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HYPERNATREMIA IN CHILDREN

DR .GH.SARVARI
PEDIATRIC NEPHROLOGIST

INFANT HYPERNATREMIA: A CASE REPORT



A 7-month-old boy presented to the ED with a history of profuse watery diarrhea for 5 days. His foster mother reported a recent decrease in urine output, vomiting of all oral intake, and a dramatic decrease in his activity level.

No temperature had been obtained at home. Past medical history included premature delivery at 36 weeks, apnea of prematurity, and gastroesophageal reflux. He was on no medications, and there were no known medical allergies.

Immunizations were up to date. Family history was unknown by the foster mother. Birth weight and recent weight prior to this illness were not known

PHYSICAL EXAMINATION

- **A rectal temperature of 38.2°C**
- **Pulse 187 beats/min**
- **Respiratory rate 32 breaths/min**
- **Blood pressure 120/86 mmHg**
- **Capillary refill was between 3 and 4 s**
- **Dry tongue and dry mucous membranes.**
- **Skin turgor was reduced**
- **He weighed 6.8 kg**

LABORATORY STUDIES

- **WBC 16,400 with 36% segmented neutrophils, 48% lymphocytes, and 14% monocytes**
- **Sodium 197 mmol/L (nL 136–145)**
- **Chloride 150 mmol/L (nL 98–107)**
- **Blood gas showed a pH of 7.24, pCO₂ of 30 mmHg, and a pO₂ of 40 mmHg and bicarbonate 9 mmol/L (nL 18–27)**
- **BUN 52 mg/dL (nL 5–15)**
- **Creatinine 1.1 mg/dL (nL 0.3– 0.5)**
- **Urinalysis revealed a pH of 5, SG= 1.031, protein greater than 300 mg, nitrite negative. WBC=15/, RBC=0, and few bacteria. Urinary sodium was 18 mmol/L, and urine osmolality was 796 mOsm/L.**

TREATMENT


After the normal saline bolus, the infant's condition improved. He became more alert and fussy, but was consolable. Capillary refill improved to less than 2 s. He was admitted to the hospital and pediatric nephrology was consulted because of the marked electrolyte abnormalities.


Based on the history of profuse diarrhea and vomiting, and the severe clinical dehydration, hypernatremic dehydration with prerenal azotemia and metabolic acidosis was the initial diagnosis.

D5 1/4 normal saline with sodium bicarbonate was started at 45 mL/h.

Hypotonic fluid was chosen because of the marked deficit in free water. The rate was estimated to provide maintenance fluid plus replace the free water deficit and on-going losses.

Sodium bicarbonate was added to the initial fluids to correct the extreme metabolic acidosis.

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- **Within 3 days of admission the child's weight had stabilized at 7.8 kg and his serum sodium had decreased to 155 mmol/L. A stool specimen was positive for rotavirus. Blood cultures were negative. Despite adequate oral rehydration solution intake, serum sodium remained between 150 and 154 mmol/L.**
 - **Urine output was 6.8 mL/kg/h. Urine osmolality was consistently less than 300 mOsm/L.**

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- In light of the persistent hypernatremia, polyuria, and dilute urine, diabetes insipidus (DI) was suspected. Pediatric endocrinology was asked to evaluate the patient.
 - Presumptive treatment for DI was recommended. Desmopressin acetate was prescribed and ultimately resulted in the serum sodium stabilizing at 136–140 mmol/L.
 - Urine output had dropped to approximately 2.5 mL/kg/h.
 - The diarrhea resolved by hospital Day 6, and he was discharged home on desmopressin acetate with no apparent sequelae of the severe hypernatremia

INTRODUCTION

Hypernatremia is typically defined as a serum or plasma sodium greater than 150 mEq/L.

Although pediatric hypernatremia is an uncommon electrolyte abnormality, there can be significant neurologic injury in patients with severe hypernatremia, especially those with acute and rapid changes in serum sodium

EPIDEMIOLOGY

- The true incidence of pediatric hypernatremia is unknown, as published data are based on hospitalized children.
- As an example, a Scottish study reported an overall incidence of hypernatremia (defined as a plasma sodium >150 mEq/L) of 0.04 percent for all pediatric hospitalizations in pediatric patients over two weeks of age over a study period from 1996 to 2006
- However, the risk of hypernatremia was 10 times greater in neonates less than two weeks of age, with an incidence of 0.4 percent.
- Neonatal hypernatremia was almost exclusively seen in breastfed infants with excessive weight loss (water loss).
- In older patients between two weeks and 17 years of age, the most common cause of hypernatremia on admission was excess water loss due to gastroenteritis or systemic infection

PATHOPHYSIOLOGY

- Plasma tonicity is tightly regulated by the release of antidiuretic hormone (**ADH**) from the posterior pituitary promoting water retention, and by thirst-prompting water ingestion.
- These homeostatic mechanisms that mediate plasma tonicity and water balance are similar in adults and children, resulting in a normal range of plasma sodium between 135 and 145 mEq/L that does not vary by age.

