Hyponatraemia – presentations and management

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ABSTRACT

Hyponatraemia is the most common electrolyte disturbance encountered in clinical practice. It is associated with significant morbidity and mortality, thus appropriate investigation and treatment is essential. Hyponatraemia presents with a spectrum of clinical presentations ranging from no symptoms to life-threatening neurological sequelae. Hyponatraemia has multiple aetiologies and distinguishing the underlying aetiology facilitates appropriate treatment. This review provides an overview of the presentations and approaches to management of this common clinical condition.

Introduction

Hyponatraemia (defined as serum sodium <135 mmol/L) is the most common electrolyte abnormality and is encountered in all areas of clinical practice.[1] Hyponatraemia is associated with increased morbidity and mortality.[2] The assessment of patients with hyponatraemia can pose a clinical challenge and strategies for its management are often suboptimal. In recent years, expert guidance and recommendations have been published that provide an evidence-based approach to diagnosis and treatment of hyponatraemia[3,4] although it should be highlighted that high-quality evidence is lacking for many aspects of hyponatraemia management. Additionally, new therapies have emerged promising a more targeted approach to regulating body water and sodium balance in certain patients with hyponatraemia.

Epidemiology

Hyponatraemia occurs in approximately 15–30% of hospitalised patients, with 1–2% of patients having a serum sodium level <125 mmol/L.[5,6] In addition, hyponatraemia is often underreported in the hospital setting.[7] In the intensive care unit, approximately 25–30% of patients will have a serum sodium <134 mmol/L.[8,9] In neurosurgical units, hyponatraemia is reported in up to 50% of patients with subarachnoid haemorrhage in retrospective[2] and prospective studies.[10] Hyponatraemia is also a common occurrence in heart failure with an incidence of approximately 20% in patients hospitalised for heart failure.[11] Age-related changes and chronic diseases are often associated with abnormalities in water homeostasis. Miller *et al*[12] have reported that more than 50% of nursing home residents had at least one episode of hyponatraemia over a 12-month study period.

Morbidity and mortality associated with hyponatraemia

Hyponatraemia is associated with increased morbidity and mortality. Acute severe symptomatic hyponatraemia is a medical emergency that carries a high mortality rate if not addressed acutely. A recent prospective observational study found a positive correlation of serum sodium and mortality, with a serum sodium <125 mmol/L associated with a substantial 1-year mortality, recurrence of hyponatraemia and rehospitalisation rate.[13] 'Asymptomatic' chronic mild hyponatraemia has previously been thought to be clinically insignificant; however, recent evidence shows that mild chronic 'asymptomatic' hyponatraemia, particularly in an older population, may contribute to impaired cognition,[14] increased risk of falls[15] and fractures.[16] Recent studies suggest

Key Points

Hyponatraemia is the commonest electrolyte abnormality in hospitalised patients and is associated with increased morbidity and mortality

Assessment of volume status and urinary sodium are key steps in the appropriate diagnosis and treatment of hyponatraemia

Symptomatic hyponatraemia is a medical emergency and needs to be treated acutely in order to reduce neurological sequelae

During the treatment of hyponatraemia careful and regular monitoring of sodium is required in order to avoid rapid overcorrection with the risk of osmotic demyelination syndrome

Many patients with syndrome of inappropriate antidiuresis may not respond to fluid restriction and will need second line therapy

KEYWORDS: Hyponatraemia, plasma osmolality, syndrome of inappropriate antidiuresis, urine sodium, vasopressin ■

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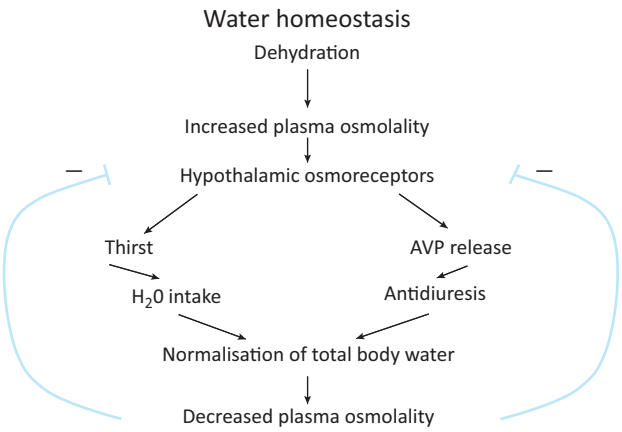

