CHAPTER 155

Correction of Water, Electrolyte, and Acid-Base Derangements by Hemodialysis and Derived Techniques

Blaithin A. McMahon, Tessa Novick, and Patrick T. Murray

OBJECTIVES

This chapter will:

1. Discuss the clinical implications of using different dialysate sodium concentrations when performing intermittent hemodialysis.
2. Describe how to safely manage patients with different degrees of hyponatremia and hypernatremia using intermittent hemodialysis.
3. Review the factors that influence potassium removal during intermittent hemodialysis.
4. Explain the effects of different dialysate calcium concentrations on patients' electrolyte abnormalities and hemodynamics.
5. Show how to adjust dialysate bicarbonate concentration to manage acid-base abnormalities and to understand its effects on serum calcium and potassium concentrations.

Acute kidney injury (AKI) frequently develops in the most critically ill patients in the intensive care unit (ICU), often as a component of multi-organ system failure. The constellations of electrolyte and acid-base abnormalities seen in these patients vary according to the clinical situation but are often highly complex. The introduction of hemodialysis can have profound effects on these metabolic perturbations, and the clinician must understand these mechanisms to optimize clinical outcomes of dialytic intervention and avoid further complications.

This chapter explores the use of intermittent hemodialysis (IHD) to correct electrolyte and acid-base abnormalities. A great deal of the literature concerning this topic comes from the end-stage renal disease (ESRD) population and must be extrapolated with caution; patients with ESRD have chronically developed compensatory physiologic responses to the uremic milieu, generally have better vascular access than patients with AKI, and are as a rule more hemodynamically stable than patients in the ICU. However, the data collected from studies on ESRD do provide valuable insight into the utility of IHD to correct acid-base and electrolyte abnormalities in patients with renal failure in the ICU. Patients with ESRD who are undergoing maintenance hemodialysis frequently are cared for in the ICU, and the presence of existing arteriovenous access (fistula or graft) is a major incentive to optimize and continue the use of intermittent dialysis in such patients whenever possible, even in the presence of low-dose vasoactive drug support, as opposed to placement of temporary dialysis access to switch to continuous renal replacement therapy (CRRT). Finally, IHD may be preferred over CRRT as the modality of choice in some cases, because it allows the clinician to remove small solutes such as potassium more rapidly and efficiently in acute life-threatening conditions.[1]

SODIUM ABNORMALITIES

Dysnatremias (hypo- and hypernatremia) are common in patients admitted to the ICU with prevalence approaching

20% to 30%.[2] Even mild degrees of hyponatremia and hypernatremia confer markedly increased risk for mortality and increased length of stay.[2] Sodium is the principal determinant of plasma and dialysate osmolality, and the use of IHD can affect dramatically a patient's osmotic homeostasis. As water flows from an area of lower osmolality to one of higher osmolality, the associated fluid shifts can affect hemodynamic stability adversely (when water moves from intravascular to tissue compartments), cerebral fluid and osmolyte homeostasis (when fluid shifts in either direction), or both. Sodium crosses hemodialysis membranes by means of diffusion or convection. Diffusion depends on the concentration gradient and the molecular weight of the solute, but not all ionized sodium is diffusible. The presence of negatively charged plasma proteins results in some cation retention to maintain electrical neutrality (the Donnan effect). However, the ionized sodium in the dialysate is completely available for diffusion, because there are no anionic proteins there. Because of this discrepancy, a diffusive gradient of zero can be achieved only by choosing an ionized sodium concentration in the dialysate of about 5 to 10 mEq/L less than the ionized sodium concentration in plasma water.[3,4] Other factors that may change the amount of sodium available for diffusion are dialysate temperature and pH, and the addition of other ions, such as carbonate, bicarbonate, and phosphate. In contrast, convective transport (ultrafiltration) of sodium occurs when plasma water is driven across the membrane by either a hydrostatic or an osmotic force.

The choice of dialysate sodium concentration depends on the goals to be achieved and has changed over the years.[5,6] In the past, a lower dialysate sodium concentration, typically less than 135 mEq/L, was used to limit interdialytic hypertension and thirst.[7] This approach, however, can be complicated by headaches, muscle cramps, nausea, and vomiting[4] and may play a role in the dialysis dysequilibrium syndrome.[8] The use of a dialysate sodium concentration below the serum sodium concentration results in fluid shifts from the extracellular compartment to the intracellular compartment, because diffusion lowers serum sodium and plasma osmolality.[7] Ultimately, the total water loss from the extracellular space exceeds the total water loss from the body. In contrast, the use of a dialysate with a higher sodium concentration than the serum sodium concentration causes water removal from intracellular and extracellular compartments and minimizes the effect of plasma volume loss.[6,7]

The mechanism by which higher dialysate sodium concentration maintains a greater proportion of plasma volume while accomplishing ultrafiltration is especially important in the context of AKI. Many patients with AKI are hypervolemic but are also hypotensive from cardiogenic or septic shock, and the ability to produce significant ultrafiltration while minimizing hemodynamic impact is an important tool in such cases. The improvement in hypertension control[9,10] and reduced thirst associated with lower dialysate sodium are optimal in the outpatient setting.[7] However, in the critically ill patient, thirst is less relevant, and hypotension may be detrimental. For this reason, the use of a dialysate sodium concentration of 140 to 145 mEq/L often is advised for acute dialysis,[6] and the same principle underlies the use of sodium modeling to prevent or manage intradialytic hypotension.

