

Dialysate Composition in Hemodialysis and Peritoneal Dialysis

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The goal of dialysis for patients with chronic renal failure is to restore the composition of the body's fluid environment toward normal. This is accomplished principally by formulating a dialysate whose constituent concentrations are set to approximate normal values in the body. Over time, by diffusional transfer along favorable concentration gradients, the concentrations of solutes that were initially increased or decreased tend to be corrected. When an abnormal electrolyte concentration poses immediate danger, the dialysate concentration of that electrolyte can be set at a nonphysiologic level to achieve a more rapid correction. On a more chronic basis the composition of the dialysate can be individually adjusted in order to meet the specific needs of each patient.

Dialysate Composition for Hemodialysis

In the early days of hemodialysis, the dialysate sodium concentration was deliberately set low to avoid problems of chronic volume overload such as hypertension and heart failure. As volume removal became more rapid because of shorter dialysis times, symptomatic hypotension emerged as a common and often disabling problem during dialysis. It soon became apparent that changes in the serum sodium concentration—and more specifically changes in serum osmolality—were contributing to the development of this hemodynamic instability. A decline in plasma osmolality during regular hemodialysis favors a

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fluid shift from the extracellular space to the intracellular space, thus exacerbating the volume-depleting effects of dialysis. With the advent of high-clearance dialyzers and more efficient dialysis techniques, this decline in plasma osmolality becomes more apparent, as solute is removed more rapidly.

Use of dialysate of low sodium concentration would tend further to enhance the intracellular shift of fluid, as plasma tends to become

even more hyposmolar consequent to the movement of sodium from

plasma to dialysate. The use of a higher sodium concentration dialysate (>140 mEq/L) has been among the most efficacious and best tolerated therapies for episodic hypotension [1–3].

The high sodium concentration prevents a marked decline in the plasma osmolality during dialysis, thus protecting the extracellular volume by minimizing osmotic fluid loss into the cells.

In the early 1960s acetate became the standard dialysate buffer for correcting uremic acidosis and offsetting the diffusive losses of bicarbonate during hemodialysis. Over the next several years reports began to accumulate that linked routine use of acetate with cardiovascular instability and hypotension during dialysis. As a result, dialysate containing bicarbonate began to re-emerge as the principal dialysate buffer, especially as advances in biotechnology made bicarbonate dialysate less expensive and less cumbersome to use. For the most part, the bicarbonate concentration used consistently in most dialysis centers is 35 mmol/L. Emphasis is now being placed on individually adjusting the dialysate bicarbonate concentration so as to maintain the predialysis tCO₂ concentration above 23 mmol/L [12–16]. Increasing evidence suggests that correction of chronic acidosis is of clinical benefit in terms of bone metabolism and nutrition.

Dialysis assumes a major role in the maintenance of a normal serum potassium concentration in patients with end-stage renal disease. Excess potassium is removed by using a dialysate with a lower potassium concentration, so that a gradient is achieved that favors movement of potassium. In general, one can expect only up to 70 to 90 mEq of potassium to be removed during a typical dialysis session. As a result, one should not overestimate the effectiveness of dialysis in the treatment of severe hyperkalemia. The total amount removed varies considerably and is affected by changes in acid-base status, in tonicity, in glucose and insulin concentration, and in catecholamine activity [17–20].

The concentration of calcium in the dialysate has implications for metabolic bone disease and hemodynamic stability. Like the other constituents of the dialysate, the calcium concentration should be tailored to the individual patient [21]. Some data suggest that lowering the dialysate calcium concentration would exac-

erbate hemodynamic instability during the dialysis procedure [21]. In this regard, the intradialysis drop in blood pressure noted in patients dialyzed against a low-calcium bath, while statistically significant, is minor in degree [22,23]. Nevertheless, for patients who are prone to intradialysis hypotension avoiding low calcium dialysate concentration may be of benefit. On the other hand, the use of a lower calcium concentration in the dialysate allows the use of increased doses of calcium-containing phosphate binders and lessens dependence on binders containing aluminum. In addition, use of 1,25-dihydroxyvitamin D can be liberalized to reduce circulating levels of parathyroid hormone and, thus, the risk of inducing hypercalcemia. With dialysate calcium concentrations below 1.5 mmol/L, however, patients need close monitoring to ensure that negative calcium balance does not develop and that parathyroid hormone levels remain in an acceptable range [24].

