Scientific Foundation SPIROSKI, Skopje, Republic of Macedonia
Open Access Macedonian Journal of Medical Sciences. 2020 Mar 25; 8(F):1-10.
https://doi.org/10.3889/oamjms.2020.4270
eISSN: 1857-9655
Category: *F - Review Articles*
Section: *Systematic Review Article*

The Available Clinical Approaches to the Management of Patients with Acute and Chronic Hypernatremia

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Edited by: Mirko Spiroski
Citation: Moradi A, Sabzghabaei F, Kalantar M. The Available Clinical Approaches to the Management of Patients with Acute and Chronic Hypernatremia. Open Access Maced J Med Sci. 2020 Mar 25; 8(F):1-10. https://doi.org/10.3889/oamjms.2020.4270
Keywords: Acute hypernatremia; Chronic hypernatremia; Clinical approach
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Received: 06-Jan-2020
Revised: 02-Feb-2020
Accepted: 10-Feb-2020

Funding: This study was supported by the Cairo University teaching hospitals
Competing Interests: The authors have declared that no competing interests exist

Abstract

Hypernatremia has been known as a conventional electrolyte problem and is defined as a serum sodium concentration growth up to a value above 145 mmol/l. This disease is also known as a hyperosmolar condition, which is resulted from a reduction in total body water compared to the electrolyte content. Since two types of hypernatremia, including acute and chronic, exist, in the present study, we will review the available clinical approaches for the management of patients with acute and chronic hypernatremia. To this end, 68 studies having the criteria of the present review and published from 2000 were chosen and their data were extracted. The inclusion criterion was to be mainly focused on hypernatremia clinical treatment and those having side topics were excluded from the study. Acute symptomatic hypernatremia is a disease that occurs in <24 h and needs to be treated immediately. On the other hand, there is a chronic hypernatremia that occurs in a duration of more than 48 h and is required to be treated at a lower speed due to cerebral edema risks during treatment. Finally, for providing beneficial outcomes to patients, both chronic and acute hypernatremia need to be compared thoroughly and also more investigation needs to be done.

Introduction

Hypernatremia has been known as any increased plasma Na concentration up to a value higher than 145 mM. This condition is often seen in intensive care units (ICUs) and it is mostly developed by admission wards. The disease leads to rise mortalities, and it also causes an extended length of stay in the ICU ward [1]. One of the recent studies on severity and duration of hypernatremia after ICU admission indicates that there are higher mortality and duration of stay in the ICU ward (an increased rate of 40% and 28%, respectively) [2].

A prospective study conducted in the ICU ward shows that almost 50% of pre-dialysis patients suffering from acute kidney injury (AKI) also have a dysnatremia, which is actually hypernatremia, and also an increased mortality rate exists particularly for severe/acute hypernatremia (a serum sodium of 156) in comparison with normonatremic patients (89.1% vs. 64.6%, respectively) [3]. In addition, pre-operative hypernatremia is relevant to increase perioperative 30-day mortality and morbidity [4].

To understand hypernatremia, one needs to be familiar with the main fluid compartments of the body and how those compartments work together. Accordingly, total body water (TBW) is known as a crucial physiological expression in such an area. TBW occupies nearly 60% and 50% of the body weight among males and females, respectively. It is also divided into two main categories, including extracellular fluid (ECF) and intracellular fluid (ICF) [5]. The former encompasses interstitial and lymph fluid, plasma, transcellular fluid within body cavities, connective tissue and bone, and finally adipose tissue while the latter occupies two-third of the water in a body [6]. Another relevant important concept is tonicity, which points to cell volume's behavior in a specific solution and also introduces the effective osmoles' action throughout a membrane. A cellular volume is extended at the time cells are bathed in a relatively hypotonic solution and contracts when bathed in a relatively hypertonic solution. The reason is that water moves inside and outside of the cell to achieve tonicity with a stable state. Active/effective osmoles are glucose and sodium as well as related anions in the ECF; this is while the major cation of the ICF is potassium and estimations for its serum or plasma concentration are not so valuable to infer total body potassium. Besides, osmolality introduces the total sum of both ineffective and effective osmoles

per kg of a body's fluid. The former osmoles, usually alcohol and urea, are able to cross throughout the cell membranes freely and thus generally do not lead to a cellular volume change. Osmolality is known as a weak sign of tonicity following to existence of such ineffective-type osmoles. Whereas the impacts of tonicity on cellular size might not be direct, serum sodium may act as a useful surrogate for tonicity in all parts of the body in a stable state [7].

