

**Hospital Acquired
Hyponatremia in children
“The Solution is in the Solution”
“الحل في ما يُحل”**

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Outline

- Introduction
- Pathogenesis of hyponatremia
- Hyponatremic Encephalopathy
- Prevention
- Risk factors
- Therapy
- Cerebral Demyelination
- Conclusion

Case Scenario

- Ahmad is one-yr-old boy who was admitted to PICU post-operatively
- Right upper lobe was resected for symptomatic congenital lobar emphysema
- IV fluid was started with D5 1/4 NS with 20 meq/L KCl at 40 cc/hr (his weight = 10 kg)
- Next day labs:
 - Serum Na = 128 (pre-op Na = 138). **Why??**

Wrong IV Fluid?

- Fluid maintenance = $100 \times 10 = 1000\text{cc}$
- Na maintenance = $2-4 \text{ meq/kg/day} = 20-40/\text{day}$
- $\frac{1}{4}$ NS = $\frac{1}{4}$ of 154 = 38 meq/L of Na (perfect)
- No hypotonic fluid bolus given

(danger)

- What went wrong?

Hyponatremia

- Common
- Tragic Brain Injury if mismanaged
- Hospital-acquired (hypotonic fluid)
- Death or neurologic injury if:
 - not recognized early
 - not treated properly

Pathogenesis of Hyponatremia

- Na = 135-145 mEq/L
- Kidney adaptation
- Hyponatremia from excess of H₂O ingestion
????
- Hyponatremia from only excess Na loss ?
- Usually:
 - A relative excess of free water with...
 - Impaired kidney ability to excrete free water

Renal Water Control

- Argenin vasopressin (AVP)
- Hypothalamus → Posterior pituitary
- ↑ Permeability to water in the collecting tubule
- Stimulation
 - Osmotic
 - Hemodynamic (››› inhibitory hypoosmolar)
 - Nonhemodynamic

Disorders in Impaired Renal Water Excretion

Depleted circulating volume:

- GI losses: vomiting, diarrhea
- Skin losses: CF
- Renal losses: diuretics, salt wasting nephropathy, cerebral salt wasting, hypoaldosteronism
- Edematous states: heart failure, cirrhosis, nephrosis, hypoalbuminemia
- Decreased SVR: sepsis, hypothyroid

Disorders in Impaired Renal Water Excretion

Euvolemic or hypervolemic:

- Renal failure: acute or chronic
- Non-hypovolemic state of ADH excess:
 - CNS: meningitis, encephalitis, tumors, head injury
 - Pulmonary disease: pneumonia, asthma, bronchiolitis
 - Cancer
 - Medications: vincristine, morphine
 - Nausea, emesis, pain, stress
 - Postoperative state
 - Cortisol deficiency

Who is at risk?

- Any hospitalized patient
- 1% of hospitalized (Na < 130)*
- Cellular swelling → Cerebral edema → Hyponatremic encephalopathy
- Incidence of hyponatremic encephalopathy:

Author	Inclusion Criteria (Na)	Incidence (%)
Wattad et al 1992*	< 125	53
Sarniak et al 1991	< 125	60
Halberthal et al 2001	< 130 in 48 hrs	78

SIADH

- High ADH:
 - No osmotic stimulus
 - No hypovolemic stimulus
- Most common:
CNS, Pulmonary, Malignancy, Medications

CNS insult (encephalitis) + Hyponatremia
± ? hypotonic IV fluid = Herniation*

*McJunkin et al NEJM 2001

Postoperative Hyponatremia

Age (year)	Setting	IV fluid	Na Value	Complication
3-5	Tonsilitis	Hypotonic	139-114	Quadriplegia
5	Tonsillectomy		141-123	Death
4	Tonsillectomy		139-115	Death
15	Tonsillectomy		141-101	Death
3-5	Tonsillectomy		138-121	Death
12	Fracture		137-120	MR
4	Fracture		139-118	Death
3	Tonsillectomy		137-113	Death
1.5	VP shunt		137-114	Vegetative
9	Fracture		137-120	Vegetative
15	Fracture		138-102	Vegetative
4	Tonsillectomy		138-107	Death
2	Orchiopexy		138-116	Death
6	Nasal packing		138-119	Death
12	Appendectomy		137-123	Death
12	Pneumonia		134-116	Vegetative

Arief et al. BMJ 1992 (mortality of 8% of postoperative hyponatremia)

Prevention

- Holliday MA, Segar WE. The maintenance need for water in parenteral fluid therapy. *Pediatrics*. 1957
- Schwartz et al. Syndrome of renal sodium loss and hyponatremia probably resulting from inappropriate secretion of antidiuretic hormone. *Am J Med*. 1957
- Holliday MA, Segar WE et al. Acute hospital induced hyponatremia in children: A physiologic approach. *J Pediatr*. 2004

Is it real risk??

