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Electrolytes in ICU

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INTRODUCTION

Electrolyte disturbances are common clinical problems encountered in the intensive care unit (ICU) and are associated with increased morbidity and mortality among critically ill patients. Unless suspected they can be missed and inappropriate therapy can lead to irreversible damage. For management of hyponatremia in ICU identifying stimuli for vasopressin secretion, judicious use of hypertonic saline, and close monitoring are essential components. Hypernatremia is associated with cellular dehydration and central nervous system dysfunction. Water deficit should be corrected with hypotonic fluid, taking into account ongoing water losses. Cardiac manifestations should be identified and treated before initiating stepwise diagnostic evaluation of potassium disturbances. Disturbances of calcium phosphorous and magnesium metabolism are also frequently encountered in some critically ill patient with trauma, burns, sepsis, pancreatitis and renal failure. Early recognition and prompt correction of these abnormalities are necessary to avoid catastrophes. A brief description electrolyte disturbance pertaining to ICU patients follows.

HYPONATREMIA

Hyponatremia may be present on ICU admission or can develop later. In either case it is associated with poor prognosis. A recent study of 151,486 adult patients from 77 intensive care units over a period of 10 years demonstrated that severity of dysnatremia is associated with poor outcome in a graded fashion. Another study reported that both ICU-acquired hyponatremia and ICU-acquired hypernatremia were associated with increased mortality. It should be noted that patients with hyponatremia may also have manifestations of concurrent volume depletion and possible underlying neurologic diseases that predispose to development of hyponatremia due to SIADH or cerebral salt wasting. Hyponatremia-induced cerebral edema occurs with sudden fall in the serum sodium concentration, usually within 24 hours. Causes of hyponatremia are mentioned in Table 1. Clinically, hyponatremia manifests with primarily neurologic symptoms. Their severity depends on rapidity of the change in the serum sodium concentration in addition to level of sodium. When serum sodium falls acutely below 120 meq/L, patients become symptomatic with lethargy, apathy, confusion, seizures and coma. Premenopausal women and young children with acute postoperative hyponatremia have high risk of brain herniation suggesting a possible hormonally-mediated decrease in the degree of osmotic adaptation. Patients with chronic hyponatremia usually do not have neurological symptoms and manifest with muscle cramps, anorexia, nausea and weakness.

In most of the cases cause of hyponatremia becomes apparent by detail clinical evaluation including medication history. Measurement of serum osmolality, urinary sodium, cortisol, thyroid hormone and relevant radiological investigations are needed in selected cases. Low uric acid levels and BUN are found in patients with SIADH, thiazide induced hyponatremia, hypopitutarism and hypervolemia. Concurrent metabolic alkalosis is seen in patients with diuretic use, vomiting and hypopitutarism while metabolic acidosis is seen in cases of diarrhea and primary adrenalin insufficiency.

Treatment

Acute hyponatemia is generally symptomatic and needs rapid correction. Treatment is recommended with 3% NaCl by giving a bolus of 100ml IV over 10 min, repeated upto maximum 3 doses, or till acute symptoms subsides. The goal is to provide an urgent correction by 4 to 6 mmol/L to prevent brain herniation. For patients with mild to moderate symptoms, 3% NaCl is infused at lower rate of 0.5-2 mL/kg/h. In chronic hyponatremia the brain undergoes gradual adaptation and there is less cerebral edema, and very rapid correction can lead to osmotic demyelination syndrome (ODS). Hence, chronic hyponatremia generally needs gradual correction. High risk of ODS is seen with serum sodium < 120meq/L