Fig 1. Normal regulation of salt and water balance. Adapted from Hannon MJ *et al.*[10] AVP = antidiuretic hormone vasopressin

the predisposition to fractures in patients with hyponatraemia not only exists because of a higher falls risk, but also as a result of associated osteoporosis.[17,18] In addition to the above, inappropriate management of hyponatraemia can lead to significant morbidity.[19]

Physiology of water balance

In healthy humans, plasma sodium concentrations are maintained within a narrow range, despite wide variations in water and salt intake.[20] Plasma sodium concentration rarely varies by more than 1–2% off baseline in normal physiological conditions, when access to water is normal. In health, plasma osmolality is very closely regulated by the sophisticated interaction between the secretion and action of the antidiuretic hormone vasopressin (AVP) and the sensation of thirst, which promotes water intake (Fig 1). Changes in plasma osmolality are detected by specialised magnocellular neurons in the anterior hypothalamus. When plasma osmolality rises, there is stimulation of synthesis and secretion of AVP. AVP binds to V2 receptors in the collecting ducts of the renal tubules, stimulating an intracellular cascade that leads to migration of vesicle bound aquaporin-2 to the luminal membrane of the collecting duct.[21] This renders the cells of the collecting duct permeable to water, enabling reabsorption of water from the urine to the blood, such that adequate urine concentration can occur. Simultaneously, the thirst centre in the cerebral cortex is stimulated, promoting water intake. Thus, AVP-mediated restriction of water excretion combined with thirst-driven water intake leads to an increase in plasma water and normalisation of plasma osmolality.[22] Changes in plasma sodium concentration are therefore a reflection of abnormal water balance, rather than the dysregulation of sodium intake and excretion.

Aetiology and classification of hyponatraemia

There are a number of aetiologies of hyponatraemia, which can be divided into:

1 hypotonic hyponatraemia (which is divided into hypovolaemic, euvolaemic and hypervolaemic causes)
2 pseudohyponatraemia
3 non-hypotonic hyponatreamia.

Other important sub-classifications include whether the hyponatraemia has developed acutely or chronically and is symptomatic or asymptomatic.

Table 1. Causes of hyponatraemia according to volume status and urinary sodium

Volume status	Clinical signs	Urinary $Na^{=}$ ≤30 mmol/L	Urinary $Na^{=}$ ≥40 mmol/L
Hypovolaemic	Dry mucous membranes	GI losses	Diuretics
	Decreased turgor	Mucosal losses	Addison's disease
	Tachycardia	Pancreatitis	Cerebral salt wasting
	Hypotension (orthostatic)	Sodium depletion post diuretics	Salt wasting nephropathy
	Raised urea, renin		
Euvolaemic	Underlying illness	Hypothyroidism	SIAD
		SIAD with ongoing fluid restriction	ACTH deficiency
Hypervolaemic	Peripheral oedema	Cirrhosis	Cardiac failure with diuretic therapy
	Ascites	Cardiac failure	
	Raised JVP	Nephrotic syndrome	
	Pulmonary oedema	Primary polydipsia	
	Underlying illness		

ACTH = adrenocorticopic hormone; GI = gastrointestinal; JVP = jugular venous pulse; SIAD = syndrome of inappropriate antidiuresis

Adapted from Smith et al.[23]

Hypotonic hyponatraemia

Hypotonic hyponatraemia can be classified, based on the estimation of extracellular volume status of the patient, as hypovolaemic, euvolaemic or hypervolaemic hyponatraemia (Table 1). In clinical practice, evaluation of volume status may be challenging and is often suboptimal.[23]

