

Treatment of Hyponatremia: What the Clinician Needs to Know

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ABSTRACT

Hyponatremia due to different pathogenetic mechanisms is the most common electrolyte abnormality and is associated with increased morbidity and mortality. However, several aspects of the proper management of these patients are not clear. In this editorial a brief overview of the basic principles for the appropriate treatment of hyponatremia are summarized.

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Key words: Hyponatremia; Serum sodium; Syndrome of inappropriate antidiuresis

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EDITORIAL

Hyponatremia (serum sodium <135mEq/L) is the most common electrolyte abnormality, is due to different pathophysiologic mechanisms, is associated with increased morbidity and mortality and its appropriate treatment is still a therapeutic challenge^[1,2]. Even though clinical practice guidelines on the treatment of hyponatremia

have been recently reported^[3,4], several aspects of the proper management of these patients are not clear^[5,6]. In this editorial some basic principles for the appropriate management of patients with decreased serum sodium levels are briefly summarized.

1) It should be stressed that non hypotonic hyponatremia (with normal or increased Posm) should be carefully excluded by a meticulous medical history and the appropriate laboratory investigation. Consequently, the initial approach to the hyponatremic patient includes the determination of Posm (by an osmometer if it is available) as well as the exclusion of pseudohyponatremia (due to severe hypercholesterolemia, hypertriglyceridemia, and hyperproteinemia) or hypertonic hyponatremia [due to the presence of osmotic active agents, such as glucose (hyperglycemia) or the administration of mannitol or glycine]^[2,7,8]. It is worth mentioning that in hyperglycemic individuals the corrected serum sodium levels should be calculated by increasing the measured serum sodium levels by 2.4 mEq/L for each 100mg/dl of glucose above normal^[4,8].

2) A growing list of drugs, including thiazides, ecstasy and SSRIs, can cause hyponatremia, while endocrine causes of hyponatremia (mainly adrenal insufficiency) should be carefully and appropriately assessed^[9,10].

3) Urine sodium in a random urine specimen is commonly used to differentiate between hypovolemia-induced hyponatremia (urine sodium <20 mEq/L) and the syndrome of inappropriate antidiuresis (SIADH, urine sodium >30 mEq/L). However, increased urine sodium levels (>30 mEq/L) can also be encountered in patients with extracellular volume contraction with renal or adrenal insufficiency, severe metabolic alkalosis, osmotic diuresis, as well as in those on thiazides^[2,8].

4) In cases of hypovolemia-associated hyponatremia, 0.9% sodium chloride solution should be administered (with potassium chloride 10% if hypokalemia is also present). In this setting potassium anions should be taken into account in the calculation of the tonicity of the infused solutions. Interestingly, the infusate formula proposed by the Adrogue-Madias and verified by Liamis et al can reliably project the effect of gaining 1L of any infusate on the patient's serum sodium (ΔNa^+) and thus can be used to calculate the rate of the administered 0.9% NaCl solution^[2,11,12].

$$\Delta Na^+s = \frac{(\text{sodium and potassium of the infusate}) - \text{serum sodium}}{\text{total body weight (55\% of body weight in men and 50\% in women)} + 1}$$

Most authorities suggest that the correction of serum sodium concentration by more than 8 mEq/L/d (or more than 18 mEq/L over the first 48h) should be avoided even in cases of acute hyponatremia^[5,6]. However, the main problem notified during treatment of hyponatremia is the rapid water diuresis observed during therapy when hypovolemia is corrected leading to an abrupt decrease of ADH and rapid increase of serum sodium levels. Thus, prompt recognition of an increased diuresis (>100 mL/h) and repeated determinations of serum sodium levels are mandatory to avoid hypercorrection of serum sodium levels leading to osmotic demyelination. Moreover, conditions such as hypokalemia, chronic alcoholism, malnutrition, underlying liver disease or serum sodium <105 mEq/L associated with high risk of this syndrome should be readily recognized^[2,8].