Hypertonicity or dehydration points to the TBW loss in such a way that cellular volume contracts, while volume depletion is an expression that is employed to represent ECF loss. These two individual conditions lead to both different clinical specifications and therapeutic reactions [8], [9].

On the other hand, according to a comparison between hypernatremia and hyponatremia, it can be said that the former signifies a water deficit relative to sodium and may be resulted from few causes, including insufficient free water intake, free water losses, and, more seldom overload of sodium (all elaborated in etiology section). In contrast to hyponatremia, hypernatremia always points to serum hyperosmolality [10].

As a result, hypernatremia permanently depicts hypertonic hyperosmolality and continually leads to cellular dehydration or transient dehydration, while chronic plasma hypertonicity correction through rehydration therapy can point to herniation, brain swelling, and even death [10]. The clinical differences between acute and chronic hypernatremia can be realized by considering the different mechanisms through which the cells inside the brain adjust their volume in a reaction to brief and sustained osmotic challenges [11]. For this reason and also for the significance of hypernatremia, the present study reviewed the clinical approaches for the management of patients with acute and chronic hypernatremia. In the methodology section, we initially provide some details on etiology and pathophysiology as well as causes of this disease, and then, we explain the treatment and clinical approaches.

Methods

The present study is actually a qualitative work and a careful review and critical analysis of the medical literature. We undertook several searches in such authoritative online databases as PubMed, MEDLINE, Link of Springer, Online Library of Wiley, Science Direct of Elsevier, Cambridge Core, and Cochrane. To this end, the special keywords (i.e., hypernatremia, acute hypernatremia, chronic hypernatremia, hypernatremia management, and hypernatremia diagnosis, clinical approaches for hypernatremia, and etiology of hypernatremia) associated with the subject of this review were determined, based on which the searches were conducted. The time range of the investigated content is limited from 2000 to 2019. Accordingly, 68 studies having the criteria of the present review and published from 2000 were chosen and their data were extracted. The inclusion criterion was to be mainly focused on hypernatremia clinical treatment and above-mentioned keywords and those having side topics were excluded from the study.

Etiology

Hypernatremia is a water problem. In other words, it usually points to inaccessibility of water or when there is a disorder or damage in thirst mechanism. The primary causes of hypernatremia could be divided into the following groups:

- Free water losses:
  - Osmotic diuresis/renal losses (e.g., poorly controlled diabetes mellitus, being recovoered from renal failure, intravenous mannitol/loop diuretics use, diabetes insipidus, being recovered from obstructive uropathy) [12], [13]
  - Gastrointestinal losses (e.g., profuse diarrhea secondary to treatment with activated charcoal/sorbitol for poisoning, prolonged vomiting/severe diarrhea, sodium polystyrene sulfonate/sorbitol use among patients suffering from hyperkalemia) [14]
  - Insensible or sweat losses (e.g., burns, exercise, heat exposure, and fever) may not lead to acute hypernatremia, but they can worsen the hypernatremia [15]
  - Within peritoneal dialysis, where the high dextrose dialysates are used (seen among patients unable to normally drink water) [16]
- Inadequate/insufficient free water intake:
  - Being unable to drink water or limited water accessibility (e.g., older patients who have dementia) [16]
  - Impaired thirst mechanism (e.g., granulomatous disease, primary hypodipsia due to brain tumors, congenital hypothalamic lesions, and the existence of subfornical organ-targeting antibody) [17].

It is noteworthy to mention that those suffering from hypernatremia show a deficit in free water intake, in the two conditions explained above, the only abnormality that is seen among them is either they are unable to drink water or they are inaccessible to water due to the disorders of their body system, inaccessibility/limited accessibility to water or the impaired thirst mechanism [18].

