Hypernatremia in critically ill patients☆,☆☆,★

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Abstract Hypernatremia is common in intensive care units. It has detrimental effects on various physiologic functions and was shown to be an independent risk factor for increased mortality in critically ill patients. Mechanisms of hypernatremia include sodium gain and/or loss of free water and can be discriminated by clinical assessment and urine electrolyte analysis. Because many critically ill patients have impaired levels of consciousness, their water balance can no longer be regulated by thirst and water uptake but is managed by the physician. Therefore, the intensivists should be very careful to provide the adequate sodium and water balance for them. Hypernatremia is treated by the administration of free water and/or diuretics, which promote renal excretion of sodium. The rate of correction is critical and must be adjusted to the rapidity of the development of hypernatremia.
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1. Introduction

Hypernatremia is defined as a serum sodium concentration exceeding 145 mmol/L [1]. The Edelman equation shows the serum sodium concentration (Na^+) as a function of the total exchangeable sodium and potassium in the body and the total body water [2].

$$[Na^+] = \frac{(Na^+_{total\ body} + K^+_{total\ body})}{total\ body\ water}$$

increase ⟹ gain of sodium

decrease ⟹ loss of free water

Equation 1 (while Na^+ total body stands for total exchangeable sodium and K^+ total body stands for total exchangeable potassium).

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Consequently, hypernatremia can only develop as a result of either a gain of sodium or a loss of free water or a combination of both. Although hyponatremia can be associated with iso-osmolality or even hyperosmolality when an additional osmotically active particle is present in excess (eg, glucose in hyperglycemia), hypernatremia is always associated with hyperosmolality [3,4]. Under normal conditions, thirst is the major defense mechanism against the development of hypernatremia [3,5]. Osmolality is regulated within narrow ranges in the healthy individual, and even slight elevations in osmolality lead to the development of thirst and the secretion of antidiuretic hormone [3]. Thus, hypernatremia usually develops only when there is no access to free water, when the person has a disturbed sensation of thirst or when he or she is unconscious. Critically ill patients are often unconscious, intubated, or sedated, and their "water intake" is mainly managed by the physician, making them prone to the development of hypernatremia [4,6].

This review provides an overview of the new findings on epidemiology and outcomes associated with hypernatremia in critically ill patients. It focuses on the pathophysiology and presents a diagnostic approach and treatment recommendations for hypernatremia in the intensive care setting.

2. Frequency and timing of hypernatremia in critically ill patients

Traditionally, hypernatremia has been considered to be mainly a problem of the elderly or infants with diarrhea [1,7,8]. Indeed, hypernatremia is rare in noncritically ill, hospitalized patients with a prevalence of 0·2% for hypernatremia upon admission and 1% for patients developing it during their hospital stays [9].

In contrast, hypernatremia is a much more common finding in critically ill patients treated in intensive care units (ICUs). Upon admission to the ICU, between 2% and 6% of patients are already hypernatremic [10,11].

Between 6% and 26% and 4% and 10% of patients become hypernatremic during the course of treatment in medical and surgical ICUs, respectively [10,12-16]. In 1 medical cohort of patients as well as in a cohort of patients admitted to the ICU after cardiothoracic surgery, the cumulative incidence of hypernatremia has demonstrated that almost all patients who have ever experienced hypernatremia during their ICU stays developed this electrolyte disturbance during their first week after admission [10,13]. This observation might be explained by the physicians' efforts to correct hypovolemia, which is often associated with the administration of large amounts of fluids,

which, on the one hand, might be hypertonic compared with the ongoing fluid losses of patients or, on the other hand, are containing potassium for correction of hypokalemia, which, in turn, can trigger the development of hypernatremia. In addition, the conjunction with the administration of loop diuretics can result in a rise in serum sodium levels.

An overview of the studies on hypernatremia in critically ill patients is given in Table 1.