Table 1: Causes of Hyponatremia

Pseudohyponatremia (normo-osmolar)	Hyperlipidemia Hyperproteinemia
Redistributive Hyponatremia (hyperosmolar)	Hyperglycemia Mannitol therapy
Hypovolemic Hyponatremia	GI losses Third space losses Diuretic therapy Cerebral salt wasting Mineralocorticoid deficiency
Euvolemic hyponatremia	SIADH Hypothyroidism Glucocorticoid deficiency Polydipsia
Hypervolemic Hyponatremia	Congestive heart failure Cirrhosis of liver Nephrotic syndrome Renal failure

or if there are comorbidities such as alcoholism, liver disease, malnutrition, or severe hypokalemia are present. However, if chronic hyponatremia is symptomatic with neurological features or is severe, aggressive therapy is indicated as for acute hyponatremia and Initial administration of 3% NaCl is needed to raise the serum sodium by 4-6 mmol above baseline.

Estimated change in plasma [Na+] following the administration of 1 L of an intravenous fluid regimen can be calculated by equations proposed by Madias and Adrogue:

Change in plasma [Na+] =Infusate [Na+] – plasma [Na+]/ Total body water + 1

There is a tendency to underestimate the achieved plasma [Na+] using this formula. Also ongoing losses have to be accounted for and close clinical and laboratory monitoring is needed. In hypovolemic hyponatremia, the initial intravenous fluid of choice should be 0.9% sodium chloride, unless the patient is symptomatic or hyponatremia is documented to have developed acutely (< 48 hours). Euvolemic asymptomatic hyponatremia does not require urgent therapy. Identification and removal of reversible causes should be done followed by fluid restriction in patients with chronic SIADH. Loop diuretics concurrently used are beneficial in patients with SIADH who have a high urine to serum electrolyte ratio (>1). Vaptans are useful for chronic hyponatremia in addition to fluid restriction and sodium chloride administration. Many cases of hypervolemic hyponatremia are associated with significant dysfunction of the heart, liver, or kidney. Treatment includes restriction of water and sodium intake, administration of loop diuretics and treatment of cause. Treatment of severe hyponatremia in patients with decompensated heart failure may require extracorporeal ultrafiltration, which has been shown to improve congestion, lower diuretic requirements, and correct hyponatremias. Vaptans can be used in cirrhotic patients for management of fluid overload with hyponatremia if water restriction and diuretics do not help.

HYPERNATREMIA

Predisposing factors for hypernatremia in ICU include the administration of sodium bicarbonate solutions for acidosis correction; selective renal water loss, use of diuretics; gastrointestinal fluid losses through nasogastric suction, and selective water losses through fever, drainage tubes, and open wounds. Acute diabetes insipidus with hypernatremia can complicate traumatic brain injury. The clinical manifestations of acute hypernatremia begin with lethargy, weakness, and irritability, and can progress to convulsions and coma if serum sodium is >160meq/L. Patients may have intense thirst initially, however most ICU patients cannot communicate same.

Treatment

Acute (<48 hours) hypernatremia is rare, occurring in patients with diabetes insipidus or is iatrogenic. The initial regimen in such patients is fluid therapy with D5-5 percent dextrose in water, intravenously, at a rate of 3 to 6 mL/kg per hour with close monitoring of serum sodium and blood glucose until the serum sodium is lowered below 145 meq/L, followed by infusion at 0.5-1 mL/kg/ hour till normonatremia is restored over 24 hours.

Chronic (>48 hours) hypernatremia is more common, even in those who present with acute changes in mentation. The initial regimen in such patients is D5 infusion, intravenously, at a rate of (1.35 x patient's weight in kg ml/hour) to lower the serum sodium by a maximum of 10 meq/L in a 24-hour period (0.4 meq/L/hour). It is likely that this regimen will lower the serum sodium by less than 10 meq/L in 24 hours, as many patients have ongoing free water losses (osmotic diuresis, diarrhea, nasogastric suction) slowing the rate of correction. Potassium can be added to the intravenous fluid in patients with concomitant hypokalemia. A potential complication of rapid administration of dextrose-containing intravenous fluids is the development of hyperglycemia, more so in patients with diabetes. Hyperglycemia can lead to an osmotic diuresis, which creates electrolyte-free water losses further limiting the reduction in serum sodium. Lower concentration e.g. 2.5% dextrose in water- solution can be used in such patients. Hypervolemic hypernatremia is usually an iatrogenic complication that develops in patients with renal failure. Renal replacement therapy is the only effective treatment in them. Composition of hemodialysis solution should be adjusted to lower sodium concentration in such patients.

