

Hospital-acquired hyponatremia—why are hypotonic parenteral fluids still being used?

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SUMMARY

Hospital-acquired hyponatremia can be lethal. There have been multiple reports of death or permanent neurological impairment in both children and adults. The main factor contributing to the development of hospital-acquired hyponatremia is routine use of hypotonic fluids in patients in whom the excretion of free water, which is retained in response to excess arginine vasopressin (AVP), might be impaired. The practice of administering hypotonic parental fluids was established over 50 years ago, before recognition of the fact that there are numerous potential stimuli for AVP production in most hospitalized patients. Virtually all neurological morbidity resulting from hospital-acquired hyponatremia has been associated with administration of hypotonic fluids. Multiple prospective studies have shown that 0.9% NaCl is effective prophylaxis against hyponatremia. There is not a single report in the literature of neurological complications resulting from the use of 0.9% NaCl in non-neurosurgical patients. Patients at greatest risk of developing hyponatremic encephalopathy following hypotonic fluid administration are children, premenopausal females, postoperative patients, and those with brain injury or infection, pulmonary disease or hypoxemia. When hyponatremic encephalopathy develops, immediate administration of 3% NaCl is essential. In this Review, we discuss the question of why administering hypotonic fluids is unphysiologic and potentially dangerous, the settings in which isotonic fluids should be administered to prevent hyponatremia, and the appropriate treatment of hyponatremic encephalopathy.

KEYWORDS brain injury, fluid therapy, hyponatremia, hypoxia, surgery

REVIEW CRITERIA

PubMed was searched for relevant articles using different combinations of the following search terms: “hyponatremia”, “fluid therapy”, “SIADH”, “vasopressin”, “peri-operative”, “post-operative”, “surgery”, “pneumonia”, “epidemiology”, and “children”. The bibliographies of retrieved articles were reviewed. The “related links” feature of PubMed was then used when relevant articles were found. The search engine Google was used to find clinical practice guidelines for “fluid therapy”.

CME

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Learning objectives

Upon completion of this activity, participants should be able to:

- 1 Describe the prevalence of hospital-acquired hyponatremia.
- 2 List 3 factors contributing to the development of hyponatremia.
- 3 List complications associated with hospital-acquired hyponatremia.
- 4 Identify patients at risk for adverse outcomes of hospital-acquired hyponatremia.
- 5 Describe strategies for the management of hospital-acquired hyponatremia.

INTRODUCTION

Hospital-acquired hyponatremia can be lethal. There have been several reports of death or permanent neurological impairment arising from this condition in both children and adults. Hyponatremia can cause cerebral edema and intracranial hypertension as a result of an influx of water into the brain parenchyma. We have argued that the main factor contributing to the development of hospital-acquired hyponatremia is routine use of hypotonic fluids in patients in whom the excretion of free water, which is retained in response to excess arginine vasopressin (AVP), is impaired.^{1–3} Virtually all hospitalized patients are at risk of developing hyponatremia as a result of the multiple potential stimuli for AVP production (Box 1). Hypotonic fluid administration in the presence of AVP excess will predictably produce hyponatremia, explaining why this condition develops in approximately 30% of hospitalized

patients.^{4,5} In 2003, we introduced the concept of using 0.9% sodium chloride (NaCl) as a maintenance parenteral fluid for the prevention of hospital-acquired hyponatremia in children.¹ This concept caused controversy in the pediatric literature about the most appropriate fluid therapy for children.^{6–10} The Royal College of Pediatrics has since issued a warning regarding the use of 0.18% NaCl,¹¹ and critics have now conceded that hypotonic fluids are overused and can be dangerous.¹² Avoidance of hypotonic fluids, and use of 0.9% NaCl as prophylaxis against hospital-acquired hyponatremia, are equally relevant to adults and children.¹³ In this Review, we explore the question of why administration of hypotonic fluids is unphysiologic and potentially dangerous, the settings in which isotonic fluids should be administered to prevent hyponatremia, and the appropriate management of hyponatremic encephalopathy.