3. Consequences of hypernatremia

Hypernatremia and the associated hyperosmolar state have a multitude of effects on bodily functions (Fig. 1). The best-known side effect of hypernatremia is its effect on neurologic function. The development of hypernatremia and, therefore, hyperosmolality leads to a shift of free water from the intracellular to the extracellular space. This shift leads to brain cell shrinkage, which can even lead to vascular rupture and permanent neurologic deficits in severe cases [1]. Cerebral demyelination, probably the most feared complication in the correction of hyponatremia, was also reported in hypernatremia of various origins [17-19]. Patients with end-stage liver disease who develop hypernatremia seem to be especially prone to cerebral

Table 1 Studies on hypernatremia in the ICU

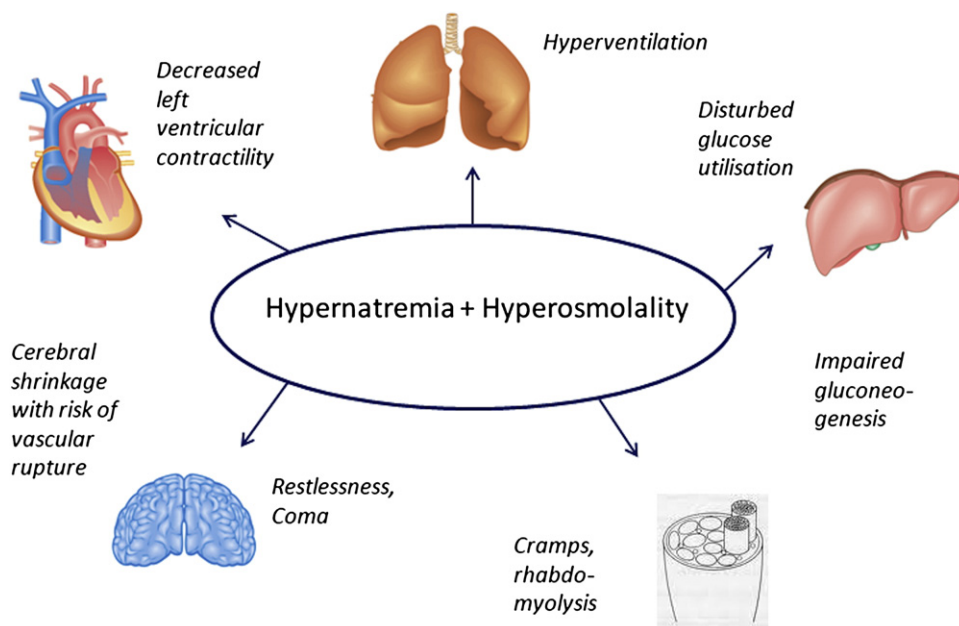| Author and year	Study type	Serum sodium cutoff defining hypernatremia	Population size (N)	ICU type	Incidence of ICU-acquired hypernatremia	Length of ICU stay (d)	Mortality
Lindner et al [13]	Retrospective	145 mmol/L	2.314	Surgical	10%	17 vs 3 ($P < .01$)	19% vs 8% ($P < .01$)
Stelfox et al [15]	Retrospective	145 mmol/L	6.727	Surgical	4%	4 vs 2 ($P = .69$)	14% vs 2% ($P < .001$)
Darmon et al [12]	Retrospective	145 mmol/L	8.441	Mixed	11% (mild) 4% (moderate to severe)	13 vs 5 ($P < .001$)	30% (mild), 46% (moderate to severe) vs 15% ($P < .001$)
O'Donoghue et al [16]	Retrospective	150 mmol/L	3.317	Mixed	8%	13 vs 2 ($P < .001$)	22% vs 3% ($P < .001$)
Stelfox et al [14]	Retrospective	145 mmol/L	8.142	Mixed	26%	7 vs 2 ($P < .001$)	23% vs 9% ($P < .001$)
Hoorn et al [45]	Retrospective	150 mmol/L	1.843	Mixed	7%	11 vs 3 ($P < .001$)	48% vs 10% ($P < .001$)
Lindner et al [10]	Retrospective	150 mmol/L	981	Medical	7%	20 vs 8 ($P < .001$)	43% vs 24% ($P < .01$)
Polderman et al [76]	Retrospective	150 mmol/L	389	Medical	6%	13 vs 5 ($P < .01$)	32 vs 20 ($P < .01$)

Fig. 1 Consequences of hypernatremia ranging from well-known brain cell shrinkage to impaired glucose utilization, muscle cramps, or decreased left ventricular contractility.

demyelination [20,21]. Neuromuscular effects of hypernatremia include muscle weakness or cramps [22]. In infants, hypernatremia has been shown to cause restlessness, lethargy, hyperpnea, and even coma [23]. It has been hypothesized that the neurologic impairment caused by the presence of hypernatremia may even lead to prolonged mechanical ventilation [11].