CONT.

- Hyponatremia is most often caused by the failure to replace water losses, which, in children, are **most commonly** due to gastrointestinal fluid loss.
- In these patients, the sodium plus potassium concentration in the fluid that **is lost is less** than the plasma sodium concentration.
- As a result, water is lost in excess of sodium plus potassium, which will **tend to increase** the plasma sodium concentration

CONT.

- In individuals with intact thirst mechanisms, the intake of free water promptly corrects any increase in plasma sodium.
- However, when water losses cannot be replaced because of a lack of free access to water, excessive loss in acute illnesses, or impaired thirst mechanism, sodium concentration increases and may result in hypernatremia.

CONT.

- Infants and children who are significantly **neurodevelopmentally impaired** are at particular risk for hypernatremia, as they may be unable to communicate their thirst and are dependent on others for fluid repletion.
- Pediatric hypernatremia also may result from urinary or skin loss of free water without adequate water replacement.
- Less commonly, pediatric hypernatremia may be caused by intake of sodium in excess of water (eg, administration of a hypertonic salt solution).
- In this setting, patients also are unable to access free water to correct the plasma tonicity.

ETIOLOGY

- Hypernatremia may be caused by a primary Na gain or a water deficit, the latter being much more common.
- Normally, this hyperosmolar state stimulates thirst and the excretion of a maximally concentrated urine.

For hypernatremia to persist, one or both of these compensatory mechanisms must also be impaired.

ETIOLOGY

- **EXCESSIVE SODIUM**
- Excess sodium bicarbonate
- Ingestion of seawater or sodium chloride
- Intentional salt poisoning (Child abuse or Munchausen syndrome by proxy)
- Intravenous hypertonic saline
- Hyperaldosteronism

ETIOLOGY

- **WATER DEFICIT-**
- Diabetes insipidus- Central, Nephrogenic
- **WATER AND SODIUM DEFICITS**
- **Gastrointestinal losses**
- Diarrhea, Emesis, Osmotic cathartics (lactulose)
- **Cutaneous losses**
- Burns, Excessive sweating
- **Increased insensible losses**
- Premature infants, Radiant warmers, Phototherapy

ETIOLOGY

- **Inadequate intake:**
- Ineffective breastfeeding, Child neglect or abuse, Adipsia
- **Renal losses**
- Osmotic diuretics (mannitol)
- Diabetes mellitus
- Chronic kidney disease (dysplasia and obstructive uropathy)
- Polyuric phase of acute tubular necrosis
- Postobstructive diuresis

EXCESS WATER LOSSES

- Loss of body fluids with a sodium plus potassium concentration that is less than serum or plasma sodium (hypotonic fluids) will result in an increase in sodium concentration if the water losses are not replaced.
- Sources of hypotonic body fluid losses include gastrointestinal fluids, dilute urine, and skin loss due to sweat or burns.
- In addition, inadequate water intake that fails to replace ongoing normal fluid losses will result in excess water loss and increases in serum or plasma sodium

GASTROINTESTINAL LOSS

- In children, the **most common** cause of hypernatremia is hypotonic gastrointestinal losses without replacement, which result in effective water loss.
- In particular, gastroenteritis due to rotavirus can present with profuse watery diarrhea and hypernatremia.
- In addition, losses due to vomiting or nasogastric drainage can lead to excess free water loss and hypernatremia

URINARY WATER LOSS

- Excessive urinary free water loss may be caused by disorders with impaired urinary concentration (eg, **diabetes insipidus [DI]**) or **osmotic diuresis**.
- Without adequate water replacement, sodium concentration will rise and may result in hyponatremia

CENTRAL DI

Central DI has multiple etiologies, including:

- **Congenital central nervous system**
- **Malformations and genetic syndromes with associated CNS anomalies**
- **Acquired causes due to CNS tumors, infiltrative processes of the hypothalamic-pituitary stalk**
- **Sequelae from neurosurgery**
- **Trauma**