Hypovolaemic hyponatraemia

Hypovolaemic hyponatraemia occurs when there is depletion of both water and body sodium with a relative excess of sodium loss. Solute loss can be classified as renal and non-renal. Thiazide diuretic-induced hyponatraemia is the leading cause

of drug-induced hyponatraemia requiring hospital admission, and can affect up to one third of older patients taking thiazide diuretics.[24] Risk factors for the development of thiazide-induced hyponatraemia include increasing age,[25] low body mass index,[26] hypokalaemia[27] and female gender.[28] Other causes of hypovolaemic hyponatraemia include gastrointestinal losses, skin losses (burns and perspiration) and renal salt loss due to salt wasting nephropathy or mineralocorticoid deficiency (eg Addison's disease).

Euvolaemic hyponatraemia

Euvolaemic hyponatraemia is caused by a relative absolute increase in body water. It is the most heterogeneous and common cause of hyponatraemia among hospitalised patients and the syndrome of inappropriate antidiuresis (SIAD) is the most frequent underlying disorder. Most hyponatraemic patients who appear to be euvolaemic by physical examination have SIAD. However, such patients may occasionally have hyponatraemia due to true volume depletion, primary polydipsia, malnutrition, glucocorticoid deficiency or severe hypothyroidism.

Syndrome of inappropriate antidiuresis

SIAD is the most common cause of euvolemic hyponatraemia in hospitalised patients.[29] It is a common complication of a wide range of clinical disorders and drug therapies. The most common causes of SIAD are malignancy, pulmonary disorders, central nervous system disorders and medications.[30,31] SIAD has been reported as an adverse effect of many drugs, including psychotropic medications[32] and chemotherapeutic drugs.[33]

The cardinal diagnostic criteria for SIAD, originally described by Bartter and Schwartz in 1967, are outlined in Box 1.[34]

Glucocorticoid deficiency

An important cause of euvolaemic hyponatraemia, which must be differentiated from SIAD, is adrenocorticotropic hormone (ACTH) deficiency leading to cortisol deficiency (this is different to patients with Addison's disease who are also lacking mineralocorticoids). The biochemical presentation is identical to that of SIAD. Patients with ACTH deficiency and hyponatraemia have elevated plasma vasopressin concentrations,[35] which may be partially baroregulated because of an associated decrease in blood pressure. In addition, cortisol is required for free water excretion, which also contributes to the development of euvolaemic hyponatraemia. In a large, prospective and well-defined cohort of euvolaemic hyponatraemia in a tertiary centre, undiagnosed secondary adrenal insufficiency co-occurred in 3.8% of cases initially diagnosed as SIAD.[36] Acute glucocorticoid insufficiency should also be considered as the cause of hyponatraemia in any patient with acute neurotrauma and in patients who have been receiving long-term glucocorticoid therapy.

Box 1. Essential diagnostic criteria for SIAD[37]

1 Plasma hypoosmolality (<275 mOsm/kg)

2 Inappropriate urine concentration (Uosm >100mOsm/kg H20)

3 Urine sodium >30mmol/L, with normal salt and water intake

4 Clinical euvolaemia

5 Exclusion of glucocorticoid deficiency or hypothyroidism (rare)

Supplementary criteria are not included as these are not used routinely in clinical Practice.

Hypothyroidism

Determination of thyroid-stimulating hormone is important for evaluation of a patient with hyponatraemia as the exclusion of hypothyroidism is one of the prerequisites for the diagnosis of SIAD.

However, the relationship between hypothyroidism and hyponatraemia is inconsistent,[37] although they often coexist, and recent data suggest that hypothyroidism-induced hyponatraemia is extremely rare and probably occurs only in severe hypothyroidism and myxoedema, with reduction in cardiac output and nonosmotic stimuli to AVP release.

