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REVIEW ARTICLE

Correction of Electrolyte Abnormalities in Critically Ill Patients

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Abstract

Introduction The majority of patients in the intensive care unit (ICU) are at risk for at least one electrolyte abnormality and critically ill patients are the most vulnerable population to the effects of suboptimal electrolyte levels. These patients have unique characteristics impacting implications of the electrolyte disturbances and management.

Areas Covered In the ICU, magnesium, potassium, calcium, phosphorous, and sodium are the most commonly encountered electrolytes that can be abnormal in the critically ill. Critical illness both is affected by and affects disturbances of these electrolytes which can result in more severe illness, longer duration of mechanical ventilation, increased dialysis support, longer length of stay, and increased mortality. Often, patients have multiple imbalances that require correction. Removal or mitigation of the cause should be undertaken whenever possible and should be concurrent with any therapeutic management used to correct the electrolyte imbalance. Selection of medication to correct electrolyte imbalances should be undertaken according to available evidence and drug-specific characteristics that impact medication delivery in the critically ill.

Electrolyte disturbances, measurements, and corrections are ubiquitous in the ICU. Published literature on the management of electrolytes in the critically ill is limited. Management should consider factors unique to the critically ill when selecting optimal treatment approach and it is essential to individualize treatment to a patient's unique needs and adapt management to the patient's chancing clinical situation.

Keywords Electrolyte · Potassium · Magnesium · Calcium · Phosphorous · Sodium

Abbreviations

ATP	Adenosine triphosphate
CRRT	Continuous renal replacement therapy
DI	Diabetes insipidus
ECF	Extracellular fluid
EKG	Electrocardiography
EN	Enteral nutrition
ICF	Intracellular fluid
ICU	Intensive care unit
IV	Intravenous
ODS	Osmotic demyelination syndrome
PN	Parenteral nutrition
PTH	Parathyroid hormone
ROMK	Luminal potassium channels
SIAD	Syndrome of inappropriate diuresis
SPS	Sodium polystyrene sulfonate

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SZC Sodium zirconium cyclosilicate
TBW Total body weight
TdP Torsade de Pointes

1 Introduction

Almost all patients in the intensive care unit (ICU) are at risk for some electrolyte abnormality. Depletion or overabundance of key electrolytes are both caused by and cause various clinical conditions and outcomes in the critically ill, the risk of which is often compounded when multiple imbalances are present [1]. Some abnormalities may be asymptomatic and/or transient; however, acknowledgment of them is important in the care of critically ill patients. In these patients, the prevalence of uncorrected imbalances has been shown to be higher in non-survivors than survivors [2]. Most imbalances can be corrected by addressing the underlying cause or augmenting the intake, clearance, or intracellular movement of the various electrolytes [3]. In the acute setting, isolated electrolyte abnormalities are not common, as often patients will have multiple imbalances that require correction. It is possible that multiple electrolyte imbalances have a common cause. Removal or mitigation of the underlying cause should be done whenever possible and should be concurrent with any therapeutic management used to correct the electrolyte abnormality. It is important that any electrolyte manipulation or replacement be purposeful as inappropriate provision or changes can cause further harm or even death [3].

There is a paucity of prospective, randomized-controlled trials on managing electrolyte abnormalities overall, with even less data specific to the ICU setting. Much of the available reviews summarize inpatient management broadly or focus on patient populations receiving continuous renal replacement therapy (CRRT). Patients in the ICU are complex, with unique needs that can be significantly different from other inpatients. They can be particularly vulnerable to the effects of suboptimal electrolyte levels. Subsequently, it is essential to evaluate available information in a context appropriate for the critically ill patient. A literature search of PubMed, Google Scholar, and SCOPUS for article published January 2000 to August 2023 was conducted using the search terms electrolyte disorder, hyponatremia, hypernatremia, hyperkalemia, hypokalemia, hypocalcemia, and hypophosphatemia was conducted. Articles published in the English language involving human subjects, applicable to the critical care setting, and evaluating pharmacologic agents or instruments to guide pharmacotherapy were included. Articles were excluded if they focused on chronic treatment of an electrolyte disorder and/or focused on outpatient pharmacotherapy. References of key articles identified were also reviewed. Studies involving twelve different pharmacologic agents or classes met criteria for inclusion. This narrative review provides guidance on the approach to monitoring and correcting the most common electrolyte disturbances in the ICU. While any abnormality can occur in a critically ill patient, not all electrolyte disturbances have the same frequency of occurrence or acute clinical significance. Hyperphosphatemia and hypermagnesemia are of less acute significance in the average critically ill patient and therefore are excluded from this review. The standard values for electrolytes can vary according to a facility's laboratory; the ranges used in this article may vary minimally from the standard ranges at any given institution.

2 Magnesium

Magnesium is the fourth most abundant mineral in the body and the second most prevalent intracellular cation [4]. The standard serum magnesium concentration ranges from 1.5 to 2.4 mg/dL. It plays an abundance of critical roles in the human body, including, but not limited to, acting as a cofactor for reactions powered by adenosine triphosphate (ATP), involvement in the active transport of calcium and potassium ions across cell membranes, economization of cardiac pump function, and utilization of certain vitamins (e.g., vitamin D and B vitamins) [4–6]. The kidneys, intestines, and bones are all involved in magnesium homeostasis [4–6]. Table 1 lists etiologies for hypomagnesemia and other common electrolyte abnormalities in the ICU.

2.1 Hypomagnesemia

Hypomagnesemia (< 1.5 mg/dL) has been associated with increased mortality, longer mechanical ventilation, and increased ICU length of stay [7]. The consequences of hypomagnesemia leading to poor outcomes include increased muscle weakness, respiratory failure, development of cardiovascular disease, dysrhythmias, and more.

Consideration of potassium must occur in patients with hypomagnesemia. Depletion of intracellular magnesium allows potassium to be freely secreted through luminal potassium channels (the renal outer medullary potassium channel, or ROMK) [8]. Therefore, magnesium replacement is often necessary before hypokalemia can be corrected [9]. Both hypomagnesemia and hypokalemia are predisposing risk factors for the development of Torsades de Pointes (TdP) [10]. Hypocalcemia may also manifest from hypomagnesemia from inhibition of the release of parathyroid hormone (PTH) [11]. Consequently, hypocalcemia may predispose patients to cardiac manifestations of hypomagnesemia.

