CHAPTER 105

Water and Electrolyte Disturbances in Acute Renal Failure

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OBJECTIVES

This chapter will:

1. Describe the common electrolyte disturbances seen in patients with acute renal failure.
2. Review the diagnosis and treatment of hyperkalemia.
3. Review the diagnosis and treatment of hyponatremia and hypernatremia.

Water and electrolyte disturbances are among the most common complications of acute renal failure. Imbalances in plasma sodium, potassium, calcium, and phosphate are the most common electrolyte disturbances and require a comprehensive approach to management.

HYPERKALEMIA

Hyperkalemia is arguably the most dramatic, and certainly most life-threatening, of the metabolic consequences of acute renal failure in the intensive care unit (ICU) setting. Estimates for mortality associated with hyperkalemia are difficult to determine for the ICU population. The 1996 US Renal Data System survey, however, estimated a mortality rate of 1.9% for 1993.[1] The incidence of hyperkalemia among all hospitalized patients has been reported to range between 1.1 and 10 patients per 100 hospitalized.[2–5] The severity of hyperkalemia most often is determined by the concomitant severity of the pathophysiologic derangements leading to acute renal failure, and certainly, because acute renal failure typically is a multifactorial process, the distinct pathophysiology of hyperkalemia in association with this disorder often is also multifactorial.

In general, factors mediating potassium balance may be separated into external factors and internal factors. External factors refer to the renal and extrarenal factors controlling potassium balance in the serum. Internal factors are those that mediate the transcellular distribution of potassium. The body loses minimal potassium in sweat. The main extrarenal site of potassium elimination is in the colon, where mineralocorticoids may affect potassium secretion. This source of potassium loss is negligible during acute renal failure but may account for up to 10% of dietary potassium elimination among patients with chronic renal failure under the direct stimulation of increased aldosterone.[6] By contrast, the kidneys are extremely efficient at excreting potassium loads. It is difficult to induce hyperkalemia among patients with normal renal function strictly by increasing ingestion of potassium. In patients who have persistent hyperkalemia, particularly those who are critically ill with associated acute renal failure, hyperkalemia nearly always is associated with a decreased glomerular filtration rate (GFR), a defect in tubular flow, or inadequate aldosterone activity.

Acidosis, also a prominent feature of acute renal failure, promotes potassium exit from the cells. Maintaining normal serum potassium concentration between 3.5 and 5 mEq/L depends on the balance of potassium ingestion and potassium excretion, as well as the distribution of potassium into its usual intracellular location. Because 98% of total body potassium is located intracellularly, small shifts of even as little as 1% to 2% can cause increases in serum potassium that indeed can be life threatening. These disorders are exacerbated dramatically in acute renal failure, in which ability to excrete this potassium load is decreased.

In acute renal failure, hyperkalemia results from either exogenous or endogenous sources. Medications including potassium and penicillin VK and some multivitamins, and potassium chloride administration, are common sources of exogenous intake among patients in the ICU (Box 105.1). Endogenous sources are more common, however. Pathomechanisms of endogenous potassium accumulation such as tissue hypoxemia, specifically from skeletal muscle necrosis or red cell lysis, resorption of hematoma, or tumor lysis, often result in a dramatic shift of potassium from the intracellular to the extracellular space, with resultant life-threatening hyperkalemia.

BOX 105.1

Drugs Associated With Hyperkalemia by Pathomechanism

Increased Potassium Intake
- KCl
- Salt substitutes
- Blood transfusion
- Penicillin (K formulation)
- Rarely multivitamin preparations

Transmembrane Shifting
- Succinylcholine
- β-Blockade
- Digitalis intoxication
- Mannitol

Cellular Lysis
- Radiation
- Chemotherapy

Decreased Potassium Excretion
- NSAIDs
- COX-2 inhibitors
- ARBs, ACE inhibitors
- Heparin
- Ketoconazole
- Aldactone
- Triamterene
- Calcineurin inhibitors
- Trimethoprim
- Amiloride

ACE, Angiotensin-converting enzyme; *ARBs,* angiotensin receptor blockers; *COX-2,* cyclooxygenase-2; *KCl,* potassium chloride; *NSAIDs,* nonsteroidal antiinflammatory drugs.