Hemodialysis of a patient with an abnormally low or elevated serum sodium concentration deserves special consideration. Dialysis is not used typically to treat these conditions but is often necessary in patients with AKI in whom dysnatremias have developed, or in critically ill patients with ESRD. The correct approach to acute dialysis of a patient with significant hyponatremia or hypernatremia depends on the severity and chronicity of the dysnatremia, and dialysis should never be initiated in such a patient without careful consideration of both factors. Hyponatremia, a common complication in the critically ill patient, is usually asymptomatic but can cause central nervous system manifestations, generally at serum sodium concentrations below 125 mEq/L. The correction of hyponatremia can be complicated by osmotic demyelination if the serum sodium concentration is raised rapidly in the setting of chronic hyponatremia (with associated cerebral accommodation to hypotonicity). Even in the symptomatically hyponatremic patient, it generally is believed that a targeted extent of correction should not exceed 8 to 10 mmol/L in the first 24 hours but may have a lower rate of correction (4-6 mmol/L in 24 hours) in select clinical situations, such as malnutrition, alcohol liver disease, and hypokalemia. Similarly, patients with severe, symptomatic hyponatremia should be treated with 3% saline given as 100-mL bolus(es) to raise the plasma sodium concentration rapidly by 4 to 6 mmol/L,[11] to achieve clinical improvement, followed by slower correction. In the setting of asymptomatic hyponatremia, there is no indication for acute correction, and the targeted rate of correction should not exceed 8 to 10 mmol/L/day.[11] During a typical average-efficiency, 4-hour hemodialysis session, the expected postdialysis serum sodium concentration is typically at the midpoint between the predialysis serum sodium concentration and the dialysate sodium concentration. Because the change in serum sodium generated with this IHD may be too rapid, it may become necessary to use a lower dialysate sodium concentration, shorter dialysis time, or a slower blood flow rate to dialyze the patient safely. Accordingly, more frequent dialysis may be necessary to achieve adequate clearance for azotemia control or hyperkalemia while safely correcting hyponatremia. If overcorrection occurs with hemodialysis, intravenous dextrose or free water administration may be required to restore the serum sodium to the desired target level.

A similar approach is necessary in the hypernatremic patient undergoing dialysis. In patients with elevated serum sodium levels that have developed suddenly (over the course of hours), rapid correction (1 mmol/L/hr) is recommended and is associated with minimal side effects. However, in the patient with hypernatremia of prolonged or unknown duration, an accumulation of organic solutes in the brain cells requires several days to dissipate. The maximal rate of correction in chronic hypernatremia should not exceed 0.5 mmol/L/hr, with a targeted drop in serum sodium concentration of up to 10 mmol/L/day.[12] As described previously, the use of a dialysate sodium concentration below the serum sodium concentration can be complicated by hemodynamic instability, as fluid shifts from the extracellular to the intracellular compartment and the plasma volume contracts. Therefore the use of a dialysate sodium concentration similar to that found in the serum, and slow correction of the hypernatremia with hypotonic intravenous fluids generally is recommended.

However, there are several published case reports describing the rapid correction of hypernatremia with hemodialysis. In one report, three patients with severe hypernatremia and volume overload were treated with low dialysate sodium concentrations (110 mEq/L), causing reductions in serum sodium of 19 to 34 mEq/L over the course of 3.5 to 4 hours.[13] Other reports have described the use of IHD, one with a dialysate sodium of 138 mEq/L in a hypovolemic hypernatremic patient who required daily 2-hour treatments,[14] and the other in burn patients with hypernatremic AKI.[15] Despite

the lack of neurologic complications seen in these selected patients, large changes in serum sodium concentrations are best avoided over the time span of IHD. Correction of severe hypernatremia with renal replacement therapy (RRT) is probably more safely achieved with less efficient, more titratable techniques, such as sustained low-efficiency daily dialysis (SLEDD) or continuous RRT.

POTASSIUM ABNORMALITIES

Hyperkalemia is a common and potentially fatal complication in critically ill patients with AKI. Regardless of the cause of the hyperkalemia, hemodialysis generally is recognized as the most rapid means of lowering the serum potassium concentration.[16] This is particularly important because the patient with AKI has not developed some of the protective measures of the patient with ESRD, such as chronically upregulated colonic potassium secretion, and often is subjected to conditions causing decreased cellular uptake of potassium, such as metabolic acidosis and catecholamines. The role of catecholamines is particularly complicated, because α-adrenergic receptor stimulation is known to cause potassium efflux from cells, whereas β-adrenergic receptor stimulation mediates cellular uptake of potassium.[17]

The rate of potassium removal with hemodialysis and the associated changes of serum potassium concentration have been the subject of many studies. The principal factors affecting these issues in the ESRD population include the pre-dialysis serum potassium concentration, the surface area of the dialyzer, the blood flow rate, the duration of treatment, type of dialysis access, and the dialysate potassium concentration.[17] An additional factor to consider in the less-stable patient is the level of potassium generation, because intracellular potassium is released into the serum. A variety of studies have evaluated patterns of potassium removal during hemodialysis (Fig. 155.1).[18–20] Mass removal of potassium is greatest in the first 60 minutes, which correlates with the greatest decrease in serum potassium concentration. The extent of potassium removal and the drop in its serum concentration are generally less impressive over the next 2 hours and plateau after 3 hours. The rate of potassium removal diminishes as the concentration gradient between serum and plasma equalibrates.

Potassium does not freely diffuse between the intracellular and extracellular compartments, and the amount removed from each compartment during hemodialysis depends on a number of factors. Several studies have shown that potassium elimination in dialysis occurs with little change in serum potassium during the fourth and subsequent hours of conventional hemodialysis (Fig. 155.2).[18,19,21] One study of nine patients undergoing dialysis for 5 hours with a dialysate potassium concentration of 1.5 mmol/L demonstrated that two thirds of extracellular potassium was removed during the first hour, and 15% was removed during the last 2 hours.[21] It has been estimated that 28% to 47% of the potassium dialyzed in a standard 4-hour treatment comes from the extracellular compartment.[17,22] These findings demonstrate the variability in the rates of potassium transport across the dialyzer and cell membranes. Thus potassium removal is difficult to predict and cannot be described adequately with a "single-pool" model.