Dialysate Composition for Peritoneal Dialysis

To meet the ultrafiltration requirements of patients on peritoneal dialysis, the peritoneal dialysate is deliberately rendered hyperosmolar relative to plasma, to create an osmotic gradient that favors net movement of water into the peritoneal cavity. In commercially available peritoneal dialysates, glucose serves as the osmotic agent that enhances ultrafiltration. Available concentrations range from 1.5% to 4.25% dextrose. Over time, the osmolality of the dialysate declines as a result of water moving into the peritoneal cavity and of absorption of dialysate glucose. The absorption of glucose contributes substantially to the calorie intake of patients on continuous peritoneal dialysis. Over time, this carbohydrate load is thought to contribute to progressive obesity, hypertriglyceridemia, and decreased nutrition as a result of loss of appetite and decreased protein intake. In addition, the high glucose concentrations and high osmolality of currently available solutions may have inhibitory effects on the function of leukocytes, peritoneal macrophages, and mesothelial cells [25]. In an attempt to develop a more physiologic solution, various new osmotic agents are now under investigation. Some of these may prove useful as alternatives to the standard glucose solutions. Those that contain amino acids have received the most attention.

The sodium concentration in the ultrafiltrate during peritoneal dialysis is usually less than that of extracellular fluid, so there is a tendency toward water loss and development of hypernatremia. Commercially available peritoneal dialysates have a sodium concentration of 132 mEq/L to compensate for this tendency toward dehydration. The effect is more pronounced with increasing frequency of exchanges and with increasing dialysate glucose concentrations. Use of the more hypertonic solutions and frequent cycling can result in significant dehydration and hypernatremia. As a result of stimulated thirst, water intake and weight may increase, resulting in a vicious cycle.

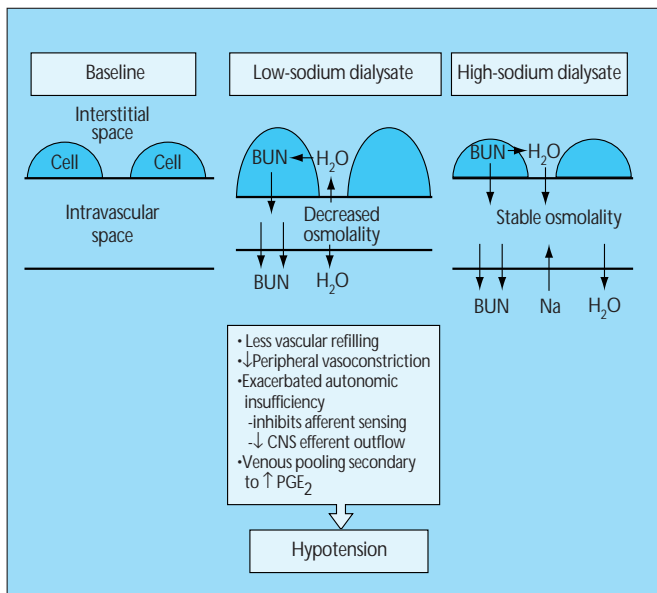
Potassium is cleared by peritoneal dialysis at a rate similar to that of urea. With chronic ambulatory peritoneal dialysis and 10 L of drainage per day, approximately 35 to 46 mEq of potassium is removed per day. Daily potassium intake is usually greater than this, yet significant hyperkalemia is uncommon in these patients. Presumably potassium balance is maintained by increased colonic secretion of potassium and by some residual

renal excretion. Given these considerations, potassium is not routinely added to the dialysate.