In vitro studies have demonstrated that the induction of hyperosmolality leads to an impairment in glucose utilization and glucagon-dependent glucose release [24,25]. In healthy volunteers, it has been shown that the slight increase in serum osmolality from 280 to 302 mosm/kg was associated with the severe impairment of insulin-mediated glucose metabolism, thus potentially contributing to the development of hyperglycemia in critically ill patients [26,27].

The cellular shrinkage induced by hyperosmolality has been demonstrated to have catabolic and antiproliferative effects [28,29]. In an animal model, hyperosmolality induced proinflammatory cytokine responses [30]. Hypernatremia has also been shown to impair hepatic gluconeogenesis and lactate clearance [31]. In patients hospitalized for diabetes mellitus who showed hyperosmolality, an increased risk for venous thromboembolism has been demonstrated [32]. Impairment in cardiac function via a decrease in left ventricular contractility has been reported in hypernatremic patients [33,34]. In addition, severe hypernatremia has been reported to cause rhabdomyolysis and consequent acute renal failure [35-43]. It is worth noting that the severity of symptoms in hypernatremia strongly depends on the rapidity of the development of hypernatremia (acute vs chronic). An overview of the consequences of hypernatremia is given in Fig. 1.

4. Influence of hypernatremia on the outcome of critically ill patients

Mortality rates in hypernatremic patients were reported to be dramatically increased as compared with normonatremic controls [44]. However, this increase in mortality was mainly attributed to the severity of the underlying disease in hypernatremic ICU patients [44].

Studies focused on the potential impact of hypernatremia on outcomes in critically ill patients on a medical ICU have shown mortality rates between 30% and 48% for patients with serum sodium levels exceeding 150 mmol/L [10,12,45]. Even for patients with only slightly elevated serum sodium levels, mortality was elevated as compared with the normonatremic controls (15% vs 30%) [12]. The same observations have been made in patients admitted to the ICU after surgery [13,15]. All of these studies have found an independent effect of ICU-acquired hypernatremia on mortality after adjusting for other risk factors. One study on hypernatremia upon admission to the ICU included more than 150 000 patients and demonstrated an independent effect of hypernatremia present at the time of admission on patient outcome after adjustment for age, severity of the underlying disease as measured by the Simplified Acute Physiology Score II, age, sex, and admission type [11]. In this study, even mild elevation of serum sodium greater than 145 mmol/L showed an independent effect on patient outcome.

All of these studies were performed retrospectively, and potential unknown confounders may not have been included in the analyses. However, hypernatremia and the following hyperosmolar state have a variety of well-known adverse effects on physiologic functions. Therefore, the association between hypernatremia and increased mortality

Table 2   Areas of uncertainty of hypernatremia in critically ill patients

Hypernatremia—areas of uncertainty	
Impact on physiologic functions	Impact of hypernatremia on central nervous system, cardiac function, metabolism, etc: studies have to be conducted to clarify the impact of hypernatremia
Causes of hypernatremia	Only few data available, larger studies to identify causes of hypernatremia in the ICU are necessary
Impact on outcome	Reason for the independent association of hypernatremia with adverse outcome remains to be clarified
Treatment	Correction rates: have not been evaluated in prospective studies
	Outcome: whether intense sodium monitoring and/or aggressive early treatment of hypernatremia results in decreased mortality is not clear

could point at causality. To clarify this issue, critically ill patients who have developed hypernatremia would need to be randomized for either treatment or observation of the disorder, which is difficult from an ethical point of view (Table 2). Alternatively, one might also randomize patients to either thorough serum sodium monitoring and intervention or a more liberal strategy allowing mild dysnatremias.

5. Pathophysiology and classification of ICU-acquired hypernatremia

To determine the origin of hypernatremia in the ICU, it is crucial to precisely document the daily volume input and output including enteral/parenteral nutrition. In any case of more significant increases or decreases in serum sodium, daily urine electrolyte analysis is indicated. Thorough analysis of the volume state and changes in serum sodium levels should ideally be performed before the development of hyponatremia or hypernatremia. In the case that an electrolyte disorder has already developed, analysis must be performed of the days during which the increase in serum sodium occurred. Fig. 2 shows a diagnostic approach for patients with hypernatremia acquired in the ICU.