NEPHROGENIC DI

- **Congenital nephrogenic DI is most often the result of mutations in the vasopressin type 2 receptor (AVPR2 and may be caused by a mutation in the aquaporin-2 gene (AQP2)**
- **Congenital nephrogenic DI is also observed in other inherited disorders, including :**
 - **Bardet-Biedl and Bartter syndromes,**
 - **nephronophthisis,**
 - **cystinosis,**
 - **familial hypomagnesemia with hypercalciuria and nephrocalcinosis**

ACQUIRED NEPHROGENIC DI

- Drug toxicity is the most common cause of acquire DI(**lithium, amphotericin, demeclocycline, ifosfamide, foscarnet, and cidofovir**)
- Hypercalcemia and hypokalemia
- Impaired urinary concentration is seen in a variety of renal diseases, including **obstructive uropathy, sickle cell disease, nephronophthisis, cystinosis, and acute or chronic kidney disease**

OSMOTIC DIURESIS

- Hyponatremia can also occur from urinary water losses due to renal excretion of nonelectrolyte, nonreabsorbed solutes, such as mannitol or **glucose** (eg, patients with diabetic ketoacidosis and hyperglycemia).

SKIN LOSS

- **Vigorous or sustained exercise, or significant febrile illness,** water losses from sweat can become more substantial and can result in hypernatremia if not corrected with water intake. Increased insensible water losses due to **burns** can also lead to hypernatremia

IMPAIRED THIRST MECHANISM

- Children with structural midline brain abnormalities include congenital abnormalities, such as **holoprosencephaly** , acquired lesions (eg, **craniopharyngioma**), and **infiltrative processes of the hypothalamic-pituitary stalk**.

EXCESS SALT INTAKE

- **Hypernatremia can be a consequence of salt intake out of proportion to water.**
- **A teaspoon of salt contains 100 mEq of sodium (Na), which can increase the serum sodium concentration in a 10 kg child by 15 mEq/L.**
- **In children, excessive salt intake is generally due to iatrogenic administration of excess sodium (eg, hypertonic saline solution), or due to salt poisoning.**
- **In either setting, patients are unable to access free water in order to restore plasma tonicity and correct hypernatremia.**

SALT POISONING

- Salt poisoning has been described both from incorrect formula preparation and as an intentional form of child abuse .
- Infants, young children, and individuals with significant developmental delay are especially susceptible due to their inability to communicate their thirst, their reliance on others for access to water, and smaller volume of distribution
- Salt poisoning causes a rapid onset of hypernatremia and tonicity, often resulting in cerebral hemorrhage and irreversible neurologic injury.
- Osmotic demyelination can occur, similar to the injury caused by a rapid elevation in serum sodium in patients with chronic hyponatremia

CLINICAL MANIFESTATIONS

- Nonspecific initial manifestations of hypernatremia include irritability, restlessness, weakness, vomiting, muscular twitching, fever, and, in infants, high-pitched cry and tachypnea.
- Severe symptoms are observed with an acute rise of sodium above 160 mEq/L and include altered mental status, lethargy, coma, and seizures.
- In the most severe cases, such as salt poisoning, the rapid rise in sodium leads to acute brain shrinkage, resulting in vascular rupture with cerebral and subarachnoid hemorrhage, demyelination, and irreversible neurologic injury

CHRONIC HYPERNATREMIA

- It appears that patients with chronic hypernatremia (defined as hypernatremia that is present more than one day) are asymptomatic due to cerebral adaption, which occurs within one to three days.
- This process involves restoration of brain volume by water movement from the cerebrospinal fluid into the brain, and generation and uptake of intracellular solutes (**osmolytes**) that promote water movement into the brain cells

TRANSIENT HYPERNATREMIA

- Transient hyponatremia (in which the serum sodium concentration can rise by as much as 10 to 15 mEq/L within a few minutes due to water loss into cells) can be induced by **severe exercise or seizures**.
- Sodium returns to normal within 5 to 15 minutes after the cessation of exercise or seizures.