WHY ARE HYPOTONIC FLUIDS USED?

Hypotonic fluids are still the parenteral fluid most commonly administered to both pediatric and adult hospitalized patients. The pediatric literature specifically addresses the topic of maintenance parenteral fluid therapy and recommends hypotonic fluid.¹⁴ The adult literature does not specifically address maintenance parenteral therapy but does make recommendations for hypotonic fluids in total parenteral nutrition and in the perioperative setting.^{15,16} We queried the adult inpatient pharmacy of the University of Pittsburgh Medical Center, and found that 0.45% NaCl with 20 mmol/l potassium chloride in 5% dextrose is the most commonly prescribed fluid for parenteral therapy. This practice seems to be common for adult patients throughout the world. The WHO recommends using 5% dextrose in water in the postoperative setting for one-third of maintenance fluids in patients unable to drink.¹⁷ In the UK, 0.18% NaCl in 4% dextrose is the most commonly used parenteral fluid.^{18–20} In a Brazilian study, about 50% of postoperative patients received 5% dextrose in water.²¹ In a recent Case Record of the Massachusetts General Hospital, 0.45% NaCl was administered to a patient with a central nervous system disorder and a serum sodium level of 131 mmol/l.²²

The use of hypotonic fluids in adults originated in part from recommendations made by Talbot *et al.* in 1953.²³ These authors generated a theoretical model of maximal and minimal

Box 1 Clinical settings in which production of arginine vasopressin is increased.

Hemodynamic stimuli (decreased effective circulatory volume)

Hypovolemia

- Vomiting
- Diarrhea
- Diuretics
- Renal salt wasting
- Hypoadosteronism

Hypervolemia

- Nephrosis
- Cirrhosis
- Congestive heart failure
- Hypoalbuminemia

Hypotension

Nonhemodynamic stimuli (syndrome of inappropriate antidiuretic hormone production)

Euvolemia

- Central nervous system disturbances such as meningitis, encephalitis, stroke, brain tumor, brain abscess, head injury and hypoxic brain injury
- Pulmonary diseases such as pneumonia, asthma, tuberculosis, empyema, chronic obstructive pulmonary disease and acute respiratory failure
- Cancers of the lung, brain, central nervous system, head, neck, breast, gastrointestinal tract, genitourinary tract, and leukemia, lymphoma, thymoma and melanoma
- Medications such as cyclophosphamide, vincristine, morphine, selective serotonin reuptake inhibitors and carbamazepine
- Nausea, emesis, pain and stress
- Postoperative state
- Cortisol deficiency

tolerances for sodium and water in parenteral fluids, based on the ranges of normal renal concentration and dilution. Their recommendation at the time was to use 40 mmol/l NaCl for maintenance fluid therapy. Hypotonic fluid use in children is partly based on recommendations made by Holliday and Segar in 1957.²⁴ These authors recommended 30 mmol/l NaCl for maintenance fluid in children. Their guidance was based in part on the recommendations of others, and also on the fact that 30 mmol/l NaCl approximates the sodium composition of human breast and cow's milk. Both Talbot's and Holliday's groups appreciated that AVP excess could impair water handling and that symptomatic

hyponatremia was a potential complication. What they did not seem to appreciate at the time was how common AVP excess was in hospitalized patients, and that hyponatremia would be an inevitable consequence of administering the maintenance fluids they advocated. Talbot's group acknowledged that a wide range of fluid compositions would be appropriate, but was not in favor of using 0.9% NaCl (154 mmol/l) on the basis of the belief that it did not provide enough free water and could, therefore, result in hypertonicity and fluid overload.

