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Hypernatremia in children. Focus on the neurological complications

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Hypernatremia is an electrolyte disorder in patients at the hospital stage of treatment. Symptomatic hypernatremia involves severe neurological disorders. The degree of dysfunction varies from mild behavioral disturbances to convulsions, coma, and depends on the duration and depth of hypernatremia. Neurological disorders are on one hand caused by the shrinkage of neurocytes along with high concentration of sodium in the blood, and on the other hand - by the development of brain edema with rapid correction of hypernatremia. Symptomatic hypernatremia is a threatening complication and involves a significant increase in mortality in children having a wide range of diseases. The paper describes current approaches to the pathophysiology, diagnosis and treatment of hypernatremia.

Key words: *hypernatremia, causes, diagnosis, forms, correction, diabetes insipidus, children.*

The concentration of sodium in the serum defines its osmolality and is a fundamental tool for monitoring the water balance of the body. Balance maintenance is supported by thirst, the synthesis of vasopressin (antidiuretic hormone), formation of endogenous water in the process of metabolism and by renal reabsorption capacity. An imbalance in this system is accompanied by pathology exchange of sodium which is known as hyponatremia or hypernatremia [1]. Increasing level of serum sodium over 145 mmol per liter signals on hypernatremia.

It is important to note that in most cases(except for the iatrogenic causes) hypernatremia is a violation of water exchange and is not a consequence of metabolic sodium [2]. Causes of this condition are numerous and include restriction of fluid due to severe chronic diseases, neurological complications, critical condition, prematurity, nutritional deficiency in breast-feeding. According to special literature data, hypernatremia was observed in more than 1% of

hospitalized patients in the U.S., while 60% of registered hypernatremia states accounted for hospitalized children [3, 4].

It should be noted that young children, especially at their first year of life, as well as patients on mechanical ventilation are considered to be a high-risk group. In addition, the physiological characteristics of the child's body - a large area of the body relative to the weight and growth, a higher body water content (70-80% in neonates, 70% of infants, 60% of young children and less than 60% of adults), significant loss of fluid from the body surface in comparison with older patients altogether predispose dehydration and development of hyponatremia.

Pathophysiology

Pathophysiological basis of this condition in most cases is characterized by a deficiency of total body water (TBW) in proportion to the total sodium content due to:

-Loss of free water (eg, diabetes insipidus);

-Loss of free water in excess of sodium loss (eg, diarrhea);

- Appointment of enteral or parenteral formulas with a high content of sodium [5].

Hypernatremia causes hyperosmolality of serum and extracellular fluid, which is accompanied by passive movement of water from the cell into the extracellular space (Fig. 1) [6]. The result is cellular dehydration which is to equalize osmolality of intra-and extracellular spaces, as it is especially critical to brain cells. Severe dehydration caused by hypernatremia is accompanied with a decrease of brain volume and damage of cerebral blood vessels, causing hemorrhagic stroke, encephalopathy, paralysis, and convulsions. It is important that the rapid rehydration using hypotonic solutions in patients having chronic hypernatremia causes swelling of the brain with a high risk of coma, convulsions and death [7].

Hypernatriemia causes

Hypernatremia reflects a deficit of total body water in proportion to the total content of sodium (Na). Due to the fact that the total amount of sodium in the body determines the amount of extracellular fluid, hypernatremia is usually considered depending on the volume of extracellular fluid: hypovolemic, normovolemic, and hypervolemic. In this context it is important to note that the volume of extracellular fluid does not completely reflect the effective plasma volume, i.e., its reduction can occur simultaneously with reduction of extracellular fluidvolume, or in different directions, such as in patients having heart failure, hypoalbuminemia, or capillary leak syndrome (capillary leak syndrome). Table. 1 shows the causes of hypernatremia in children.

Hypovolemic hypernatremia

In patients with hypovolemic hypernatremia there was observed loss of total body water, prevailing over the loss of sodium. The most common causes of this type of dehydration in children are diarrhea and vomiting, with possible different scenarios - both hyper-and hyponatremia. According to the literature data, acute dehydration in hypernatremia in infants may be due to the use of activated charcoal on the basis of 70% sorbitol with an overdose of theophylline [8]. The concentrated sorbitol acts as an osmotically active agent and causes the movement of free water from the bloodstream into the lumen of the intestine, causing diarrhea. In such cases, there is a high urine osmolality and low sodium concentration in it (<20 mmol / l).

Renal causes of hypovolemic hypernatremia include the use of diuretics, hyperosmolar states. So, loop diuretics inhibit reabsorption of sodium in the concentrating portion of the nephron and increase water clearance. Mannitol, glycerol, urea less damageconcentrating renal function with further development of hypernatremia. The most common cause of osmotic diuresis is hyperglycemia in patients with diabetes mellitus. In such cases there has place hypoosmolality or izoosmolality of urine with sodium concentration of 20 mmol / l.