- Sodium overload:
  - Prescription of high volumes of solutions of hypertonic sodium bicarbonate (e.g., patients

who are suffering from metabolic acidosis) or hypertonic saline [19].

- Surplus use of mineralocorticoid (e.g., Cushing syndrome and primary aldosteronism), whereas hypernatremia is usually mild and such patients typically suffer from a concomitant abnormality in their water accessibility, developing an acute hypernatremia [20]
- Salt intake at a high volume (e.g., inadvertent infusion with 5% saline, deliberate ingestion of household-strength bleach, improperly high concentration of either sodium chloride or sodium bicarbonate in dialysate for the treatment of hemodialysis, seawater drowning [thereof in survivors], and ingestion of bamboo salt or general excessive salt ingestion which usually occurs among children/pediatric patients when salt might be mistaken for sugar) [21], [22].

According to the details of the etiology of hypernatremia, as mentioned earlier, Figure 1 depicts a diagram of possible etiologies of this disease.

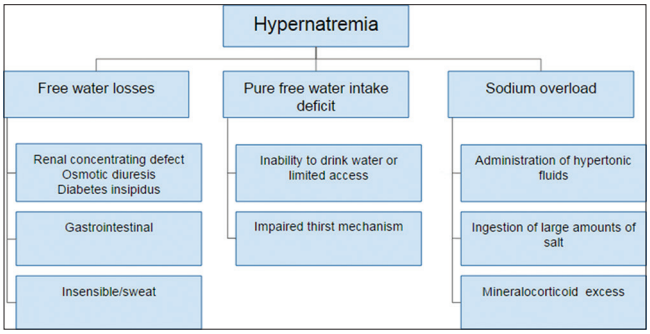

Figure 1: Possible etiologies of hypernatremia

As mentioned above, dementia patients usually suffer from a concomitant infection, and free water losses and inadequate free water intake may be seen concurrently [23].

Nevertheless, diabetes insipidus is an unconventional reason for hypernatremia incidence since the patient's thirst mechanism is intact enough to tackle electrolyte abnormalities development [13]. Two types of diabetes insipidus exist:

- Nephrogenic:
  - Acquired: Causes include specific drugs (e.g., demeclocycline, lithium, cisplatin, foscarnet, amphotericin B, aminoglycosides, Vitamin A or D excess, penicillin derivatives, vinblastine, colchicine, and vasopressin receptor antagonists) [24], [25], amyloidosis, sickle cell disease, obstructive uropathy, additional tubulointerstitial diseases, hypercalcemia, and hypokalemia [26]
  - Congenital: Although it is resulted from a mutation at the corresponding gene for the receptor vasopressin (V2) in the majority of cases and is X-linked, a low rate of patients has mutations in the aquaporin 2 collecting duct (AQP2) gene [27].
- Central/hypothalamic:
  - Acquired: A history of traumatic brain injury or any other damage to the brain (e.g., infections, vascular syndromes, aggressive surgery for craniopharyngioma, tumors, Rathke cleft cyst, or other types of hypothalamic tumors) often exists [19]. In a study, for the 1st time, two case studies having apparent temozolomide-induced central diabetes insipidus were described [28]. Temozolomide (an alkylating agent) is active in the central nervous system, may improve the treatment of advanced metastatic melanoma [29]. Faje *et al*. [28] concluded that, although the prevalence of central diabetes insipidus is rare, it may be referred to as a reversible side effect of treatment with temozolomide. This type of diabetes insipidus is relevant to acute myelogenous leukemia, as well [30].
  - Congenital: This is rarely seen [27].

Dexmedetomidine, a sedative used before and within surgical procedures, is reported to result in polyuria and urinary concentrating defect through a not known mechanism, which can lead to partial central or nephrogenic diabetes insipidus [31].

Pathophysiology

In general, the serum sodium concentration (Na^+) could be considered as a function of the total exchangeable sodium and potassium in the body as the TBW. In doing so, hypernatremia may merely develop as a result of either a loss of free water or a gain of sodium or a combination of both. Nevertheless, a high percentage of patients with hypernatremia are still hypervolemic despite a high urine output; this is due to formerly received vast amounts of normal saline and being massively edematous [32], [33].

