Part 10.1: Life-Threatening Electrolyte Abnormalities

Electrolyte abnormalities are commonly associated with cardiovascular emergencies. These abnormalities may cause or contribute to cardiac arrest and may hinder resuscitative efforts. In some cases therapy for life-threatening electrolyte disorders should be initiated before laboratory results become available.

Potassium (K$^+$)

The magnitude of the potassium gradient across cell membranes determines excitability of nerve and muscle cells, including the myocardium. Rapid or significant changes in the serum potassium concentration can have life-threatening consequences.

Evaluation of serum potassium must consider the effects of changes in serum pH. When serum pH falls, serum potassium rises because potassium shifts from the cellular to the vascular space. When serum pH rises, serum potassium falls because potassium shifts from the vascular space into the cells. Effects of pH changes on serum potassium should be anticipated during therapy for hyperkalemia or hypokalemia and during any therapy that may cause changes in serum pH (eg, treatment of diabetic ketoacidosis).

Hyperkalemia

Although hyperkalemia is defined as a serum potassium concentration >5 mEq/L, it is moderate (6 to 7 mEq/L) and severe (>7 mEq/L) hyperkalemia that are life-threatening and require immediate therapy. Hyperkalemia is most commonly seen in patients with end-stage renal disease. Other causes are listed in the Table. Many medications can contribute to the development of hyperkalemia. Identification of potential causes of hyperkalemia will contribute to rapid identification and treatment.[1–3]

Signs and symptoms of hyperkalemia include weakness, ascending paralysis, and respiratory failure. A variety of electrocardiographic (ECG) changes suggest hyperkalemia. Early findings include peaked T waves (tenting). As the serum potassium rises further, flattened P waves, prolonged PR interval (first-degree heart block), widened QRS complex, deepened S waves, and merging of S and T waves can be seen. If hyperkalemia is left untreated, a sine-wave pattern, idioventricular rhythms, and asystolic cardiac arrest may develop.

Treatment of Hyperkalemia

The treatment of hyperkalemia is determined by its severity and the patient's clinical condition. Stop sources of exogenous potassium administration (eg, consider supplements and maintenance IV fluids) and evaluate drugs that can increase serum potassium (eg, potassium-sparing diuretics, angiotensin-converting enzyme [ACE] inhibitors, nonsteroidal anti-

inflammatory agents). Additional treatment is based on the severity of the hyperkalemia and its clinical consequences. The following sequences list the treatments for hyperkalemia in order of priority.

For *mild* elevation (5 to 6 mEq/L), remove potassium from the body with

1. Diuretics: furosemide 40 to 80 mg IV
2. Resins: Kayexalate 15 to 30 g in 50 to 100 mL of 20% sorbitol either orally or by retention enema

For *moderate* elevation (6 to 7 mEq/L), shift potassium intracellularly with

1. Glucose plus insulin: mix 25 g (50 mL of D$_{50}$) glucose and 10 U regular insulin and give IV over 15 to 30 minutes
2. Sodium bicarbonate: 50 mEq IV over 5 minutes (sodium bicarbonate alone is less effective than glucose plus insulin or nebulized albuterol, particularly for treatment of patients with renal failure; it is best used in conjunction with these medications[4,5])
3. Nebulized albuterol: 10 to 20 mg nebulized over 15 minutes

For *severe* elevation (>7 mEq/L with toxic ECG changes), you need to shift potassium into the cells and eliminate potassium from the body. Therapies that shift potassium will act rapidly but they are temporary; if the serum potassium rebounds you may need to repeat those therapies. In order of priority, treatment includes the following:

TABLE. Common Causes of Hyperkalemia

Endogenous Causes

- Chronic renal failure
- Metabolic acidosis (eg, diabetic ketoacidosis)
- Pseudohypoaldosteronism type II (also known as Gordon's syndrome; familial hyperkalemia and hypertension)
- Chemotherapy causing tumor lysis
- Muscle breakdown (rhabdomyolysis)
- Renal tubular acidosis
- Hemolysis
- Hypoaldosteronism (Addison's disease, hyporeninemia)
- Hyperkalemic periodic paralysis

