Hyperkalemia in End-Stage Renal Disease: Mechanisms and Management¹,²

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ABSTRACT
Clinical investigations in the past few years have enhanced the understanding of the mechanisms of hyperkalemia in patients with ESRD. The results of these studies have led to modifications in the acute treatment and prevention of hyperkalemia in this patient population. They have confirmed the efficacy of intravenous insulin, while raising doubts about the utility of intravenous bicarbonate, for the acute treatment of hyperkalemia. Moreover, the ß-adrenergic agonist albuterol has been shown to be a useful adjunct to insulin for acutely lowering plasma potassium. Finally, there has been enhanced recognition of nondietary factors that can predispose to hyperkalemia in patients with ESRD, including prolonged fasting and the use of nonselective ß-adrenergic blockers. These new insights may improve the clinical management of hyperkalemia in patients with renal failure.

Key Words: Potassium, insulin, albuterol, epinephrine, bicarbonate

Recent review articles have discussed in depth the pathogenesis and management of potassium disorders in patients with ESRD (1,2). The goal of this editorial review is to focus primarily on recent clinical investigations that have enhanced our understanding of potassium homeostasis in hemodialysis patients and to consider their implications for the treatment and prevention of hyperkalemia in dialysis patients.

ACUTE TREATMENT OF HYPERKALEMIA IN ESRD PATIENTS

The definitive treatment of severe hyperkalemia in ESRD patients is the removal of excess potassium by emergent hemodialysis. Because the initiation of dialysis often involves a 1- to 2-h delay, more immediate temporizing measures are used. After the myocardium is stabilized with intravenous calcium, therapy is directed at decreasing plasma potassium acutely, by shifting potassium from the extracellular to the intracellular fluid compartment. Until recently, the administration of intravenous insulin and bicarbonate was recommended uniformly to promote this shift. Only in the past few years have these textbook recommendations been examined critically in carefully designed, prospective studies. These investigations have confirmed the efficacy of insulin, while casting doubts about the utility of bicarbonate therapy. Moreover, these studies have established ß-adrenergic agonists as useful adjuncts to insulin for the acute treatment of hyperkalemia. The following section will examine some of the studies that have led to a change in our thinking.

To understand the rational treatment and prevention of hyperkalemia in ESRD patients, it is necessary to understand the physiologic mechanisms that regulate potassium homeostasis. Extracellular potassium concentration is determined by two distinct regulatory systems (3) (Figure 1). The first system maintains external potassium balance by regulating potassium excretion according to dietary intake. On a typical American diet containing approximately 100 mmol of potassium per day, 90 to 95 mmol is excreted by the kidneys and 5 to 10 mmol is excreted by the gut. The excretion of an acute potassium load is a relatively slow process, requiring several hours for completion (4). In ESRD patients, there is an adaptive increase in potassium excretion by the gut (5-9). Nevertheless, this adaptation is insufficient to compensate for the loss of renal excretory capacity.

The second homeostatic system maintains internal potassium balance by regulating potassium shifts between the intracellular and extracellular fluid compartments. Internal balance can be achieved much faster than external balance: an acute potassium load is shifted into the cells within minutes (2). Total body potassium is about 3,300 mmol. Only 2% (about 65 mmol) is in the extracellular fluid compartment, whereas 98% is in the intracellular fluid compartment, primarily in skeletal muscle and to a lesser extent in liver. This uneven distribution means that relatively small shifts of potassium from the intracellular to the extracellular fluid compartment can produce severe hyperkalemia. Conversely, relatively small potassium shifts from the extracellular to the intracellular fluid compartment can produce a marked decrease in plasma potassium. Extrarenal potassium disposal (shifts from the extracellular to the intracellular fluid compartment) assumes a criti-
Figure 1. Internal and external potassium balance in humans. Reproduced with permission from Ref. 3. GI, gastrointestinal; RBC, red blood cells.

Figure 2. Changes in plasma potassium during the intravenous infusion of 8.4% bicarbonate, epinephrine, or insulin in glucose and during hemodialysis. Values represent means ± SE. Reproduced with permission from Ref. 16.