Treatment of Hyperkalemia in Acute Renal Failure

Surprisingly, despite the dogmatic approach that has been advocated, actual evidence-based evaluation of treatment for life-threatening hyperkalemia is fairly scant. Review of the available literature reveals the woeful inadequacy of current knowledge about effective treatments for hyperkalemia.[7–9] In general, treatment of hyperkalemia is guided by three major tenets. Initially, antagonism of the membrane effects of the increased potassium should be facilitated with the administration of calcium and, potentially, the use of hypertonic sodium if the patient is notably hyponatremic in association with the hyperkalemia. Thereafter, the administration of glucose plus insulin and sodium bicarbonate, to induce shifting of potassium from the extracellular to the intracellular space, should be the next step. Finally, removal of the excess potassium must be facilitated by either renal or extrarenal mechanisms. Specifically, in diuretic-responsive states, use of diuretics is indicated. Among patients who are oliguric, cation exchange resins such as sodium polystyrene sulfonate (Kayexalate) or extracorporeal therapy with dialysis, or both, also is indicated. Fig. 105.1 shows recommended specific therapies for hyperkalemia. Evidence of efficacy of polystyrene sulfonate is modest at best. A retrospective case-controlled trial revealed a statistically significant but clinically minimal difference among hospitalized patients with mild hyperkalemia treated with polystyrene sulfonate versus conservative measures (0.14 mmol vs. controls).[10] Another retrospective analysis of AKI patients who received a dose of Kayexalate showed a 1-week average of 0.93 mmol/L decrease in potassium levels.[11]

Much evidence exists regarding the danger of colonic administration of cation exchange resins such as Kayexalate. Particularly among patients who are critically ill, colonic necrosis associated with use of this preparation has been reported widely.[12–16] Furthermore, the sodium content of Kayexalate is only 4 mEq/g. Because sodium ions exchange theoretically one for one with potassium ions, a 30-g dose of Kayexalate would maximally remove only 120 mEq of potassium. This degree of exchange does not occur physiologically in the gastrointestinal tract, however. The limited exchange becomes obvious on evaluation of the potassium concentration in the lumen of the bowel: at no point in the bowel lumen does the potassium concentration reach 120 mEq/L. Actual data reporting the degree of serum potassium decrease with the use of Kayexalate are nonexistent. Thus, particularly among critically ill patients, Kayexalate enemas are likely to be ineffective and are potentially dangerous.

New potassium binders have been introduced into the treatment armamentarium recently: zirconium cyclosilicate and patiromer. Although these agents have differing potentials for therapy in AKI-associated hyperkalemia, neither has yet been shown to be efficacious in the ICU.[17]