Hypomagnesemia can influence myocardial excitability [12]. The consequences of hypomagnesemia have been

Table 1 Causes of electrolyte abnormalities in critically ill patients [2, 3, 5, 6, 8, 19, 21, 50, 66, 68, 72]

	Drug-induced	Non-drug induced
Hypomagnesemia	Loop diuretics and thiazide diuretics Amphotericin B Aminoglycosides Capreomycin Pentamidine Platinum-based chemotherapy Calcineurin inhibitors Cetuximab Panitumumab Matuzumab Proton pump inhibitors Foscarnet, Cardiac glycosides	Malnutrition Malabsorption Chronic diarrhea Hyperparathyroidism Hyperthyroidism Hyperaldosteronism Acute or chronic alcoholism Diabetes Severe burns Refeeding syndrome
Hypokalemia	Loop and thiazide diuretics Corticosteroids Aminoglycosides Bicarbonate therapy Penicillins Cisplatin Beta-2 agonists (albuterol, epinephrine, salbutamol) Insulin Theophylline	Nephrogenic diabetes insipidus Renal tubular disorders Certain congenital conditions Cushing's syndrome Ileostomy Hemodialysis on a low potassium dialysate Hyperaldosteronism Hypothermia (including therapeutic hypothermia) Alkalosis Refeeding syndrome Hypomagnesemia
Hyperkalemia	Potassium-sparing diuretics Renin–angiotensin–aldosterone system (RAAS) inhibitors Calcineurin inhibitors Trimethoprim Pentamidine Nonsteroidal anti-inflammatory drugs Heparin Succinylcholine (dose-dependent) Mannitol Digoxin Beta blockers (nonselective > selective) Potassium administration Potassium-containing cardioplegia solutions	Acute renal failure Chronic renal failure Type 4 renal tubular acidosis Addison's Disease Acute adrenal insufficiency Tumor lysis syndrome Rhabdomyolysis Massive blood transfusion Hemolysis Acidosis Insulin deficiency Increased potassium intake Blood transfusion (usually massive transfusion and/or blood stored > 12 days)
Hypocalcemia	Aminoglycosides Bisphosphonates Phosphate preparations Calcitonin Loop diuretics Foscarnet	Sepsis Pancreatitis Cytokine-mediated inflammatory response Rhabdomyolysis Tumor lysis syndrome Hypoparathyroidism COVID-19 (association) Decreased vitamin D Hypomagnesemia Hyperphosphatemia Blood transfusion Acute renal failure Alkalosis Citrate anticoagulation with renal replacement therapy
Hypercalcemia	Thiazide diuretics Lithium Vitamin D supplementation	Malignancy Hyperparathyroidism Prolonged immobility

Table 1 (continued)

	Drug-induced	Non-drug induced
Hypophosphatemia	Corticosteroids Dopamine Estrogen Insulin Beta-agonists Sodium bicarbonate	Metabolic acidosis Respiratory alkalosis Malnutrition Diarrhea Vitamin D deficiency Decreased vitamin D activation Thyroid hormone Refeeding syndrome Parathyroidectomy Hungry bone syndrome Diabetic ketoacidosis Renal replacement therapy Open heart surgery Gram-negative bacteria infection
Hyponatremia		
Hypertonic	Mannitol	Diabetic Ketoacidosis
Hypotonic hypovolemic	Thiazide diuretics	Osmotic diuresis Cerebral salt wasting Salt wasting nephropathy Gastrointestinal losses Burns Third spacing Mineralocorticoid deficiency Blood loss/hemorrhage
Hypotonic euvolemic	Tricyclic antidepressants Selective serotonin reuptake inhibitors Carbamazepine Oxcarbazepine Valproic acid Cisplatin Carboplatin Methylenedioxymethamphetamine (Ecstasy)	Syndrome of inappropriate diuresis Malignancy Pneumonia Traumatic brain injury Hypothyroidism Cortisol insufficiency Psychogenic polydipsia Beer potomania
Hypotonic hypervolemic	None	Congestive heart failure Renal failure Nephrotic syndrome Hepatic failure
Hypernatremia		
Hypovolemic	Loop diuretics	Diarrhea Excessive sweating Respiratory losses Glycosuria
Euvolemic	None	Diabetes insipidus Insensible losses
Hypervolemic	Hypertonic saline Sodium bicarbonate Salt tablets Normal saline diluents in intravenous medications Corticosteroids	Hyperaldosteronism Cushing's Syndrome

correlated to an increased risk of abnormal rhythms, including atrial and ventricular arrhythmias [13]. Concurrent electrocardiography (EKG) findings with hypomagnesemia include flattened T-waves, U-waves, prolonged QT interval, and widened QRS complexes [14].

Table 2 provides concise recommendations for the management of common electrolyte disturbances in critically ill patients. Magnesium replacement can be completed both via enteral or intravenous (IV) supplementation. Enteral supplementation may be utilized when hypomagnesemia is mild with minimal or no symptoms, but use may be limited by gastrointestinal (GI) intolerance and should be avoided in patients with nausea, vomiting, diarrhea and high output ostomy. Several oral magnesium options exist with different salt formulations, with magnesium oxide and magnesium lactate being commonly selected choices.

Table 2 Recommendations for managing electrolyte abnormalities in critically ill patients [5, 6, 8, 15, 16, 19, 20, 23, 24, 32, 34, 56, 76–80, 87–91]

Electrolyte abnormality	Severity	Treatment	Monitoring	Comments
Hypomagnesemia	Mild to moderate (1.0–1.5 mg/dL)	1–1.5 mg/dL: 2–4 g of IV magnesium sulfate over 4–12 h 1.6–1.9 mg/dL: 1–2 g of IV magnesium sulfate over 1–2 h	Check magnesium at least 2 h after completion of infusion given the slow equilibrium of magnesium Patients with symptomatic hypomagnesemia or renal dysfunction should consider having magnesium rechecked	The treatment regimen may vary depending on the disease's state Caution in patients with reduced renal function, consider reduction of dose
	Severe (< 1 mg/dL)	4–8 g of IV magnesium sulfate each gram administered over a maximum rate of 1 g/hour		
Hypokalemia	Mild to moderate (2.5–3.4 mEq/L)	Oral or IV potassium, 10–20 mEq 3–4 times per day until normalized	EKG for arrhythmia, muscle weakness, ileus Monitor potassium daily for mild (3.0–3.5 mEq/L) or every 6–12 h for moderate (2.5–2.9 mEq/L)	Potassium chloride is preferred due to its high potassium content. If the patient has a functional GI tract, oral is preferred due to the risk of phlebitis with IV KCl Due to the potential for gastrointestinal adverse reactions and limited absorption, oral doses of potassium should not exceed 40 mEq at one time, and delayed release formulations are preferred With normal renal function, 10 mEq typically increases serum potassium by 0.1 mEq/L. If serum potassium is less than 3.0 mEq/L, 10 mEq typically results in a slower increase of 0.05 mEq/L Magnesium levels should be checked, and magnesium should be replaced if low
	Severe (< 2.5 mEq/L)	IV KCl 10 mEq/h via peripheral line or 20 mEq/h via central line until normalized	EKG for arrhythmia, muscle weakness, ileus Repeat potassium level for every 40–60 mEq KCl administered	Patients should have continuous cardiac monitoring when receiving more than 10 mEq/h IV potassium. Up to 40 mEq/h may be used in life-threatening situations When levels are < 3.0 mEq/L, 10 mEq potassium increases serum potassium by approximately 0.05 mEq/L Magnesium levels should be checked and magnesium should be replaced if low