AVP AND THE PATHOGENESIS OF HYPONATREMIA

Three factors can contribute to the development of hyponatremia: excessive water ingestion; hypertonic urinary losses (i.e. a urine concentration of Na⁺ plus K⁺ that exceeds that of plasma); and impaired ability to excrete free water. Excess water ingestion alone is unlikely to produce hyponatremia, as a healthy adult male can excrete more than 15 l of fluid a day to maintain sodium homeostasis. There are few clinical situations in which hypertonic urinary losses of electrolytes will result in hyponatremia in the absence of fluid administration. These scenarios are idiosyncratic reactions to thiazide diuretics and cerebral salt wasting. Thus, the main factor that contributes to development of hyponatremia is impaired ability to excrete free water generated in response to AVP excess.

The body's main defense against the development of hyponatremia is excretion of free water by the kidney. This process has two prerequisites: the delivery of solutes and water to the ascending limb of the loop of Henle and the capacity to suppress AVP production. Excretion of free water will be impaired, therefore, when there is a marked reduction in glomerular filtration rate, renal hypoperfusion or AVP excess. AVP increases the permeability of the collecting duct to water, leading to retention of free water. Hospitalized patients have numerous nonosmotic stimuli for AVP production that put them at risk of developing hyponatremia (Box 1). These nonosmotic stimuli are either hemodynamic (resulting from effective circulatory volume depletion) or nonhemodynamic (essentially conditions that can result in syndrome of inappropriate secretion of antidiuretic hormone [SIADH]-like states).

Stimuli for AVP production can occur in states of hypovolemia, euvoolemia or hypervolemia.

Administration of hypotonic fluids to a patient in any of these clinical states can produce hyponatremia. Hypovolemic and hypervolemic states of AVP excess are usually associated with avid salt and water retention; administration of hypotonic fluids results in dilutional hyponatremia. In euvolemic states of AVP excess, hyponatremia results from a combination of free water retention and urinary sodium losses due to a natriuresis that preserves volume at the expense of serum sodium. Virtually every hospitalized patient requiring parenteral fluids has a potential stimulus for AVP excess and should be considered to be at risk for development of hyponatremia.²⁵ Studies of hospitalized children and adults with hyponatremia have detected nonosmotic secretion of AVP in most patients.^{26–28}

HYPOTONIC FLUID ADMINISTRATION AND HYPONATREMIA

We have previously reported on the relationship between hypotonic fluid administration and development of hyponatremia in children.¹ There have been more than 50 reports of death or neurological injury associated with hypotonic fluid administration in children.³ Tragically, most of the deceased were otherwise healthy children undergoing minor surgery or suffering common childhood illnesses. In 1992, Ayus and Arieff's group reported on 16 otherwise healthy children who died or suffered permanent neurological impairment as a result of acute hospital-acquired hyponatremia. All 16 had received hypotonic fluids, most following minor surgical procedures.²⁹ Halberthal *et al.* reported similar findings in 2001 in 23 children with acute hyponatremia; all had received hypotonic fluids, most in the postoperative setting, and 6 died or suffered permanent neurological impairment.³⁰ In 2004, Hoorn and colleagues showed that 10% of children admitted to the emergency department with a normal serum sodium level went on to develop acute hyponatremia; all had received hypotonic fluids.⁵ In a prospective study of an unselected group of pediatric patients receiving intravenous fluids, 78% received hypotonic fluids and 24% of the total developed hyponatremia (serum sodium level <135 mmol/l).³¹

Hypotonic fluid administration in excess of maintenance or as part of deficit therapy is an additional risk factor for development of hospital-acquired hyponatremia. Deaths

have, however, occurred at fluid volumes less than or equal to standard maintenance doses. In a prospective study by Coulthard *et al.*, postoperative administration of one-third normal saline at two-thirds of the standard maintenance dose caused serum sodium levels to drop; 37% of patients developed hyponatremia.³²