Normovolemic hypernatremia

Children with marked hypernatremia normovolemic suffer from equivalent loss of both total body water and sodium. Extrarenal causes of this condition are perspirational fluid loss, including respiratory losses: tachypnea, hyperventilation, mechanical ventilation with no adequate hydration of breathing mixture, the loss of water from the skin surface (hyperthermia, prematurity, phototherapy and the use of sources of radiant heat without adequate replenishment of water).Among other reasons of normovolemis hypernatriemia it is important to note a gained or congenital central diabetes insipidus, or renal genesis [9, 10]. Causes of diabetes insipidus are presented in Table 2. As it can be seen from the table, among the most common causes of acquired diabetes insipidus there are injured central nervous system (CNS) tumors, infections, lesions of hypoxic origin, neurosurgery, death of brain of non-traumatic origin. It is important to note that the course of this disease can be divided into three phases:

1) The initial phase of polyuria (lasting from several hours to several days);

2) Phase of antidiuresis, probably caused by the release of antidiuretic hormone from damaged axons (lasting from from several hours to several days);

3) The second phase of the polyuria, the duration of which depends on the nature of the damage.

Hypervolemic hypernatremia

Hypervolemic hypernatremia in most cases is an iatrogenic problem caused by the appointment of hypertonic solutions of sodium bicarbonate during cardiopulmonary

resuscitation, correction of metabolic acidosis. Another common cause is conducting fluid therapy, including hypertonic solutions of sodium chloride for hyponatremia correction. Patients with CNS injury are also at risk (conduction of osmotherapy in order to reduce intracranial hypertension is often accompanied by hypernatremia). Among non-iatrogenic reasons of hypervolemic hypernatremia there is primary hyperaldosteronism. In addition, this pathological condition develops during drowning in sea water.

Clinical evidences

Clinical manifestations of hypernatremia are primarily due to CNS disabilities, as well to symptoms of dehydration in the case of hypovolemia. The severity of the patients' state and thus severity of clinical manifestations depend on the depth and pace of hypernatraemia development. In 70-75% of children with hypernatremia that occurred within 48 h, there was marked irritability, high pitched screaming, disturbances of consciousness ranging from somnolence to coma, normal or increased muscle tone, and convulsions. In addition, this group of patients may suffer from hyperglycemia and hypocalcemia.

The clinical manifestation of hypernatremia in newborns and infants is presented by nausea, vomiting, fever, respiratory distress syndrome, spasticity, tonical and clonical convulsions, and coma. In the experiment, it was established that death due to respiratory failure is observed in animals with serum osmolality of 430 mOsm / L [11]. According to special literature data, mortality in children having acute hypernatremia varies within 10-45%; up to 15% of those who have had hypernatremia, had neurological complications, including intellectual deficits, convulsions, spastic paralysis. In case of chronic hypernatremia mortality rate is 10% [7, 12].

Diagnosis

Diagnosis oa hypernatremia is based on verification of the underlying disease (clinical history, physical examination, laboratory and instrumental methods), determining the level of serum sodium, aldosterone, cortisol, antidiuretic and adrenocorticotropic hormone, glucose, urine output, urine sodium levels, serum osmolality and urine. It is necessary to conduct a differential diagnosis of poliurinal conditions, including diabetes insipidus renal and central origin in patients having polyuria. A two-stage combined functional and pharmacological test with deprivation of water and the subsequent introduction of vasopressin (SVI) is a reliable method of differential diagnosis of various forms of polyuria.

Treatment

Before treating hypernatremia a clinician should know the answer to two critical questions:

- What is the volemic status of the child?
- How long has hyponatremia (chronic or acute) developed?

Normalization of serum sodium with parallel correction of hypovolemia is the main purpose of treatment at hypovolemic hypernatremia. Rehydration tactics is determined depending on the degree of dehydration. Oral dehydration is carried out at exsicosis of I-II degree in patients having no severe pathology of the gastrointestinal tract.

Severe forms of exsicosis (II-III degree), impaired mental status, symptoms of hypovolemic shock, the ineffectiveness of oral rehydration therapy, severe dysfunction of the gastrointestinal tract (uncontrollable vomiting, increase in diarrhea syndrome), oliguria and anuria, which are not amenable to correction with oral rehydration, are indications for parenteral rehydration [13].

Conditionally-infusion therapy consists of two phases.

I. Emergency care. Severe dehydration causes development of hypovolemic shock, which determines the urgency of ongoing activities:

- Provision of intravenous, or intraosseous access, if intravenous access is impossible;
- bolus introduction (within 15 min) of isotonic crystalloidon 20 ml / kg of body weight (such as Ringer's lactate, 0.9% sodium chloride solution);
- additional bolus administration of crystalloids, depending on the severity of dehydration and clinical response to the ongoing infusion.