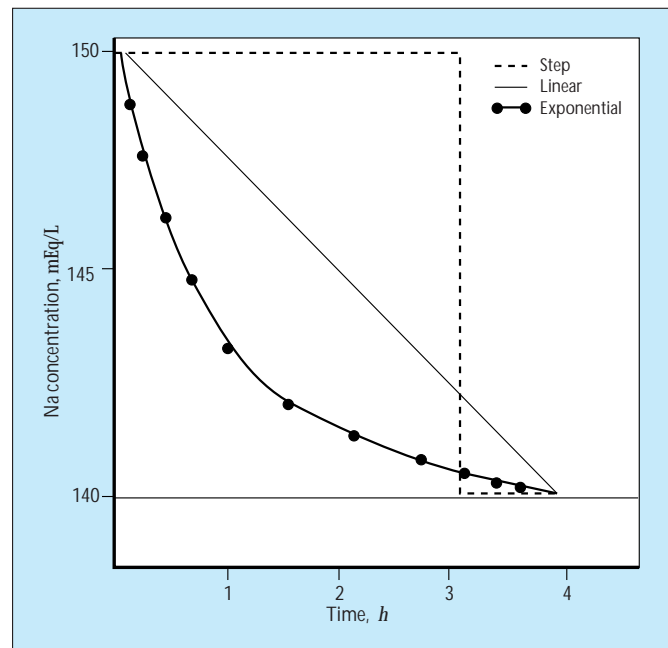
The buffer present in most commercially available peritoneal dialysate solutions is lactate. In patients with normal hepatic function, lactate is rapidly converted to bicarbonate, so that each mM of lactate absorbed generates one mM of bicarbonate. Even with the most aggressive peritoneal dialysis there is no appreciable accumulation of circulating lactate. The rapid metabolism of lactate to bicarbonate maintains the high dialysate-plasma lactate gradient necessary for continued

absorption. The pH of commercially available peritoneal dialysis solutions is purposely made acidic by adding hydrochloric acid to prevent dextrose from caramelizing during the sterilization procedure. Once instilled, the pH of the solution rises to values greater than 7.0. There is some evidence that the acidic pH of the dialysate, in addition to the high osmolality, may impair the host's peritoneal defenses [25,26].

To avoid negative calcium balance—and possibly to suppress circulating parathyroid hormone—commercially available peritoneal dialysis solutions evolved to have a calcium concentration



of 3.5 mEq/L (1.75 mmol/L). This concentration is equal to or slightly greater than the ionized concentration in the serum of most patients. As a result, there is net calcium absorption in most patients treated with a conventional chronic ambulatory peritoneal dialysis regimen. As the use of calcium-containing phosphate binders has increased, hypercalcemia has become a common problem when utilizing the 3.5 mEq/L calcium dialysate. This complication has been particularly common in patients treated with peritoneal dialysis, since they have a much greater incidence of adynamic bone disease than do hemodialysis patients [27]. In fact, the continual positive calcium balance associated with the 3.5-mEq/L solution has been suggested to be a contributing factor in the development of this lesion. The low bone turnover state typical of this disorder impairs accrual



of administered calcium, contributing to the development of hypercalcemia. As a result, there has been increased interest in using a strategy similar to that employed in hemodialysis, namely, lowering the calcium content of the dialysate. This strategy can allow increased use of calcium-containing phosphate binders and more liberal use of 1,25-dihydroxyvitamin D to effect decreases in the circulating level of parathyroid hormone. In this way, development of hypercalcemia can be minimized.

Dialysate Na in Hemodialysis

INDICATIONS AND CONTRAINDICATIONS FOR USE OF SODIUM MODELING (HIGH/LOW PROGRAMS)

Indications

- Intradialysis hypotension
- Cramping
- Initiation of hemodialysis in setting of severe azotemia
- Hemodynamic instability (eg, intensive care setting)

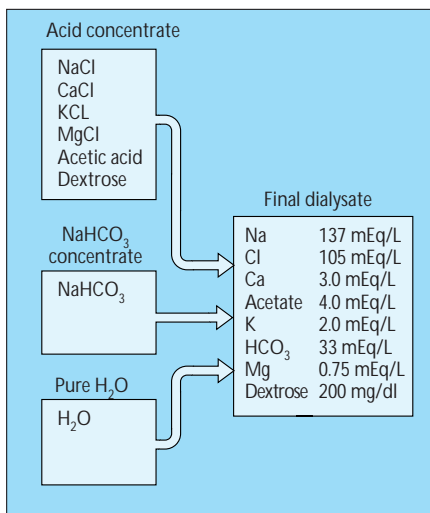
Contraindications

- Intradialysis development of hypertension
- Large interdialysis weight gain induced by high-sodium dialysate
- Hypernatremia