Our group used data collected since 2000 to evaluate the risk factors for death or neurological impairment from hyponatremic encephalopathy.³³ We found hospital-acquired hyponatremia caused by hypotonic fluid administration to be one of the primary risk factors. Virtually all reports of hospital-acquired hyponatremic encephalopathy in children are of cases in which hypotonic fluids were administered.^{5,34,35} Even a small amount of supplemental hypotonic fluid can produce hyponatremia. A prospective study of jaundiced neonates revealed that 8 h of supplementation with 50 ml/kg body weight of 0.18% NaCl resulted in acute hyponatremia.^{36,37}

There is evidence to suggest that hypotonic fluid administration is the primary factor leading to hospital-acquired hyponatremia and hyponatremic encephalopathy in adult patients. In three studies of patients with neurological sequelae from hospital-acquired hyponatremic encephalopathy, most had received hypotonic parenteral fluids with a sodium concentration of ≤ 77 mmol/l.^{38–40} In a series of 15 women with hyponatremia and permanent neurological impairment following elective surgery, 11 had received 5% dextrose in water.³⁸ In a series of 65 postoperative patients with hyponatremic encephalopathy, all had received hypotonic fluids.³⁹ In a series of 30 patients with noncardiogenic pulmonary edema as a complication of postoperative hyponatremic encephalopathy, all had received hypotonic fluids.⁴⁰ These results are consistent with those of a prospective study by Chung *et al.*, which revealed that 94% of patients with postoperative hyponatremia (Na^+ concentration < 130 mmol/l) were receiving hypotonic fluids.⁴¹ A prospective study by Aronson and colleagues showed that the amount of electrolyte-free water administered was the most predictive factor for the development of clinically significant hyponatremia following cardiac catheterization.⁴² The odds ratio for developing hyponatremia was 3.7 for each liter of electrolyte-free water administered to a 70 kg patient.

0.9% NaCl AS PROPHYLAXIS AGAINST HYPONATREMIA

Several prospective studies in children and adults have shown that administration of 0.9% NaCl is effective prophylaxis against the development of hyponatremia.^{42–49} Even in patients with SIADH and hyponatremia, administration of normal saline does not aggravate hyponatremia.⁵⁰ We conducted a meta-analysis of 550 postoperative patients, 50 of whom were children, managed with either 0.9% NaCl or a more-hypotonic fluid. Hyponatremia was effectively prevented by 0.9% NaCl, whereas more-hypotonic fluids—including Ringer's lactate—consistently caused a drop in serum sodium level.⁵¹ Ringer's lactate, which has a sodium concentration of 130 mmol/l, is hypotonic to plasma water and can produce hyponatremia.⁵² Avoidance of hypotonic fluids, and administration of 0.9% NaCl when parenteral fluids are required, is the most physiologic approach to preventing hyponatremia. Administration of 0.9% NaCl is safe; there has never been a report of neurological complications of hyponatremia resulting from use of 0.9% NaCl in non-neurosurgical patients. Neurosurgical patients can develop cerebral salt wasting. In such cases, 0.9% NaCl might not be sufficient for prophylaxis against hyponatremia, and 3% NaCl might need to be administered in order to maintain normal serum sodium levels.

Hyponatremia is not a benign condition. Several studies have shown that mortality and hospitalization rates are elevated in patients with hyponatremia.⁵³ Mortality is highest in patients with hospital-acquired hyponatremia. Active measures must be taken to prevent hyponatremia in patients at risk for AVP excess (Box 1). In these disease states, parenteral fluid therapy should consist of normal saline rather than a more-hypotonic fluid. There are certain subsets of patients for whom adaptation of the brain to hyponatremia is impaired and even mild hyponatremia can be lethal (Table 1). In these groups of patients, prophylaxis with normal saline is crucial.

Postoperative setting

Most of the deaths and neurological dysfunction resulting from hyponatremic encephalopathy in both children and adults have occurred in postoperative patients. Postoperative patients have multiple nonosmotic stimuli for AVP production, such as subclinical volume depletion, pain, stress, nausea and vomiting, narcotic use and

Table 1 Risk factors for development of hyponatremic encephalopathy.