As can be seen in the Edelman equation (Equation 1), hypernatremia can only develop through either a loss of free water or a gain of serum sodium [2]. However, in the critical care setting, a combination of the 2 mechanisms is responsible for most cases of hypernatremia. Fig. 3 shows factors contributing to ICU-acquired hypernatremia in 45 patients [46]. A third rare mechanism for hypernatremia is seen in transient hypernatremia: This form of hypernatremia occurs after severe exertion, and serum sodium may rise 10 to 15 mmol/L—a consequence of a shift of free water from the extracellular to the intracellular space [3]. It was suggested that the reason for the shift of water is a breakdown of
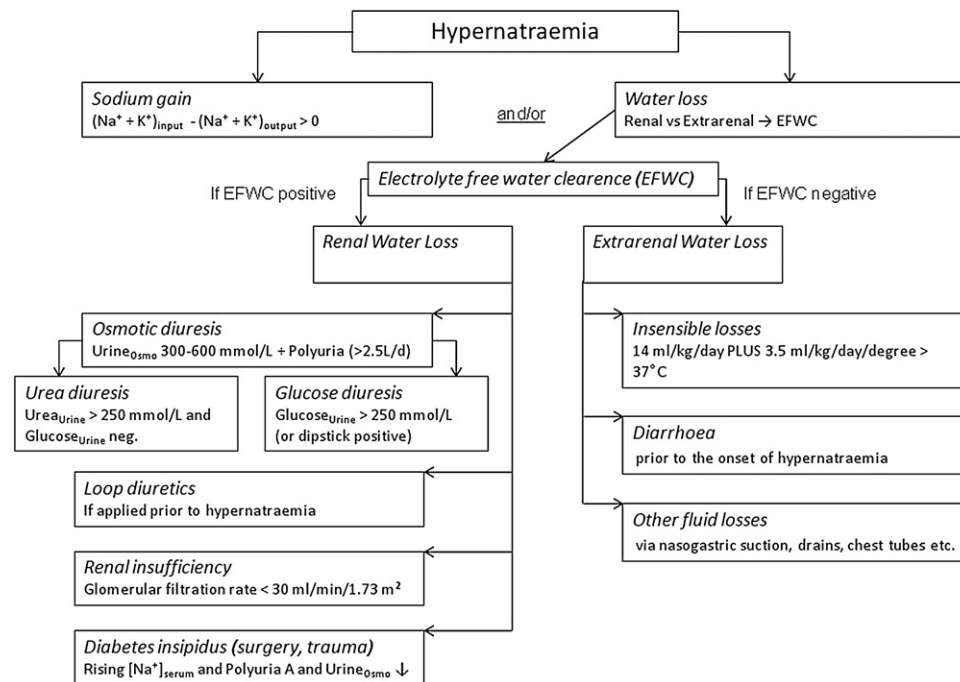

Fig. 2   Diagnostic approach to critically ill patients with rising serum sodium/hypernatremia showing the two possible mechanisms to develop hypernatremia: loss of free water or gain of sodium. In the ICU, a combination of both mechanisms will contribute to the development of hypernatremia in most cases. Water loss is further divided into renal and extrarenal water loss.
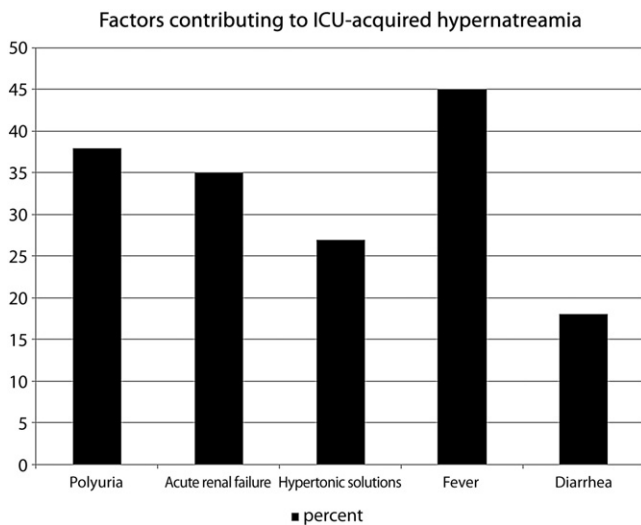
Fig. 3 Factors contributing to the development of hypernatremia in 45 patients in a medical ICU [46].

glycogen into smaller molecules such as lactate and a consequent gain of osmolytes.