Variability in potassium removal often is coupled with a significant "rebound" of serum potassium in the hours after dialysis, a phenomenon that has been well documented.[23] An average of 35% of the serum potassium concentration reduction achieved during dialysis is reversed within the first

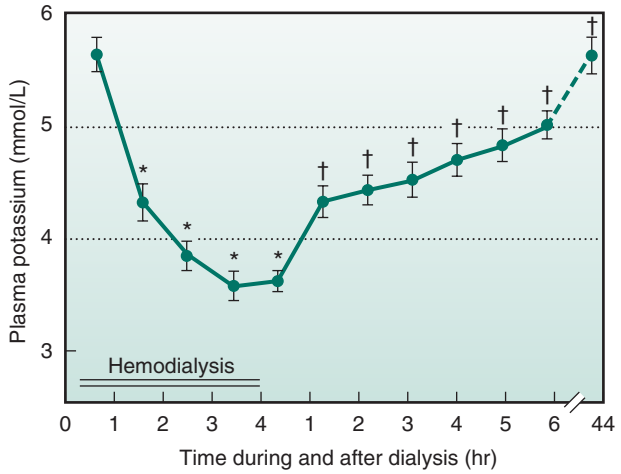

FIGURE 155.1 Changes in plasma potassium (mmol/L) during and up to 6 hours after hemodialysis. *, Significantly lower than predialysis value ($p < .001$); †, significantly higher than end-dialysis value ($p < .001$). (From Blumberg A, Roser HW, Zehnder C, Müller-Brand J. Plasma potassium in patients with terminal renal failure during and after haemodialysis: Relationship with dialytic potassium removal and total body potassium. *Nephrol Dial Transplant.* 1997;12:1629–1634.)

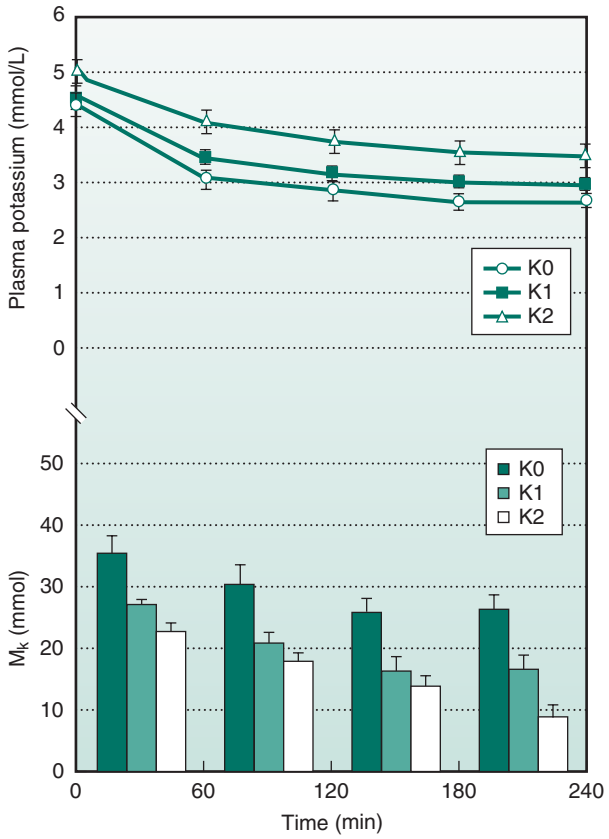

FIGURE 155.2 Plasma potassium concentrations *(top)* and potassium mass removed (M_K) *(bottom)* during standardized high-flux hemodialysis with potassium-free (K0), potassium 1 mmol/L (K1), and potassium 2 mmol/L (K2) dialysates. Potassium concentrations and M_K values were measured at 60-minute intervals. (From Zehnder C, Gutzwiller J-P, Huber A, et al. Low-potassium and glucose-free dialysis maintains urea but enhances potassium removal. *Nephrol Dial Transplant.* 2001;16:78–84.)

hour after dialysis, and a further 35% is reversed within 6 hours.[18,19,23,24] Although the extent of rebound is not entirely predictable, a close correlation between the predialysis and 6-hour postdialysis serum potassium concentrations has been described and accounts for one of the factors responsible for the high incidence of sudden cardiac death in the 12 hours after dialysis.[24,25] This finding should be considered in the patient who has severe hyperkalemia; a greater rebound should be expected after the treatment.[23–25] Unlike the patient with ESRD, the patient with AKI treated with conventional hemodialysis may require repeated courses of dialysis more often than thrice weekly to control refractory hyperkalemia.

The amount of potassium removed by a single hemodialysis session varies depending on the dialysate potassium concentration. Most studies have used dialysate baths with potassium concentrations ranging from 0 to 3 mmol/L.[18,19,22,26] Zehnder et al.[20] measured potassium removal in 12 patients with ESRD who underwent high-flux hemodialysis with a polysulfone filter using a blood flow rate of 300 mL/min and a dialysate flow rate of 500 mL/min over a 4-hour session. In these patients, potassium removal was 117.1 mmol ± 10.3 mmol with the zero-potassium bath and 63.3 ± 5.2 mmol with the 2 mmol/L dialysate. The greater potassium removal with low-potassium dialysate is tempered by the concern for intradialytic or early postdialytic hypokalemia and its complications.[26] There is conflicting evidence in the ESRD population regarding the association between lower dialysate potassium levels, ventricular arrhythmias, and mortality, and recommended dialysate potassium concentration varies according to monthly predialysis potassium level.[26,27] For this reason, zero-potassium bath concentrations should be avoided. The study by Basile et al. confirmed that the rate of potassium removal during dialysis is largely a function of the predialysis plasma potassium concentration, the higher the initial plasma concentration, the greater the gradient between plasma and dialysate, and therefore the greater the potassium removal.[27] However, there are no data on the impact of dialysate potassium in patients with AKI. Another factor that must be considered is the blood flow rate, which is typically lower with the use of temporary catheters in the setting of AKI. In a crossover prospective study reported by Gutzwiller et al., 13 patients with ESRD underwent dialysis using blood flow rates of 200, 250, and 300 mL/min. Potassium removal was significantly higher with the use of higher blood flow rates.[28] This finding provides further evidence that methods that improve solute clearance, such as higher blood flow rates and limiting of recirculation, should be expected to improve the efficacy of potassium removal. Furthermore, observations of SLEDD have shown significant declines in potassium levels over longer periods,[29] but these findings require further study and comparison with results in IHD.

Furthermore, several clinical situations can affect the transport of potassium between the intracellular and extracellular compartments and the extent of potassium removal.[30] A higher dialysate sodium concentration results in a higher serum sodium concentration, which causes a significant rise in serum potassium. Twelve patients were enrolled in a crossover trial to receive hemodialysis using a dialysate sodium concentration of 143 mmol/L or 138 mmol/L; the treatments using the higher sodium bath were associated with a greater rebound in potassium, which was statistically significant at 1 hour after dialysis.[31] The underlying mechanism is thought to be a solvent drag caused by the increased tonicity of the extracellular fluid, which inhibits the transfer of potassium into cells.