Risk factor	Pathophysiologic mechanism
Childhood	Higher brain-to-intracranial volume ratio
Female sex	Sex steroids (estrogens) inhibit adaptation of brain to hyponatremia Higher arginine vasopressin levels than males Cerebral vasoconstriction Hypoperfusion of brain tissue
Hypoxemia	Impairs adaptation of brain to hyponatremia Decreased cerebral perfusion Causes brain injury
Brain injury	Vasogenic cerebral edema Cytotoxic cerebral edema

third spacing, which puts them at risk for hyponatremia. Premenopausal females are at highest risk of developing hyponatremic encephalopathy, as their postoperative AVP levels are 40 times those of young males.⁵⁴ The relative risk of death or permanent neurological dysfunction is approximately 30 times greater for women than for men, and about 25 times greater for menstruant females than for postmenopausal females.³⁹ Children under the age of 16 years are also at high risk of developing postoperative hyponatremic encephalopathy, as seizures occur at higher serum sodium concentrations in this group than in adults. This phenomenon occurs because children have a larger brain-to-intracranial volume ratio than adults. There can be no justification for administering electrolyte-free water, including Ringer's lactate, in the postoperative setting.³

Brain injury and infection

Hyponatremia is poorly tolerated in patients with brain injury. Even a small drop in serum sodium level can aggravate cerebral edema.^{22,35,55} Brain injury can produce cerebral edema via vasogenic and cytotoxic mechanisms. Vasogenic edema is accumulation of fluid in the extracellular brain parenchyma following disruption of the blood-brain barrier by, for example, a brain tumor or abscess. Cytotoxic cerebral edema is accumulation of fluid in the intracellular space, as in hypoxic brain injury or hyponatremia.⁵⁶ These mechanisms are not mutually exclusive. Volume regulation of brain cells is impaired in patients with brain injury, and the movement of additional water into the brain as a result of even mild hyponatremia can be lethal. In a study of children with Lacrosse encephalitis, mild hyponatremia was associated with neurological deterioration.³⁵

The serum sodium level of patients with neurological deterioration was only 2 mmol/l less than that of those without deterioration (131.9 vs 133.8 mmol/l). A drop in serum sodium concentration of only 4 mmol/l resulted in neurological deterioration. There is no 'safe' degree of hyponatremia in patients with brain injury, and 0.9% NaCl is one of the most important prophylactic measures for prevention of hyponatremia in this population.

Pulmonary disease (hypoxemic states)

Hyponatremia is common in patients with pulmonary disease, affecting approximately 25% of patients with pneumonia.⁵⁷ Hyponatremia markedly increases the risk of death from community-acquired pneumonia.⁵⁸ The underlying mechanism is probably hypoxia, a major risk factor for the development of hyponatremic encephalopathy. The majority of neurological morbidity in patients with hyponatremia has been in those who experienced a respiratory arrest.^{59–61} Recent studies have found respiratory compromise to be a comorbidity factor in patients with hyponatremia.^{5,62,63} Studies of hyponatremic animals have revealed that hypoxia impairs volume regulation of brain cells, decreases cerebral perfusion, and increases the probability of neuronal lesions developing.⁶⁴ Adaptation of the brain to hyponatremia largely depends on extrusion of sodium from the intracellular space via sodium-potassium ATPase pumps. This energy-dependent process is impaired under hypoxic conditions. The combination of systemic hypoxia and hyponatremia is more deleterious than is either condition alone, because hypoxia impairs the ability of the brain to adapt to hyponatremia, worsening hyponatremic encephalopathy.⁶¹

POTENTIAL COMPLICATIONS OF 0.9% NaCl

No single fluid therapy will be optimal for all patients. Patients with ongoing urinary free water losses resulting from renal concentrating defects, or extrarenal free water losses secondary to diarrhea or fever, will probably require a more-hypotonic fluid. Patients with hypernatremia will need a more-hypotonic fluid to correct the free water deficit. In general, normal saline will not cause hypernatremia, as the kidney can generate free water by producing hypertonic urine. Prolonged administration of normal saline to a patient who is avidly fluid restricted could cause hypernatremia. Administration of