Hypervolaemic hyponatraemia

In hypervolaemic hyponatraemia, there is an increase in both total body water and total body sodium, with a relative excess of total body water, leading to dilutional hyponatraemia. In both cardiac failure and cirrhosis there is a fall in mean arterial pressure (particularly within the splanchnic circulation). This stimulates baroregulated vasopressin secretion, baroregulated activation of the renin-angiotensin-aldosterone axis and increases sympathetic tone. Increased AVP leads to water retention, and the activation of the renin-angiotensin axis promotes sodium and water retention.[38]

Pseudohyponatraemia

Pseudohyponatraemia, originally described in the 1950s,[39] is caused by a displacement of serum water by significantly elevated concentrations of serum lipids or proteins. It occurs when blood specimens with high concentrations of either lipid or protein are analysed by either a flame photometer or an ion-selective electrode that requires sample dilution before assay.[40]

Non-hypotonic hyponatraemia

Hyponatraemia with normal or increased effective osmolality can occur when the serum contains additional osmoles, which reduce serum sodium concentration by attracting water from the intracellular compartment. Hypertonic hyponatraemia may occur as a consequence of hyperglycaemia. Hyperglycaemia will result in an osmotic shift of water from the intracellular to the extracellular fluid compartment, thus diluting serum sodium levels, which can be calculated by correcting the measured serum [Na^+] for the glucose elevation.[41] It is imperative to control the rate at which plasma glucose is lowered, to minimise the associated risk of cerebral oedema that can occur.[42]

Clinical presentation of hyponatraemia

The symptoms associated with hyponatraemia are varied and are related to the severity and rapidity of the fall in the plasma sodium concentration as well as the coexistence of neurological disease or other electrolyte abnormalities. Symptoms are

far more likely if the fall in plasma sodium is rapid, whereas chronic hyponatraemia (hyponatraemia of >72-hour duration) may present as a relatively asymptomatic condition, even in cases where hyponatraemia is biochemically significant. In acute hyponatraemia, the main pathological consequence is the development of cerebral oedema, which leads to raised intracranial pressure with the risk of cerebral herniation, hypoxia and even death.[43] In chronic hyponatraemia there is a lower risk of acute neurological symptoms because of the presence of chronic cerebral adaptive mechanisms.[44]

Diagnosis and investigations

The initial diagnostic approach to the adult patient with hyponatraemia consists of a directed history and physical examination, supported by laboratory tests. There should be a focus on assessment of extracellular fluid volume status, symptoms and signs of hyponatraemia, the rate at which hyponatraemia developed and the biochemical severity of hyponatraemia. Measurement of urinary sodium is crucial in the distinction of hyponatraemia aetiology (Table 1). In hypovolaemic hyponatraemia, urinary sodium allows differentiation between renal (high urine sodium; >30 mmol/L) and extra-renal (low urine sodium; <30 mmol/L) salt loss. These are not absolute values; they are a guide as they may also be determined by solute intake. In euvolaemic hyponatraemia, urinary sodium levels are high in SIAD and glucocorticoid insufficiency, but low in hyponatraemia associated with hypotonic fluid replacement or in patients with low solute intake. However, low urinary sodium is also an early feature of the recovery phase from diuretic use (within hours) or SIAD, highlighting the complexities in forming a diagnostic algorithm for hyponatraemia. Recent studies have focused on the use of a novel parameter, co-peptin, as a surrogate marker for vasopressin and its potential role as a diagnostic parameter in the differential diagnosis of hyponatraemia has been discussed.[45] However, as AVP is elevated in almost all causes of hyponatraemia co-peptin is unlikely to be of significant clinical utility at present. In patients with primary polydipsia, a low co-peptin may be a useful diagnostic tool.[46] Fenske *et al*[47] have also recently reported that measurement of fractional excretion of urea (FEurea) or uric acid (FEUA) levels were valuable parameters for discriminating between SIAD and other hyponatraemia aetiologies, irrespective of diuretic use.[47]

Management of hyponatraemia

Management of hyponatraemia needs to be targeted to the underlying aetiology. The urgency of intervention is determined by the severity of symptoms and the potential for an adverse outcome.