Table 2 (continued)

Electrolyte abnormality	Severity	Treatment	Monitoring	Comments
Hyperkalemia	Asymptomatic (> 5 mEq/L)	Regular insulin 10 units IV (if CKD or ARF reduce dose to 5 units) with concomitant dextrose 50% 25–50 g IV Furosemide 20–100 mg IV (consider prior loop diuretic exposure, renal function, to determine optimal dose) Sodium polystyrene sulfonate 30 g PO for 1 dose, or Sodium zirconium cyclosilicate 10 g TID for a maximum of 48 h	Check blood glucose 30 min after insulin administration, then every 1 h for 3 h. Extended monitoring in renal dysfunction, at least 2 h Re-assess serum potassium 30–60 min after insulin or albuterol; 2 h after elimination therapies	Monitor closely for hypoglycemia Sodium bicarbonate is not recommended for routine management of hyperkalemia; may consider if concomitant metabolic acidosis No data to support routine use of albuterol in critically ill patients; may consider 10–20 mg nebulized over 15 min. May exacerbate tachycardia
	Symptomatic (> 5 mEq/L accompanied by EKG changes)	Calcium gluconate 1–2 g in 50–100 mL 0.9% NaCl or D5W IV over 2–3 min if unstable; over 10–20 min if stable Consider dialysis based on potassium elevation and persistence of EKG changes Rest of management same as mild hyperkalemia	Repeat EKG 10 min after calcium administration	If EKG changes persist, may repeat calcium administration Calcium gluconate is preferred due to lower risk of necrosis in case of extravasation
Hypocalcemia	Mild to moderate (< 8.6 mmol/L or ionized calcium concentration of 1–1.2 mmol/L)	*Calcium gluconate 1–2 g in 50–100 mL 0.9% NaCl or D5W IV over 30–60 min, repeated every 6 h as needed Maximum rate of IV infusion = 1.5 mEq calcium/minute	Monitor heart rate and blood pressure Recheck serum calcium concentrations within 4–6 h after the dose Monitor ionized calcium in hypoalbuminemia	May give IV push over in an emergency; may increase risk of cardiac toxicities Patients on CRRT with citrate require calcium replacement per institutional protocol
	Severe (< 7.5 mmol/L or ionized calcium concentration < 1 mmol/L)	Calcium gluconate 3–4 g calcium gluconate in 50 mL or 150 mL of 0.9% NaCl or D5W over 4 h; repeat as needed or calcium chloride 1 g IV push; repeat as needed	Patients should be reassessed within 24 h after the first dose, and another calcium infusion may need to be given to some patients	Calcium chloride should be administered via a central line to avoid extravasation; however, a peripheral line may be used when the benefit outweighs the risk Calcium chloride provides three times more elemental calcium than calcium gluconate
Hypercalcemia	Mild asymptomatic (total serum calcium concentration of 10.3–11.9 mg/dL)	May not need treatment until workup completed	Volume overload	Caution in heart failure and end-stage renal disease

Table 2 (continued)

Electrolyte abnormality	Severity	Treatment	Monitoring	Comments
	Moderate to severe associated with renal or neurologic symptoms, (total calcium of ≥ 12 mg/dL)	Requires prompt management with 1–2 L 0.9% NaCl as an initial bolus followed by maintenance fluids of 150–300 mL/h for the next 2–3 days or until hypervolemic Bisphosphonates onset of action 48 h, may repeat every 3–4 weeks Pamidronate 60–90 mg IV over 2–6 h Zoledronic acid 3–4 mg IV over 15–30 min Calcitonin 4–8 units/kg SQ q 6–12 h, the onset of action 4–6 h. Calcitonin: tachyphylaxis develops after 48 h Denosumab 120 mg SQ weekly for 4 weeks and monthly thereafter, onset of action 7–10 days Hydrocortisone 200–400 mg per day for 3–4 days and then prednisone 10–20 mg daily for 7 days, or prednisone 40–60 mg daily for 10 days	Monitor corrected calcium after 7–10 days	Bisphosphonates should be given within 48 h of diagnosis. The response typically takes 2–4 days Pamidronate: Avoid use if the glomerular filtration rate is less than 30 ml/min Zoledronic acid: Nephrotoxicity, infusion site reaction, bone pain, and flu-like illness may occur for the first 1 to 2 days after the infusion. May repeat dose after at least 7 days. Reduce dose in renal impairment Calcitonin: tachyphylaxis develops after 48 h Though not recommended for critically ill patients due to the tendency to cause prolonged hypocalcemia. Denosumab may be used for bisphosphonate refractory serum calcium level > 12.5 mg/dl and who had received bisphosphonates within 7 days to 30 days. monitor for arthralgias, nausea, diarrhea, dyspnea, and osteonecrosis of the jaw If prednisone is not helpful after 10 days, it should be discontinued
Hypophosphatemia	Mild (asymptomatic) (> 2.5 mg/dL) Moderate to severe (< 2.5 mg/dL)	1–2 packets oral phosphorous per dose 15–45 mmol sodium or potassium phosphate IV diluted in 100–250 mL NS or D5W over 4 to 6 h Weight-based protocol preferred	Serum phosphorus levels daily in patients with sepsis, malnutrition, or respiratory failure Individualized frequency of monitoring for other patients based on severity of hypophosphatemia and other risk factors Levels should be collected in the morning	Avoid overcorrection

Table 2 (continued)