- Hanna et al.
Incidence of hyponatremia and hyponatremic seizure in severe RSV bronchiolitis.
Acta Paediatr 2003

33% of infants transferred to PICU with
bronchiolitis had hyponatremia
4% had hyponatremic encephalopathy

Preventive Strategy

- Moritz ML, Ayus JC. Prevention of hospital-acquired hyponatremia: a case for using isotonic saline. *Pediatrics* 2003

Adjusting Maintenance Parenteral Fluids for Disease States

Isotonic (0.9%)	Fluid Restriction	Hypotonic
Dehydration	CHF	Hypernatremia
Salt-wasting nephropathy	Nephrosis	Nephrogenic DI
Decreased SVR	Cirrhosis	Sickle cell
CNS diseases	Hypoalbuminemia	Obstructive uropathy
Pulmonary	Renal insufficiency	Reflux nephropathy
Cancer		Renal dysplasia
Medications		Nephronophthisis
Nausea, emesis, pain, stress		Interstitial nephritis
Posoperative state		Burn
Glucocorticoid deficiency		Prematurity
		Fever
		Infectious diarrhea

The use of isotonic fluid as maintenance therapy prevents iatrogenic hyponatremia in pediatrics: A randomized, controlled open study

Alvarez-Montanana et al. *Pediatr Crit Care Med* 2008

- **Study Design:** One hundred twenty-two pediatric patients hospitalized in intensive care unit requiring maintenance fluid therapy were randomized to receive
 - isotonic fluids (isotonic group, NaCl 140 mEq/L) or
 - hypotonic fluids (hypotonic group, NaCl <100 mEq/L).
- **Results:** At 24 hrs, the percentage of hyponatremia in the hypotonic group was 20.6% as opposed to 5.1% in the isotonic group ($p = 0.02$).
No differences in the number of adverse events other than hyponatremia were observed between groups.

Clinical Manifestation of Hyponatremic Encephalopathy

- Headache, nausea, vomiting, weakness
- Behavioral changes & impaired response
- Advanced symptoms:
 - Seizure, respiratory arrest, neurogenic pulmonary edema, dilated pupils, decorticate posturing, even arrhythmias
- Slow or fast progress

Risk Factors

- Young age (< 16 yrs)
Larger brain to intracranial volume ratio
Brain = adult size by 6,
Skull = adult size by 16
- Average Na (encephalopathy)*:
 - Children = 120
 - Adult = 111

Children will have high morbidity

*Sarniak et al. Crit Care Med 1991.

*Bruce et al. Pediatrics 1997

Risk Factors

- Hypoxia + Hyponatremia = Disaster
- Hypoxia impairs brain cell volume regulation (more edema)
- Hyponatremia lead to more hypoxia
 - Decrease CBF
 - Respiratory Failure
(pulmonary edema, respiratory depression)

Hypoxia is the strongest predictor of mortality in patients with symptomatic hyponatremia

Therapy of HE

- Asymptomatic hyponatremia = Slow correction
- Symptomatic hyponatremia = Medical Emergency
- ABC ... support
- Hypertonic Saline (3%, 513 mEq/L NaCl)
- Rate: Increase Na by 1 mEq/L per hr until the patient is alert and seizure free.
- Optimal correction rate: 15-20 mEq in 48 hr
- 1 mL/kg of 3% NaCl will raise the Na level by 1
- ? Furosemide can be added

Cerebral Demyelination

- Rare complication
- Associated with rapid correction of hyponatremia (> 25 in 24 hrs) in animal*

?More complex:

- Co morbid conditions (hypoxemia, liver disease)
- The magnitude of correction (to hypernatremia)

*Ayus et al. Rapid correction of severe hyponatremia in the rat. *Am J Physiol* 1985

Cerebral Demyelination

- Biphasic pattern:
 - Encephalopathy →
 - Improvement →
 - Deterioration (2-7 days later)
- Pontine: mutism, dysarthria, spastic quadriplegia, pseudobulbar palsy, pseudo-coma and ataxia
- Extrapontine: Behavioral changes and movement disorders
- Diagnosis by MRI 14 days post correction

Key Message

The primary cause of brain damage in patient with hyponatremia is not cerebral demyelination, but cerebral edema and herniation

Caution

High risk for over correction of hyponatremia:

- Water intoxication
- Diarrheal dehydration
- Thiazide diuretics
- dDAVP

Stop the cause, urine will get diluted... ta ta

SIADH is saline resistant hyponatremia

Thank You