Exogenous Causes

- Medications: K$^+$-sparing diuretics, ACE inhibitors, nonsteroidal anti-inflammatory drugs, potassium supplements, penicillin derivatives, succinylcholine, heparin therapy (especially in patients with other risk factors), β-blockers
- Blood administration (particularly with large transfusions of older "bank" blood)
- Diet (rarely the sole cause), salt substitutes
- Pseudohyperkalemia (due to blood sampling or hemolysis, high white blood cell count, high platelets, tumor lysis syndrome)

- *Shift potassium into cells:*

1. Calcium chloride (10%): 500 to 1000 mg (5 to 10 mL) IV over 2 to 5 minutes to reduce the effects of potassium at the myocardial cell membrane (lowers risk of ventricular fibrillation [VF])
2. Sodium bicarbonate: 50 mEq IV over 5 minutes (may be less effective for patients with end-stage renal disease)
3. Glucose plus insulin: mix 25 g (50 mL of D_{50}) glucose and 10 U regular insulin and give IV over 15 to 30 minutes
4. Nebulized albuterol: 10 to 20 mg nebulized over 15 minutes[5–7]

- *Promote potassium excretion:*

5. Diuresis: furosemide 40 to 80 mg IV
6. Kayexalate enema: 15 to 50 g plus sorbitol PO or per rectum
7. Dialysis

Hypokalemia

Hypokalemia is defined as a serum potassium level <3.5 mEq/L. The most common causes of low serum potassium are gastrointestinal loss (diarrhea, laxatives), renal loss (hyperaldosteronism, severe hyperglycemia, potassium-depleting diuretics, carbenicillin, sodium penicillin, amphotericin B), intracellular shift (alkalosis or a rise in pH), and malnutrition.

The major consequences of severe hypokalemia result from its effects on nerves and muscles (including the heart). The myocardium is extremely sensitive to the effects of hypokalemia, particularly if the patient has coronary artery disease or is taking a digitalis derivative. Symptoms of mild hypokalemia are weakness, fatigue, paralysis, respiratory difficulty, constipation, paralytic ileus, and leg cramps; more severe hypokalemia will alter cardiac tissue excitability and conduction. Hypokalemia can produce ECG changes such as U waves, T-wave flattening, and arrhythmias (especially if the patient is taking digoxin), particularly ventricular arrhythmias. Pulseless electrical activity or asystole may develop.

Treatment of Hypokalemia

The treatment of hypokalemia consists of minimizing further potassium loss and providing potassium replacement. IV administration of potassium is indicated when arrhythmias are present or hypokalemia is severe (potassium level of <2.5 mEq/L). Gradual correction of hypokalemia is preferable to rapid correction unless the patient is clinically unstable.

Administration of potassium may be empirical in emergent conditions. When indicated, the maximum amount of IV potassium replacement should be 10 to 20 mEq/h with continuous ECG monitoring during infusion. A more concentrated solution of potassium may be infused if a central line is used, but the tip of the catheter used for the infusion should not extend into the right atrium.

If cardiac arrest from hypokalemia is imminent (ie, malignant ventricular arrhythmias are present), rapid replacement of potassium is required. Give an initial infusion of 10 mEq IV over 5 minutes; repeat once if needed. *Document in the patient's chart that rapid infusion is intentional in response to life-threatening hypokalemia.*

Sodium (Na$^+$)

Sodium is the major intravascular ion that influences serum osmolality. An acute increase in serum sodium will produce an acute increase in serum osmolality; an acute decrease in serum sodium will produce an acute fall in serum osmolality.