The presence of glucose in dialysate also influences potassium removal. Studies comparing dialysate glucose concentrations of 0 and 200 mg/dL have shown that the higher glucose bath is associated with less potassium removal but a similar decline in serum potassium concentration.[22] The higher dialysate glucose concentration results in higher serum glucose and insulin levels, which in turn cause the transport of potassium into the cells, lowering the serum potassium concentration. However, the corresponding decrease in serum potassium concentration results in a diminished potassium gradient between the serum and dialysate, impairing diffusive dialytic potassium clearance. Similarly, some of the methods used to lower serum potassium acutely in the patient with AKI act by shifting potassium into cells, decreasing the efficacy of dialytic potassium removal, and cause greater rebound levels in the following hours. For example, a study examining the effects of nebulized albuterol on potassium removal in seven patients with ESRD showed that the albuterol caused a substantial decrease in the magnitude of potassium removal by dialysis.[32]

Theoretically, intracellular potassium shifts induced by insulin or glucose therapy and, perhaps, sodium bicarbonate similarly could degrade the efficacy of dialytic potassium removal. In fact, acute administration of sodium bicarbonate can have paradoxical effects on serum potassium levels; the associated acute increase in osmolality actually shifts potassium out of tissue and raises serum potassium transiently. However, ultimately, alkalinization results in intracellular potassium shift, and this in turn may impair dialytic potassium removal.[24] One study that examined the effects of different dialysis bicarbonate concentrations, ranging from 27 to 39 mmol/L, during the hemodialysis of eight patients with ESRD found that the serum potassium diminished significantly more with the higher bicarbonate bath, with a difference seen in the first 15 minutes of treatment. However, the cumulative potassium removal was not significantly different among the different treatments, suggesting a large effect of intracellular potassium shift.[33] Similarly, for patients with hypokalemia, lower dialysate bicarbonate concentration (25 mmol/L) and higher potassium should be used.

ABNORMALITIES OF DIVALENT IONS

Calcium abnormalities are very common in the critically ill population. The diagnosis of hypocalcemia is complicated by limitations in the interpretation, which are principally the result of the effects of hypoalbuminemia and disorders of acid-base balance on the total calcium concentration. For this reason, we rely on measurements of ionized calcium to assess an individual's true serum calcium levels.[34]

Hypocalcemia is associated with AKI because of phosphate retention, impaired formation of 1,25-dihydroxycholecalciferol, and parathyroid hormone resistance.[35] Severe hypocalcemia, defined as iCa<1 mmol/L, independently predicts mortality in patients with AKI needing renal replacement therapy.[36–38] Therefore the effect of dialytic therapy on calcium homeostasis is critical in the ICU.

The diffusion of calcium during hemodialysis depends on the gradient between serum and dialysate calcium concentrations. Ultrafiltration (UF) is a critical component as well, especially in modalities using larger UF volumes with replacement fluid (hemofiltration and hemodiafiltration), because the calcium losses by convective transport can exceed the gain of calcium by diffusion.[30] Calcium mass balance studies have shown that in the normocalcemic patient undergoing long-term dialysis, a dialysate calcium

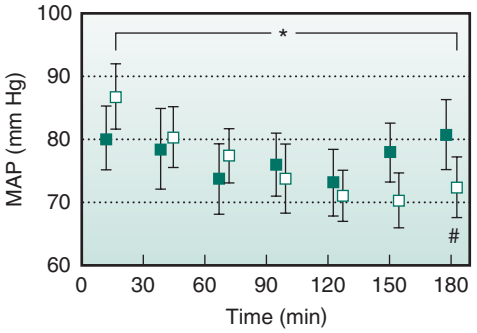

FIGURE 155.3 Mean arterial pressure (MAP) with 1.25 mmol/L dialysate calcium concentration *(open squares)* and 1.75 mmol/L dialysate calcium *(closed squares)* during 3 hours of hemodialysis. Measurements are given every 30 minutes. (From Van der Sande FM, Cheriex EC, van Kuijk WHM, Leunissen KML. Effect of dialysate calcium concentrations on intradialytic blood pressure course in cardiac-compromised patients. *Am J Kidney Dis.* 1998;32:125–131.)

concentration of 2.5 mEq/L is associated with a negative calcium balance during treatment and a concentration of 3.5 mEq/L is associated with a gain of calcium balance.[30] Given these findings, the standard dialysate calcium concentration for chronic hemodialysis in many institutions has been reduced to 2.5 mEq/L to decrease the potential long-term impact of dialysate-derived calcium on vascular calcification in atherosclerotic patients and to avoid hypercalcemic suppression of parathyroid hormone as a potential contributor to adynamic bone disease.[30,39–41] However, that approach is not recommended in the setting of AKI, particularly in the hemodynamically compromised patient. Serum ionized calcium concentration during dialysis has been shown to correlate directly with myocardial contractility and vascular reactivity.[42] Similarly, small studies comparing dialysate calcium concentrations of 2.5 mEq/L and 3.5 mEq/L have found significantly lower blood pressures in patients dialyzed with the lower calcium concentration, with more clinically relevant differences in patients who have a greater degree of heart dysfunction.[43,44] (Fig. 155.3). Dialysate calcium concentrations of 2.5 mEq/L also have been associated with an increased QT dispersion, increasing risk for ventricular arrhythmias.[30,33] On the basis of these studies, a dialysate calcium concentration of 3.0 mEq/L or greater generally is recommended for the patient with AKI. This is especially true in the patient with combined hypocalcemia and metabolic acidosis; the alkalinizing effect of acute dialysis initiation in such a patient may precipitate tetany by lowering serum ionized calcium concentration. Accordingly, the use of a lower-concentration bicarbonate bath (25 mEq/L) also is recommended for initial dialytic therapy of severely hypocalcemic patients with AKI, even if they have concomitant metabolic acidosis, to decrease the potential for precipitating this complication. Challenges in treating these patients can persist despite modifications in bicarbonate bath concentrations. A retrospective study examining 44 patients who received IHD with a dialysate calcium concentration of 3.5 mEq/L found that there was no change in the proportion of patients with calcium abnormalities, which remained near 50% of the sample, although hypercalcemia made up 36.1% of these abnormalities after treatment.[45]