Both urinary loss and diarrhea may lead to hypernatremia. In the case of the former, electrolyte-free water excretion (also referred to as electrolyte-free water clearance) is found through the following equation known as electrolyte-free water excretion formula [34].

$$V \times \left(1 - \frac{U_{Na} + U_K}{P_{Na}}\right)$$

Where,

V denotes urine flow rate, U_{Na} refers to sodium's urine concentration (mEq/L), U_K shows potassium's urine concentration (mEq/L), and PNa denotes plasma concentration of sodium (mEq/L).

A negative or positive value can be obtained for electrolyte-free water excretion [24]:

- $U_{Na} + U_K < P_{Na}$ (Positive): A process tending to increase the concentration of serum sodium
- $U_{Na} + U_K > P_{Na}$ (Negative): A process tending to decrease the concentration of serum sodium.

Where, U_{Na}, U_K, and P_{Na} denote sodium's urine concentration, potassium's urine concentration, and sodium's plasma concentration, respectively.

The people who have a normal renal function and also the individuals who receive huge amounts of saline are likely to focus their urine on excreting their received sodium load, and, as a result, they will have minimal electrolyte-free water excretion. Nevertheless, patients with diabetes insipidus or kidney dysfunction are not able to excrete the extra sodium load and are likely to develop hypernatremia [19], [35], [36].

In an acute type of hypernatremia (typically characterized by the onset of signs <48 h), the higher osmolality in the extracellular space will lead the water to move out of brain cells and thus resulting in shrinkage of the brain. Such shrinkage may result in neurological outcomes, including weakness, lethargy, and irritability. In the case of severe types, adverse manifestations may contain seizures, intracranial hemorrhage, coma, stupor, and death [19], [37]. Chronic hypernatremia (typically developing over >48 h) causes fewer variations in brain cell volume since the brain cells can be matched with the chronic hyperosmolality through increased intracellular osmolality. Brain cells accomplish it first by accumulating potassium chloride and sodium chloride and then by increasing intracellular brain solutes including taurine, glutamate, and myoinositol [37], [38].

In central type of diabetes insipidus, no vasopressin (which is also referred to as arginine vasopressin or antidiuretic hormone) exists due to a congenital/acquired condition which impairs vasopressin synthesis. Nevertheless, in nephrogenic type of diabetes insipidus, the kidneys provide no proper response to the secretion of vasopressin [39].

Patients with hypernatremia mostly have a high creatinine level and blood urea nitrogen (BUN). The high BUN level may make the hypernatremia worse through an osmotic diuresis. Therefore, the amounts of potassium and sodium excreted in the urine will be relatively small (i.e., $U_{Na} + U_K < P_{Na}$), increasing the excretion/clearance of electrolyte-free water [40].

Treatment

As in other diseases, the treatment of hypernatremia should be first undertaken by addressing the primary causes and then taking appropriate actions (e.g., treating fever, stopping the offending medication, relieving the urinary obstruction, giving insulin, and discontinuing the sodium sources), as well as substitution of any free water deficit and ongoing fluid losses, and simultaneously, keeping an eye on serum sodium concentration to make sure all levels are returning to the correct range at the desired rate. However, no consensus exists on the ideal correction rate. Rapid correction of concentration of the serum sodium is of high importance due to the cerebral edema's risk; in contrast, an investigation indicated that prolonged correction of concentration of the serum sodium could be harmful, as well [41]. Another systematic review reports an absence of good-quality evidence (observational controlled or randomized trials) for active correction of hypernatremia among resuscitated patients who are recovered from a critical disease [42].

On the other hand, the following factors can be pointed out as risk factors of hypernatremia:

- Advanced age
- Uncontrolled diabetes (solute diuresis)
- Mental or physical impairment
- Diuretic therapy
- Primary polyuria disorders
- Hospitalization
- Residency in nursing home, inadequate nursing care [10].