0.9% NaCl can be dangerous in the setting of a renal concentrating defect, especially diabetes insipidus. Patients with head injuries might initially require 0.9% NaCl to prevent hyponatremia; however, if central diabetes insipidus develops, 0.9% NaCl can result in severe hypernatremia. Patients at risk of developing central diabetes insipidus should be monitored closely for the development of hyperosmolality while they are receiving fluid therapy. In patients with a fixed inability to excrete free water and a urine osmolality greater than 500 mmol/kg H₂O, even 0.9% NaCl can cause serum sodium levels to drop.⁵⁰

The optimal fluid therapy for patients with congestive heart failure or cirrhosis is a matter of debate. Excessive sodium administration can lead to fluid overload, but hypotonic fluid administration can also lead to hyponatremia, which increases the risk of mortality.^{65,66} Sodium and water need to be avidly restricted in patients with these conditions. Either 0.9% NaCl or a more-hypotonic fluid could be used safely, provided that there is adequate fluid restriction and patient monitoring.

Parenteral fluid therapy, including 0.9% NaCl, should not be thought of as benign, as serious complications can develop. Continuous fluid administration in excess of standard maintenance doses—generally accepted to be 1,600 ml/m²/day—should be avoided. Volume depletion is best corrected by administering 0.9% NaCl as bolus therapy until volume repletion, rather than via prolonged administration of parenteral fluids at a rate in excess of standard maintenance. Even standard maintenance therapy can result in fluid overload in patients with advanced chronic renal failure, oliguric acute renal failure, acute glomerulonephritis or an edematous state such as nephrosis, cirrhosis or congestive heart failure. The monitoring of patients who are receiving parenteral fluids should take the form of daily weights, frequent vitals, strict intake and output measures, and daily chemistries, and is especially important within the first 72 h of fluid therapy. Prolonged administration of parenteral fluids should be avoided unless there is a specific indication. In patients requiring prolonged administration of parenteral fluids (such as those receiving total parenteral nutrition), a more-hypotonic fluid could be used and monitoring performed less frequently, provided there is no acute illness resulting in AVP excess.

There is a misconception that administration of 0.9% NaCl as a maintenance fluid will result in acidosis. This solution has a pH of 5 (which does not differ from that of 0.45% or 0.2% NaCl) and is not more likely to produce acidosis than is a more-hypotonic parenteral fluid. Administration of 0.9% NaCl in large volumes for fluid resuscitation can result in a dilutional acidosis. Ringer's lactate does have an advantage over normal saline in that the lactate can be metabolized to bicarbonate; however, Ringer's lactate is a slightly hypotonic fluid that, in cases of severe liver disease, sepsis or severe hypoperfusion, can contribute to lactic acidosis. There are currently no FDA-approved parenteral fluids containing bicarbonate because of the instability of bicarbonate in solution. Acidosis can develop following administration of any parenteral fluid to a patient with renal dysfunction or multi-system organ failure. Additional prospective studies are needed to assess the safety and efficacy of administering 0.9% NaCl.

TREATMENT OF HYPONATREMIC ENCEPHALOPATHY

Hyponatremic encephalopathy is a medical emergency that requires early recognition and treatment. Neurological sequelae of hyponatremic encephalopathy are the result of inadequate therapy rather than rapid correction.^{59,60} This fact has been confirmed by three recent studies in adults, which found a poor outcome to be associated with inadequate therapy.^{62,63,67} We have studied risk factors for poor neurological outcome in hyponatremic encephalopathy in children, and have found lack of therapy to be the main contributory factor.³³