Hypercalcemia is encountered less commonly in the ICU but can occur in a patient with AKI, especially in the setting of a malignancy. Hemodialysis is indicated in the presence of severe symptoms refractory to medical therapy or when the presence of renal or cardiac failure prevents the administration of large volumes of intravenous fluids to lower calcium levels. In these cases, calcium removal can be achieved with low dialysate calcium concentrations (such as 1 to 2 mEq/L), but in general, calcium-free hemodialysis should be avoided. In one retrospective analysis of 33 patients undergoing calcium-free hemodialysis for management of severe hypercalcemia, adverse cardiovascular effects occurred in 43% of patients, and its use should be restricted to patients with severe clinical symptoms or advanced renal impairment.[46]

Hyperphosphatemia in critically ill patients with AKI is not uncommon. When tissue breakdown results in AKI and severe hyperphosphatemia, such as in tumor lysis syndrome or rhabdomyolysis, hypocalcemia may be life threatening, and acute dialysis (intermittent or continuous) is required to safely raise serum calcium concentration while lowering serum phosphate concentration. Similar to the rebound seen in potassium levels after hemodialysis, there is a postdialysis hyperphosphatemia due to release of phosphate from bones. When serum phosphate levels were drawn from six patients with ESRD every 30 minutes during their treatments, a nadir was reached at 30 to 150 minutes, but phosphate levels 4 hours after dialysis did not differ significantly from the predialysis levels.[47,48]

In patients with ESRD, who generally are able to achieve higher blood flow rates with superior hemodialysis access, only approximately 900 mg of phosphorus is removed with each treatment.[49] Improved clearance has been demonstrated with 8-hour nocturnal hemodialysis, suggesting that longer periods of treatment with higher solute clearance may be useful in patients with greatly elevated phosphate concentrations.[50] A similar improvement was noted in a series of SLEDD therapies performed over 12 hours. In this study of 145 treatments, there was a drop in average serum phosphate concentration from 5.9 ± 2.1 mg/dL before treatment to 3.4 ± 1.0 mg/dL 1 hour after treatment was completed.[29] There is no significant difference in the prevalence of hypophosphatemia in patients undergoing different durations of extended daily hemodialysis of 10 versus 6 hours.[51]

Continuous RRT also effectively lowers serum phosphorus levels, typically requiring supplementation within 1 to 2 days of initiation.[52] This modality may be preferred for control of severe hyperphosphatemia in patients with tumor lysis syndrome or other tissue breakdown and may be combined with an initial hemodialysis therapy to lower the serum potassium concentration rapidly if severe hyperkalemia is also present.

AKI in malnourished patients, or patients who are severely catabolic with prolonged ICU stays, can be accompanied by hypophosphatemia. In these cases, it is especially important to provide oral or intravenous phosphorous supplementation before initiating hemodialysis to prevent worsening of the hypophosphatemia with resultant multi-organ dysfunction. Methods of using phosphate-enriched hemodialysate for patients with normal phosphate levels who have acute overdose of dialyzable intoxicants requiring prolonged dialysis (e.g., lithium, ethylene glycol, methanol) also have been described; the dialysate can be prepared by adding sodium phosphate salts to liquid concentrates of a bicarbonate-based dialysate generating system.[50]

Magnesium has significant effects on the stability of excitable membranes and hemodynamic stability. Although hypomagnesemia increases risk for cardiac arrhythmias, higher levels of magnesium may be detrimental because the substance acts as a vasodilator and can contribute to hypotension in the unstable patient.[39,53] The kidneys are the dominant site of magnesium excretion, which typically measures 100 mg a day, so AKI often is accompanied by

hypermagnesemia. Hypomagnesemia is associated positively with intradialytic hypotension.[54,55] Dialysates with lower magnesium concentrations are available, but the use of zero-magnesium dialysate often is complicated by severe muscle cramps. Interestingly, one study showed that when a dialysate solution contains low magnesium (0.5 mEq/L) and a calcium concentration of 2.5 mEq/L, hypocalcemia and hypomagnesemia can be induced, causing a greater degree of intradialytic hypotension.[56] The changes in calcium and magnesium are more dramatic when convective clearance becomes dominant, such as with the higher ultrafiltration volumes used in hemofiltration and hemodiafiltration.

ACID-BASE ABNORMALITIES

Hemodialysis plays an important role in management of acid-base abnormalities associated with AKI. Normally, a decrease in renal function causes an accumulation of acids and a corresponding decline in serum bicarbonate levels, resulting in metabolic acidosis.[57] In the critically ill patient, however, the acid-base abnormalities can be highly complex and less predictable. In the context of metabolic acidosis, hemodialysis provides a buffer source that moves by diffusion into the blood to replace the bicarbonate titrated by the excess acid. Historically, this buffer source has been bicarbonate or acetate, but acetate no longer is used routinely as an alkali source in patients with AKI.[58] Although sodium acetate undergoes oxidation to become bicarbonate in the blood, the delivery of acetate has been shown to exceed the body's capacity to metabolize it. Acetate acts as a direct peripheral vasodilator and myocardial depressant, and its accumulation can have severe clinical ramifications in the critical care setting. Several factors play a role in contributing to this complication, including those related to the influx of acetate from the dialysate to the patient, such as shorter treatment time, higher efficiency dialyzers, and higher blood flow rates, and those related to the acetate metabolism, such as a reduction in muscle mass, malnutrition, increased age, hepatic dysfunction, and female gender.[59,60]