5) In asymptomatic or oligosymptomatic cases of SIADH water restriction (to 1L/day) can increase serum sodium levels. However, its effectiveness is limited by the restricted ability of some patients to excrete water. Thus, the calculation of the electrolyte-free water clearance ($C_{H_2O}^e$) is necessary to predict if water restriction can increase serum sodium levels.

$$C_{H_2O}^e = V_{\text{urine}} \times \left(1 - \frac{\text{Urine sodium} + \text{urine potassium}}{\text{Serum sodium}}\right)$$

A negative value of the $C_{H_2O}^e$ suggest diminished ability to excrete water; if this is the case water restriction is unable to increase serum sodium levels. Alternatively, the urine/plasma electrolyte ratio (U/P) using spot urine values for sodium and potassium should be calculated by the equation^[13,14].

$$\frac{U}{P} \text{ ratio} = \frac{\text{urine sodium} + \text{urine potassium}}{\text{serum sodium}}$$

When this ratio is <0.5, fluid restriction to <1L/d could increase serum sodium levels. On the contrary, a ratio >1 should be considered as a predictor of the probable failure of fluid restriction given that the electrolyte free water excretion is negative. Under these circumstances water intake must be severely restricted (< 500 mL/d).

In these cases of asymptomatic/oligosymptomatic solute administration by increasing the dietary intake of sodium chloride and proteins as well as by urea administration can also substantially increase water diuresis and serum sodium levels in SIADH patients^[8,15]. Furthermore, demeclocycline (which can down regulate aquaporin 2 channels)^[16] and vaptans (vasopressin antagonists), recently approved for the treatment of hyponatremia, can also be used for managing these patients^[17,18].

6) In patients with SIADH 0.9% sodium chloride solution should not be used to treat hyponatremia. In fact, since these patients are usually euvoletic, aldosterone is suppressed and sodium is rapidly excreted in the urine. Thus, the failure of 0.9% NaCl solution to increase serum sodium levels should raise the suspicion of the presence of SIADH. Additionally, in such cases urine osmolality is relatively fixed, and its value determines the urine volume. Indeed, if Uosm greatly exceeds 300 mosmol/kg, 0.9% sodium chloride solution (308 mosmol) can be excreted in a smaller urine volume leading to water retention and further decrease of serum sodium levels (especially if Uosm is > 530 mosmol/kg)^[2,6,8].

7) In hyponatremic patients with hyponatremic encephalopathy a 3% sodium chloride solution should be used according to the recently published guidelines^[3,4]. A 100 mL (or 150 mL) volus (2 mL/kg body weight) of 3% saline should be administered at 10-minute intervals to a total of 3 nodes if necessary to control symptoms or until a

target of a 5mEq/L increase in serum sodium concentration in 1h is achieved. However, excessive correction (>6 mEq/L) in the first 6h should be avoided^[3]. Alternatively, Ayus et al proposed that a total of 500ml of 3% sodium chloride solution over a 6h period should be administered^[19]. On the contrary, Adrogué and Madias suggest that these procedures can lead to overcorrection of hyponatremia^[5]. Thus, in patients with symptomatic hyponatremia a 3% sodium chloride solution should be carefully used, while the Adrogué and Madias infusate formula should be at first used to appropriately calculate the amount and rate of the hypertonic solution needs to be given^[2,5].

8) In cases of SIADH, the solute load given is excreted in the urine having a fixed Uosm. To increase the water diuresis furosemide (20 mg ×2/d) should be used. In fact the furosemide-induced decrease in Uosm leads to a profound increase in urine volume and subsequently to serum sodium. However, frequent determinations of serum and urine electrolytes as well as of Uosm (if an osmometer is available) are necessary during management of patients with hyponatremia^[2,5,8].

9) During treatment of hyponatremia when ongoing fluid losses (mainly renal) are substantial (>1L/d), the fluid loss formula should be used, since it projects the effect of losing 1L of any fluid (mainly urine) on the patient's serum sodium (ΔNa^+_s)^[2].

$$\Delta Na^+_s = \frac{\text{serum sodium} - \text{urine (sodium} + \text{potassium)}}{\text{total body water} - 1}$$

Thus, when urine output is increased this formula can be used to appropriately change treatment to avoid inappropriate overcorrection. When this formula predicts a rather inappropriate increase of serum sodium levels proper modifications of the infused solutions should be performed (f.e. administration of hypotonic sodium solutions or even 5% dextrose in water, or simultaneous administration of desmopressin (a synthetic vasopressin) to prevent and reverse inadvertent overcorrection of hyponatremia^[20,21].

We conclude that patients' careful surveillance is necessary during treatment of hyponatremia. Water restriction and the cautious administration of the proper saline solutions (isotonic or hypertonic) can safely increase serum sodium levels. Frequent sampling for serum sodium levels as well as sodium and potassium excretion in the urine are needed to adjust the treatment and avoid inappropriate under or mainly overcorrection of hyponatremia.

CONFLICT OF INTERESTS

The authors declare no conflict of interest.

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