5.1. Sodium gain

Pure sodium gain is seldom the only cause for the development of hypernatremia. In cases of salt poisoning, hypernatremia is typically acute and can be severe. In most cases, salt is unintentionally ingested by infants, but reports have also been published on forced salt ingestion as a form of punishment [47-52]. In an ICU setting, sodium gain often contributes to the development of hypernatremia. In a study evaluating the total water and electrolyte input and output (ie, tonicity balances) of critically ill patients with hypernatremia, 56% of patients demonstrated a positive sodium balance [46]. These results confirmed the findings of a prior study on this issue [45]. The gain of sodium might be attributed to the administration of hypertonic solutions such as sodium bicarbonate, but isotonic solutions such as 0.9% saline can also lead to sodium accumulation if dilute urine is excreted [45,46,53]. In patients with multiorgan failure in which large amounts of saline are administered during the course of illness, hypervolemic hypernatremia is common [54]. In these cases, hypernatremia is thus considered to be of iatrogenic origin [53]. A common cause of sodium accumulation in the ICU is the administration of sodium-rich antibiotics (eg, fosfomycin) [55]. Table 3 contains an overview of the sodium content of commonly prescribed infusion solutions and antimicrobial agents. Whether a pure sodium gain has contributed to the development of hypernatremia can be detected by calculation of the sodium balance:

$$(Na^+ + K^+)_{infused} - (Na^+ + K^+)_{excreted} > 0. \qquad (2)$$

Equation 2 should be calculated on a 24-hour basis. For calculation of the amount of excreted sodium and

Table 3 Overview of the sodium content of commonly prescribed infusion solutions and antimicrobials in grams and millimoles of sodium per gram of drug

Name of solution	Sodium content	
	Grams (per L)	mmol (per L)
Isotonic saline (0.9% NaCl)	3.5	154
Lactated Ringer	3	130
Ringer solution	3.4	147
Sodium bicarbonate (8.4%)	23	1000
Sodium chloride (3%)	11.8	513
Sodium chloride (10%)	39.4	1711
Name of intravenous antimicrobial agent	Grams (per g)	mmol (per g)
Fosfomycin	0.33	14.5
Ticarcillin	0.12	5
Ampicillin	0.07	3
Amoxicillin/clavulanic acid	0.06	2.8
Piperacillin	0.04	2
Ceftriaxone	0.08	3.6
Cefazolin	0.05	2
Ceftazidime	0.05	2
Ciprofloxacine	1.8	78
Fluconazole	1.7	75
Voriconazole	1.1	48
Foscarnet	0.23	10
Ganciclovir	0.09	4

Only intravenous drugs were considered. Sodium content may vary with different manufacturers.

potassium, measurements of 24 hours urine sodium and potassium are crucial.

A positive sodium balance demonstrates a contribution of sodium gain to the rise in serum sodium. In critically ill patients, the total amount of sodium administered is easy to calculate by adding the sodium content of infusates and enteral/parenteral nutrition. Excretion can only be estimated because losses via stool are difficult to measure and not part of daily practice. Daily urine electrolyte analysis is indicated in situations of rising serum sodium, and this process allows for the calculation of electrolyte losses via urine.

5.2. Water loss

Water loss can be caused by either renal or extrarenal mechanisms [46].

Serum and plasma osmolalities can be of help in the evaluation of causes for hypernatremia. A urine osmolality exceeding serum osmolality indicates retention of free water by the kidney and, therefore, a water loss via a nonrenal route—a relationship, which is used in the free water clearance formula. However, the relationship is not useful in osmotic diuresis where a large part of osmolytes in urine is represented by glucose or urea (see below) [3].

The current state of renal water handling (ie, whether the kidney retains or excretes free water) and, therefore, the discrimination between renal and extrarenal water loss can easily be determined by calculating the electrolyte free water clearance (EFWC) [3]:

$$EFWC = urinevolume \times \left[1 - \left(Na^+_{Urine} + K^+_{Urine}\right) / Na^+_{Serum}\right], \quad (3)$$

with urine volume calculated in liters and Na^+ and K^+ in millimoles per liter.