Bicarbonate solutions are prepared separately from the remainder of the dialysate because of the low solubility of sodium bicarbonate and its incompatibility in combined solution with calcium. The two components (bicarbonate and calcium-containing) then are combined in a given proportion by the dialysis machine, offering a wide range of final bicarbonate concentrations depending on the clinical situation. In the majority of patients with kidney failure, the dialysate bicarbonate concentration is kept at 32 to 38 mmol/L to maintain a more physiologic pH.[39,46] The correction of acid-base disturbances with IHD occurs through the mechanism of diffusion, which is well suited for clearing the small solutes that factor into the calculation of pH and the strong ion difference (SID). The performance of hemodialysis is one of many factors in determining a patient's serum bicarbonate concentration and depends on the dialysate composition, type of RRT, the duration of the treatment, the membrane used, blood and dialysate flow rates, and the extent of ultrafiltration.[58,61] The mechanism of convection plays a larger role with other forms of intermittent RRT, such as hemofiltration and hemodiafiltration. The same solutes that determine pH and SID easily cross the membrane with the ultrafiltration. As a result, maintenance of the serum bicarbonate concentration depends on the contents of the replacement fluid.[62] The administration of bicarbonate through hemodialysis is part of a larger discussion regarding the role of bicarbonate in the treatment of metabolic and respiratory acidoses. It has been argued that alkali therapy can be used to maintain a more physiologic pH in the patient with severe acidosis to prevent or reverse the detrimental consequences of severe acidemia.[63] Routine use of bicarbonate for treatment of severe acidemia and lactic acidosis in the critically ill is a controversial subject, and current opinion does not favor routine use of bicarbonates.[64–66]

Reasons for the absence of clear advantage from bicarbonate administration include increased plasma $PaCO_2$, hyperosmolality, hypernatremia, volume overload, and pH overcorrection resulting in metabolic alkalosis. Additional risks of sodium bicarbonate administration include reduction of ionized calcium, which, in turn, decreases cardiac output, and cellular swelling and dysfunction resulting from acceleration of cellular influx of sodium and calcium in response to worsening intracellular acidosis.[64,67] However, much of the risk surrounding bicarbonate administration is centered around intravenous bicarbonate use, and not with bicarbonate buffering seen during hemodialysis, a setting in which risks of hypernatremia, hyperosmolality, and volume overload are regulated.

Hemodialysis is often necessary in patients with severe acidemia who have a respiratory acidosis that cannot be metabolically compensated for by the injured kidneys. In these cases, the use of a higher bicarbonate concentration on hemodialysis is recommended to maintain a more physiologic pH and provide more comprehensive renal support.

The advent of hybrid therapies, such as SLEDD and sustained low-efficiency daily diafiltration (SLEDDF), has changed the management of critically ill patients in many centers. Specific information related to handling of the acid-base balance using these therapies still is being acquired, but previous studies have shown a general increase in serum bicarbonate after treatment. In a study of 37 patients who underwent SLEDD using a dialysate flow rate of 100 mL/min, a blood flow rate of 200 mL/min, and a dialysate bicarbonate concentration of 35 mmol/L over 12 hours, the average serum bicarbonate level after treatment was 24.4 ± 3.2 mmol/L.[29] A study of 56 treatments using sustained low-efficiency daily diafiltration in 24 critically ill patients with similar flow rates over a span of 8 hours using a dialysate bicarbonate concentration of 26 mmol/L resulted in an average serum bicarbonate level of 23.3 ± 2.7 mmol/L after treatment.[68]

CONCLUSION

IHD continues to play an important role in the management of critically ill patients with AKI. Many of the electrolyte and acid-base disturbances present in these individuals can be corrected with proper management and an understanding of the capabilities and limitations of hemodialysis and other renal replacement techniques. Some critical electrolyte abnormalities are best corrected rapidly with acute hemodialysis, particularly severe hyperkalemia. Other abnormalities, however, such as symptomatic hyponatremia with severe renal failure, are probably better managed with slower, more titratable techniques such as CRRT. A combination approach using IHD followed by CRRT to prevent rebound elevation of serum potassium and phosphorus with recurrent acidosis is probably optimal for patients with tissue necrosis or some intoxications, such as with lithium. Despite the growing range of renal replacement modality options, IHD remains an essential option for RRT in the ICU setting.

Key Points

1. A higher dialysate sodium concentration, 140 to 145 mEq/L, typically is used in the setting of acute kidney injury to improve hemodynamic stability.
2. A primary goal of intermittent hemodialysis should be to limit dramatic changes in the serum sodium concentration, especially in the setting of chronic hyponatremia.
3. Potassium removal by hemodialysis and its subsequent rebound are subject to several factors, including the sodium and glucose content of the dialysate.
4. The bicarbonate concentration of dialysate can be manipulated at the time of hemodialysis to control the delivery of alkali to the patient with acid-base abnormalities.
5. The choice of calcium and magnesium concentrations used in dialysate can have clinical implications for the hemodynamically unstable patient.

Key References

2. Rosner MH, Ronco C. Dysnatremias in the intensive care unit. *Contrib Nephrol.* 2010;165:292-298.
6. Mc Causland FR, Waikar SS. Optimal dialysate sodium-what is the evidence? *Semin Dial.* 2014;27(2):128-134.
11. Verbalis JG, Goldsmith SR, Greenberg A, et al. Diagnosis, evaluation, and treatment of hyponatremia: expert panel recommendations. *Am J Med.* 2013;126(10 suppl 1):S1-S42.
24. Hung AM, Hakim RM. Dialysate and serum potassium in hemodialysis. *Am J Kidney Dis.* 2015;66(1):125-132.
37. Steele T, Kolamunnage-Dona R, Downey C, et al. Assessment and clinical course of hypocalcemia in critical illness. *Crit Care.* 2013;17(3):R106.
57. Marano M, Marano S, Gennari FJ. Beyond bicarbonate: complete acid-base assessment in patients receiving intermittent hemodialysis. *Nephrol Dial Transplant.* 2016.
64. Velissaris D, Karamouzos V, Ktenopoulos N, et al. The use of sodium bicarbonate in the treatment of acidosis in sepsis: A literature update on a long term debate. *Crit Care Res Pract.* 2015;2015:605830.