Treatment strategy

In all patients, the primary treatment strategy involves the following steps:

- Making the deficiency of free water calculated
- Estimating proceeding losses of free water (if applicable)
- Determining a suitable serum sodium correction rate
- Designing a suitable fluid repletion program that takes into account the estimated free water deficit, the desired serum sodium correction rate, and any ongoing free water losses
- More specific treatment is guided by the existence of signs or symptoms, severity of symptoms, time of onset, and volume status of the patient [10].

Severe or acute hypernatremia must always be treated in hospital, whereas mild/chronic hypernatremia can be controlled in the outpatient conditions, as well [10].

Chronic hypernatremia

Most of the patients with hypernatremia are suffering from chronic type. The brain matches itself to hypernatremia through idiogenic osmoles generation. It is a protective mechanism that begins on the 1st day

and continues to be completed within a few days, and it decreases cerebral edema. Due to the prevalence and importance of the chronic type of hypernatremia, first, we elaborate the chronic hypernatremia and its different types as follows:

Chronic hypernatremia is categorized into three main forms: Hypovolemic, euvolemic, and hypervolemic, each of which has specific treatment considerations [43]. Figure 2 compares each mentioned form.

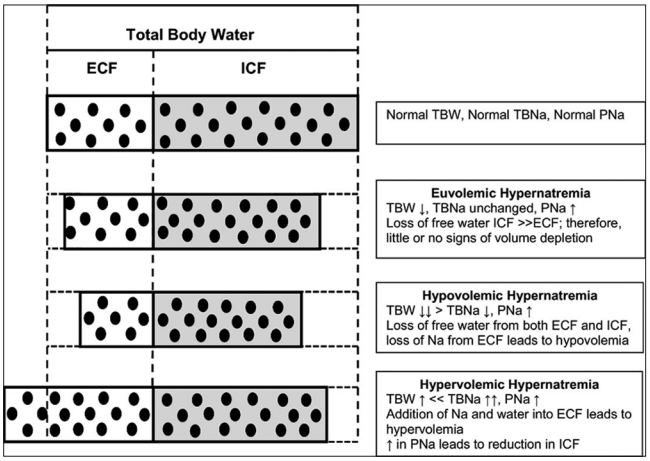

Figure 2: Hypernatremia caused by variations in total body water and total body sodium. The circles in black introduce the sodium (Na) [10]

Furthermore, enhanced plasma osmolality due to hypernatremia leads to water movement outside the brain cells and will thus cause shrinkage of the brain cells. Next, the brain will experience some adaptive processes which aim at additional solutes' accumulation to recover the volume of the brain, which is composed of slower organic osmolytes' accumulation and rapid inorganic ions' accumulation. Such an adaptive process for chronic hypernatremia is considered for the incidence of lower neurologic signs/symptoms in a comparison to acute hypernatremia with similar severity [44]. While a patient is being recovered from chronic hypernatremia, the brain's organic solute content will be slowly back to normal levels within 24–48 h. As a result, chronic hypernatremia correction needs to occur gradually for the prevention of rapid fluid motions into the brain cells and the relevant development of cerebral edema [45]. Most specialists recommend not to exceed sodium correction from 0.5 mEq/L/h to 10–12 mEq/L/d among patients suffering from hypernatremia for the duration above 24 h [44]. Nevertheless, no randomized trial is available to support such a recommendation. Studies conducted on animals and children/pediatric patients report that quicker rates may result in neurologic symptoms [46], [47]. The ingredients and composition of the fluid, which is supposed to be given, is considerably dependent on the lost fluid type and any simultaneous electrolyte disorders. The water deficiency, which is presented with pure water loss (no change in the total content of cation in the body), may be estimated through the following equation (inferred of the Edelman equations): Water deficiency = TBW × (ongoing concentration of serum sodium/140−1). This equation helps to estimates the amount of positive water balance needed to take the concentration of serum sodium back to 140 mEq/L, while traditional approaches recommend to replace half of the calculated water deficiency within the first 24 h and the rest within the next 48–72 h [48].