EVALUATION

- **The evaluation in pediatric hypernatremia is focused on determining the underlying etiology**
- **Because pediatric hypernatremia is most often due to unreplaced hypotonic fluid losses, the history focuses on whether there are increased body fluid losses (eg, diarrhea) or inadequate fluid intake.**
- **History of excess gastrointestinal losses because of the presence of watery stools with documentation of the frequency and amount, or loss from nasogastric or colostomy drainage.**
- **History of impaired urinary concentration based on excessive urine output (polyuria) and dilute appearance.**

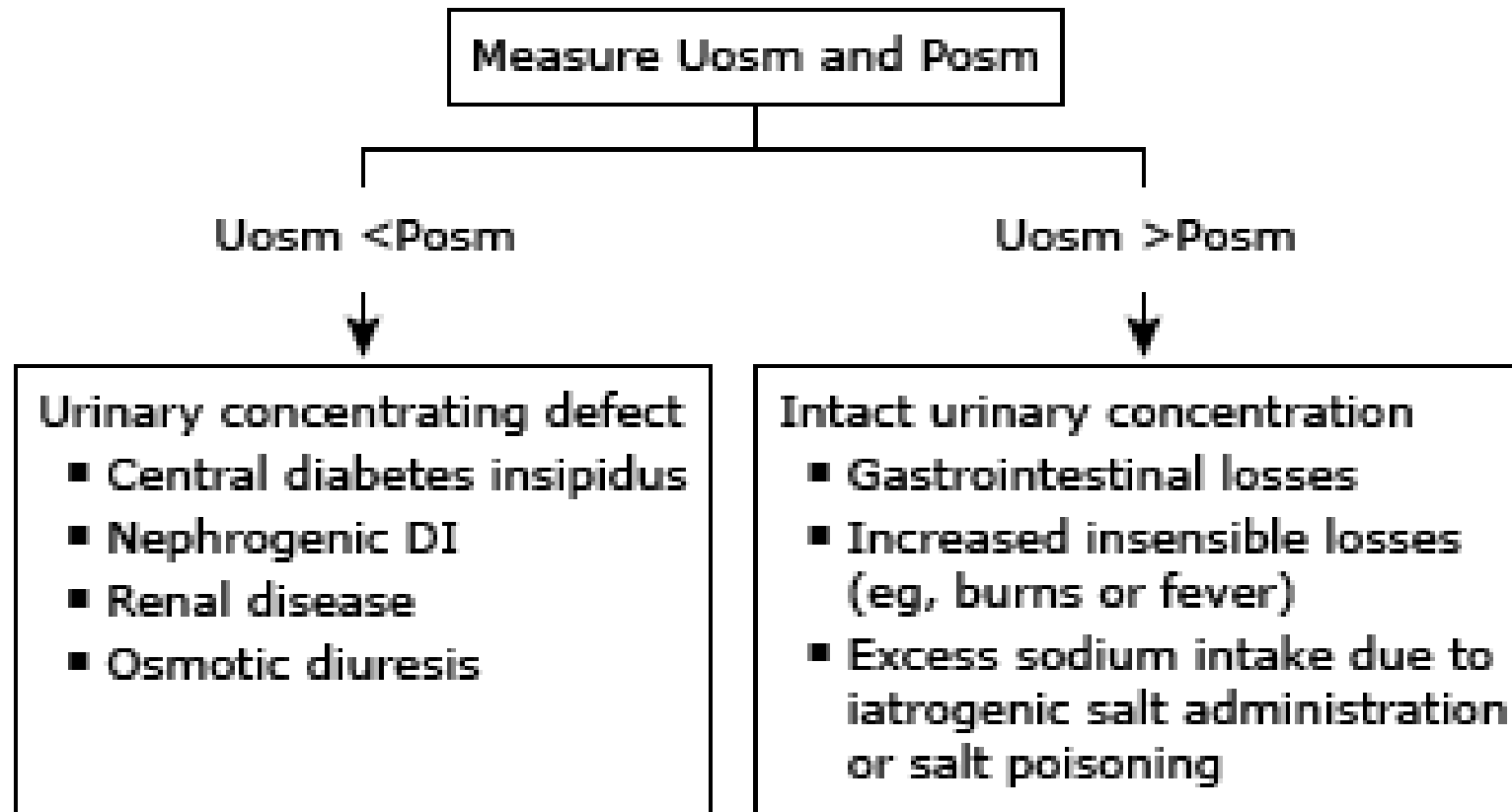
CONT.

- **Total urinary sodium excretion is appropriately increased with salt poisoning, and is appropriately reduced with hypovolemia due to unreplaced water losses.**
- **The fractional excretion of sodium (FENa) may be useful in a patient with hypernatremia, as a FENa greater than 2 percent in a volume-replete (well hydrated) patient is strongly suggestive of salt poisoning, whereas a FENa less than 1 percent is suggestive of dehydration caused by water loss.**

LABORATORY EVALUATION

- Laboratory studies should preferably be obtained before significant fluid intervention has taken place, although fluid therapy should never be delayed in the severely ill patient.
- When the underlying diagnosis remains uncertain, comparing the urine with plasma osmolality may be helpful in establishing the underlying mechanism and diagnosis (algorithm 1).