Sodium concentration and osmolality in the intravascular and interstitial spaces equilibrate across the vascular membrane. *Acute* changes in serum sodium will produce free water shifts into and out of the vascular space until osmolality equilibrates in these compartments. An acute fall in serum sodium will produce an acute shift of free water from the vascular into the interstitial space and may cause cerebral edema.[8,9] An acute rise in serum sodium will produce an acute shift of free water from the interstitial to the vascular space. Rapid correction of hyponatremia has been associated with development of pontine myelinolysis and cerebral bleeding.[10–12] For these reasons, monitor neurologic function closely in the patient with hypernatremia or hyponatremia, particularly during correction of these conditions. Whenever possible, correct serum sodium slowly, carefully controlling the total change in serum sodium over 48 hours and avoiding overcorrection.[13,14]

Hypernatremia

Hypernatremia is defined as a serum sodium concentration >145 to 150 mEq/L. It may be caused by a primary gain in Na$^+$ or excess loss of water. Gains in sodium can result from hyperaldosteronism (excess mineralocorticoid), Cushing's syndrome (excess glucocorticoid), or excessive hypertonic saline or sodium bicarbonate administration. Loss of free water can result from gastrointestinal losses or renal excretion (eg, osmotic diuresis or diabetes insipidus).

Hypernatremia may cause neurologic symptoms such as altered mental status, weakness, irritability, focal neurologic deficits, and even coma or seizures. The severity of symptoms is determined by the speed and magnitude of the change in serum sodium concentration.

Treatment of Hypernatremia

Treatment of hypernatremia includes reduction of ongoing water losses (by treating the underlying cause) and correction of the water deficit. For stable, asymptomatic patients, replacement of fluid by mouth or through a nasogastric tube is effective and safe.

In hypovolemic patients the extracellular fluid (ECF) volume is typically restored with normal saline or a 5% dextrose in half-normal saline solution to prevent a rapid fall in the serum sodium concentration. Avoid D_5W because it will reduce the serum sodium too rapidly. During rehydration, monitor serum sodium closely to ensure a gradual fall (and prevent rapid fall) in serum sodium.

The quantity of water needed to correct hypernatremia can be calculated by using the following equation:

$$\text{Water deficit (in liters)} = \frac{\text{plasma } Na^+ \text{ concentration} - 140}{140} \times \text{total body water}$$

Total body water is approximately 50% of lean body weight in men and 40% of lean body weight in women. For example, if a 70-kg man had a serum Na^+ level of 160 mEq/L, the estimated free water deficit would be

$$\frac{160 - 140}{140} \times (0.5 \times 70) = 5 \text{ L}$$

Once the free water deficit is calculated, administer fluid to lower serum sodium at a rate of 0.5 to 1 mEq/h with a decrease of no more than approximately 12 mEq/L in the first 24 hours and the remainder over the next 48 to 72 hours.

Hyponatremia

Hyponatremia is defined as a serum sodium concentration <130 to 135 mEq/L. It is caused by an excess of water relative to sodium. Most cases of hyponatremia are caused by reduced renal excretion of water with continued water intake or by loss of sodium in the urine. Impairment of renal water excretion may be caused by

- Use of thiazide diuretics
- Renal failure
- ECF depletion (eg, vomiting with continued water intake)
- Syndrome of inappropriate antidiuretic hormone (SIADH) secretion
- Edematous states (eg, congestive heart failure, cirrhosis with ascites)
- Hypothyroidism
- Adrenal insufficiency

Most cases of hyponatremia are associated with low serum osmolality (so-called hypo-osmolar hyponatremia). The one common exception to this is in uncontrolled diabetes, in which hyperglycemia leads to a hyperosmolar state despite a serum sodium that is below normal (hyperosmolar hyponatremia).

Hyponatremia is usually asymptomatic unless it is acute or severe (<120 mEq/L). An abrupt fall in serum sodium produces a free water shift from the vascular to the interstitial space that can cause cerebral edema. In this case the patient may present with nausea, vomiting, headache, irritability, lethargy, seizures, coma, or even death.