Management of acute symptomatic hyponatraemia

There is a high mortality associated with symptomatic hyponatraemia given the risk of cerebral oedema and brain herniation and, as such, plasma sodium needs to be elevated acutely (the risk of not increasing the plasma sodium needs to be weighed against the risk of osmotic demyelination syndrome).[48] Evidence available in the literature regarding the treatment of acute severe hyponatraemia is limited. Recently, a number of guidelines, which differ slightly in their approach to the management of severe symptomatic hyponatraemia in adult patients, have been published.[3,4,49]

The US consensus guidelines recommend an initial rise in serum sodium of 4–6 mmol/L over 4 hours, using intravenous boluses of hypertonic (3%) sodium chloride.[3] This is based on published experience with hypertonic saline to treat cerebral oedema in normotraemic patients with neurosurgical conditions, where a 5 mmol/L rise in serum sodium reversed the clinical signs of herniation and reduced intracranial pressure by almost 50% within the first hour.[50]

The Society for Endocrinology guidelines recommend 150 mL bolus of hypertonic saline, aiming for a rise of 5 mmol/L in serum sodium within the first hour.[49]

For severe symptoms, a 100 mL bolus of 3% saline infusion should be given over 10 minutes and repeated up to three times, if necessary, depending on clinical improvement. For mild to moderate symptoms with a low risk of cerebral herniation, 3% saline infusion is again recommended but at a slower rate of 0.5–2 mL/kg/h. Patients who are treated with hypertonic saline need to be managed in a critical care setting to allow for frequent monitoring of plasma sodium in order to ensure that there is not a rapid overcorrection of hyponatraemia.

In true acute hyponatraemia (where the decrease in plasma sodium has been documented to be in the prior 24–48 hours), the rate of correction need not be restricted as tightly as in chronic hyponatraemia as there is a lower risk of osmotic demyelination. However, if there is any uncertainty as to the rapidity of onset of hyponatraemia (chronic verses acute), then the target limits for correction of chronic hyponatraemia should be adhered to.

Management of chronic hyponatraemia

Rapid overcorrection of chronic hyponatraemia can lead to neurological sequelae due to osmotic demyelination syndrome (ODS; previously known as pontine or extra-pontine myelinolysis). This syndrome manifests clinically as progressive quadriplegia, opthalmoplegia or with extrapyramidal features such as ataxia. The mainstay of diagnosis is clinical suspicion and examination, aided by T1-weighted magnetic resonance imaging, which may have the classic appearances of a hypointense pons on sagittal imaging but a hyperintense pons on coronal imaging. Prognosis is variable but usually poor, with many patients developing persistent neurological deficit.

Current recommendations suggest a target rise in serum sodium concentration in patients with chronic hyponatraemia stratified by the risk of developing ODS (Table 2). They suggest a target maximum rise of 4–8 mmol/L per day in patients with low risk of ODS, with a target maximum limit not to exceed 10–12 mmol/L in any 24 hours or 18 mmol/L in any 48 hours. For those at high risk of ODS, they suggest a lower maximum target rise of 4–6 mmol/L per day, with a maximum target limit not to exceed 8 mmol/L in any 24-hour period. Factors that place a patient at high risk of developing ODS with correction of chronic hyponatraemia include starting serum sodium concentration ≤105 mmol/L, hypokalaemia, alcoholism, malnutrition and advanced liver disease (Table 2).[3]

Table 2. Targets for elevation in plasma sodium in hyponatraemic patients

	Goal of minimal correction of plasma sodium in first 24 hours (mmol/L)	Limits not to exceed in plasma sodium per 24 hours (mmol/L)
Normal risk patient	**4–8**	**10–12***
High risk of ODS	**4–6**	**8**
Patients with pNa^+ <105 mmol/L, hypokalaemia, alcoholism, malnutrition, liver disease		

*Not >18 mmol/L in 48 hours in normal risk patients.
ODS = osmotic demyelination syndrome

Management of hypovolaemic hyponatraemia

In hypovolaemic hyponatraemia, the aim is to correct plasma sodium and also restore intravascular volume. Most cases will respond to intravenous infusion of physiological saline. Diuretic therapy should be discontinued and any other underlying causes sought and treated.