Electrolyte abnormality	Severity	Treatment	Monitoring	Comments
Hyponatremia	Mild to moderate	Depends on etiology Hypotonic hypovolemic hyponatremia- volume expansion with isotonic fluids Hypotonic euvolemic hyponatremia- discontinue offending agents, water restriction Hypotonic hypervolemic hyponatremia- water and sodium restriction	Serum Na at least every 24 h	Evaluate volume status to determine the etiology of hyponatremia Treatment of underlying conditions and discontinuation of contributing medications Water restriction, generally to 1000–1500 mL/day. IV medications, PN solutions, and EN formulas should be concentrated as able
	Severe and or symptomatic	Hypertonic saline, administered as either continuous IV infusion or intermittent IV boluses	Serum Na 20 min after 3% bolus doses, at least every 2–4 h while receiving 3% continuous IV infusions, and at least 6–12 h once Na concentrations stable	Avoid overcorrection- limit rise to 10–12 mEq/L in 24 h for acute hyponatremia and 6–8 mEq/L in 24 h for chronic hyponatremia *For Moderately severe symptoms, the European guidelines suggest* treating less aggressively, using 150 mL 3% saline over 20 min with a target increase of 5 mEq/L in 24 h and maximum increase of 10 mEq/L in the first 24 h and then subsequently 8 mEq/L per day, until serum sodium is ≥ 130 mEq/L. [93] For severe symptoms, the European guidelines suggest 150 mL 3% saline (or 2 ml/kg if a lower volume) over 20 min with a repeat bolus dose afterward. This can be repeated twice until serum sodium increases by 5 mEq/L. If symptoms improve, hypertonic saline can be discontinued, and the individual type of hyponatremia can be treated. If symptoms do not improve, the 3% sodium infusion should be continued, with a goal rise of 1 mEq/L/hr, until symptoms improve or the serum sodium is ≥ 130 mEq/L
Hypernatremia	Mild to severe	Hypovolemic hypernatremia- free water replacement Euvolemic hypernatremia- treat etiology, free water replacement Hypervolemic hypernatremia- sodium restriction, discontinue the offending medications	Serum Na at least every 12 h	Avoid overcorrection- generally limit decrease to 8–10 mEq/L in 24 h

Table 2 (continued)

ARF Acute renal failure, *CKD* chronic kidney disease, *D5W* dextrose 5% in water, *dL* deciliter, *EKG* electrocardiogram, *IV* intravenous, *KCl* potassium chloride, *kg* kilogram, *L* liter, *mEq* milliequivalent, *mg* milligram, *mL* milliliter, *mmol* millimol, *Na* sodium, *NaCl* sodium chloride, *NS* normal salinine, *PO* by mouth, *SQ* subcutaneous, *TID* three times a day

*1 g calcium gluconate (10%) = 4.56 mEq calcium, preferred agent. 1000 mg calcium chloride = 13.6 meq calcium

Parenteral magnesium is administered to patients with moderate to severe hypomagnesemia, patients with pre-existing GI abnormalities (nausea, vomiting, diarrhea, high output ostomy), and/or patients with a lack of enteral access [15, 16]. Most patients with clinically significant hypomagnesemia should receive 1 to 2 g given over one hour followed by 4–8 g given slowly over 12–24 h [8, 15, 17]. However, in some critical situations where the potential benefit of faster administration exceeds the risk of hypotension, IV magnesium may be administered faster than the usual slow infusion. For example, in TdP, 1–2 g of IV magnesium may be administered over 15 min [10]. In preeclampsia, a 4–6 g loading dose can be administered over 15–30 min, followed by 1–2 g/h continuous infusion [18]. Close monitoring of magnesium levels is warranted when a continuous infusion is ongoing.

As with any electrolyte abnormality, follow-up monitoring after replacement therapy is a key part of the management. Up to 50% of an IV dose of magnesium may be excreted in the urine. Due to variability in renal function in critically ill patients, it may be prudent to perform a follow-up magnesium level after 2 h to check for repletion [9]. Most patients will tolerate even large doses without toxicity, but some patients, such as those with acute kidney injury, may still be at risk for overcorrection.

3 Potassium

Potassium is the most abundant cation in the human body, with total body potassium stores of 50–75 mEq/kg body weight [19, 20]. A primarily intracellular electrolyte, 98% of total potassium stores are located in the cells which generate a concentration gradient critical to cellular excitability and function [19]. To maintain this gradient, serum potassium levels are carefully regulated between 3.5 and 5 mEq/L [19, 21]. Although serum levels may not necessarily correlate with total body stores, small changes in levels can drastically alter the cellular gradient and lead to dangerous deficiencies in cellular function [22, 23]. Approximately 90% of potassium excretion occurs via the kidney and the remaining 10% via theGI tract [19]. Other than renal function, factors that play a critical role in regulating potassium distribution include catecholamines, insulin, aldosterone, and acid–base balance [21].

3.1 Hypokalemia

Hypokalemia is defined as a serum potassium level less than 3.5 mEq/L, with severe hypokalemia typically defined as a level less than 2.5 mEq/L [19]. Mild hypokalemia is often asymptomatic. Moderate or severe hypokalemia can cause muscle weakness and fatigue that can lead to muscle

paralysis, slowed GI transit and ileus, metabolic acidosis, and polyuria [19]. Life-threatening complications of severe hypokalemia include cardiac arrhythmias such as TdP and ventricular fibrillation [19, 24]. Patients with ischemic heart disease or heart failure, or on digoxin therapy, are at an increased risk of arrhythmias from hypokalemia [19, 22].

In critically ill patients, hypokalemia may be caused by excess renal or extrarenal losses or transcellular shifting of potassium. Measurement of urine potassium levels and the urine potassium-to-creatinine ratio may help to differentiate between renal and non-renal causes of hypokalemia [20, 25]. The optimal dosing and rate of potassium replacement depend on several factors, including kidney function, body weight, IV access, and the presence of symptoms, especially EKG changes. As previously discussed, low intracellular magnesium levels can result in hypokalemia that is refractory to treatment; therefore, hypomagnesemia must be corrected to prevent further potassium wasting [26]. Intravenous potassium is generally provided as potassium chloride and must be diluted prior to infusion. Solutions containing 10 mEq/100 mL may be administered via a peripheral line, while solutions with 20 mEq/100 mL should be given via a central line [19]. Oral potassium is available in tablet, capsule, and liquid formulations and is generally preferred over intravenous administration due to its high bioavailability and the potent vesicant potential of intravenous potassium. Although oral potassium is associated with GI effects, including nausea, vomiting, diarrhea, abdominal discomfort, and small bowel ulcerations, most patients can tolerate enteral replacement at doses of 40 mEq or less [19]. In patients with feeding tubes, liquid formulations or powder packets can be utilized but should be diluted to prevent osmotic diarrhea [23]. Occasionally, potassium sparing diuretics can be used to prevent or treat hypokalemia in patients with volume overload and normal renal function that have an indication for these agents [19].

In severe cases (< 2.5 mEq/L), patients with arrhythmias, severe vomiting, impaired oral absorption, or those without enteral access, IV supplementation is required (Table 2) [19]. A combination of oral and IV doses may be administered simultaneously to provide more rapid correction. Potassium chloride must be diluted prior to IV administration to minimize phlebitis [19]. Many hospitals utilize nurse-driven potassium replacement protocols to improve standardization and reduce unnecessary or inappropriate repletion. To ensure appropriate repletion of potassium and avoidance of hyperkalemia, serum potassium should be measured after every 40–60 mEq administered, with more frequent monitoring recommended for patients with severe kidney injury [23]. Potassium should be administered slowly, no faster than 10 mEq/h through a peripheral line and 20 mEq/h through a central line to prevent cardiac effects. In life-threatening situations, rates of administration as fast as 40 mEq/h have been suggested [19]. However, the optimal dosing and infusion rate of potassium in the setting of imminent or actual cardiac arrest is unknown [22]. In the absence of robust data, rapid administration of potassium administration should be limited to rare cases with a clear benefit-to-risk ratio.