Treatment of Hyponatremia

Treatment of hyponatremia involves administration of sodium and elimination of intravascular free water. If SIADH is present, the treatment is restriction of fluid intake to 50% to 66% of estimated maintenance fluid requirement. Correction of asymptomatic hyponatremia should be gradual: typically increase the Na^+ by 0.5 mEq/L per hour to a maximum change of about 12 mEq/L in the first 24 hours. Rapid correction of hyponatremia can cause coma, which may be associated with osmotic demyelination syndrome or central pontine myelinolysis, lethal disorders thought to be caused by rapid fluid shifts into and out of brain tissue.[10−12]

If the patient develops neurologic compromise, administer 3% saline IV immediately to correct (raise) the serum sodium at a rate of 1 mEq/L per hour until neurologic symptoms are controlled. Some experts recommend a faster rate of correction (ie, increase concentration 2 to 4 mEq/L per hour) when seizures are present. After neurologic symptoms are controlled, provide 3% saline IV to correct (raise) the serum sodium at a rate of 0.5 mEq/L per hour.

To determine the amount of sodium (eg, 3% saline) required to correct the deficit, calculate the total body sodium deficit. The following formula may be used:

Na^+ deficit=(desired $[Na^+]$−current $[Na^+]$)×0.6*×body wt (kg) (*use 0.6 for men and 0.5 for women).

Once the deficit is estimated, determine the volume of 3% saline (513 mEq/L Na^+) necessary to correct the deficit (divide the deficit by 513 mEq/L). Plan to increase the sodium by 1 mEq/L per hour over 4 hours (or until neurologic symptoms improve); then increase the sodium by 0.5 mEq/L per hour. To calculate this amount, use the amount you wish to correct the sodium in an hour (eg, 0.5 mEq/L) and multiply by 0.6 (or 0.5 in women) and then multiply by the body weight; that will calculate the amount of sodium to administer that hour. Check serum sodium frequently and monitor neurologic status.

Magnesium (Mg^{++})

Magnesium is the fourth most common mineral and the second most abundant intracellular cation (after potassium) in the human body. Because extracellular magnesium is bound to serum albumin, magnesium levels do not reliably reflect total body magnesium stores. Magnesium is necessary for the movement of sodium, potassium, and calcium into and out of cells, and magnesium plays an important role in stabilizing excitable membranes. Low potassium in combination with low magnesium is a risk factor for severe arrhythmias. Thus, magnesium balance is closely tied to sodium, calcium, and potassium balance.

Hypermagnesemia

Hypermagnesemia is defined as a serum magnesium concentration >2.2 mEq/L (normal: 1.3 to 2.2 mEq/L). The most common cause of hypermagnesemia is renal failure. Note that pre-eclampsia in pregnant women is treated with magnesium administration, often titrated to maintain the serum magnesium near the maximum normal concentration, without complications of hypermagnesemia.

Neurologic symptoms of hypermagnesemia are muscular weakness, paralysis, ataxia, drowsiness, and confusion. Moderate hypermagnesemia can produce vasodilation; severe hypermagnesemia can produce hypotension. Extremely high serum magnesium levels may produce a depressed level of consciousness, bradycardia, cardiac arrhythmias, hypoventilation, and cardiorespiratory arrest.[15]

Treatment of Hypermagnesemia

Hypermagnesemia is treated with administration of calcium, which removes magnesium from serum. It is important to eliminate sources of ongoing magnesium intake. Cardiorespiratory support may be needed until magnesium levels are reduced. Administration of 10% solution of calcium chloride (5 to 10 mL [500 to 1000 mg] IV) will often correct lethal arrhythmias. This dose may be repeated if needed.

Dialysis is the treatment of choice for severe hypermagnesemia. If renal function is normal and cardiovascular function adequate, IV saline diuresis (administration of IV normal saline and furosemide [1 mg/kg]) can be used to increase renal excretion of magnesium until dialysis can be performed. Diuresis can also increase calcium excretion; the development of hypocalcemia will make signs and symptoms of hypermagnesemia worse.