HYPOKALEMIA

This is a common electrolyte disturbance in ICU patients resulting from GI losses (diarrhea, vomiting, nasogastric suction), renal losses (diuretics, diuretic phase of renal failure, RTA), trans-cellular shifts or drugs (beta stimulants, insulin, aminoglycosides, amphotericin B). Clinical manifestations of hypo and hperkalemia are enumerated in Table 2. The most dreaded complications

Table 2: Clinical manifestations of Hypokalemia and Hyperkalemia

	Manifestations of Hypokalemia	Manifestations of Hyperkalemia
GI manifestations	Anorexia, nausea, vomiting, paralytic ileus	Nausea, vomiting, diarrhea, intestinal cramps
Neuromuscular Manifestations	Muscle cramps, weakness, paraesthesia, paralysis	Paraesthesia, weakness, muscle cramps, dizziness
Cardiovascular Manifestations	Postural hypotension, ECG changes, cardiac dysrhymias	ECG changes, risk of cardiac arrest
Associated Acid Base Disorders	Metabolic alkalosis	Metabolic acidosis

of hypokalemia are cardiac arrhythmias, especially in patients with hypertension and IHD, heart failure and neuromuscular paralysis. ECG changes seen in patients with hypokalemia include ST-segment depression, T-wave flattening followed by inversion, and the presence of U waves. In presence of life threatening symptoms like respiratory muscle paralysis or changes in ECG, therapy should precede investigations. In cases where cause is not obvious clinically, urinary potassium excretion should be measured. If it is appropriately low (urine K+ < 20 mEq/day then trans-cellular shift or extrarenal K+ loss should be suspected. If urinary K+ excretion is high, trans-tubular potassium gradient (TTKG), acid-base status, and the presence or absence of hypertension help in identifying cause of hypokalemia.

Treatment

Parentral therapy is reserved for patients with severe symptoms and ECG changes. Infusion of > 10–20 mEq/hr of potassium requires a central venous catheter, as infusion via peripheral line causes phlebitis. Total amount of daily K+ replacement should be less than 240–300 mEq with close monitoring. Parenteral K+ replacement should be given in dextrose-free vehicle. Hypocalcemia and hypomagnesemia should be suspected and corrected if hypokalemia persists despite adequate potassium supplementation. Milder hypokalemia should be corrected with oral therapy.

HYPERKALEMIA

It is seen in 1-2% of hospitalized patients. Increased intake, impaired renal excretion, hypoaldosteronism, transcellular shifts (acidosis, drugs, periodic paralysis, exercise) and cellular injury are important causes. Pseudohyperkalemia due to hemolysis of sample, leukocytosis, thrombocytosis and laboratory error should be suspected in absence of obvious cause, symptoms and ECG changes. ECG changes include tall T waves, low p wave, prolongation of PR interval and widening of QRS complex. Table 2 enumerates clinical manifestations. Initial step after exclusion of pseudohyperkalemia is to identify the cause of trans-cellular potassium shift, and discontinuation of medications responsible for hyperkalemia. The next step is to assess urinary potassium excretion. If there is relatively low urinary K+ excretion, calculation of TTKG should follow. A low TTKG may warrant further tests to differentiate between aldosterone deficiency and resistance to aldosterone. If ECG abnormality of hyperkalemia is present, emergency management should be started before further investigations. Intravenous calcium gluconate is the first therapy to antagonize the depolarizing effect of hyperkalemia. Administration of Insulin with 50% glucose follows. It takes 30 minutes to produce effect that lasts for 4-6 hours. Nebulization with beta stimulants lower potassium levels for at least 2 hours. Sodium bicarbonate should be avoided in patients with extracellular fluid volume overload. Infusion of 44 meq over 5-15 minutes lowers serum potassium for approximately 2 hours. In case of emergency and in presence of renal failure or rhabdomyolysis, hemodialysis is most effective therapy. Exchange resins are advocated in long term management in chronic cases.