The two major physiologic factors that stimulate extrarenal potassium disposal are insulin and epinephrine. Flatman and Clausen (10) observed the stimulation of potassium influx in isolated skeletal muscle fibers incubated with insulin or epinephrine. Simultaneous exposure to both hormones produced an additive effect on potassium influx, suggesting different cellular mechanisms. These observations would suggest that both insulin and epinephrine may be useful for the treatment of hyperkalemia in dialysis patients. Whereas insulin is routinely used for this purpose in clinical practice, epinephrine is not.

The potassium-lowering effect of insulin in normal individuals is well established and dose dependent; it is increased progressively, going from moderate physiologic doses to pharmacologic doses (11). The effect of insulin on potassium uptake is distinct from that of epinephrine, because β-adrenergic blockade does not attenuate the decrease in plasma potassium during insulin administration (12, 13). Several studies have documented the efficacy of intravenous insulin in the acute treatment of hyperkalemia in ESRD patients (14–17) (Figure 2). The magnitude of decrease in plasma potassium after insulin administration in hemodialysis patients is comparable to that obtained in normal controls (14). Interestingly, the effect of insulin on cellular potassium uptake can be dissociated from its effect on glucose uptake. This dissociation was demonstrated in an elegant clinical study that measured plasma potassium in the brachial artery and vein of normal controls before and during a continuous infusion of insulin into the brachial artery (18). Insulin increased the arteriovenous gradient for both potassium and glucose. However, the concomitant infusion of ouabain with insulin prevented the stimulation of potassium uptake, without affecting glucose uptake. Thus, the effect of insulin on potassium uptake appears to be mediated by enhanced activity of the Na-K pump, whereas the stimulation of glucose uptake is achieved by a membrane-bound glucose transporter (19). These two effects of insulin are often dissociated in hemodialysis patients. As a result, ESRD patients are relatively resistant to the glucose-lowering effect of insulin (20–22), yet responsive to its potassium-lowering action (14).

When treating hyperkalemia, dextrose is routinely administered in conjunction with insulin, to avoid the anticipated hypoglycemia. Because exogenous glucose stimulates endogenous insulin secretion, one might be tempted to administer dextrose alone. Such an approach is ill advised in the emergent situation. If endogenous insulin is not secreted (as might occur in insulin-dependent diabetics or in patients with inadequate insulin reserve), the resulting hyperglycemia is likely to aggravate the hyperkalemia (23–26). An acute worsening of hyperkalemia is not unique to hyperglycemia; any maneuver that increases plasma osmolality promotes potassium shifts from the intracellular to the extracellular fluid compartments. Thus, for example, acute infusions of mannitol, hypertonic saline, and hypertonic arginine in dialysis patients also raise plasma potassium acutely (27–29). The hyperkalemic effect of hyperosmolality is independent of changes in plasma insulin, catecholamines, or acid-base status (28).

Epinephrine at physiologic doses produces hypokalemia acutely in normal controls (30–34). The stimu-
lation of extrarenal potassium disposal by epinephrine is mediated by β-2 adrenergic receptors. It is prevented by β-2 selective blockers and by nonselective β blockers, but not by β-1 selective blockers (30,32,35). The ability of intravenous β-2 agonists to induce hypokalemia in normal individuals (36,37) suggests their potential utility for acute therapy of hyperkalemia in hemodialysis patients. Montoliu et al. (38) first reported that intravenous albuterol (0.5 mg), a β-2 agonist, acutely lowers plasma potassium in hemodialysis patients. The effect was maximal (1.1 mmol/L reduction) at 30 min and was sustained for at least 3 h. In several patients, hyperkalemic electrocardiographic changes resolved after the administration of albuterol alone, in the absence of intravenous calcium or any other measures to lower plasma potassium. Subsequent studies have confirmed the efficacy of intravenous albuterol in the acute treatment of hyperkalemia in patients with renal failure (17,39,40).