A complete reference list can be found online at ExpertConsult.com

References

1. Vanholder R, Van Biesen W, Hoste E, et al. Pro/con debate: continuous versus intermittent dialysis for acute kidney injury: a never-ending story yet approaching the finish? *Crit Care*. 2011;15(1):204.
2. Rosner MH, Ronco C. Dysnatremias in the intensive care unit. *Contrib Nephrol*. 2010;165:292-298.
3. Locatelli F, Ponti R, Pedrini L, et al. Sodium kinetics and dialysis performances. *Contrib Nephrol*. 1989;70:260-266.
4. Flanigan MJ. Role of sodium in hemodialysis. *Kidney Int Suppl*. 2000;76:S72-S78.
5. Van Stone JC, Bauer J, Carey J. The effect of dialysate sodium concentration on body fluid distribution during hemodialysis. *Trans Am Soc Artif Intern Organs*. 1980;26:383-386.
6. Mc Causland FR, Waikar SS. Optimal dialysate sodium-what is the evidence? *Semin Dial*. 2014;27(2):128-134.
7. Munoz Mendoza J, Arramreddy R, Schiller B. Dialysate Sodium: Choosing the Optimal Hemodialysis Bath. *Am J Kidney Dis*. 2015;66(4):710-720.
8. Port FK, Johnson WJ, Klass DW. Prevention of dialysis disequilibrium syndrome by use of high sodium concentration in the dialysate. *Kidney Int*. 1973;3(5):327-333.
9. Inrig JK, Molina C, D'Silva K, et al. Effect of low versus high dialysate sodium concentration on blood pressure and endothelial-derived vasoregulators during hemodialysis: a randomized crossover study. *Am J Kidney Dis*. 2015;65(3):464-473.
10. Shah A, Davenport A. Does a reduction in dialysate sodium improve blood pressure control in haemodialysis patients? *Nephrology (Carlton)*. 2012;17(4):358-363.
11. Verbalis JG, Goldsmith SR, Greenberg A, et al. Diagnosis, evaluation, and treatment of hyponatremia: expert panel recommendations. *Am J Med*. 2013;126(10 suppl 1):S1-S42.
12. Adrogue HJ, Madias NE. Hypernatremia. *N Engl J Med*. 2000;342(20):1493-1499.
13. Pazmino PA, Pazmino BP. Treatment of acute hypernatremia with hemodialysis. *Am J Nephrol*. 1993;13(4):260-265.
14. Yang CW, Kim YS, Park IS, et al. Treatment of severe acute hypernatremia and renal failure by hemodialysis. *Nephron*. 1995;70(3):372-373.
15. Chai J, Diao L, Sheng Z, et al. Heparin-free hemodialysis in the treatment of hypernatremia in severely burned patients. *Burns*. 2000;26(7):634-637.
16. Lameire N, Van Biesen W, Vanholder R, et al. The place of intermittent hemodialysis in the treatment of acute renal failure in the ICU patient. *Kidney Int Suppl*. 1998;66:S110-S119.
17. Ahmed J, Weisberg LS. Hyperkalemia in dialysis patients. *Semin Dial*. 2001;14(5):348-356.
18. Feig PU, Shook A, Sterns RH. Effect of potassium removal during hemodialysis on the plasma potassium concentration. *Nephron*. 1981;27(1):25-30.
19. Blumberg A, Roser HW, Zehnder C, et al. Plasma potassium in patients with terminal renal failure during and after haemodialysis; relationship with dialytic potassium removal and total body potassium. *Nephrol Dial Transplant*. 1997;12(8):1629-1634.
20. Zehnder C, Gutzwiller JP, Huber A, et al. Low-potassium and glucose-free dialysis maintains urea but enhances potassium removal. *Nephrol Dial Transplant*. 2001;16(1):78-84.
21. Williams AJ, Barnes JN, Cunningham J, et al. Effect of dialysate buffer on potassium removal during haemodialysis. *Proc Eur Dial Transplant Assoc Eur Ren Assoc*. 1985;21:209-214.
22. Ward RA, Wathen RL, Williams TE, et al. Hemodialysate composition and intradialytic metabolic, acid-base and potassium changes. *Kidney Int*. 1987;32(1):129-135.
23. Pani A, Floris M, Rosner MH, et al. Hyperkalemia in hemodialysis patients. *Semin Dial*. 2014;27(6):571-576.
24. Hung AM, Hakim RM. Dialysate and serum potassium in hemodialysis. *Am J Kidney Dis*. 2015;66(1):125-132.
25. Genovesi S, Valsecchi MG, Rossi E, et al. Sudden death and associated factors in a historical cohort of chronic haemodialysis patients. *Nephrol Dial Transplant*. 2009;24(8):2529-2536.
26. Abuelo JG. Low dialysate potassium concentration: an overrated risk factor for cardiac arrhythmia? *Semin Dial*. 2015;28(3):266-275.
27. Basile C, Libutti P, Lisi P, et al. Ranking of factors determining potassium mass balance in bicarbonate haemodialysis. *Nephrol Dial Transplant*. 2015;30(3):505-513.
28. Gutzwiller JP, Schneditz D, Huber AR, et al. Increasing blood flow increases kt/V(urea) and potassium removal but fails to improve phosphate removal. *Clin Nephrol*. 2003;59(2):130-136.
29. Marshall MR, Golper TA, Shaver MJ, et al. Chatoth DK. Sustained low-efficiency dialysis for critically ill patients requiring renal replacement therapy. *Kidney Int*. 2001;60(2):777-785.
30. Basile C, Lomonte C. A neglected issue in dialysis practice: haemodialysate. *Clin Kidney J*. 2015;8(4):393-399.
31. De Nicola L, Bellizzi V, Minutolo R, et al. Effect of dialysate sodium concentration on interdialytic increase of potassium. *J Am Soc Nephrol*. 2000;11(12):2337-2343.
32. Allon M, Shanklin N. Effect of albuterol treatment on subsequent dialytic potassium removal. *Am J Kidney Dis*. 1995;26(4):607-613.
33. Heguilen RM, Sciurano C, Bellusci AD, et al. The faster potassium-lowering effect of high dialysate bicarbonate concentrations in chronic haemodialysis patients. *Nephrol Dial Transplant*. 2005;20(3):591-597.
34. Kelly A, Levine MA. Hypocalcemia in the critically ill patient. *J Intensive Care Med*. 2013;28(3):166-177.
35. Zaloga GP. Hypocalcemia in critically ill patients. *Crit Care Med*. 1992;20(2):251-262.
36. Afshinnia F, Belanger K, Palevsky PM, et al. Effect of ionized serum calcium on outcomes in acute kidney injury needing renal replacement therapy: secondary analysis of the acute renal failure trial network study. *Ren Fail*. 2013;35(10):1310-1318.
37. Steele T, Kolamunnage-Dona R, Downey C, et al. Assessment and clinical course of hypocalcemia in critical illness. *Crit Care*. 2013;17(3):R106.
38. Egi M, Kim I, Nichol A, et al. Ionized calcium concentration and outcome in critical illness. *Crit Care Med*. 2011;39(2):314-321.
39. Locatelli F, La Milia V, Violo L, et al. Optimizing haemodialysate composition. *Clin Kidney J*. 2015;8(5):580-589.
40. Langote A, Ahearn M, Zimmerman D. Dialysate Calcium Concentration, Mineral Metabolism Disorders, and Cardiovascular Disease: Deciding the Hemodialysis Bath. *Am J Kidney Dis*. 2015;66(2):348-358.
41. Gotch FA, Kotanko P, Thijssen S, et al. The KDIGO guideline for dialysate calcium will result in an increased incidence of calcium accumulation in hemodialysis patients. *Kidney Int*. 2010;78(4):343-350.
42. Fellner SK, Lang RM, Neumann A, et al. Physiological mechanisms for calcium-induced changes in systemic arterial pressure in stable dialysis patients. *Hypertension*. 1989;13(3):213-218.
43. van Kuijk WH, Mulder AW, Peels CH, et al. Influence of changes in ionized calcium on cardiovascular reactivity during hemodialysis. *Clin Nephrol*. 1997;47(3):190-196.
44. van der Sande FM, Cheriex EC, van Kuijk WH, et al. Effect of dialysate calcium concentrations on intradialytic blood pressure course in cardiac-compromised patients. *Am J Kidney Dis*. 1998;32(1):125-131.
45. Tan HK, Bellomo R, M'Pisi DA, et al. Ionized serum calcium levels during acute renal failure: intermittent hemodialysis vs. Continuous hemodiafiltration. *Ren Fail*. 2002;24(1):19-27.
46. Camus C, Charasse C, Jouannic-Montier I, et al. Calcium free hemodialysis: experience in the treatment of 33 patients with severe hypercalcemia. *Intensive Care Med*. 1996;22(2):116-121.
47. DeSoi CA, Umans JG. Phosphate kinetics during high-flux hemodialysis. *J Am Soc Nephrol*. 1993;4(5):1214-1218.
48. Minutolo R, Bellizzi V, Cioffi M, et al. Postdialytic rebound of serum phosphorus: pathogenetic and clinical insights. *J Am Soc Nephrol*. 2002;13(4):1046-1054.
49. Coladonato JA. Control of hyperphosphatemia among patients with ESRD. *J Am Soc Nephrol*. 2005;16(suppl 2):S107-S114.
50. Mucsi I, Hercz G, Uldall R, et al. Control of serum phosphate without any phosphate binders in patients treated with nocturnal hemodialysis. *Kidney Int*. 1998;53(5):1399-1404.
51. Albino BB, Balbi AL, Abrao JM, et al. Dialysis complications in acute kidney injury patients treated with prolonged intermittent renal replacement therapy sessions lasting 10 versus 6 hours: results of a randomized clinical trial. *Artif Organs*. 2015;39(5):423-431.