Hypomagnesemia

Hypomagnesemia, defined as a serum magnesium concentration <1.3 mEq/L, is far more common than hypermagnesemia. Hypomagnesemia usually results from decreased absorption or increased loss of magnesium from either the kidneys or intestines (diarrhea). Alterations in thyroid hormone function and certain medications (eg, pentamidine, diuretics, alcohol) can also induce hypomagnesemia.

Hypomagnesemia interferes with the effects of parathyroid hormone, resulting in hypocalcemia. It may also cause hypokalemia. Symptoms of low serum magnesium are muscular tremors and fasciculations, ocular nystagmus, tetany, altered mental state, and cardiac arrhythmias such as torsades de pointes (multifocal ventricular tachycardia). Other possible symptoms are ataxia, vertigo, seizures, and dysphagia.

Treatment of Hypomagnesemia

The treatment of hypomagnesemia is determined by its severity and the patient's clinical status. For severe or symptomatic hypomagnesemia, give 1 to 2 g of IV MgSO$_4$ over 5 to 60 minutes. For torsades de pointes with cardiac arrest, give 1 to 2 g of MgSO$_4$ IV push over 5 to 20 minutes. If torsades de pointes is intermittent and not associated with arrest, administer the magnesium over 5 to 60 minutes IV. If seizures are present, give 2 g IV MgSO$_4$ over 10 minutes. Administration of calcium is usually appropriate because most patients with hypomagnesemia are also hypocalcemic.[16]

Calcium (Ca^{++})

Calcium is the most abundant mineral in the body. Many processes depend on intracellular calcium, such as enzymatic reactions, receptor activation, muscle contraction, cardiac contractility, and platelet aggregation. Calcium is essential for bone strength and neuromuscular function. Half of all calcium in the ECF is bound to albumin; the other half is in the biologically active, ionized form. Calcium concentration is normally regulated by parathyroid hormone and vitamin D.

Total serum calcium is directly related to the serum albumin concentration. The total serum calcium will increase 0.8 mg/dL for every 1 g/dL rise in serum albumin and will fall 0.8 mg/dL for every 1 g/dL fall in serum albumin.

Although total serum albumin is directly related to total serum calcium, the ionized calcium is *inversely* related to serum albumin. The lower the serum albumin, the higher the portion of the total calcium that is present in ionized form. In the presence of hypoalbuminemia, although total calcium level may be low, the ionized calcium level may be normal.

Calcium antagonizes the effects of both potassium and magnesium at the cell membrane. For this reason it is extremely useful for treating the effects of hyperkalemia and hypermagnesemia.

Hypercalcemia

Hypercalcemia is defined as a total serum calcium concentration >10.5 mEq/L (or an elevation in ionized calcium >4.8 mg/dL). Primary hyperparathyroidism and malignancy account for >90% of reported cases.[17] In these and most forms of hypercalcemia, release of calcium from the bones and intestines is increased, and renal clearance may be compromised.

Symptoms of hypercalcemia usually develop when the total serum calcium concentration is ≥12 to 15 mg/dL. Neurologic symptoms are depression, weakness, fatigue, and confusion at lower levels. At higher levels patients may experience hallucinations, disorientation, hypotonicity, seizures, and coma. Hypercalcemia interferes with renal concentration of urine; the diuresis can cause dehydration.

Cardiovascular symptoms of hypercalcemia are variable. Myocardial contractility may initially increase until the calcium level reaches >15 mg/dL. Above this level myocardial depression occurs. Automaticity is decreased and ventricular systole is shortened. Arrhythmias occur because the refractory period is shortened. Hypercalcemia can worsen digitalis toxicity and may cause hypertension. In addition, many patients with hypercalcemia develop hypokalemia. Both of these conditions contribute to cardiac arrhythmias.[18] The QT interval typically shortens when the serum calcium is >13 mg/dL, and the PR and QRS intervals are prolonged. Atrioventricular block may develop and progress to complete heart block and even cardiac arrest when the total serum calcium is >15 to 20 mg/dL.