Treatment of hyponatremia should be based on neurological symptoms and not on the absolute serum sodium concentration. Patients with symptomatic hyponatremia need aggressive management with 3% NaCl (513 mmol/l; Figure 1). Fluid restriction alone has no role in the management of symptomatic hyponatremia. Treatment of hyponatremic encephalopathy should precede any neuroimaging studies to confirm cerebral edema and should occur in a monitored setting in which the airway can be secured and serum sodium level measured every 2 h until the patient is stable. Patients with severe symptoms such as seizures, respiratory arrest or neurogenic pulmonary edema should receive 100 ml of 3% NaCl as a bolus over 10 min in order to rapidly reverse brain edema.⁶⁸ This

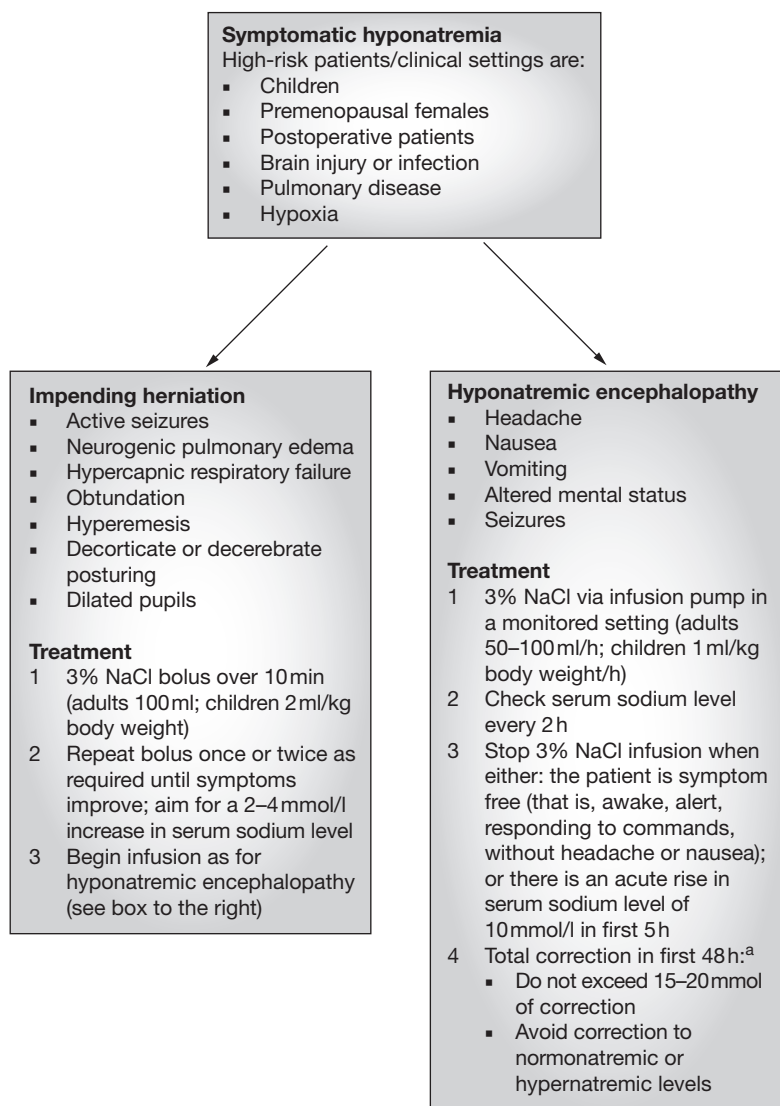


Figure 1 Treatment algorithm for symptomatic hyponatremia. ^aIn cases of rapid free water diuresis (e.g. psychogenic polydipsia, water intoxication, thiazide diuretic), administration of DDAVP (desmopressin) might be required to prevent overcorrection of hyponatremia; a physician experienced in managing this condition should be consulted.