FIGURE 2-1

Use of a low-sodium dialysate is more often associated with intradialysis hypotension as a result of several mechanisms [4]. The drop in serum osmolality as urea is removed leads to a shift of water into the intracellular compartment that prevents adequate refilling of the intravascular space. This intracellular movement of

Dialysate Buffer in Hemodialysis



water, combined with removal of water by ultrafiltration, leads to contraction of the intravascular space and contributes to the development of hypotension. High-sodium dialysate helps to minimize the development of hypo-osmolality. As a result, fluid can be mobilized from the intracellular and interstitial compartments to refill the intravascular space during volume removal. Other potential mechanisms whereby low-sodium dialysate contributes to hypotension are indicated. Na—sodium; BUN—blood urea nitrogen; PGE₂—prostaglandin E₂.

FIGURE 2-2

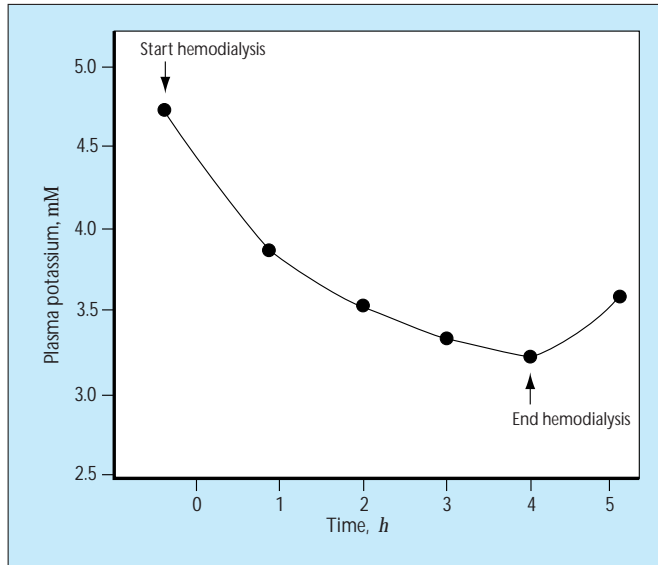
There has been interest in varying the concentration of sodium (Na) in the dialysate during the dialysis procedure so as to minimize the potential complications of a high-sodium solution and yet retain the beneficial hemodynamic effects. A high sodium concentration dialysate is used initially and progressively the concentration is reduced toward isotonic or even hypo-

MECHANISMS BY WHICH ACETATE BUFFER CONTRIBUTES TO HEMODYNAMIC INSTABILITY

- Directly decreases peripheral vascular resistance in approximately 10% of patients
- Stimulates release of the vasodilator compound interleukin 1
- Induces metabolic acidosis via bicarbonate loss through the dialyzer
- Produces arterial hypoxemia and increased oxygen consumption
- ?Decreased myocardial contractility

tonic levels by the end of the procedure. The concentration of sodium can be reduced in a linear, exponential, or step pattern. This method of sodium control allows for a diffusive sodium influx early in the session to prevent a rapid decline in plasma osmolality secondary to efflux of urea and other small-molecular weight solutes. During the remainder of the procedure, when the reduction in osmolality accompanying urea removal is less abrupt, the dialysate sodium level is set lower, thus minimizing the development of

hypertonicity and any resultant excessive thirst, fluid gain, and hypertension in the interdialysis period. In some but not all studies, sodium modeling has been shown to be effective in treating intradialysis hypotension



and cramps [5-11].

FIGURE 2-3

Indications and contraindications for use of sodium modeling (high/low programs). Use of a sodium modeling program is not indicated in all patients. In fact most patients do well with the dialysate sodium set at 140 mEq/L. As a result the physician needs to be aware of the benefits as well as the dangers of sodium remodeling.