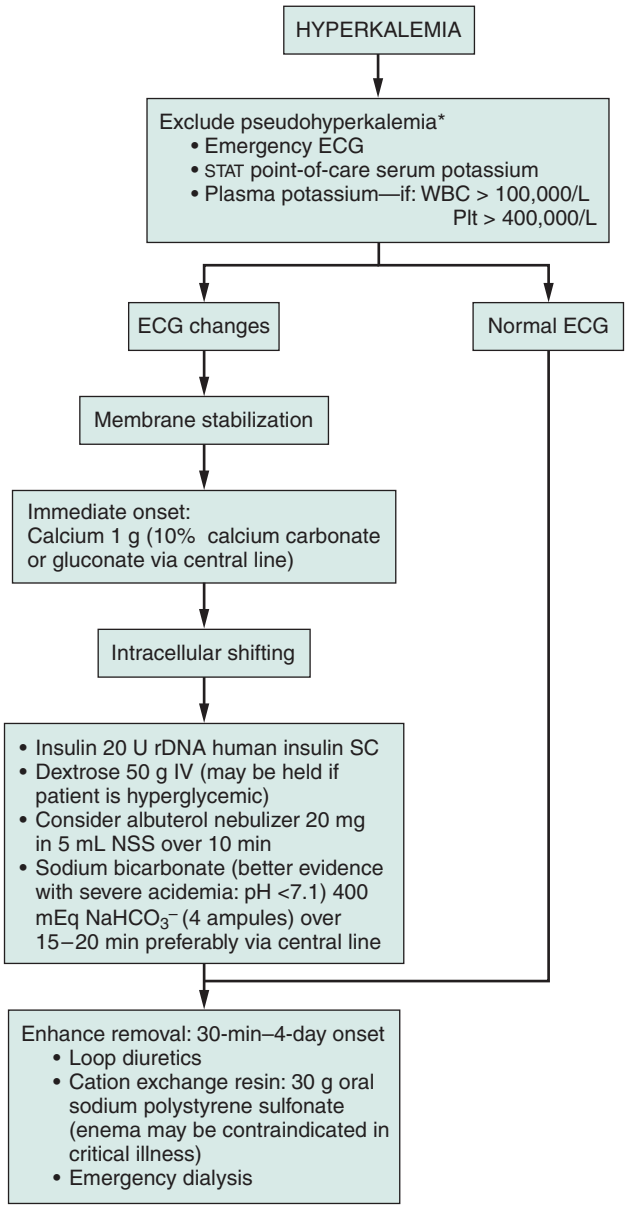

FIGURE 105.1 Algorithm for treatment of hyperkalemia. *ECG,* Electrocardiogram; *IV,* intravenously; *NSS,* normal saline solution; *Plt,* platelet count; *SC,* subcutaneously; *WBC,* white blood cell count.

Optimally, dialysis should be considered the primary modality for removal of potassium during an episode of acute renal failure and critical illness–associated hyperkalemia. Obviously, this protocol will require mobilization of resources for placement of intravenous access safely and expeditiously, and the availability of urgent dialysis. The most effective route of potassium removal for decreasing serum potassium in patients with acute renal failure is dialysis. Peritoneal dialysis, intermittent hemodialysis (IHD), and continuous venovenous hemodialysis (CVVHD) may be considered.

Peritoneal dialysis yields variable results with respect to control of emergent hyperkalemia, particularly among patients with acute renal failure. Complications arising from placement of a temporary peritoneal dialysis access are common. Reliable control of potassium with peritoneal dialysis is difficult to achieve. Removal of potassium with peritoneal dialysis is related to the relative size of the fluid-membrane contact surface area, as well as the blood flow to the peritoneal surface. These factors often are extraordinarily variable among critically ill patients. Peritoneal fluid generally has a zero potassium bath, so exchange should be conducted roughly on an hourly basis for life-threatening hyperkalemia. With the possible exception of pediatric patients and patients in whom intravenous access cannot be achieved, peritoneal dialysis has a very limited role in the management of acute renal failure–associated hyperkalemia in the ICU.

The preferred method for control of hyperkalemia in acute renal failure is use of blood-based dialytic techniques. Very little evidence is available, however, regarding the reliable decrement of plasma potassium with respect to dialysis potassium baths. Several concerns must be addressed with respect to rapid shifts in potassium among critically ill patients. One study evaluated the use of a 1-mEq/L potassium bath for 1 hour. A decrease in serum potassium by 1.34 mEq/L was noted.[9] Stepwise approach to management of acute hyperkalemia may be reasonable. In fact, a study performed in 1996 showed better tolerance from the perspective of decreasing ventricular dysrhythmias by means of a stepwise potassium modeling approach to dialytic potassium concentration.[18] In general, a reasonable recommendation would be a dialytic potassium concentration of approximately 2 to 3 mEq below the current plasma potassium (depending on the current situation) for approximately 1 hour, with stepwise hourly increases in dialysate potassium concentration as treatment progresses.