The diagnosis of Addison's disease is suggested by history, examination and the presence of hyperkalaemia. Although the biochemical abnormalities of Addison's disease will respond to high-dose corticosteroids, patients are often profoundly fluid deplete and require intravenous saline to expand blood volume and replace body sodium. Current guidelines recommend a rapid intravenous infusion of 1,000 mL of isotonic saline infusion within the first hour, followed by further intravenous rehydration as required (usually 4–6 L in 24 hours, with careful monitoring for volume overload in the elderly or in renal impairment).[51] Intravenous dextrose may also be needed if the patient if hypoglycaemic (close monitoring is required as dextrose can exacerbate hyponatraemia).

Management of SIAD

Owing to a relative lack of randomised controlled trials, the treatment of SIAD is largely based on expert opinion. The current European guidelines and US consensus recommendations diverge in relation to the use of interventions after fluid restriction has failed.

Fluid restriction

The first-line therapy for mild to moderate asymptomatic hyponatraemia secondary to SIAD is fluid restriction. Several factors may predict failure of fluid restriction, including high urine osmolality (>500 mOsm/kg H_2O), low 24-hour urine volume (<1,500 mL/day) and a urinary sodium and potassium that are greater than plasma sodium. In addition, failure of fluid restriction may prompt reconsideration for the presence of underlying causes, such as malignancy, or the presence of clinically unapparent hypovolaemia.

Fluid restriction of 800–1,200 mL/day is generally advised, according to severity of hyponatraemia. As long as background water losses from the kidney, skin and lungs exceed this amount, there is progressive depletion of total body water and a gradual rise in plasma sodium concentration. The principle drawback is that patients find it extremely difficult to maintain fluid restriction, as thirst in SIAD is inappropriately normal because of a downward resetting of the osmotic thirst threshold.[15] Hospitalised patients who can be supervised tend to do better with fluid restriction than outpatients. However, hospitalised patients who are receiving intravenous fluids, as part of cytotoxic or antibiotic regimens, often find it hard to comply with fluid restriction.

Demeclocycline

Demeclocycline is a tetracycline derivative that is utilised in the treatment of SIAD because it causes nephrogenic diabetes insipidus in about 60% of patients. The degree of vasopressin resistance is not predictable; in a significant proportion of patients, it does not work. When it does work, the onset of action is also unpredictable, usually occurring after 2–5 days, but occasionally taking longer. In some patients, polyuria can be profound and patients can become markedly symptomatic, occasionally developing hypernatraemia if access to water is compromised. Nephrotoxicity can arise, particularly in patients with cirrhosis, and although renal impairment is usually reversible with discontinuation, cases with permanent renal failure have been reported.[16] It has also been associated with photosensitive skin rash and appropriate UV protection is recommended.

Urea

A relatively small number of centres have experience in the use of urea. It is recommended for use in the recent European hyponatraemia guidelines; however, it is unavailable in many countries. Human studies have shown that long-term (5-year) treatment of hyponatraemia with urea is effective[24] and the same group have published data in a rat model of SIAD that suggest that treatment of hyponatraemia with urea may protect against brain complications, such as osmotic demyelination syndrome.[25,26]

Frusemide

Frusemide was shown some years ago to be effective in the rapid correction of hyponatraemia in SIAD,[27] but it is of limited efficacy in long-term treatment as the diuresis that it induces includes a natriuresis, which can occasionally worsen hyponatraemia.

Vaptans

The development of specific vasopressin receptor antagonists (vaptans) represents a novel therapeutic option in euvolaemic hyponatraemia. The vaptans are vasopressin receptor antagonists with V1a (relcovaptan) or V2 (tolvaptan, lixivaptan) selectivity or non-selective activity (conivaptan), which may be advantageous in some disorders. The V2 receptors located primarily in the collecting tubules mediate free water absorption while the V1B receptors are located in the anterior pituitary and mediate ACTH release.[52]

The V1a/V2 non-selective vasopressin antagonist conivaptan was the first vaptan approved by the US Food and Drug Administration for the treatment of euvolaemic and hypervolaemic hyponatraemia as an intravenous infusion. Its efficacy for the treatment of hyponatraemia has been assessed in several double-blind, placebo-controlled clinical trials.[53,54] Like other vasopressin antagonists, its use is contraindicated in patients with hypovolaemic hyponatraemia.