Neither albuterol nor any other β-2 selective agonist is available for intravenous use in the United States. However, selective β-2 agonists are available in nebulized form for the treatment of asthma. Moreover, nebulized albuterol (and other β-agonists) produces hypokalemia in normal controls (41–44), indicating significant systemic absorption of the inhaled drug. To determine whether nebulized albuterol was useful for the acute treatment of hyperkalemia in ESRD patients, we studied ten hemodialysis patients in a double-blinded, crossover trial (45). Each subject received 10 or 20 mg of nebulized albuterol or nebulized placebo (saline) inhaled over 10 min. Plasma potassium decreased by about 0.6 mmol/L after 10 mg of albuterol and by about 1.0 mmol/L after the 20-mg dose (Figure 3). A significant decrease in plasma potassium was first noted after 30 min. Albuterol was equally efficacious in diabetic and nondiabetic patients. In contrast, nebulized placebo did not lower plasma potassium. Subsequent studies have confirmed the utility of nebulized albuterol (10 to 20 mg) in lowering plasma potassium acutely (15,40,46).

The doses of albuterol required to achieve a significant reduction in plasma potassium are fourfold to eightfold higher than those used to treat asthma, raising concerns about potential adverse cardiovascular effects. The mean increase in heart rate in our double-blinded study was 6 beats/min with 10 mg of albuterol and 8 beats/min with 20 mg of albuterol (45) (Figure 3). There were no significant changes in blood pressure, and no patient developed chest pain or arrhythmias. Several subsequent investigations have similarly reported stable blood pressures and clinically insignificant increases in heart rate after the nonblinded administration of albuterol at similar nebulized doses to ESRD patients (15,40,46). An increase in plasma glucose after intravenous and nebulized albuterol has been observed in a number of studies, but this has not been clinically significant (−2 to 3 mmol/L).

A direct comparison between intravenous (0.5 mg) and nebulized (10 mg) albuterol in ESRD patients revealed a similar magnitude of decrease in plasma potassium (40). The onset of the potassium-lowering effect was somewhat slower with the nebulized drug than with the intravenous form. On the other hand, nebulized albuterol produced less tachycardia than the intravenous form. Thus, nebulized albuterol may be safer than the intravenous form in patients with known or suspected coronary artery disease.

It is important to note that a subset of ESRD patients are refractory to the potassium-lowering effect of albuterol (ΔK ≤ 0.4 mmol/L). In various studies, these have ranged from 20 to 40% of dialysis patients studied (15,40,45). Similarly, even pharmacologic doses of epinephrine do not lower plasma potassium in some dialysis patients (47,48). The reason for this resistance has not been elucidated. Because we cannot prospectively identify which patients are resistant to albuterol, it is critical to treat severe hyperkalemia with intravenous insulin, as well as albuterol. The potassium-lowering effect of albuterol in ESRD patients is additive to that of insulin. We found that intravenous insulin (10 U bolus) and albuterol (20 mg nebulized over 10 min) each lowered plasma potassium by approximately 0.6 mmol/L, whereas in combination, they lowered plasma potassium by about 1.2

![Figure 3](image-url)
mmol/L (15). A similar additive effect has also been reported with intravenous albuterol and insulin (17). This additive effect is consistent with the in vitro observations in isolated skeletal muscle fibers (10).

Albuterol may also attenuate insulin-induced hypoglycemia in hemodialysis patients. Dextrose is administered routinely with intravenous insulin to prevent the predictable hypoglycemia. Nevertheless, hypoglycemia (frequently asymptomatic) may be a common event after such therapy. For example, we documented hypoglycemia (plasma glucose < 3 mmol/L) in 9 of 12 hemodialysis patients 1 h after they received 10 U of regular insulin and 25 g of dextrose as an intravenous bolus (15). The high incidence of hypoglycemia may reflect, in part, a defect in the activation of counterregulatory sympathetic discharge in ESRD patients (49). When nebulized albuterol was given concurrently with the same regimens of insulin and dextrose, only 2 of 10 patients developed hypoglycemia. This salutary action of albuterol is likely mediated by the β-adrenergic stimulation of gluconeogenesis (50).

