Clinical approach to electrolyte abnormalities

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Abstract

Electrolyte disorders are common, confer significant morbidity and may be life threatening. They are frequently multifactorial and are both caused by and causative of dysfunction of multiple organ systems. There is considerable co-dependence in electrolyte homeostasis and several abnormalities may emerge simultaneously. Effective treatment is dependent on early recognition, an understanding of physiological principles underlying the disorder, judicious corrective therapy and adequate monitoring. Decades of research have shed considerable light on the molecular mechanisms underlying the pathophysiology of these conditions. This has led to recent therapeutic advances such as the use of V2 receptor blockade in the treatment of the syndrome of inappropriate antidiuretic hormone (SIADH).

Keywords acidosis; alkalosis; electrolytes; hypercalcaemia; hyperkalaemia; hypermagnesaemia; hypernatraemia; hyperphosphataemia; hypocalcaemia; hypokalaemia; hypomagnesaemia; hyponatraemia; hypophosphataemia

Introduction

Electrolyte abnormalities are extremely common in the hospital setting. While some aspects of physiology and therapy are controversial and complex, the great majority can be managed safely and effectively by applying basic principles consistently. This review is intended as a practical, working guide for the hospital physician.

Sodium and water disorders

Sodium disorders are disorders of both sodium and water balance, with dysregulation of water balance being, in many cases, the primary abnormality. Water moves freely between body fluid compartments. Sodium is the dominant extracellular cation but, unlike water, its ability to move across cell membranes is limited. The presence of sodium in the extracellular fluid (ECF) is critical to maintenance of circulating blood volume. Changes in ECF and osmolality elicit compensatory mechanisms that involve changes in renal sodium handling and variation in renal free water clearance.

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Hyponatraemia

Hyponatraemia is common in hospital settings and appropriate and timely management is of great importance. The clinical manifestations of hyponatraemia depend on whether it is associated with a genuine decline in osmolality (not the case in translocational or pseudohyponatraemia), and on the severity and the rate of decline of serum sodium concentration. Hypovolaemic, euvolaemic and hypervolaemic hyponatraemia need to be distinguished in order to identify the cause and institute appropriate treatment. The first investigative step is to establish whether vasopressin is active, by measuring urine osmolality, which normally exceeds 100 mmol/kg. A urine osmolality of 50–100 mmol/kg suggests hypo-osmolar hyponatraemia. The clinical circulatory assessment then defines whether vasopressin activity is expected (hypovolaemia or reduced affective circulating volume seen in heart or liver failure) or due to the syndrome of inappropriate antidiuretic hormone secretion (SIADH), in which case the patient will be euvolaemic. In SIADH, urine sodium concentration is generally high as in this context the kidneys conserve water alone (rather than salt and water). Urine Na^+ may also be high in hypovolaemic hyponatraemia because of renal salt wasting (e.g. Addison's disease).

The treatment strategy in patients with hyponatraemia is defined by the urgency of correction, the chronicity and the underlying cause. There are no reliable formulae for therapy; treatment must be titrated with adequate monitoring, including regular frequent sodium measurement and assessment of urinary free water and sodium excretion.

Hypovolaemia, if present, should be corrected concomitantly with colloid or sodium chloride 0.9%. The rate of correction of sodium should not exceed 12 mmol/litre/24 hours. When severe neurological symptoms are present, the serum sodium may need to be corrected more rapidly. Hypertonic sodium chloride (3%) should be infused (a standard recommendation is 2 ml/kg/hour), aiming for a rise in serum sodium of 1–2 mmol/litre/hour until symptoms have resolved (usually when serum sodium >120 mmol/litre).

Symptomatic hyponatraemia should be corrected with great care, particularly if there is evidence of chronicity (>48 hours duration), because of the potential risk of central pontine myelinolysis (CPM). Hypovolaemia should be corrected with sodium chloride 0.9% or colloid. Thereafter, hypertonic sodium chloride should be infused cautiously with regular monitoring of serum sodium. The rate of correction should not exceed 0.5–1.0 mmol/litre/hour or 12 mmol/litre/24 hours. Symptoms will usually abate when serum sodium reaches 120 mmol/litre.

Acute therapy of hyponatraemia may be augmented with furosemide, which increases solute delivery to the distal tubule, facilitating free water excretion.

In chronic asymptomatic hyponatraemia (with euvolaemia or hypervolaemia), if there is an excess of arginine vasopressin (AVP), fluid restriction (usually 1 litre/24 hours) is effective. The degree of water restriction required will vary according to the free water excretory capacity of the individual. This may be augmented with demeclocycline (300–600 mg orally twice daily), which inhibits cyclic adenosine monophosphate (cAMP) in the collecting duct, inducing nephrogenic diabetes insipidus and AVP resistance. More recently, V2 receptor antagonists

(conivaptan intravenously (IV) and tolvaptan orally) have been deployed in these clinical situations.