3.2 Hyperkalemia

Hyperkalemia is defined as a serum potassium level greater than 5 mEq/L, although patient-specific factors such as cardiac morphology, physiologic adaptation, acute illness, and medications affect the threshold at which toxicity will manifest. Rapid increases in serum potassium lower cardiac resting membrane potential that may be accompanied by sequential EKG changes: peaked T-waves, prolonged PR interval, flattened or absent P-waves, QRS prolongation, sinus wave pattern, ventricular fibrillation, asystole, and pulseless electrical activity. In a prospective study, only 46% of patients with serum potassium levels greater than 6 mEq/L had corresponding EKG changes. Physical symptoms (e.g., paresthesia, weakness, depressed tendon reflexes, and flaccid paralysis) are often overshadowed by the clinical illness causing hyperkalemia and may not be apparent in sedated or obtunded patients [22].

Emergency management of hyperkalemia consists of cardiac membrane stabilization, intracellular shifting of potassium, and enhancement of potassium elimination. Definitive management requires addressing the underlying cause. In patients with EKG changes, stabilization of the cardiac membrane is achieved by raising the cardiac action potential threshold through calcium administration. Evidence of calcium use is limited to animal studies and case reports; consequently, the optimal calcium salt, dose or dosing frequency is unknown [27, 28]. Calcium gluconate is preferred but some clinicians may elect to use calcium chloride 10%. This is theoretically accompanied by a greater risk of tissue necrosis in the event of extravasation due to the greater availability of ionized calcium, consequently central line administration is preferred [29]. The effect of calcium administration is expected to be rapid but brief; repeat dosing up to every five minutes may be required if dysrhythmias recur [30].

Shifting of potassium intracellularly is achieved through the administration of insulin, beta-adrenergic agonists, or sodium bicarbonate. Insulin stimulates the Na+–H+ antiporter to shift sodium intracellularly, which activates the Na+ K+ ATPase to exchange intracellular sodium for potassium [22]. Lowering of serum potassium occurs within 10–20 min and lasts several hours [28]. Generally, regular insulin is administered as an IV bolus rather than an infusion due to ease of administration and faster onset of action [31]. Insulin is excreted by the kidneys and patients with kidney

dysfunction can require lower insulin doses. Recently, some studies demonstrate similar potassium lowering efficacy with fewer hypoglycemic events when lower flat doses or weight based doses are used as opposed to the conventional dose of 10 units [32–37]. Other strategies to reduce hypoglycemic complications include standardized blood glucose monitoring, increased dextrose dose, or the use of dextrose infusions [37–40]. There are theoretical benefits to the use of a dextrose infusion as insulin's duration of effect exceeds that of a dextrose bolus. A shortage of dextrose 50% vials led one institution to substitute dextrose 10% infusions; a retrospective evaluation of the practice change revealed similar rates of hypoglycemia [41]. Some clinicians may hold dextrose if patients are hyperglycemic (blood glucose > 200 mg/dL); however, this practice should take patient-specific risks into consideration, and monitoring for hypoglycemia is still required [30].

Nebulized albuterol at doses of 10–20 mg over 10 min is approximately as effective as insulin and can decrease serum potassium by up to 1 mEq/L for 2 h [28]. Beta-agonists bind beta-2 receptors, activating adenylate cyclase's consumption of ATP, resulting in Na+ K+ ATPase moving potassium intracellularly [22]. Albuterol may be less effective in patients receiving beta-blockers and those with end-stage renal disease [28, 30]. Most studies with beta-agonists have occurred in non-critically ill inpatients. The efficacy and safety of beta-agonists for hyperkalemia in critically ill patients remains sub-optimally studied. Although still considered a viable treatment option, the most common adverse effect, tachycardia, often limits the use of albuterol.

Sodium bicarbonate increases the extracellular concentration of H+ which in turn increases intracellular Na+ via Na+ –H+ antiporter resulting in an intracellular shift of sodium that activates the Na+ K+ ATPase to exchange intracellular sodium for potassium [22]. There is little evidence for the use of sodium bicarbonate monotherapy in hyperkalemia; several studies suggest a lack of or delayed efficacy [30]. There may be a role for administration in patients with metabolic acidosis. The BICAR-ICU trial, which evaluated the impact of sodium bicarbonate 4.2% administration on mortality and organ dysfunction in critically ill patients with acidemia, is one of the only studies demonstrating a statistically significant reduction in serum potassium levels ($p = 0.0341$); however, this was a safety endpoint that requires further evaluation [42]. In the absence of metabolic acidosis, sodium bicarbonate should not be used for routine management of hyperkalemia, given the availability of more effective treatment options without the risk of fluid overload.

Potassium is ultimately removed using diuretics, dialysis, or exchange resins. Loop diuretics are administered to patients who are non-oliguric, although there is no data specifically supporting their use and clinicians should be careful to monitor volume status [26, 30]. Dialysis is the most effective means of potassium removal from the body. The degree of potassium removal achieved through dialysis depends on the modality, potassium concentration, and bicarbonate concentration of the dialysate and the blood flow rate [22]. Hyperkalemia accompanied by kidney insufficiency, persistent EKG changes, or insufficient response to temporizing therapies is considered an urgent indication for dialysis, although definitive recommendations on the timing of initiation are lacking [30]. There are theoretical concerns that pre-dialysis pharmacologic-induced potassium shifting may impair the efficacy of dialysis. A retrospective evaluation of emergency department patients receiving hemodialysis after potassium shifting therapies found no increase in the incidence of recurrent hyperkalemia or need for repeat dialysis within 24 h [43]. Exchange resins remove potassium via the GI tract. Sodium polystyrene sulfonate (SPS) is the longest in-use exchange resin. One randomized study suggests a greater initial reduction in serum potassium compared to placebo but the loss of effect by day seven [44]. SPS use is limited by erratic onset and duration of action, poor GI tolerance, and risk of colonic necrosis. Although the risk is extremely low, colonic necrosis is a potentially fatal complication reported in postoperative patients, critically ill patients, those with ileus, and rectal administration of SPS with 70% sorbitol [45]. Patiromer, a novel exchange resin, does not expand in the GI tract, possibly further lowering the risk of colonic necrosis compared to SPS, but its delayed onset of action limits utility in acute hyperkalemia [46]. Sodium zirconium cyclosilicate (SZC) similarly has a lower rate of GI side effects compared to SPS. SZC's rapid onset of one hour makes it the most attractive candidate for emergency treatment of hyperkalemia. Unfortunately, the ENERGIZE study failed to demonstrate a significant reduction in serum potassium at one hour with SZC plus insulin compared to insulin alone in emergency department patients [47, 48]. The lack of significant difference may be due to the small sample size and early dominant effect of insulin; it should be noted that serum potassium assessments at two hours suggest a possible benefit with SZC. No exchange resins have been evaluated in the critically ill population. The ongoing KBindER study will help further delineate the role of SPS and SZC in the management of acute hyperkalemia [49].