The EFWC describes the amount of water (free of sodium and potassium) removed from the body by the kidneys during the time over which the urine volume was collected. In the case of rising serum sodium, a negative EFWC (ie, the kidney retains free water) indicates extrarenal water loss. Conversely, a positive EFWC (ie, the kidney excretes free water) under circumstances of a rising serum sodium and serum osmolality indicates renal water loss.

5.2.1. Renal water loss

Renal water loss can be triggered by a variety of causes. In a study on the pathophysiology of ICU-acquired hypernatremia, 38% of patients were polyuric, and most of those patients demonstrated osmotic diuresis [46]. Osmotic diuresis can be caused by hyperglycemia and consequent glucosuria, mannitol administration, or urea [56-59]. Osmotic diuresis due to urea is often the cause of renal loss of free water and the consequent rise in serum sodium concentration in critically ill patients [60]. This phenomenon can be observed in patients who are tube fed or in a catabolic state. High amounts of urea are generated and excreted in the urine. This process leads to high renal output of osmoles and the consequent loss of water as in glucosuria.

Another common cause of the loss of free water in the ICU is the use of diuretics [46]. The administration of loop diuretics in particular leads to loss of hypertonicity in the renal medulla, which causes a concentration defect in the kidney [3]. Depending on the dose and frequency of administration, the use of diuretics can result in significant losses of free water. In an observational study on mannitol use in a neurologic ICU, hypernatremia was observed in up to 21% of patients during a 7-day mannitol treatment [61].

Water diuresis can also be caused by diabetes insipidus, which is further divided into central and nephrogenic diabetes insipidus. Central diabetes insipidus is often observed in response to central nervous system damage or surgery [62-65]. It is associated with a reduced secretion of antidiuretic hormone, while nephrogenic diabetes insipidus is caused by a reduced susceptibility to the water retaining effects of antidiuretic hormone [66]. Causes for nephrogenic diabetes insipidus are multiple ranging from hereditary to drug-induced cases [67]. Examples for drugs associated with nephrogenic diabetes insipidus include lithium, foscarnet, amphotericin B, or ifosfamide [67]. Moreover, hypercalcemia can lead to diabetes insipidus, but generally, the hypercalcemia must be chronic [68,69]. Hypokalemia can also cause renal concentration defects with loss of free water [3,70]. For the diagnosis of diabetes insipidus, the following criteria should be present: polyuria (ie, 24 hours urine volume exceeding 2.5 L or 40 mL/kg per day) and a high normal or even elevated (as in the case of critically ill patients) serum sodium levels especially in the presence of a serum osmolality higher than the urine osmolality [3]. As a next step, the differentiation between central and nephrogenic diabetes insipidus is established by the administration of desmopressin [5,66]. If urine osmolality rises to more than 600 mosm/kg, the test can be considered positive, and central diabetes insipidus is present. However, diabetes insipidus seems to account for only a few cases of hypernatremia in the medical ICU, although it probably plays a larger role in the neurologic ICU [46,71]. Nevertheless, a correct diagnosis of diabetes insipidus is essential because an effective and simple treatment is available for the disorder.

Renal insufficiency per se can result in renal free water loss. Although the glomerular filtration rate is reduced in renal insufficiency, the urine output may be normal or even above normal. This observation is due to a defect in urine diluting as well as the concentrating ability of the kidney. Although a healthy kidney produces urine with osmolality ranging from 50 to 1200 mosm/kg, this output may be reduced to only 200 to 300 mosm/kg in the event of failure. Such a defect in renal dilution is referred to as hyposthenuria [72-74]. This defect may cause significant water loss and even the development of hypernatremia if the hypo-osmolar losses are replaced by isotonic or hypertonic solutions.

5.2.2. Extrarenal water loss

Extrarenal water loss can occur via several routes and cause or contribute to the development of hypernatremia in more than half of critically ill patients [46]. Usually, insensible losses account for 14 mL/kg per day or a total of 980 mL/day for a 70-kg person. However, in the presence of a fever, an additional 3·5 mL/kg per day per 1°C must be added [75]. Fever has been identified as being responsible for 20% of hypernatremia cases in a Dutch medical ICU [76]. Other potential sources of extrarenal water loss include diarrhea, nasogastric suction, and fluid loss via tubes or drains. Overzealous administration of lactulose, for example, in patients with hepatic encephalopathy, has been reported to result in hypernatremia [77,78].