52. Chua HR, Baldwin I, Ho L, et al. Biochemical effects of phosphate-containing replacement fluid for continuous venovenous hemofiltration. *Blood Purif*. 2012;34(3-4):306-312.
53. Zafar MS, Wani JI, Karim R, et al. Significance of serum magnesium levels in critically ill-patients. *Int J Appl Basic Med Res*. 2014;4(1):34-37.
54. Elsharkawy MM, Youssef AM, Zayoon MY. Intradialytic changes of serum magnesium and their relation to hypotensive episodes in hemodialysis patients on different dialysates. *Hemodial Int*. 2006;10(suppl 2):S16-S23.
55. Pakfetrat M, Roozbeh Shahroodi J, Malekmakan L, et al. Is there an association between intradialytic hypotension and serum magnesium changes? *Hemodial Int*. 2010;14(4):492-497.
56. Kyriazis J, Kalogeropoulou K, Bilirakis L, et al. Dialysate magnesium level and blood pressure. *Kidney Int*. 2004;66(3):1221-1231.
57. Marano M, Marano S, Gennari FJ. Beyond bicarbonate: complete acid-base assessment in patients receiving intermittent hemodialysis. *Nephrol Dial Transplant*. 2016.
58. Claure-Del Granado R, Claure R, Bouchard J. Acid-base and electrolyte abnormalities during renal support for acute kidney injury: recognition and management. *Blood Purif*. 2012;34(2): 186-193.
59. Diamond SM, Henrich WL. Acetate dialysate versus bicarbonate dialysate: a continuing controversy. *Am J Kidney Dis*. 1987;9(1):3-11.
60. Gennari FJ. Acid-base balance in dialysis patients. *Semin Dial*. 2000;13(4):235-239.
61. Feriani M. Acid-base homeostasis with the high convective dialysis treatments. *Nephrol Dial Transplant*. 2003;18(suppl 7):vii26-vii30, discussion vii56-7.
62. Fall P, Szerlip HM. Continuous renal replacement therapy: cause and treatment of electrolyte complications. *Semin Dial*. 2010;23(6):581-585.
63. Adrogue HJ, Madias NE. Management of life-threatening acid-base disorders. First of two parts. *N Engl J Med*. 1998; 338(1):26-34.
64. Velissaris D, Karamouzos V, Ktenopoulos N, et al. The Use of Sodium Bicarbonate in the Treatment of Acidosis in Sepsis: A Literature Update on a Long Term Debate. *Crit Care Res Pract*. 2015;2015:605830.
65. Cuhaci B, Lee J, Ahmed Z. Sodium bicarbonate controversy in lactic acidosis. *Chest*. 2000;118(3):882-884.
66. Forsythe SM, Schmidt GA. Sodium bicarbonate for the treatment of lactic acidosis. *Chest*. 2000;117(1):260-267.
67. Claure-Del Granado R, Bouchard J. Acid-base and electrolyte abnormalities during renal support for acute kidney injury: recognition and management. *Blood Purif*. 2012;34(2):186-193.
68. Marshall MR, Ma T, Galler D, et al. Sustained low-efficiency daily diafiltration (SLEDD-f) for critically ill patients requiring renal replacement therapy: towards an adequate therapy. *Nephrol Dial Transplant*. 2004;19(4):877-884.