MAGNESIUM IMBALANCE

It is second most abundant intracellular cation but only 1% of body's Mg is present in ECF. Hypomagnesemia is common finding in hospitalised patients (10-20%) especially in emergency department and ICU patients (as high as 50%). It may result from impaired intake (alcoholism, starvation, malabsorption, TPN), increased losses (diuretics, DKA, hyperaldosteronism, magnesium losing kidney disease). Drugs like aminoglycosides, amphotericin, beta agonists, diuretics and PPIs predispose to hypomagnesemia. Severe hypomagnesemia can result in ECG changes, arrhythmias including torsades de pointes, seizures, coma, and death. Neuromuscular manifestations are muscle weakness, tremors and hyperreflexia. Hypomagnesemia can also lead to refractory hypokalemia and hypocalcemia. Severe hypomagnesemia(serum Mg < 1mg/dl) is treated with IV infusion of 1.5 meq/Kg $MgSO_4$ over 12-24 hours with monitoring of serum Mg level and renal function. Hypermagnesemia is rare but can be seen in ICU patients following administration of IV $MgSO_4$ for eclampsia, Mg containing laxatives and in patients with renal failure. It manifests with lethargy, hyporeflexia, hypotension, confusion and coma and respiratory paralysis. Treatment of hypermagnesemia includes stopping Mg supplementation, IV Calcium infusion in severe cases, hydration, loop diuretics and dialysis for patients with life threatening manifestations.

CALCIUM IMBALANCE

Hypocalcemia is a frequent electrolyte abnormality encountered in the ICU. Prevalence of hypocalcemia measured as ionized calcium is estimated to be about 15–20%. Hypocalcemia is also associated with increased mortality in ICU patients. Spuriously low concentration of calcium can be seen following the administration of gadolinium based contrast, as gadolinium interferes with calorimetric calcium assays. Common causes of hypocalcemia in ICU patients are trauma, renal failure, sepsis, pancreatitis, massive transfusion, post parathyroidectomy, associated hypomagnesemia and vitamin D deficiency. The symptoms and signs of severe acute hypocalcemia include tetany, seizures, cardiovascular manifestations such as prolonged QT interval and ventricular arrhythmias. Calcium chloride should be preferred over calcium gluconate for urgent situations, since it contains three times more elemental calcium. Hypomagnesemia should be suspected and corrected if hypocalcemia is not getting corrected by repeated calcium administration. If metabolic acidosis is present concomitantly, hypocalcemia should be corrected first as the treatment of acidosis with bicarbonates further decreases level of ionized calcium, precipitating tetany or cardiac arrest. Hypercalcemia is seen in ICU patients with hyperparathyroidism, prolonged immobilization, malignancies, use of thiazide diuretics and milk alkali syndrome. Clinical manifestations are vomiting, constipation, hypertension, renal dysfunction and CNS

disturbances including coma. Management is with saline hydration, followed by loop diuretics. Biphosphonates, calcitonin, steroids and plicamycin have role in chronic and severe cases. Dialysis is required in patients with renal failure or fluid overload.