Frequency and duration of serum potassium, EKG, and blood pressure monitoring in acutely hyperkalemic patients should be tailored to the severity of hyperkalemia, administered treatment and response, and clinical manifestations of hyperkalemia. Potassium levels are expected to rebound a few hours after administration of shifting therapies, necessitating continued reevaluation if potassium has not been eliminated from the body by means of medications or dialysis. For insulin therapy, standardized approaches to monitoring

can help improve the detection and treatment of hypoglycemic events [40].

4 Calcium

Normal total serum ranges 8.6–10.2 mg/dL or ionized serum calcium ranges 1.12–1.30 mmol/L [50, 51]. Nearly 99% of total body calcium resides in the bones, and the remaining 1% in the extracellular fluid (ECF) [50–52]. About half of circulating calcium is bound to albumin, and the remaining is ionized calcium, which is biologically active and maintains physiologic functions [50–52]. Calcium homeostasis depends on the regulation of calcium fluxes in relation to the intestinal tract, bone, and kidneys [50]. Calcium is regulated predominantly by PTH and calcitriol (1,25-dihydroxy vitamin D3 (1,25(OH)2D3) [50]. Hypoalbuminemia decreases total calcium with minimal effect on the ionized calcium. Conversely, acidemia reduces protein binding but increases ionized calcium [50, 52]. Correction formulas are proposed for adjusting for low albumin and pH, but studies have demonstrated a poor correlation between corrected calcium and ionized calcium [52–54]. To guide calcium correction, ionized calcium should be used whenever possible.

4.1 Hypocalcemia

Hypocalcemia is defined as total serum calcium concentration of < 8.6 mg/dL or ionized calcium concentration of < 1.1 mmol/L. Hypocalcemia is multifactorial, reported in up to 90% of inpatients, with hypocalcemia measured by ionized calcium reported in 20% of ICU patients [50, 55, 56]. Recent studies have observed hypocalcemia with a negative impact on disease severity in SARS-CoV-2 infected patients owing to the hyperinflammatory response, suggesting an emerging "osteo-metabolic phenotype" in COVID-19 [57, 58].

Symptoms of hypocalcemia usually correlate with the severity and rapidity of serum calcium decrease. The hallmark manifestation of severe acute hypocalcemia is tetany. Other manifestations include seizures and cardiac rhythm disturbances due to prolonged QT interval [50–52]. Symptoms attributable to low calcium are not well described in the critically ill. Despite a paucity of data on the benefits of calcium measurement and correction, calcium correction is a common practice aimed at normalizing serum levels instead of being guided by response to therapy or relief of symptoms [50–62]. Notably, a few studies suggest correction may be harmful [63–65]. Collage et al. reported a retrospective study of 526 ICU patients with low ionized calcium where 18% received IV calcium. After adjusting for the severity of illness and demographic covariates, mortality was higher in patients that received calcium [63]. Despite uncertainty on the benefits of correcting ionized calcium, calcium should be corrected in cases with concurrent hypomagnesemia, nutritional deficits, medication-induced hypocalcemia, blood transfusions, and extracorporeal devices.

Treatment for hypocalcemia depends on severity and etiology. Symptomatic and severe hypocalcemia warrants IV calcium. Intravenous calcium gluconate is preferred for correcting symptomatic moderate (total serum calcium concentration 7.5–8.0 mg/dL) or severe hypocalcemia (total serum calcium concentration < 7.5 mg/dL or ionized calcium concentration < 0.9 mmol/L) [66–68]. Calcium chloride can be administered via peripheral line in emergent situations (e.g., cardiac arrest) but a central line is preferred when available [66–68]. In select cases such as massive blood transfusion, plasmapheresis, or citrate anticoagulation, a continuous infusion of calcium may be required, and serum calcium level should be monitored every 6 h.

4.2 Hypercalcemia

Hypercalcemia (> 10.2 mg/dL) occurs in approximately 15% of patients [69]. It is categorized as mild to moderate (total serum calcium concentration of 10.5–11.9 mg/dL) or severe (total calcium of ≥ 12 mg/dL) [70]. Hypercalcemia of malignancy secondary to PTH-related increased bone resorption is the most common etiology of hypercalcemia [69]. Patients with severe hypercalcemia are often volume depleted and symptomatic. Neurologic manifestations of hypercalcemia include anorexia, confusion, and obtundation. Cardiac manifestations include arrhythmias and EKG changes (shortened QT) [69].

As with hypocalcemia, symptoms, and treatment associated with hypercalcemia correlate with the severity and rapidity of the rise in serum calcium. The goal of treating hypercalcemia includes increased elimination, reduced gastrointestinal absorption, and decreased bone resorption. Initial treatment includes aggressive volume resuscitation, which promotes the excretion of calcium. Normal saline infusion is initiated, and furosemide can be added to promote calciuresis. Recent studies have questioned this practice, and it should be reserved for hypervolemic patients or those with heart failure [71]. Severe hypercalcemia requires aggressive interventions. Bisphosphonate therapy is the cornerstone of treatment for symptomatic hypercalcemia as they inhibit osteoclast-mediated bone resorption [72–74]. Pamidronate and zoledronic acid are the two most used bisphosphonates [72, 73]. Zoledronic acid has been shown to be more potent than pamidronate, but both are considered acceptable therapies [74].

Denosumab, a monoclonal antibody that targets osteoclast-induced bone resorption is effective for hypercalcemia refractory to IV bisphosphonates [75]. Denosumab may be useful in patients with kidney impairment as

bisphosphonates should not be used. Denosumab is not renally cleared, but the effect may be more prominent in kidney impairment and a dose reduction is recommended in these patients to avoid hypocalcemia [75].

Calcitonin is also used to acutely reduce calcium levels. When used with bisphosphonates, it can reduce calcium more rapidly than either agent alone. Calcitonin is usually reserved for rapid reduction of hypercalcemia in emergencies such as arrhythmias [72]. Calcitonin reduces bone resorption with mild calciuric effects and has a rapid onset of action [72]. Clinicians should be aware that prolonged administration of calcitonin can result in tachyphylaxis. Glucocorticoids may be useful in cases of hypercalcemia caused by overproduction of calcitriol (125-dihydroxyvitamin D).