Gastrointestinal symptoms of hypercalcemia include dysphagia, constipation, peptic ulcers, and pancreatitis. Effects on the kidney include diminished ability to concentrate urine; diuresis, leading to loss of sodium, potassium, magnesium, and phosphate; and a vicious cycle of calcium absorption in the intestines and calcium release from the bones that worsens hypercalcemia.

Treatment of Hypercalcemia

Treatment for hypercalcemia is required if the patient is symptomatic (typically a total serum concentration of approximately >12 mg/dL) or if the calcium level is >15 mg/dL. Immediate therapy is directed at restoring intravascular volume and promoting calcium excretion in the urine. In patients with adequate cardiovascular and renal function this is accomplished with infusion of 0.9% saline at 300 to 500 mL/h (saline diuresis) until any fluid deficit is replaced and diuresis occurs (urine output ≥200 to 300 mL/h). Once adequate rehydration has occurred, the saline infusion rate is

reduced to 100 to 200 mL/h. During this therapy, monitor and maintain potassium and magnesium concentrations closely because the diuresis can reduce potassium and magnesium concentrations.

Hemodialysis is the treatment of choice to rapidly decrease serum calcium in patients with heart failure or renal insufficiency.[19] Chelating agents (eg, 50 mmol PO_4 over 8 to 12 hours or EDTA 10 to 50 mg/kg over 4 hours) may be used for extreme conditions.

Use of furosemide (1 mg/kg IV) for treatment of hypercalcemia is controversial. In the presence of heart failure, administration of furosemide is required, but it can actually foster release of calcium from bone, thus worsening hypercalcemia.

Hypocalcemia

Hypocalcemia is defined as a serum calcium concentration <8.5 mg/dL (or ionized calcium <4.2 mg/dL). Hypocalcemia may develop with toxic shock syndrome, with abnormalities in serum magnesium, after thyroid surgery, with fluoride poisoning, and with tumor lysis syndrome (rapid cell turnover with resultant hyperkalemia, hyperphosphatemia, and hypocalcemia).

Symptoms of hypocalcemia usually occur when ionized levels fall to <2.5 mg/dL. Symptoms include paresthesias of the extremities and face, followed by muscle cramps, carpopedal spasm, stridor, tetany, and seizures. Hypocalcemic patients show hyperreflexia and positive Chvostek and Trousseau signs. Cardiac effects include decreased myocardial contractility and heart failure. Hypocalcemia can exacerbate digitalis toxicity.

Treatment of Hypocalcemia

Treatment of hypocalcemia requires administration of calcium. Treat acute, symptomatic hypocalcemia with 10% calcium gluconate, 93 to 186 mg of elemental calcium (10 to 20 mL) IV over 10 minutes. Follow this with an IV infusion of 540 to 720 mg of elemental calcium (58 to 77 mL of 10% calcium gluconate) in 500 to 1000 mL D_5W at 0.5 to 2 mg/kg per hour (10 to 15 mg/kg). Alternatively, administer 10% calcium chloride, giving 5 mL (136.5 mg of elemental calcium) over 10 minutes, followed by 36.6 mL (1 g) over the next 6 to 12 hours IV. Measure serum calcium every 4 to 6 hours. Aim to maintain the total serum calcium concentration at 7 to 9 mg/dL. Correct abnormalities in magnesium, potassium, and pH simultaneously. Note that untreated hypomagnesemia will often make hypocalcemia refractory to therapy. Therefore, evaluate serum magnesium when hypocalcemia is present and particularly if hypocalcemia is refractory to initial calcium therapy.

Summary

Electrolyte abnormalities are among the most common causes of cardiac arrhythmias, and they can cause or complicate attempted resuscitation and postresuscitation care. A high degree of clinical suspicion and aggressive treatment of underlying electrolyte abnormalities can prevent these abnormalities from progressing to cardiac arrest.

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