FACTORS RELATED TO DIALYSIS THAT AFFECT DISTRIBUTION OF POTASSIUM BETWEEN CELLS AND THE EXTRACELLULAR FLUID

Factors that enhance cell potassium uptake

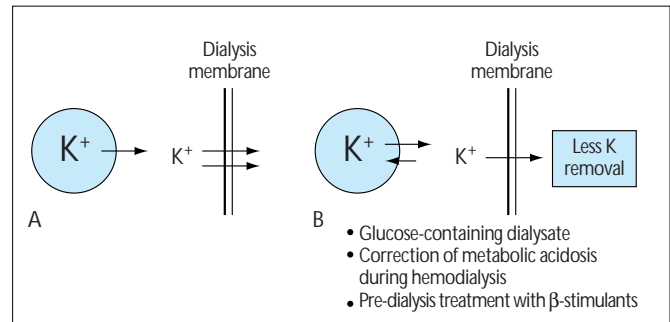
- Insulin
- β_2 -adrenergic receptor agonists
- Alkalemia

Factors that reduce cell potassium uptake or increase potassium efflux

- β_2 -adrenergic receptor blockers
- Acidemia (mineral acidosis)
- Hypertonicity
- α -adrenergic receptor agonists

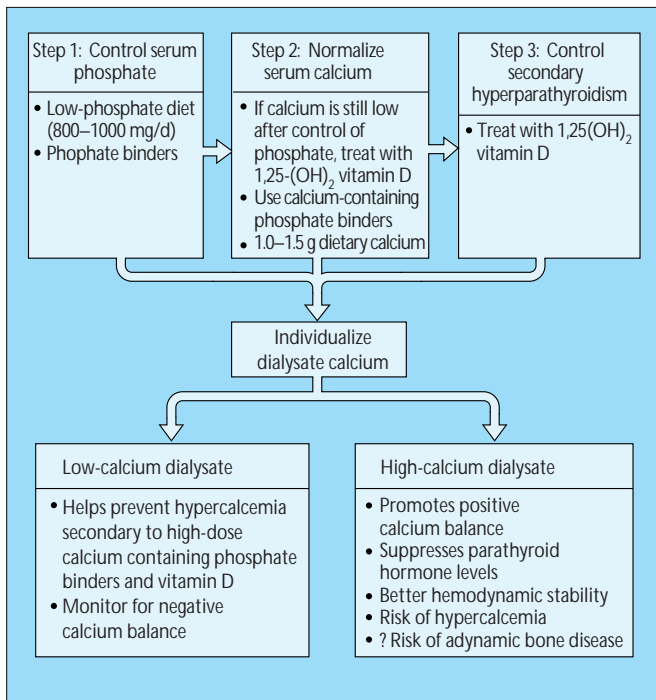
FIGURE 2-4

The current utilization of a bicarbonate dialysate requires a specially designed system that mixes a bicarbonate and an acid concentrate with purified water. The acid concentrate contains a small amount of lactic or acetic acid and all the calcium and magnesium. The exclusion of these cations from the bicarbonate concentrate prevents the precipitation of magnesium and calcium carbonate that would otherwise occur in the setting of a high bicarbonate concentration. During the mixing procedure the acid in the acid



concentrate reacts with an equimolar amount of bicarbonate to generate carbonic acid and carbon dioxide. The generation of carbon dioxide causes the pH of the final solution to fall to approximately 7.0-7.4. The acidic pH and the lower concentrations in the final mixture allow the calcium and magnesium to remain in solution. The final concentration of bicarbonate in the dialysate is approximately 33-38 mmol/L.

FIGURE 2-5



Mechanisms by which acetate buffer contributes to hemodynamic instability. Although bicarbonate is the standard buffer in use today, hemodynamically stable patients can be dialyzed safely using as acetate-containing dialysis solution. Since muscle is the primary site of metabolism of acetate, patients with reduced muscle mass tend to be acetate intolerant. Such patients include malnourished and elderly patients and women.