ALGORITHM 1




CONT.

- Other laboratory studies that may be included:
- Serum **BUN and creatinine** to determine renal function. Serum creatinine is also used to calculate the fractional excretion of sodium (**FENa**).
- **Serum/plasma and urine measurements of sodium and creatinine.**
- Urine sodium is typically low (<25 mEq/L) in patients with hypernatremic hypovolemia, generally due to gastrointestinal losses.
- Urine sodium exceeds 200 mEq/L in patients with salt poisoning
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TREATMENT

- **General principles —** Correction of hypernatremia requires both the administration of dilute fluids to correct the water deficit and, when appropriate, interventions to limit further water loss.
- Many pediatric patients also have a concurrent volume isotonic deficit usually due to gastrointestinal losses. Such patients with hypernatremia will require replacement of both water and electrolyte deficits

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- **In cases where hypernatremia alone is the primary abnormality, therapy is aimed at correcting the plasma sodium by providing free water and determining a rate of desired correction.**

ISSUES THAT NEED TO BE ADDRESSED WHEN TREATING PEDIATRIC HYPERNATREMIA ARE:

- **What is the volume status of the patient? Is there an emergent need for fluid resuscitation to restore intravascular volume and tissue perfusion?**
- **What is the magnitude of the water deficit that needs to be restored?**
- **At what rate should the hypernatremia be corrected (as lowering the sodium concentration too rapidly may lead to neurologic injury)?**
- **Is there a concurrent ongoing fluid loss that needs to be addressed?**
- **What is the underlying cause of hypernatremia and are there specific interventions that need to be considered?**

VOLUME STATUS AND EMERGENT FLUID RESUSCITATION

- **In any child with significant volume depletion, first management steps should be directed toward ensuring cardiovascular stability.**
- **In patients with moderate to severe hypovolemia, emergent fluid resuscitation with isotonic fluid is administered to restore intravascular volume and tissue perfusion.**
- **However, overzealous fluid resuscitation needs to be avoided to prevent inadvertent volume overload, which may be associated with cerebral edema**

CALCULATING THE FREE WATER DEFICIT

- The volume of free water to be provided can be calculated using one of two common approaches
- Free water deficit in milliliters = Current total body water x $\left[\frac{\text{current plasma Na}}{140} - 1\right]$
- Free water deficit in milliliters = $(4 \text{ mL/kg}) \times (\text{weight in kg}) \times (\text{desired change in plasma Na})$

RATE OF CORRECTION

- For children with chronic hypernatremia (plasma sodium ≥ 150 mEq/L for greater than 24 hours) or those with acute severe hypernatremia (plasma sodium > 160 mEq/L), we and other experts recommend that a rate of correction does not exceed a fall of sodium greater than 0.5 mEq/L per hour (ie, 10 to 12 mEq/L per day).

TREATMENT OF HYPERNATREMIC DEHYDRATION

Restore intravascular volume:

Normal saline: 20 mL/kg over 20 min (repeat until intravascular volume restored)

Determine time for correction on basis of initial sodium concentration:

- [Na] 145-157 mEq/L: 24 hr
- [Na] 158-170 mEq/L: 48 hr
- [Na] 171-183 mEq/L: 72 hr
- [Na] 184-196 mEq/L: 84 hr

Administer fluid at constant rate over time for correction:

Typical fluid: 5% dextrose + half-normal saline (with 20 mEq/L KCl unless contraindicated)

Typical rate: 1.25-1.5 times maintenance

Follow serum sodium concentration

Adjust fluid on basis of clinical status and serum sodium concentration:

Signs of volume depletion: administer normal saline (20 mL/kg)

Sodium decreases too rapidly; either:

- Increase sodium concentration of IV fluid
- Decrease rate of IV fluid

Sodium decreases too slowly; either:

- Decrease sodium concentration of IV fluid
- Increase rate of IV fluid

Replace ongoing losses as they occur

TREATMENT OF SPECIFIC ETIOLOGIES

Although most young children develop hypernatremia related to acute illness or inability to take in fluid, in cases where a chronic condition is identified, such as nephrogenic or central diabetes insipidus, therapy directed to the underlying condition (eg, administration of desmopressin) should be initiated in addition to providing free water replacement

A night desert landscape with rolling sand dunes. A bright star with a large lens flare is in the center of the sky. Several shooting stars are streaking across the dark blue sky. The text "THANK you!" is written in a yellow, cursive font across the middle of the image. Below the text, a row of ten smiley face icons is displayed.

THANK you!

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