dose might need to be repeated once or twice until symptoms subside, with the remainder of therapy delivered via continuous infusion. Patients with less-severe symptoms, such as headache, nausea, vomiting or lethargy, can be treated via an infusion pump to achieve a correction of 4–8 mmol/l in the first 4 h. To prevent complications arising from excessive therapy, 3% NaCl should be discontinued when symptoms subside, the rate of correction should not exceed 20 mmol/l in the first 48 h, and correction should be to mildly hyponatremic values,

avoiding normonatremia and hypernatremia in the first 48 h. In general, 1 ml/kg body weight of 3% NaCl will increase the serum sodium level by about 1 mmol/l. A continuous infusion of 3% NaCl at a rate of 50–100 ml/h administered over 4 h is usually sufficient to reverse symptoms. In children with acute hyponatremic encephalopathy, 12 ml/kg body weight of 3% NaCl infused over 4 h has been used without apparent neurological sequelae.^{69,70} Much of the change in serum sodium level is a function of the renal response to therapy, making formulae unreliable for predicting the change in serum sodium.

Patients with SIADH are at low risk of overcorrection of hyponatremia. Patients with hyponatremia resulting from diuretics or psychogenic polydipsia will have a brisk free water diuresis during therapy and are prone to overcorrection.³ In these patients, active measures might be needed to prevent overcorrection of hyponatremia, including a switch to hypotonic fluids or DDAVP (desmopressin). Administration of DDAVP will stop the free water diuresis, and a controlled rate of sodium correction can be achieved with a combination of fluid restriction, 0.9% NaCl and 3% NaCl as needed. Recently, vasopressin V₂ receptor antagonists have received FDA approval for the treatment of hyponatremia.⁷¹ Preliminary data support a role for these agents in the management of asymptomatic euvolemic or hypervolemic hyponatremia,⁷² but there is currently no evidence to support their use in acute treatment of symptomatic hyponatremia.

CONCLUSIONS

The routine practice of administering hypotonic fluids to hospitalized patients should be abandoned, as it is causing hospital-acquired hyponatremia and iatrogenic deaths. The basis for widespread administration of hypotonic fluids is the erroneous assumption that parenteral fluid composition should reflect normal urinary losses. What has not been appreciated is that hospitalized patients have multiple stimuli for AVP production that put them at risk for hyponatremia. Administration of hypotonic fluids to a patient with excess AVP is unphysiologic and potentially dangerous. The parenteral fluid of choice should be 0.9% NaCl unless there is a free water deficit (hypernatremia), or ongoing renal or extrarenal free water losses. In edematous states such as congestive heart failure, cirrhosis and nephrosis, 0.9% NaCl can be used, provided

fluid restriction and patient monitoring are adequate. No single fluid composition will work for all patients, and there is no substitute for sound physician judgment.

Further prospective studies are needed to assess the safety and efficacy of 0.9% NaCl in a variety of disease states in children, adults and the elderly. Current literature reveals that 0.9% NaCl is the safest parenteral fluid; hypotonic fluids have been consistently associated with neurological complications due to hyponatremia. Administration of parenteral fluids should be thought of as an invasive procedure requiring close monitoring including daily electrolytes, weight, intake and output measurements, physical examination, and vital signs. Hypotonic fluids are contraindicated in the postoperative setting, in patients with brain injury, and in those with pulmonary diseases. When hyponatremic encephalopathy develops, prompt treatment with 3% NaCl is required, as delayed or insufficient treatment can be fatal.

KEY POINTS

- Hospitalized patients have numerous stimuli for arginine vasopressin production and are at risk of developing hyponatremia
- Routine administration of hypotonic parenteral fluid to hospitalized patients can result in fatal hyponatremic encephalopathy
- 0.9% NaCl (154 mmol/l) should be administered as prophylaxis against hyponatremia, except in the setting of a free water deficit or ongoing free water losses
- Patients at greatest risk of developing neurological complications secondary to hyponatremia are children, premenopausal females, postoperative patients, and those with brain injury, brain infection or hypoxemia
- 3% NaCl (513 mmol/l) is an essential treatment for hyponatremic encephalopathy

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Competing interests

The authors declared they have no competing interests.

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