5 Phosphorous

Phosphorous, an intracellular anion, is essential in cellular function and other processes. Normal serum phosphate ranges from 2.5 to 4.5 mg/dL (0.8–1.45 mmol/L) [76–79]. Levels depend on an intricate combination of dietary intake, intra to extracellular transfer, kidney function, and tubular phosphate reabsorption [76]. Occurring in only 5% of all inpatients, up to 50% of ICU patients experience hypophosphatemia, particularly in the first week of admission, and risk factors for hypophosphatemia exist in almost all ICU patients [76–84]. Serum phosphate concentrations have a circadian pattern and should preferentially be collected in the morning [77–79]. Phosphate homeostasis depends on numerous transporters, hormones, and other mechanisms affected by a variety of factors. Additionally, critically ill patients experience shifts in phosphate faster than seen with chronic hypophosphatemia [80].

5.1 Hypophosphatemia

Mild to moderate hypophosphatemia may not be problematic in most patients; it may be asymptomatic, transient, or reversible by correcting the underlying cause [76–79]. In contrast, severe hypophosphatemia (< 2 mg/dL) can cause many complications, including arrhythmias, muscle weakness, and respiratory failure [77, 78, 80, 83]. In the ICU, hypophosphatemia has been associated with increases in illness severity, longer mechanical ventilation, longer ICU and hospital stays, and higher mortality up to six months after hospitalization [80, 83–85]. Like other electrolyte abnormalities, hypophosphatemia can be caused by medications and physiologic conditions; it may also occur subsequent to the use of other management strategies in critical illness, most notably CRRT which is known to remove phosphorus [66]. There are no guidelines to explicitly direct phosphate dosing to correct serum levels. Dosing appropriately is essential not only to restoring levels, but to mitigate the risk of producing hyperphosphatemia. It is important to replenish phosphorous without overcompensating. Compared to patients with normophosphatemia or hypophosphatemia alone, patients who experience both hypophosphatemia and hyperphosphatemia in the ICU have a significantly higher mortality rate, longer duration of mechanical ventilation, longer CRRT duration, and longer ICU length of stay [81, 86]. Asymptomatic patients or those with mild deficiencies can be managed with oral replacement. However, though rapidly absorbed in the small intestine, oral phosphate is excreted into the urine within hours requiring frequent administration and is unlikely to achieve stable serum phosphate levels in those with more pronounced deficiencies [77].

Unfortunately, there are few published studies on phosphorous replacement in the acute setting. From the data available, treating severe or symptomatic (regardless of deficiency level) hypophosphatemia in ICU patients is important for optimal outcomes. Phosphate replacement reduces oxygen requirements and is associated with fewer infections, new onset arrhythmias, myocardial infarctions, and ICU deaths [82, 83]. Over 72% of ICUs, independent of type, use IV phosphate infusions for symptomatic and severely depleted patients, of which sodium phosphate or potassium phosphate are the most common [77, 82, 83, 87, 88]. There is no standard preparation for IV phosphate, but intermittent infusions should be diluted in at least 100–250 mL normal saline or dextrose 5% [88]. Potassium phosphate is advantageous in patients with co-existing hypokalemia with minimal risk of hyperkalemia. Explicit dosing of phosphate varies throughout the literature. One study recommended a maximum dose of 0.25 mmol/kg dose in patients whose serum levels were > 0.5 mg/dL and a 0.5 mmol/kg dose for those with serum levels < 0.5 mg/dL [87]. The authors suggested that doses be based on ideal body weight in obesity but did not support the recommendation with data from their study [87]. Protocols for phosphorus replacement have been used since the 1970s [88]. Protocols standardize replacement and significantly increase the number of patients who are treated, reduce time to replacement, and result in more optimal dosing [80, 89]. Protocols can help decrease infusion times safely through standardization. Charron et al. evaluated a protocol in which patients with moderate hypophosphatemia (< 2.015 mg/dL) were administered 30 mmol potassium phosphate over 2 or 4 h and those with severe hypophosphatemia (< 1.24 mg/dL) were given 45 mmol potassium phosphate IV over 3 or 6 h [88]. Groups with the shorter infusion rates had a faster repletion ($p < 0.05$) and there were no differences in adverse reactions or abnormalities in potassium or calcium. However, more studies in this area are required before faster infusions become standard of practice. Phosphorous loss in many patients may be higher than anticipated, particularly those requiring renal

replacement therapy [66]. It is essential to remain vigilant about any patient requiring phosphorus replacement and provide additional supplementation, when necessary.

The frequency of phosphorus monitoring varies widely, and the ideal monitoring frequency has not been fully evaluated [82, 83]. Daily levels do not appear to identify a higher incidence of hypophosphatemia than when levels are obtained less frequently [82]. Therefore, it is reasonable to obtain daily levels in high-risk patients such as those with sepsis, kidney dysfunction, or malnutrition while the frequency of levels for other ICU patients can be individualized according to the presence and severity of other hypophosphatemia etiologies and risk factors [66, 82]. Depending on the approach, patients on CRRT may warrant more vigilant monitoring as phosphorous levels are known to fluctuate frequently, though the literature is lacking in regards to specifically how often levels should be obtained [66, 82].

6 Sodium

Standard serum sodium concentrations are 135–145 mEq/L. Sodium is the predominant extracellular cation and helps regulate ECF volume and water distribution [66, 90, 91]. Sodium abnormalities are independent risk factors for in-hospital mortality in ICU patients [92]. Both hyponatremia and hypernatremia occur due to either an increase or decrease of water in relation to serum sodium; thus, to adequately diagnose and treat sodium abnormalities, volume status must be evaluated [66, 90, 91].

6.1 Hyponatremia

Hyponatremia (< 135 mEq/L) occurs in up to 30% of ICU patients and is associated with increased mortality and length of stay [90–92]. Mild to moderate signs and symptoms of hyponatremia include nausea, confusion, headache, weakness, and gait instability [90, 91]. Severe hyponatremia can manifest as seizures, respiratory failure, and coma [90, 91, 93]. Signs and symptoms of hyponatremia may be more pronounced with serum < 125 mEq/L or with acute hyponatremia [90, 91, 93]. Serum osmolality should be measured as osmotic pressure, and serum osmolality regulate water distribution between fluid compartments [90, 91, 93]. Water moves from areas of lower osmolality to areas of higher osmolality until equilibrium occurs [92, 93]. Normal serum osmolality is generally 280–295 mOsm/kg [93]. Urine sodium may indicate whether renal sodium losses are occurring [90, 91].