Dialysate Potassium in Hemodialysis

FIGURE 2-6

ADVANTAGES AND DISADVANTAGES OF INDIVIDUALIZING VARIOUS COMPONENTS OF HEMODIALYSATE

Dialysate component and adjustment	Advantages	Disadvantages
Sodium: Increased	More hemodynamic stability, less cramping	Dipsogenic effect, increased interdialytic weight gain, ? chronic hypertension
Decreased (rarely used)	Less interdialytic weight gain	Intradialytic hypotension and cramping more common
Calcium: Increased	Suppression of PTH, promotes hemodynamic stability in HD	Hypercalcemia with vitamin D and high-dose calcium-containing phosphate binders, ? contribution to adynamic bone disease in PD
Decreased	Permits greater use of vitamin D and calcium containing phosphate binders	Potential for negative calcium balance, stimulation of PTH, slight decrease in hemodynamic stability
Potassium: Increased	Less arrhythmias in setting of digoxin or coronary heart disease ? improved hemodynamic stability	Limited by hyperkalemia
Decreased	Permits greater dietary intake of potassium with less hyperkalemia ? improvement in myocardial contractility	Increased arrhythmias, may exacerbate autonomic insufficiency
Bicarbonate: Increased	Corrects chronic acidosis thereby benefits nutrition and bone metabolism	Post-dialysis metabolic alkalosis
Decreased	Less metabolic alkalosis	Potential for chronic acidosis
Magnesium: Increased	? Less arrhythmias, ? hemodynamic benefit	Potential for hypermagnesemia
Decreased	Permits greater use of magnesium containing phosphate binders which in turn permits reduced dose of calcium binders and results in less hypercalcemia	Symptomatic hypomagnesemia

Plasma potassium concentration can be expected to fall rapidly in the early stages of dialysis, but as it drops, potassium removal becomes less efficient [17,18]. Since potassium is

freely permeable across the dialysis membrane, movement of potassium from the intracellular space to the extracellular space appears to be the limiting factor that accounts for the smaller fractional decline in potassium concentration at lower plasma potassium concentrations.

COMPOSITION OF A
COMMERCIALLY AVAILABLE
PERITONEAL DIALYSATE

Solute	Dianeal PD-2
Sodium, mEq/L	132
Potassium, mEq/L	0
Chloride, mEq/L	96
Calcium, mEq/L	3.5
Magnesium, mEq/L	0.5
D, L-Lactate, mEq/L	40
Glucose, g/dL	1.5, 2.5, 4.25
Osmolality	346, 396, 485
pH	5.2

Presumably, the movement of potassium out of cells and into the extracellular space is slower than the removal of potassium from the extracellular space into the dialysate, so a disequilibrium is created. The rate of potassium removal is largely a function of its predialysis concentration. The higher the initial plasma concentration, the greater is the plasma-dialysate gradient and, thus, the more potassium is removed. After the completion of a standard dialysis treatment there is an increase in the plasma concentration of potassium secondary to continued exit of potassium from the intracellular space to the extracellular space in an attempt to re-establish the intracellular-extracellular potassium gradient.

FIGURE 2-7

The total extracellular potassium content is only about 50 to 60 mEq/L. Without mechanisms to shift potassium into the cell, small potassium loads would lead to severe hyperkalemia. These mech-

anisms are of particular importance in patients with end-stage renal disease since the major route of potassium excretion is eliminated from the body by residual renal clearance and enhanced gastrointestinal excretion.

FIGURE 2-8

During a typical dialysis session approximately 80 to 100 mEq/L of potassium is removed from the body. **A**, Potassium (K) flux from the extracellular space across the dialysis membrane exceeds the flux of potassium out of the intracellular space. **B**, The movement of potassium between the intra- and extracellular spaces is controlled by a number of factors that can be modified during the dialysis procedure [17,18]. As compared with a glucose-free dialysate, a bath that contains glucose is associated with less potassium removal [19]. The presence of glucose in the dialysate stimulates insulin release, which in turn has the effect of shifting potassium into the intracellular space, where it becomes less available for removal by dialysis. Dialysis in patients who are acidotic is also associated with less potassium removal since potassium is shifted into cells as the serum bicarbonate concentration rises. Finally, patients treated with inhaled β stimulants, as for treatment of hyperkalemia, will have less potassium removed during dialysis since β stimulation causes a shift of potassium into the cell [20].