty
 - Use hypertonic saline to ↑ sNa to 125 mmol/L or symptoms resolve