Hyponatremia can be further categorized by volume status. Hypertonic hyponatremia occurs when an osmotically active substance besides sodium in the ECF pulls fluid from the intracellular fluid (ICF) into the ECF, resulting in dilutional hyponatremia [66, 91, 93]. Diabetic ketoacidosis is a common cause and for every 100 mg/dL blood glucose > 100 mg/dL, the serum sodium is 1.6–2.4 mEq/L higher than reported [94, 95]. The underlying cause should be corrected, and no treatment is required [94, 95]. Isotonic hyponatremia is a laboratory artifact from a now infrequently used assay, resulting from elevated concentrations of lipids or proteins in the nonaqueous portion of plasma, causing serum sodium to appear low [93].

Hypotonic hypovolemic hyponatremia is characterized by the loss of both total body sodium and total body water (TBW), but the decrease in total body sodium is greater. Signs and symptoms of hypovolemia occur, including hypotension and hemodynamic instability, tachycardia, dry mucous membranes, and decreased skin turgor [90, 91].

Hypotonic euvolemic hyponatremia involves normal salt handling in the setting of increased TBW, with a small portion of excess water in the ECF [90, 91]. Physical symptoms of hypovolemia or volume overload are not present [90]. The syndrome of inappropriate antidiuretic hormone secretion (SIADH) is a common cause of euvolemic hyponatremia, where antidiuretic hormone (vasopressin) is secreted inappropriately, resulting in water retention and dilutional hyponatremia. [90, 91]. In some cases, SIADH can be treated with vasopressin-2 receptor antagonists, such as conivaptan or tolvaptan, which cause water loss with no effect on sodium excretion [90, 91, 93, 96].

Hypotonic hypervolemic hyponatremia occurs when total body sodium is increased, but TBW is increased to a larger degree, causing serum sodium to appear low. Physical signs of volume overload (e.g., edema, pulmonary congestion) are present. Management involves sodium and water restriction. IV fluids should be discontinued, enteral nutrition (EN) solutions should be concentrated, and parenteral nutrition (PN) solutions should restrict both sodium and fluid [90, 91]. Medications with higher sodium content (e.g., piperacillin-tazobactam, ampicillin-sulbactam, nafcillin) should be evaluated, though alteration of regimens may not always be possible [97]. Loop diuretics and vasopressin antagonists may be required to treat refractory cases [90, 91, 93, 96].

Hypertonic saline should be reserved for patients with severe and/or symptomatic hyponatremia. There are many dosing strategies and concentrations of hypertonic saline, though few studies have specifically evaluated its use in ICU patients and some dosing strategies are extrapolated from data in exercise-associated hyponatremia [93, 96].

In general, sodium levels should not be corrected by more than 10–12 mEq/L/day in acute hyponatremia or 6–8 mEq/L in chronic hyponatremia [90, 91, 93]. Overcorrection can lead to rapid fluid shifts and osmotic demyelination syndrome (ODS), which results in neurologic symptoms, including seizures, quadriparesis, movement disorders, and "locked in" syndrome [98, 99]. If overcorrection occurs,

sodium replacement therapy should be discontinued. Although there is no robust evidence, hypotonic fluids and desmopressin may be utilized in some instances to counteract overcorrection [91]. Historically it has been recommended to infuse hypertonic saline only through central IV access devices due to concerns for extravasation and phlebitis. More contemporary data indicate hypertonic saline may be safely infused via peripheral access devices, which allows additional flexibility, particularly in emergent situations where rapid administration of hypertonic saline is indicated [100–102].

6.2 Hypernatremia

Hypernatremia (> 145 mEq/L) is a hypertonic state that results from a decrease in TBW relative to total body sodium [103]. The presence of hypernatremia is an independent risk factor for mortality in ICU patients [92, 104]. Mild to moderate symptoms are nonspecific and include increased thirst, hypotension, and nausea/vomiting. Severe symptoms, including seizures and coma, may not be present until serum sodium concentrations are significantly elevated (> 160–180 mEq/L) and are associated with higher mortality [90, 103, 106].

Hypernatremia can also be categorized by volume status. Hypovolemic hypernatremia involves both water and sodium losses, but the loss of TBW is greater [103]. Signs and symptoms may include hypotension, tachycardia, and decreased skin turgor [103]. If hemodynamic instability is present, isotonic fluids should be used to increase blood pressure [103, 106]. Once the hemodynamic status has normalized, IV or enteral hypotonic fluids should be utilized to replace the water deficit [90, 103]. The water deficit can be calculated as Water deficit (L) = TBW × [(serum Na/140) – 1] [103]. The water deficit does not reflect ongoing losses and requires reevaluation. No more than 50% of the water deficit should be corrected in the first 24 h and the remaining 50% can be corrected over the next 24–48 h [66, 103, 105]. Water and sodium content can be increased in PN formulations (up to stability limits) and less concentrated EN formulas should be utilized with increased water flushes if possible [103]. Euvolemic hypernatremia involves a loss of TBW with normal total sodium. Patients will be clinically euvolemic though water loss is occurring from the ICF and the ECF [103]. Treatment is directed at the etiology of the hypernatremia and can include discontinuation of medications that may cause diabetes insipidus (DI), desmopressin for treatment of central DI, and water replacement [66, 90, 105]. Other management includes hypotonic fluids to replace the water deficit and manipulation of EN and PN solutions as discussed for hypotonic hypervolemia [103]. Hypervolemic hypernatremia occurs due to an increase in total body sodium with normal TBW [103]. Treatment involves discontinuing the offending agent and sodium removal. Loop diuretics with hypotonic fluids may be required [68]. Sodium should also be decreased or removed from PN solutions [103].

It is generally recommended to limit hypernatremia correction to 8–10 mEq/day due to the risk of seizures and cerebral edema [90, 105]. This has been observed more in pediatric patients and there is little data regarding correction rates in adult ICU patients. A retrospective evaluation of the Medical Information Mart for Intensive Care-III (MIMIC-III) database found that rapid correction of hypernatremia was not associated with higher incidences of death or cerebral edema [107]. Acute hypernatremia can be corrected at a rate of 2 mEq/L/hr until serum sodium reaches 145 mEq/L [90]. Serum sodium should be measured at least twice daily in asymptomatic patients and at least every 4 h in symptomatic patients [105].

7 Conclusion

Electrolyte disturbances, measurements, and corrections are ubiquitous in the ICU. In most cases, electrolyte correction is guided by laboratory values rather than other measurements such as symptom relief. Data on the management of electrolyte abnormalities in the critically ill is limited. Most management strategies have been extrapolated from studies involving the general inpatient population. Further research is needed in electrolyte management in this vulnerable population. While many of these strategies have been successfully employed for years in the ICU, it is important to consider factors unique to the critically ill when selecting the optimal treatment approach. Multiple algorithms have been proposed and used to guide evaluation and treatment for standardization. As with the management of any critical illness, the most important aspect of managing a patient in the ICU with an electrolyte abnormality is to individualize the treatment to the patient's unique needs and adapt management to the patient's changing clinical situation.

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