Another equation, also inferred from the Edelman equations, was reported by Madias and Adrogué and Madias [10]. It is broadly employed in clinical settings for the management of hypernatremia and also has been investigated prospectively in the management of patients suffering from hypernatremia, particularly chronic ones [49].

$$\Delta[Na] = \frac{[Na + K]_{infusate} - [Na]_{serum}}{Total body water + 1}$$

The equation mentioned above estimates the forecasted impact of retaining 1 L of the prescribed solution on the concentration of serum sodium. Application of either the former or latter formula needs body weight to measure and estimate TBW accurately. Furthermore, such a formula is not considered for current losses, which might change considerably over the treatment course. Both losses, including renal and extrarenal, need to be taken into consideration and also included in the overall fluid administration [10], [50]. Such data provide the conditions for individual analysis of the net balance of water, potassium, and sodium. Proper regulation in the fluid administration needs to be directed through frequent evaluation of the clinical status of the patient as well as serial monitoring of laboratory values within the treatment. This mostly pertains to iterated serum sodium measurements every 6–8 h over the initial therapy [51].

Although hypervolemic hypernatremia accounts for the least conventional form of hypernatremia, it is regarded as an excessive prescription of sodium (hypertonic saline solution infusion, hypertonic sodium bicarbonate, and accidental salt overloading) [52]. In this case, the replacement of non-renal losses or hypotonic urinary with isotonic solutions leads to a hypertonic solution's net retention and hypernatremia development. This scenario may happen over the treatment of some common disorders, including burns, septic/hypovolemic shock, prolonged nasogastric suction, uncontrolled sorts of diabetes, and being recovered from severe azotemia [7], [46]. Hypervolemic type of hypernatremia is identified recently in critical care conditions [46]. Balance investigations on water and electrolytes (i.e., tonicity balance studies) approve such a fact that the mentioned issue is basically due to the prescription of isotonic fluids within the context of weak maximal urinary concentrating ability, along with the associated limitation of water intake [50]. This issue is elaborated as "shallow content of water and very high content of salt" [46].

Here, some case presentations for chronic hypernatremia are discussed as follows:

An analysis undertaken on 130 critical patients suffering from hypernatremia indicated that in a rate of 92% of cases, hypernatremia was seen over an ICU stay, and the primary cause relevant to hypernatremia was loss in renal water. Deficient correction, with shallow content of free water and very high content of the hypertonic solution, accompanied these cases, as well [46]. Such a mechanism is revealed in a patient in Robertson *et al*. [47] during a representative 24 h period when he required aggressive fluid resuscitation. In this case report, Al-Absi *et al*. [48] evaluated a 73-year-old man with obesity who was presented with severe hypotension due to acute/severe bleeding in lower gastrointestinal. The disease that was diagnosed in this patient was a hypervolemic hypernatremia type. The patient carried on the restricted mobility and reduced sensation of thirst, which left him with a high risk of experiencing chronic hypernatremia. In the time of the study, the family members of mentioned patient provided him with a time planned fluid intake. In the follow-up phase, the concentration of serum sodium was 145 mEq/L (145 mmol/L).

The development and treatment of hypervolemic hypernatremia in the patient investigated by Al-Absi *et al*. [48] are presented in Tables 1 and 2.

Table 1: Development of hypervolemic hypernatremia in the patient investigated by Al-Absi *et al*. [48] according to the effect of isotonic saline solution administration and effect of furosemide with either fluid restriction or water replacement