II. Correction of blood volume, exsicosis and the current pathological losses. The daily volume of fluid for rehydration is tentatively defined as the sum of the physiological needs of the child in the liquid during the day, the amount needed to correct exsicosis, and the amount of current pathological losses.

Calculation of fluid required to reimburse exsicosis, can be performed using the following formula:

- Total body water (TBW) in adults and older children makes 60% of body weight (in infants and young children TBW exceeds 70%), and therefore there can be made the following calculation: OBO = 0,6 × m, where m - body weight in kg;
- shortage of liquid (L) = 0,6 × m × [(Na serum mmol / L: 140 mmol / l) -1].

The composition of infusion media in the second phase depends on the degree of volemia. So, in hypovolemic hypernatremia there should be used a 0.45 or 0.2% sodium chloride solution for creating euvolemia and exclusion of rapid normalization of sodium levels. In hypervolemic hypernatremia caused by transfusion of sodium bicarbonate and concentrated solutions of sodium, it is advisable to use 5% glucose in water in combination with loop diuretics.

In hypernatremia normovolemic fluid deficit should be corrected by 0.45% sodium chloride solution or 5% glucose solution (in clinical practice, the most appropriate option is 0.9% sodium chloride solution and 5% glucose solution in a 1:1 ratio). When hypernatremia is combined with hyperglycemia, it is recommended to use 0.25% glucose solution in water, due to the fact that rapid correction of hyperglycemia, particularly when using insulin, is associated with brain swelling.

The main purpose of rehydration in the second phase is to correct fluid deficits, and normalize levels of sodium. It is important to note that the rate of decrease in serum sodium concentration should not exceed 10-12 mmol / L at 24 h or 0.5 mmol / h. Exceeding this speed is associated with catastrophic neurological disorders, including cerebral edema and death. The safest mode of therapy is the normalization of sodium concentration within 48-72 hours. It is recommended to check sodium level every 4 hours.

If the rate of sodium level decrease is less than 0.5 mmol / L per hour, it is recommended to reduce the concentration of sodium in the starting solution. It is important that hypernatryemic dehydration is often accompanied by hyperglycemia, and hypocalcemia, and therefore requires dynamic control of these parameters. When diagnosing and treating children with hypernatremia is necessary to use help of professionals such as a nephrologist, intensivist, an endocrinologist. Treatment of symptomatic hypernatremia should be conducted in the intensive care unit [14].

Treatment of diabetes insipidus is determined by the form of the disease. The main method of treatment is treatment of the underlying disease; and with organic and idiopathic forms of the disease it is a diet with a limited introduction of sodium, and protein replacement therapy using synthetic analogs of vasopressin (Minirin).

In conclusion, it is necessary to draw the reader's attention to the paradox of hypernatryemia: it is possible to damage the central nervous system both at the stage of hypernatremia development (wrinkling neurocytes), and on the background of inadequate (ie, fast) treatment of that (cerebral edema), with further development of severe neurological complications associated with high mortality and disability in patients – in both cases.