Tolvaptan is an oral, selective non-peptide V2 receptor antagonist. The results of two large multicentre, randomised, placebo-controlled, double-blind trials of oral tolvaptan have been reported in patients with hyponatraemia (due to chronic heart failure, cirrhosis and SIAD).[55] Approximately 55% of patients in the tolvaptan group had normal serum sodium concentrations after 1 month of treatment (without the need for water restriction) compared with 25% in the placebo group. However, the benefit on serum sodium was more effective in SIAD patients compared with heart failure and cirrhotic patients. Excessive correction of serum sodium concentrations was noted in this study (>12 mmol/L per day in 3%). The SALTWATER trial, an extension of the SALT study (Study of Ascending Levels of Tolvaptan in Hyponatremia), showed that the effect of tolvapton was sustained for the duration of the observation period, a maximum of 214 weeks.[56]

The US consensus recommendations suggest certain precautions with the use of vaptans to avoid overcorrection and subsequent ODS. Clinicians should monitor serum sodium levels frequently during the active phase of correction of the hyponatraemia. In addition, fluid restriction should not be recommended, thereby allowing the patient's own thirst mechanism to compensate for the induced aquaresis. Goals and limits for safe correction are similar to those described above in the treatment of chronic hyponatraemia. Hepatotoxicity with tolvaptan is a concern based on the TEMPO trial (this trial examined the effect of tolvaptan, at high dose, on the progression of polycystic kidney disease);[57] it is therefore recommended to check liver enzymes in patients taking tolvaptan. Another potential limitation to the use of vaptan therapy is that its cost may be prohibitive.

Saline infusion in SIAD

There is data to suggest that plasma sodium concentration will rise in some patients with SIAD who are treated with intravenous normal (0.9%) saline.[28] However, treatment with normal saline is reserved for patients in whom the differentiation between hypovolaemia and euvolaemia is difficult. In this situation, intravenous saline is a safer first-line treatment than fluid restriction, but careful monitoring is required in order to ensure improvement in sodium concentrations while on saline.

Management of hypervolaemic hyponatraemia

In hypervolaemic hyponatraemia, therapy is aimed at treating the underlying cause. In congestive cardiac failure and cirrhosis, the mainstays of therapy are a combination of dietary sodium restriction, diuretics and fluid restriction to restore total body water to normal, in combination with inhibition of the renin angiotensin aldosterone system using angiotensin converting enzyme inhibitors, angiotensin receptor blockers or spironolactone. The use of vasopressin receptor antagonists in hypervolaemic hyponatraemia results in increased solute-free excretion without activation of the neurohumoral systems, as compared with loop diuretics. This provides a rationale for substitution in the management of heart failure. This was recently demonstrated in normonatraemic heart failure patients. The efficacy of vaptans in hypervolaemic hyponatraemia and cirrhosis is limited[58] and, given the potential hepatotoxicity seen with tolvaptan, it is recommended that tolvaptan should not be given to patients with chronic liver disease.

Conclusion

Hyponatraemia is the commonest electrolyte abnormality encountered in clinical practice and is a biochemical manifestation of a spectrum of illnesses. It is associated with a significant morbidity and mortality. The aetiology of hyponatraemia needs to be systematically determined and is the critical step to ensure adequate treatment. SIAD is the most common cause of euvolaemic hyponatraemia in hospitalised patients. Clinical practice guidelines and consensus statements provide recommendations to help evidence-based practice. Acute hyponatraemia should be promptly managed to protect from neurological sequelae, while chronic hyponatraemia should be investigated to establish aetiology and cautiously treated to avoid overcorrection. ■

Conflicts of Interest

CJT and MS have received honoraria for lectures from Otsuka. RD has no conflicts of interest to declare.

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