Continuous therapies (CVVHD, continuous venovenous hemodiafiltration) have been used effectively for treatment of hyperkalemia. In severe acute hyperkalemia, however, continuous therapies may not remove the potassium quickly enough. Therefore a combination approach of dialytic modalities has been advocated. An initial session of intermittent hemodialysis, followed by institution of continuous therapies, has been used with success in many centers, including our own. This approach may be particularly advantageous among critically ill patients with hypoperfusion and ongoing shock.

HYPONATREMIA

Patients with acute renal failure typically have hypervolemic hyponatremia. As in patients without renal failure, however, a systematic approach to diagnosis is recommended. A rational stepwise approach is shown in Fig. 105.2. Patients who clinically appear to be hypervolemic have accumulated an excess of sodium but proportionately more water. These patients most often are edematous and hyponatremic. Commonly, these patients are those suffering from severe congestive heart failure, hepatic dysfunction, and renal failure.

Fortunately, cellular mechanisms directed at rectifying the movement of water from the extracellular to the intracellular space are stimulated by hypo-osmolality—most often caused by hyponatremia. Initially, cells combat this swelling by exporting potassium, sodium, and chloride. The decrease in these "osmolytes" may be seen within minutes to hours after induction of hyponatremia.[19] At a certain point, however, the cells have exhausted their capacity to quickly decrease intracellular tonicity, and the exporting of other organic osmolytes is affected. These substances include glutamine, creatine, taurine, myoinositol, glutamine, and glycerol phosphorylcholine. Their export requires a carrier-mediated

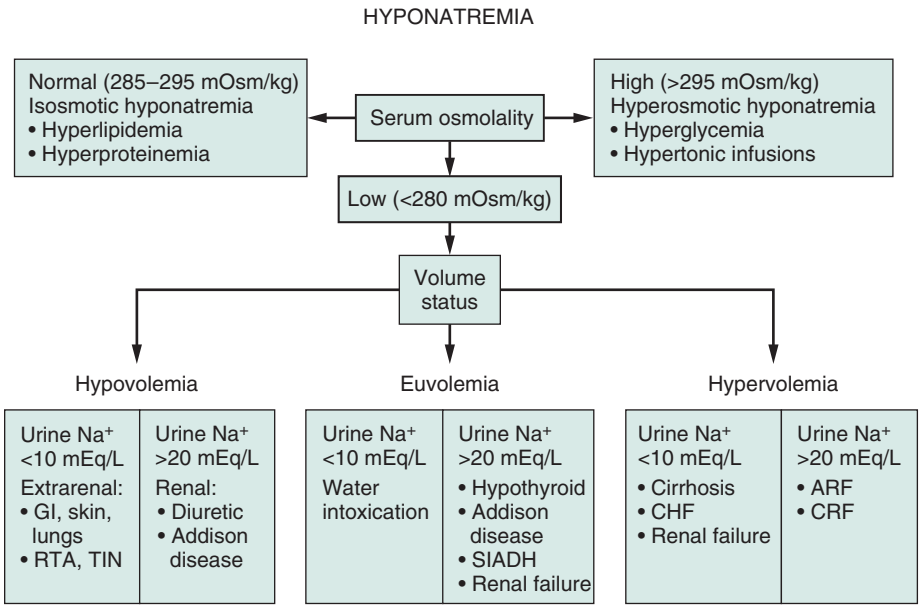

FIGURE 105.2 Algorithm for diagnosis of hyponatremia. *ARF,* Acute renal failure; *CHF,* congestive heart failure; *CRF,* chronic renal failure; *GI,* gastrointestinal; *RTA,* renal tubular acidosis; *SIADH,* syndrome of inappropriate antidiuretic hormone (secretion); *TIN,* tubulointerstitial necrosis.

process that can take days to weeks.[20] These acute and chronic processes lead to adaptation, whereby neuromuscular homeostasis is maintained and catastrophic herniation and decrease in cerebral blood flow is avoided. These processes—particularly the organic ion transport pathways—are reversed slowly, however. Therefore correction of hyponatremia must be accomplished with extraordinary care to avoid rapid increases in serum tonicity.