In contrast to β-adrenergic stimulation, which enhances potassium influx into the cells, α-adrenergic stimulation enhances potassium efflux out of the cells (51,52). Hence, the effect of epinephrine, a mixed α- and β-blocker, on plasma potassium reflects the relative effects of α- and β-adrenergic stimulation on plasma potassium. Hemodialysis patients are resistant to the potassium-lowering effect of epinephrine. For example, Gifford et al. (34) found that a low physiologic dose of epinephrine (0.015 μg/kg per min) lowered plasma potassium by about 0.4 mmol/L in normal controls but had no effect in hemodialysis patients. Similarly, Blumberg et al. (16) observed no significant change in plasma potassium during the infusion of epinephrine at high physiologic doses (0.05 μg/kg per min) in hemodialysis patients (Figure 2). These findings are in contrast to the potassium-lowering effects of β-2 agonists in ESRD patients, suggesting a possible imbalance between α- and β-adrenergic effects on potassium in dialysis patients.

To evaluate this possibility, we gave ESRD patients and normal controls a graded infusion of epinephrine at three physiologic doses (0.01 to 0.04 μg/kg per min) (33). In normal controls, increasing doses of epinephrine produced progressively greater decreases in plasma potassium. In contrast, in hemodialysis patients, epinephrine at the lowest dose actually increased plasma potassium, suggesting a predominant α-adrenergic effect. Even the highest dose of epinephrine did not significantly decrease plasma potassium in ESRD patients (Figure 4). To indirectly assess the α-adrenergic component of epinephrine, the identical infusion protocol was repeated during concurrent β-blockade with propranolol. α-Adrenergic stimulation raised plasma potassium in a dose-dependent manner in both experimental groups. The magnitude of this increase was significantly greater, however, in dialysis patients (0.7 mmol/L) than in normal controls (0.3 mmol/L). Finally, the concomitant infusion of the

Figure 4. Changes in serum potassium concentration (means ± SE) from baseline during the infusion of intravenous epinephrine at three doses in normal controls, hemodialysis patients, and renal transplant patients (serum creatinine <2 mg/ml). The upper panel shows the effect of epinephrine alone (α plus β-adrenergic stimulation), the middle panel shows the effect of epinephrine during β-blockade (“pure” α effect), and the lower panel shows the calculated pure β effect. The changes in potassium in the upper and middle panels were significantly (P < 0.05) different in the dialysis patients as compared with those in the controls and transplant patients. Reproduced with permission from Ref. 2.
α-blocker phentolamine overcame the resistance to the potassium-lowering effect of epinephrine in the dialysis patients (33). In summary, these studies suggest that the resistance to the potassium-lowering effect of epinephrine in hemodialysis patients is due to an enhanced α-adrenergic response. Interestingly, this acquired resistance is reversed after successful renal transplantation (2) (Figure 4).

Bicarbonate therapy has long been assumed to be effective for the acute treatment of hyperkalemia in dialysis patients. It is presumed that the metabolic acidosis of renal failure promotes hyperkalemia by stimulating net potassium shifts from the intracellular to the extracellular fluid compartment and that alkalization should reverse this action. However, the effect of acute acid infusion on plasma potassium is inconsistent. In nephrectomized animals, the acute (1- to 3-h) administration of mineral acids raises plasma potassium, whereas organic acids have no effect (53-56). The effect of acute acid administration on plasma potassium in dialysis patients has not been reported. Acute (1- to 3-h) bicarbonate administration to nephrectomized animals has lowered plasma potassium in some studies (56,57), but not in others (54,55). Sodium bicarbonate infusion in hyperkalemic dialysis patients lowers plasma potassium after 6 to 24 h (58). However, to be useful for acute therapy, the changes should occur within about 1 h. Blumberg et al. (16) found that neither hypertonic nor isotonic intravenous bicarbonate lowered plasma potassium in hemodialysis patients during 60 min of observation. This was in contrast to the ability of both insulin and hemodialysis to lower plasma potassium (Figure 2). Even 3 h after intravenous bicarbonate (hypertonic or isotonic) administration, there was no significant decrease in plasma potassium in ESRD patients, despite substantial increases in plasma bicarbonate (59). In fact, serial plasma potassium measurements for 6 h after bicarbonate administration found the earliest decrease at 4 h (60). In summary, although bicarbonate administration lowers plasma potassium chronically in ESRD patients, it does not do so in a timeframe useful for the emergent treatment of hyperkalemia. Of course, bicarbonate therapy is still indicated for the acute management of severe metabolic acidosis.