PHOSPHOROUS IMBALANCE

Hypophosphatemia is a frequent disorder in critically ill patients with Gram-negative sepsis, DKA, malnutrition, alcoholism, diuretic therapy and cardiac surgery (20-25%). Hypophosphatemia may result from decreased intestinal phosphate absorption, increased renal loss, and trans-cellular shift of phosphate to intracellular space. Rapid infusion of glucose containing solution to chronically malnourished patients can precipitate hypophosphatemia by causing trans-cellular shift know as re-feeding syndrome. It may manifest with leukocyte, erythrocyte, and platelet dysfunction. Clinical features are muscular weakness, confusion, ataxia, convulsions and coma; respiratory failure and cardiac arrhythmias. Hypotension and ventilator dependence are frequent problems encountered in ICU due to hypophoaphatemia. Symptomatic or severe hypophosphatemia (< 1.0 mg/dL) should be treated with intravenous sodium or potassium phosphate with initial intravenous infusion of 2–5 mg/kg of inorganic phosphate dissolved in 0.45% saline given over 6–12 hours and repeated as needed. Monitoring for hypocalcemia is required during IV phosphate infusion. Patients on CRRT need higher dose. Milder hypophosphatemia is treated with oral supplementations such as potassium phosphate.

Hyperphosphatemia can result from increased phosphate intake, decreased phosphate excretion, or shift of intracellular phosphate to extracellular space. It is an independent risk factor for mortality in ICU patients. Rhabdoomyolysis, acidosis, tumor lysis and acute hemolysis can cause hyperphosphatemia due to cellular shifts. Renal failure and hypoparathyroidism are common causes of hyperphosphatemia due to decreased loss. Most patients are asymptomatic but occasionally have symptoms of hypocalcemia, such as muscle cramps, tetany, and perioral numbness or tingling. Bone and joint pain, pruritus, and rash are other symptoms. Carpopedal spasms and seizures can develop in patients with acute hyperphophatemia. Treatment is by restricting supplementation, hydration, infusion of glucose with insulin and dialysis in severe cases. Aluminium or calcium containing phosphate binders are commonly used to retard absorption. Sevelamer is a non calcium/aluminium containing binder with additional effect on lipid profile.

CONCLUSION

Various types of electrolyte imbalances are found in critically ill patients along with fluid and acid base disturbances. In majority of cases there are no symptoms and even if present are non-specific. Thus high index of suspicion is needed to identify these disorders depending on predisposing conditions in these patients. Their prompt recognition and appropriate treatment are of utmost importance as some of these can be fatal if left untreated. Treatment is simple for most of disturbances but patients fluid status, renal function, pre-existing conditions have to be considered and close monitoring is required to avoid complications of too rapid correction with long term sequel.

REFERENCES

1. Funk GC, Lindner G, Druml W, et al. Incidence and prognosis of dysnatremias present on ICU admission. *Intensive Care Med* 2010; 36:304-311.
2. Stelfox HT, Ahmed SB, Khandwala F, Zygun D, Shahpori R, Laupland K: The epidemiology of intensive care unit-acquired hyponatraemia and hypernatraemia in medical-surgical intensive care units. *Crit Care* 2008; 12:R162.
3. Sahay M, Sahay R. Hyponatremia: A practical approach. *Indian J Endocr Metab* 2014;18:760-71.
4. Verbalis JG, Goldsmith SR, Greenberg A, Korzelius C, Schrier RW, Sterns RH, et al. Diagnosis, evaluation and treatment of hyponatremia: Expert panel recommendations. *Am J Med.* 2013; 126:S1–42.
5. Liamis G, Kalogirou M, Saugos V, Elisaf M: Therapeutic approach in patients with dysnatraemias. *Nephrol Dial Transplant* 2006; 21:1564-1569.
6. Lee JW. Fluid and Electrolyte Disturbances in Critically Ill Patients. *Electrolyte Blood Press* 2010; 8:72-81.
7. Pandey CK, Singh RB. Fluid and electrolyte disorders. *Indian J Anaesth* 2003; 47:380-87.
8. Gibbs R, Macnaughton P. Electrolyte and metabolic disturbances in critically ill patients. *Anaesthesia & Intensive Care Medicine* 2007; 8:529 -533.