Cellular contraction resulting from osmotic movement of water from the intracellular to the extracellular space may result from overly rapid correction of hyponatremia. The theoretical sudden decrease in cellular volume may be a leading cause of mechanical shear stress, causing disruption of myelin and leading to the radiologically and apparent manifestations of central pontine myelinolysis. Often these lesions are not apparent for weeks after the hyponatremic event.[21,22] Certain patient groups seem to be at particular risk for brain damage and pontine myelinolysis: patients with hypokalemia, malnutrition, alcoholism, or cirrhosis of the liver; perhaps young menstruant female patients; and burn-injured patients.[23]

Correction and Therapy of Hyponatremia

A guiding tenet in therapy for hyponatremia beyond the laboratory assessment of osmolality and clinically effective tissue perfusion is that of symptomatic presentation. The severity of symptoms dictates the aggressiveness of therapy. Another guiding tenet must be the overarching goal of conservative correction: keeping the actual increase in serum sodium concentration to 12 mEq/L or less in 24 hours and approximately 20 mEq/L over 48 hours. These conservative correction rates are guided by retrospective clinical studies evaluating the occurrence of permanent neurologic sequelae among patients with severe hyponatremia.[24] In general, the more rapid the development and more severe the degree of hyponatremia, the more likely this condition is to prove symptomatic.

Renal failure rarely results in severe hyponatremia except in combination with exogenous water loading. Correction of the underlying pathophysiology usually helps correct the hyponatremia. Among patients with hypervolemic hypotonic hyponatremia with renal failure—a very common scenario in the ICU—often the sole option available may be extracorporeal therapy (dialysis or hemofiltration).

HYPERNATREMIA

Hypernatremia is less common in patients with acute renal failure, and hypervolemic hypernatremia most often is iatrogenic. It most commonly is induced by administration of sodium bicarbonate in intravenous fluids, often in the setting of resuscitation during critical illness with severe acidosis. Mineralocorticoid excess syndrome such as primary aldosteronism or exogenous hypercortisolism, in addition to congenital adrenal hyperplasia and Cushing syndrome, also should be considerations in the differential diagnosis. These scenarios share a common pathophysiologic sodium gain exceeding water retention. Renal dysfunction exacerbates these conditions and is a common covariable.

Patients with oligoanuric acute renal failure–associated hypernatremia with mental status changes may require urgent dialytic support. Standard intermittent hemodialysis may correct sodium too rapidly in these situations. Prescribing an increased dialysate sodium to target less dramatic changes in serum sodium level seems to be a reasonable approach. Alternatively, continuous renal replacement therapy (CRRT) may offer a less dramatic change in the rate of serum sodium correction and may be warranted among critically ill patients.[25]

DISORDERS OF CALCIUM AND PHOSPHATE BALANCE

Calcium and phosphate imbalances are extremely common in patients with acute renal failure. These disorders are discussed in detail in Chapter 58.

Acknowledgment

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Key Points

1. Hyperkalemia is the most life-threatening of the metabolic consequences of acute renal failure in the intensive care unit setting.
2. Hyponatremia and, less commonly, hypernatremia may occur in patients with acute renal failure. Proper diagnosis and management are essential to avoid serious complications.
3. Dialytic therapy frequently is required to correct severe potassium and sodium imbalances.
4. Hemodialysis may be more effective for hyperkalemia because it results in rapid potassium removal.
5. Continuous renal replacement therapy may be better suited to correcting sodium imbalances because it has a slower onset of effect and therefore is less likely to result in rapid shifts, which can be dangerous to the central nervous system.

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