A recent abstract suggested that bicarbonate administration may potentiate the potassium-lowering action of insulin in hemodialysis patients (61). Whereas bicarbonate administration by itself had no significant effect on plasma potassium after 60 min in eight hemodialysis patients, it enhanced the potassium-lowering effect of insulin. Plasma potassium was decreased by 0.6 mmol/L after insulin alone and by 1.0 mmol/L after insulin plus bicarbonate. The cellular mechanism of this synergism is unexplained but may involve pH-dependent changes in the insulin receptor. If this study is confirmed, it may provide a rationale for the administration of bicarbonate for the acute treatment of hyperkalemia in ESRD patients.

Whether a similar synergism exists between bicarbonate and β-2 adrenergic agonists is unknown.

The removal of potassium by hemodialysis is largely determined by the potassium concentration gradient between the plasma and the dialysate (62,63). Measures that acutely shift potassium from the extracellular to the intracellular fluid compartment will reduce this gradient and thereby attenuate potassium removal by the subsequent dialysis treatment. Such an effect of insulin is suggested by studies demonstrating less dialytic potassium removal with glucose-containing dialysate as compared with glucose-free dialysis (64). Thus, one might anticipate that aggressive therapy with insulin and albuterol for hyperkalemia may attenuate the removal of potassium in the subsequent dialysis treatment. Such a phenomenon might potentially lead to a rebound hyperkalemia several hours after the dialysis session.

PREVENTION OF HYPERKALEMIA IN ESRD PATIENTS

Given the central role of the kidneys in maintaining potassium homeostasis, dietary potassium restriction clearly plays an important role in the prevention of hyperkalemia. As nephrologists, we tend to assume dietary excess whenever we encounter hyperkalemia in hemodialysis patients. We then ask the dietitians to provide the patients with appropriate dietary guidelines. It is important, however, to recognize some nondietary factors that may predispose to hyperkalemia in hemodialysis patients.

Thus, for example, there is convincing evidence for the impairment of extrarenal potassium disposal in ESRD patients. In a recent study, we gave fasted hemodialysis and control subjects a small oral potassium load (0.25 mmol/kg, or about 20 mmol for an 80-kg patient). The mean increase in plasma potassium was substantially greater in hemodialysis patients than in controls (0.8 versus 0.4 mmol/L) and could not all be accounted for by renal excretion (65). Similar observations were reported by Fernandez et al. (66). These clinical observations in ESRD patients are also in agreement with the impairment of ouabain-inhibitable rubidium uptake by skeletal muscle from uremic rats (67,68).

Patients do not usually eat potassium by itself. They eat foods that contain potassium, as well as carbohydrate. The endogenous insulin that is released in response to the carbohydrate promotes extrarenal potassium disposal. We found that the ingestion of 50 g of glucose along with an oral potassium load (0.25 mmol/kg) attenuated the mean rise in plasma potassium from 0.8 to 0.3 mmol/L (65). If one assumes that the extracellular fluid compartment is approximately 20% of total body water and that all the ingested potassium (0.25 mmol/kg) remains in the extracellular fluid compartment, then one would predict a 1.25 mmol/L increase in plasma potassium. The actual measured increases suggest that endogenous insulin approximately doubles extrarenal potassium dis-
posal, from 36 to 76%. Thus, dietary carbohydrate constitutes a major defense against life-threatening hyperkalemia after an oral potassium load in dialysis patients.