Hypernatraemia

Hypernatraemia (serum sodium >145 mmol/litre) is a common electrolyte disorder affecting between 1% and 5% of hospitalized patients, which is associated with very high mortality (40–75%) when severe. It is caused by a loss of total body free water or a gain in total body sodium (Table 1). The former is by far the commoner scenario and may be related to impaired thirst, reduced access to water, impaired AVP release or impaired AVP responsiveness.

Clinical assessment of patients with hypernatraemia should establish volume and hydration status, look for complications of hypernatraemia, and measure urine volume, renal function, calcium, potassium and glucose, and paired urine/serum.

In more chronic hypernatraemia, neuronal intracellular osmolytes are increased as a compensatory mechanism and rapid correction of chronic hyponatraemia will lead to neuronal oedema.

As in the case of hyponatraemia, when hypernatraemia has developed in a short period (<48 hours), compensatory neuronal changes will not have occurred and hypernatraemia may be corrected rapidly. Otherwise, correction must be cautious: a maximum rate of 1 mmol/litre/hour is recommended, with a total maximum decrease of 10 mmol/litre in 24 hours.

Hypovolaemia should be corrected with colloid or sodium chloride 0.9%. Thereafter, hypotonic fluid must be given as either oral or nasogastric water, intravenous glucose 5% or 'half-strength' sodium chloride (0.45%). Total water deficit may be calculated as 0.6 × weight × [1−(140/serum sodium)]. This assumes that 60% of ideal weight is water. In the elderly a calculation factor of 0.5 (rather than 0.6) may be used. This water deficit is not a prescription for replacement, as it does not account for ongoing renal or other losses. Titration with regular measurement and clinical assessment is critical.

In hypervolaemic hypernatraemia, sodium excretion may be increased using diuretics (which waste salt and water) and salt restriction. Neurohypophyseal diabetes insipidus is treatable with nasal or oral desmopressin (Table 2). Patients with chronic profound polyuria should have surveillance ultrasound to check for 'functional' high-pressure obstruction as well as checks of renal function.

Potassium disorders

Potassium is the main intracellular cation with an intracellular concentration of approximately 100 mmol/litre. The potassium concentration gradient between the extracellular fluid and intracellular fluid is actively maintained and is an essential determinant of the membrane potential and excitatory activity of cells. Insulin and β-adrenoreceptor agonists stimulate Na^+-K^+-ATPase, causing movement of K into cells; β-blockade has the opposite effect and may cause hyperkalaemia.

Causes of hypernatraemia

Hypovolaemic hypernatraemia

- Hypotonic renal fluid losses
  - diuretics
  - glycosuric osmotic diuresis
  - tubular damage
  - post-obstructive diuresis
- Gastrointestinal losses
  - vomiting
  - diarrhoea
  - surgical drains
- Excessive sweating

Euvolaemic hypernatraemia

Pure water deficit, with preserved total body sodium

- Restricted access to water
- Impaired thirst and common in the elderly
- Hypotonic insensible losses from the lung (respiratory disease and hyperventilation)
- Diabetes insipidus

Hypervolaemic hypernatraemia

Total body salt and water are increased, but more salt than water. Extracellular fluid volume is expanded. Clinical signs of hypervolaemia, such as hypertension and oedema.

- Excessive administration of salt-rich fluids in patients with limited capacity to excrete salt
- Sodium chloride 0.9% has a sodium content of 155 mmol/litre, as do the colloids Gelofusine® and salt-poor albumin

Table 1

Diabetes insipidus

Cranial diabetes insipidus (CDI)

Inadequate secretion of arginine vasopressin (AVP) in response to osmotic stimulus.

Acquired causes

Central nervous system (CNS) tumours

CNS infection

Brain traumatic injury and surgery

Granulomatous diseases such as sarcoid and histiocytosis X. (Rare)

Inherited causes

Mutations in genes encoding AVP and associated proteins

AVP-NPII (encodes AVP), its carrier protein neurophysin II and its co-peptide

Nephrogenic diabetes insipidus (NDI)

Impaired response to high circulating levels of AVP.

Acquired causes

Lithium

Demeclocycline

Chronic hypokalaemia

Chronic hypercalcaemia

Tubular damage (free light chains in myeloma, autoimmune disease such as Sjögren's syndrome and drug toxicity)

Inherited causes

90% of inherited NDI is due to mutation in *AVPR2*, which is on the X-chromosome

10% of patients with inherited NDI have autosomal recessive disease caused by mutations in aquaporin-2 (*AQP2*)

Table 2