6. Treatment of hypernatremia in the ICU

6.1. Assessment of the cause of hypernatremia

In general, it should be determined whether hypernatremia is due to gain of sodium or loss of free water or whether a combination of the 2 is present, which will be the case in most patients with ICU-acquired hypernatremia.

In any case of hypovolemia, volume resuscitation by administration of isotonic solutions should be performed before efforts to correct hypernatremia take place. Assessment of hypovolemia is problematic, and physical signs are often misleading [79]. Hypotension, a fractional excretion of sodium less than 1% in patients with normal renal function or prerenal acute renal failure can be helpful for the detection of hypovolemia, whereas on basis of often used parameters such as central venous pressure, a diagnosis of hypovolemia should not be made [80,81]. However, new methods, such as passive leg raising, to evaluate whether a patient is hypovolemic and will respond to fluid administration are promising [82,83].

If a loss of free water alone is present, it should be treated by the administration of free water in the form of a 5% dextrose solution, which is safe in terms of hemolysis. As an alternative to 5% dextrose, distilled water can be given via a central venous line. If pure sodium gain is the case, natriuresis should be induced through the application of loop diuretics. At the same time, fluid loss during loop diuretic therapy must be restored with the administration of fluid that is hypotonic to the urine. In critically ill patients who require renal replacement therapy, correction of hypernatremia can be performed by either intermittent or continuous renal replacement therapy. Dialysate sodium concentrations should be chosen to be as close to the actual serum sodium concentration as technically possible. However, the correction of hypernatremia in critically ill patients by continuous/intermittent renal replacement therapy has not been studied systematically, but case series on the issue reported positive results [84-86]. In any case, correction of hypernatremia by renal replacement therapy should be performed with caution. Fig. 4 provides an algorithm for the treatment of hypernatremia in the ICU, based on expert recommendations [1,3-5]. In case of serum glucose levels, which are hard to control, half isotonic saline can be used as an alternative to 5% dextrose solution to avoid glucose lapses. However, the addition of loop diuretics to induce natriuresis at the same time should be considered.

6.2. Assessment of the rapidity of the onset of hypernatremia

Before the correction of hypernatremia, differentiation should be made as to whether hypernatremia is acute or chronic. The diagnosis of acute hypernatremia should only be made if the rise in serum sodium has a documented onset within the last 48 hours. If this is the case, the rapid correction of hypernatremia (up to 8-12 mmol/L per day) is indicated because compensatory mechanisms such as an uptake of solutes into the brain cells have not yet begun [3,87]. In the case of chronic hypernatremia, compensatory mechanisms have already begun, and too rapid correction may result in cerebral oedema, which can even lead to herniation and death [1]. Therefore, correction rates of 8 to 10 mmol/L per day must not be exceeded. Special attention should be paid to patients with acute on chronic hypernatremia: These patients are at risk to be classified as having chronic hypernatremia, although rapid lowering of serum sodium would be indicated.