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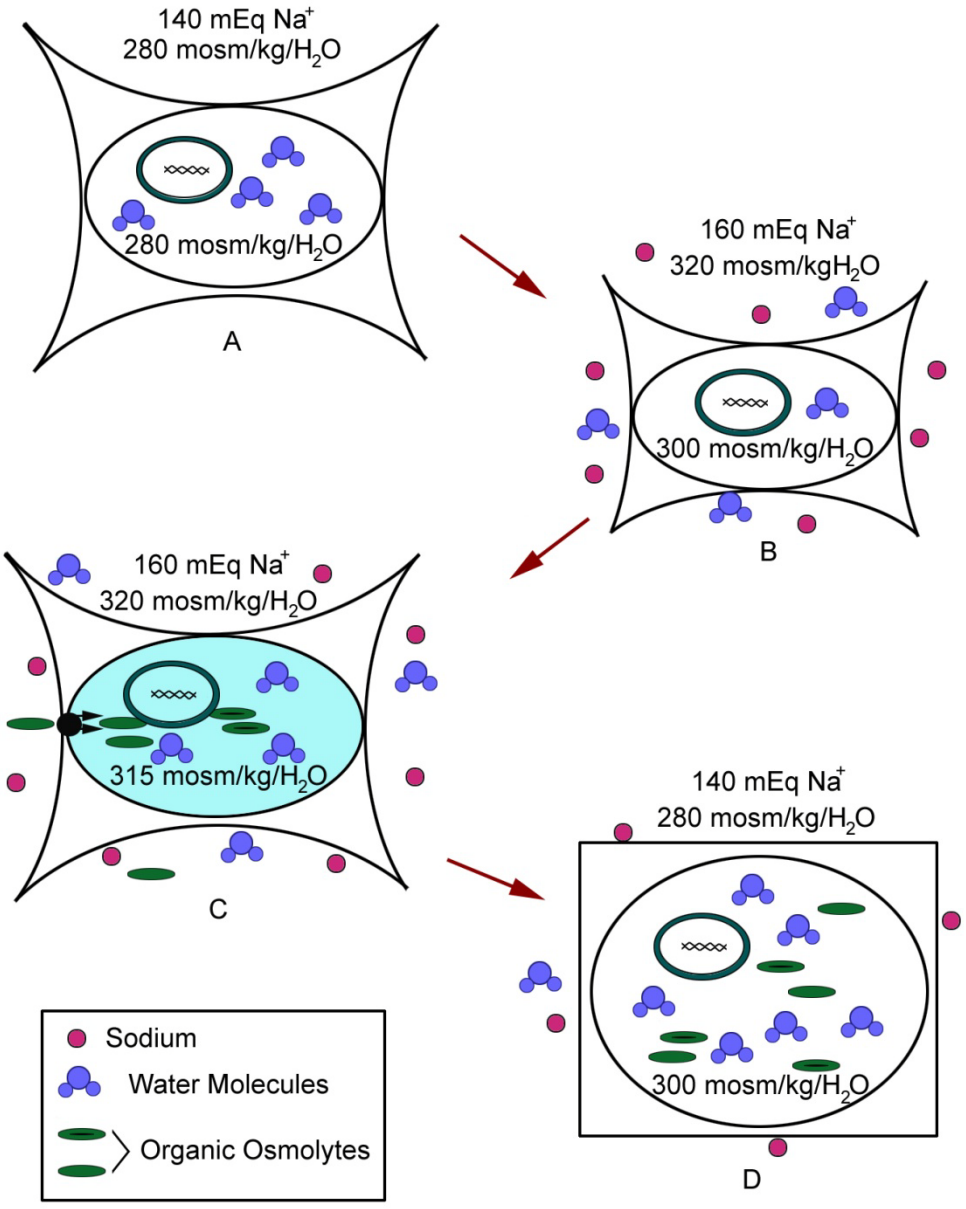

Fig. 1. A - normal cell; B - cells in response to hyperosmolality of extracellular space: passive osmosis - movement of water from the cell into the extracellular space with a decrease in cell volume, C - in response to hyperosmolality of extracellular space and a decrease in cell volume there has place active transport of organic osmolytes from the extracellular space and intracellular synthesis of osmolytes; D - quick correction of extracellular hyperosmolality leads to passive osmosis of water into the cell into relatively hyperosmolal cellular space, causing swelling of the cells, their damage and death [6]

Table 1. Hypernatriemia causes in children

Description	**Fluid loss option**	**Example**
Hypovolemic hypernatremia		
Loss of PSBs dominate over losses of sodium (Na), the total content of Na in the body is reduced	Losses through the gastrointestinal tract	Diarrhea Vomiting
	Loss through the skin	Burns Excessive sweating
	Loss through the kidneys	Kidney disabilities Osmotic diuresis (Hyperglicemia, urea, mannitol)
Normovolemic hypernatremia		
Losses from the TBW content in the body Na, close to normal proportion	Respiratory losses	Tachypnea Mechanical ventilation of lungs
	Loss through the skin	Excessive sweating Hyperthermia The sources of radiant heat Phototherapy
	Loss through the kidneys	Central diabetes insipidus Nephrogenic diabetes insipidus Syndrome reinstall osmostata
Hypervolemic hypernatremia		
The total content of Na in the body against a background of normal or elevated levels of TBW	Appointment of solutions with high contents of Na	Hypertonic solutions of NaCl Na bicarbonate Unbalanced parenteral nutrition

Notice. TBW - the total body water; GI - gastro-intestinal tract.

Table 2. Causes of diabetes insipidus

Central	Congenital	Hereditary
		Idiopathic
	Acquired	Head and eye traumas
		Tumors of the central nervous system (CNS)
		Infection: • encephalitis • meningitis • cindrom Guillain-Barre syndrome - hypoxia (newborns)
		Condition after neurosurgery
		CNS vascular pathology: • aneurysm • thrombosis • hemorrhage
		Mixed reasons: • histiocytosis • granulomatosis (sarcoidosis, tuberculosis, Wegener's granulomatosis) • non-traumatic brain death
Kidney-originated	Congenital	VR2-mutation, X-linked mutation of AQP2
	Acquired	Chronic renal failure
		Tubulointerstitial kidney disease
		Hypercalcemia
		Hypokalemia
		Side effects of drugs, alcohol, lithium, diuretics, amphotericin B, demeklotsiklin
		Crescent cell anemia
		Errors of diet: primary polydipsia, a limited introduction of sodium chloride, protein