Effect of isotonic saline solution administration
24 h intake: 4.0 L of isotonic saline; 4×154 mEq/L=616 mEq of sodium
24 h output: 2.0 L of urine; urine osmolality 350 mEq/L
Urine sodium plus potassium concentration (lost in urine)= ~100 mEq/L; 2×100 mEq=200 mEq
Net positive cation balance: 616–200=416 mEq
Net positive water balance: 4.0–2.0=2.0 L
Tonicity of retained fluid: 416 mEq/2.0 L=208 mEq/L, which would increase [Na] ~1.0 mEq/L
Effect of furosemide with either fluid restriction or water replacement:
Before furosemide administration: Serum sodium concentration: 146 mEq/L
Body weight=113 kg; TBW=0.6×113 kg=68 L; note: 0.6×body weight used due to generalized edema
Total body cation content: 68 L×146 mEq/L=9928 mEq
24 h water intake: <1.0 L, similar to insensible and stool losses
24 h output: 4.0 L of urine; urine sodium plus potassium concentration=~100 mEq/L
Net cation balance: 0 intake−4×100 mEq/L=−400 mEq
Net water balance: ~0–4 L=−4 L
New total body cation content: 9928–400=9528 mEq; new TBW=64 L
Predicted new serum sodium concentration: 9528 mEq/64 L=149 mEq/L
Measured serum sodium concentration after furosemide was 149 mEq/L
If 2 L of water were administered and retained, net water balance would be−2.0 L
New TBW=66 L; predicted serum sodium concentration: 9528/66=144 mEq/L
Administration and retention of 4.0 L of water: 9528/68=140 mEq/L with no change in TBW
Alternative analysis (assuming a 4.0 L relative water deficit): Furosemide yields a urine Na + K of ~100 mEq/L, which can be considered equivalent to excretion of 0.67 L of isotonic saline solution and 0.33 L of free water. Replacement of such urine output 1:1 with free water would result in the addition of 0.67 L of water per 1 L of urine output. Thus, the replacement of 6.0 L of urine output with 6.0 L of free water would be necessary to correct the 4.0 L water deficit over the desired time frame, assuming no other losses

TBW: Total body water.

Treatment of hypervolemic hypernatremia has two goals: (1) Achievement of water equilibrium and negative sodium for the correction of hypervolemia and (2) gradual correction of hypernatremia. These goals can be achieved through restriction of sodium, diuresis with loop diuretics along with water replacement, or undertaking the hemodialysis [51]. Correction of both diseases, including hypervolemia and hypernatremia, can be done only on an excess of a negative sodium and potassium balance from a negative water equilibrium/balance [53]. Prescription of furosemide alone causes excretion of urine with an osmolality content of ~300 mOsm/kg and urinary sodium in addition to the concentrations of potassium as many as ~100 mEq/L. This fact reveals that excretion of water exceeds that of cation, resulting in worsened hypernatremia. Prescription of 5% dextrose in water and furosemide may result in resolution of either hypernatremia or hypervolemia [53].

Table 2: Treatment procedure of hypervolemic hypernatremia in the patient investigated by Al-Absi *et al*. [48] in two settings

Setting 1: A 73-year-old man with [Na^+] of 163 mmol/L, body weight of 94 kg, TBW=0.4×94=37.6 La; selected solution is 0.9% normal saline (sodium concentration, 154 mEq/L)
$\Delta[Na^+]_{serum} = \frac{154-163}{37.6+1} = -0.23\,\text{mEq / L / 1 L of infusate}$
Patient received 3.0 L of 0.9% normal saline solution
Predicted $\Delta[Na^+]_{serum}$=~−0.7 mEq/L
Observed $\Delta[Na^+]_{serum}$=~0.0 mEq/L
Setting 2: Subsequent therapy with dextrose 5% in water as replacement solution
$\Delta[Na^+]_{serum} = \frac{0-163}{37.6+1} = -4.2\,\text{mEq / L / 1 L of infusate}$
For a goal of Δ[Na^+]serum of 10 mEq/L/24 h, 10/4.2=2.3 L of infusate required; given the patient's estimated ongoing losses (GI and insensible losses of ~2.0 L), the rate of infusion becomes 4300 mL/24 h=179 mL/h
Predicted Δ[Na^+]serum=~−10 mEq/L
Observed Δ[Na^+]serum=−7.0 mEq/L

The key role of accurate measurement of body weight and the succeeding estimation of TBW is clear because any failure to acquire iterated measurements of body weight may result in remarkable mistakes in TBW estimation. In addition, the TBW, estimated as 0.6 × body weight, is valid merely for healthy males at relatively younger ages. Among female cases and the elderly ones, 0.5 × body weight is considered as a closer approximation for TBW under euvolemic circumstances. In the case of dehydration in a patient with older ages, another adjustment of 0.4 × body weight will make the approximation of TBW more closely [54].