It has been proposed that calculations of tonicity balances could be of assistance in the treatment of hyponatremia and hypernatremia [88,89]. Tonicity balance calculations allow for separate analysis of total water and electrolyte input and
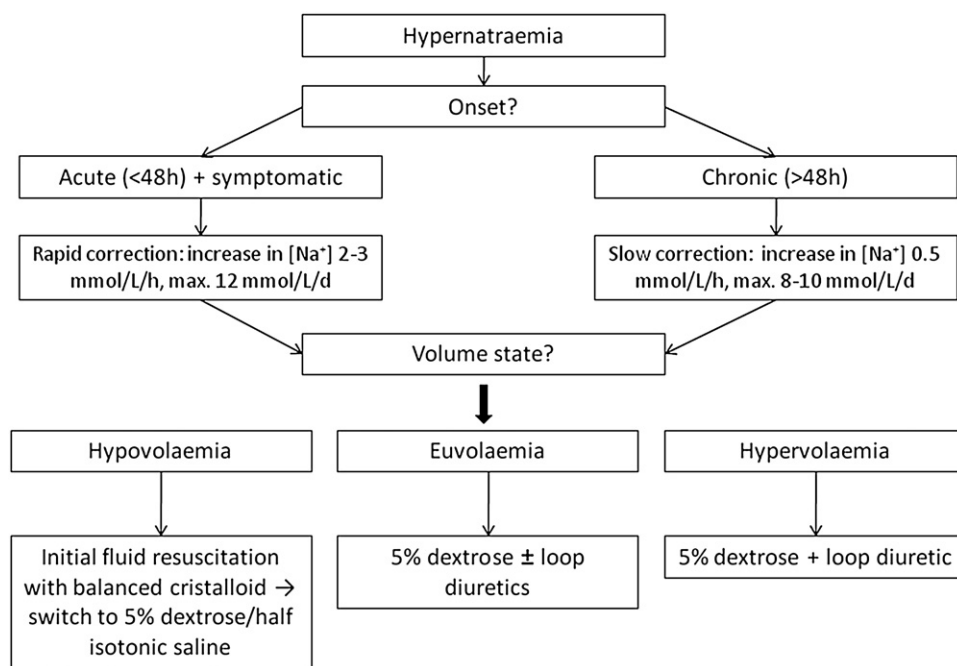

Fig. 4 Therapeutic algorithm for the treatment of hypernatremia based on the onset of hypernatremia and volume state of the patient.

output. Therefore, they show the physician whether a negative sodium balance was achieved or if enough free water was infused. Again, the determination of urine chemistry is crucial.

6.3. Correction rate and its adjustment

Although it has been shown that hypernatremia is a common and potentially life-threatening event in critically ill patients, there is no prospective study on the treatment of hypernatremia in the ICU. Data on the safety and rapidity of correction of hypernatremia stem primarily from pediatric patients [90-92]. These data suggest that the maximum rate of correction of serum sodium should not exceed 0.5 mmol/L per hour. This suggestion accounts for the often-postulated correction rate of 12 mmol/L per day.

Formulas to assist the physician in determining the rate of infusion during the correction of dysnatremias have been proposed [93-95]. The Adrogué-Madias formula has been tested in a cohort of 204 patients with hyponatremia and 117 with hypernatremia [96]. In this study, the predicted serum sodium values well correlated with measured serum sodium. However, maximum deviations of the anticipated from the measured values were not reported. Later, all proposed formulas have been tested in a retrospective analysis on a collective of hypernatremic, critically ill patients [97]. The authors reported that although all the formulas correlated well with the real changes in serum sodium concentration, individual variations exceeded 10 mmol/L. Thus, it was concluded that these formulas could only serve as rough guides in the correction of hypernatremia and should not be relied upon. Another recent study demonstrated that the formula proposed by Adrogué and Madias underestimated the change in serum sodium during the correction of hyponatremia [98]. However, use of the formulas may be helpful in establishing the initial infusion rate for the correction of hypernatremia. Nevertheless, because the formulas might underestimate the change in serum sodium achieved by infusion in some cases, we recommend starting with only 50% to 75% of the rate calculated by the formula and performing a laboratory control after 2 hours of infusion. This precaution allows for adjustment of the infusion rate depending on the results of the laboratory control. An application to calculate the initial infusion rate to correct hypernatremia with the option to choose the infusion solution is freely available at www. medcalc.com. On this platform, an option to choose between the classic and the Adrogué-Madias formula is available: Given that the Adrogué-Madias formula was tested twice should give preference for it over the classic formula [96,97]. In addition, a multitude of applications is available for smartphones and handheld computers to calculate infusion rates, electrolyte free water clearance, and others at the bedside.

In any case of the correction of hypernatremia, narrow control of the serum sodium concentration is crucial. This control allows the physician to further increase or decrease the rate of infusion as necessary to correct hypernatremia. In the case of accidental too-rapid correction of hypernatremia with imminent neurologic symptoms, a reinduction of hypernatremia by the infusion of hypertonic saline might be protective. However, research is still lacking on this important issue.

7. Conclusion

Hypernatremia is a common and largely preventable complication of intensive care. It has various adverse physiologic consequences and is associated with poor outcomes. Efforts should focus on the prevention of hypernatremia and adequate correction of the electrolyte disturbance.

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