The following items have been represented as the risk factors of the development of hypernatremia: Restricted mobility, weakened thirst, limited access to water, a urinary concentrating defect associated with a chronic kidney injury, and non-renal losses from the ileostomy as well as AKI which often escorts the hypernatremia, specifically in the case of diarrhea or osmotic diuresis with depletion of intravascular volume [55]. Although AKI is hardly ever considered as the direct source of hypernatremia, it might play a role in its development through restricted urinary concentrating capability from weakened medullary hypertonicity generation [56].

The beginning step for the treatment of hypernatremia consists of the administration of isotonic saline solution for 18–24 h to put back the hemodynamics. This kind of fluid therapy will lead to no variation in concentration of serum sodium [48]. The

next therapy based on 5% dextrose in water will result in successive correction of concentration of serum sodium within 48 h [48]. Too rapid correction of chronic hypernatremia is considerably regarded as high risk; however, some observational investigations have also indicated that a gradual correction of hypernatremia over the first 24 h is likely to result in a higher rate of mortality [57]. As a result, another therapy as the alternative may be a prescription of 1–2 L of normal saline solution for quick restoration of plasma volume on hypotonic fluids for the promotion of hypernatremia correction [58].

Intravenous replacement of free water as 5% dextrose in water is typically nominated versus oral free water intake for euvolemic hypernatremia management among hospitalized patients. The hyperglycemia caused by 5% dextrose in water might not be seen in the case of infusion rates of <300 mL/h. Nevertheless, one of the necessary solutions may be insulin therapy, which is employed for the prevention of hyperglycemia and osmotic diuresis among diabetic patients. Intravenous solution with 0.22% sodium chloride is reported to be applied successfully as a replacement fluid; however, a small risk of hemolysis is possible followed by using this solution [58].

Overall, every chronic type of hypernatremia is likely to be treated securely and efficiently through sound quantitative evaluation and clinical reasoning of output and intake, specifically output of urine. All types of hypernatremia somehow point to an absolute or relative water loss. In doing so, the primary control and management of this disease will be to identify the main reason for hypernatremia and correct specification of the volume status and body weight of the patient to provide the conditions to calculate the water insufficiency. Classification of chronic hypernatremia into three categories, including hypovolemic, euvolemic, and hypervolemic, allows us to have a beginning point to formulate what type and rate of fluid are supposed to be prescribed. Continual clinical evaluation as well as serial laboratory/experimental data are necessary to make sure of hypernatremia's gradual correction up to a value of ~0.5 mEq/L in each hour, not a value above 10 mEq/L within 24 h [10].

Furthermore, in another case study, a patient suffering from chronic hypernatremia but not having thirst sensation was investigated. This patient was presented with weakness of muscles to whom water intake was the administration method which led to successful treatment. This approach is considerably challenging but gave rise to the reduction of serum sodium with resolution of all symptoms of the patient [59].

Acute hypernatremia

The following steps are to be taken for cases with acute hypernatremia [10]:

- A report should be established for disease onset. It should be noted that the acute form is <24 h, and the chronic form is above 24 h
- The serum sodium should be corrected at a primary rate of 2–3 mEq/L/h (for a duration of 2–3 h) (maximum total value of 12 mEq/L/d)
- Every 1–2 h, the serum and urine electrolytes should be measured
- Serial neurologic examinations should be undertaken and the rate of correction should be reduced with improvement in symptoms
- In the event of existence of volume deficiency and hypernatremia, intravascular volume needs to be restored by isotonic sodium chloride before administration of free water [10]
- Patients need to be provided with intravenous 5% dextrose, in case of patients' inability for oral water toleration [58].

Other recommendations for chronic hypernatremia are also recommended and applicable for acute type. In addition, training of ambulatory care is recommended to facilitate looking after such patients in a hospital [60] and in orthopedic ward [61], [62], [63], [64].

Conclusion

Acute hypernatremia is the disease happening at a duration of <24 h and needs to be corrected quickly. On the other hand, chronic hypernatremia (<48 h) is required to be corrected gradually and in lower speed due to cerebral edema risks during treatment. Finally, this area needs more prospective investigations to compare interventions for both chronic and acute hypernatremia to beneficial outcomes for such patients.

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