The ability of exogenous insulin to lower plasma potassium acutely has been discussed earlier. What is less well appreciated is that even the low circulating insulin concentrations present during prolonged fasting constitute an important defense against hyperkalemia. Thus, the inhibition of endogenous insulin secretion in normal, fasting controls results in a significant increase in plasma potassium (69). Fasting insulin levels may be particularly important in the defense against hyperkalemia in dialysis patients. This conclusion is suggested by the finding that acute somatostatin administration to fasting rats produced a greater increase in plasma potassium in uremic rats than in control animals (68).

The decrease in plasma insulin that occurs in the transition from a postprandial state to a fasting state is not sufficient to raise plasma potassium in individuals with normal renal function (70). Presumably, the excess potassium that is shifted from the intracellular to the extracellular fluid compartment is excreted by the kidneys. In the absence of renal excretory function, however, prolonged fasting may predispose to hyperkalemia. Thus, Gifford et al. (34) fasted nondiabetic hemodialysis patients and normal controls for 26 h. Plasma potassium increased by about 0.5 mmol/L in ESRD patients but did not change in the controls. This observation suggests that prolonged fasting may be an important cause of hyperkalemia when hemodialysis patients are fasted for surgery or a diagnostic procedure.

To determine whether fasting hyperkalemia could be prevented by exogenous insulin, we fasted 10 nondiabetic hemodialysis patients for 18 h and measured serial plasma potassium concentrations (70). On a second occasion, the same patients received a continuous infusion of 10% dextrose with 20 U of regular insulin per liter, infused at 50 mL/min (or 1 U of insulin/h). This insulin infusion regimen doubled fasting plasma insulin from 10 to 20 mU/L and completely prevented the 0.6 mmol/L increase in potassium observed during fasting (Figure 5). Even low doses of exogenous insulin can potentially produce hypoglycemia. To evaluate whether exogenous glucose can prevent fasting hyperkalemia, by stimulating endogenous insulin secretion, we restudied some patients with an infusion of 10% dextrose alone. This attenuated the rise in plasma potassium during prolonged fasting but was not as effective as dextrose with insulin (70).

Hyperkalemia is much less common in patients on continuous ambulatory peritoneal dialysis than in hemodialysis patients (71). This is due, in part, to the continuous removal of potassium with continuous ambulatory peritoneal dialysis. However, another contributory factor is the continuous absorption of glucose from the dialysate, which results in increased fasting plasma insulin concentrations, thereby promoting extrarenal potassium disposal (72,73).

Because β-2 agonists decrease plasma potassium, one might expect β-blockers to increase plasma potassium. This is not a significant problem in individuals with normal renal function, because potassium transferred from the intracellular to the extracellular fluid compartment can be excreted by the kidneys. In the absence of renal excretory function, β blockade can aggravate hyperkalemia in ESRD patients. Thus, for example, a 10-day course of propranolol, a nonselective β-blocker, increased predialysis potassium by 0.7 mmol/L in a group of hemodialysis patients. In contrast, the β-1 selective blocker atenolol did not increase plasma potassium in the same group of patients (74). Similarly, exercise-induced hyperkalemia in ESRD patients is augmented by the nonselective
Hyperkalemia in ESRD

β-adrenergic blocker propranolol but is not affected by the β-1 selective blocker metoprolol (75) (Figure 6). Thus, one should preferentially prescribe β-1 selective blockers in dialysis patients.

A recent abstract described the potential utility of chronic oral β-adrenergic administration (albuterol, 2 mg twice daily) in the prevention of hyperkalemia in hemodialysis patients (76). The predialysis plasma potassium was decreased by 0.6 mmol/L after 2 wk of oral albuterol. However, 3 of the 12 patients withdrew from the study because of unacceptable palpitations and tremor. Further studies are indicated to evaluate this prophylactic measure in hemodialysis patients with persistent hyperkalemia not responsive to dietary potassium restriction.

Mineralocorticoids play an important role in maintaining potassium homeostasis in normal animals and humans fed a high-potassium diet by enhancing renal potassium excretion (77,78). In addition, there is conflicting experimental evidence on the effect of mineralocorticoids on extrarenal potassium disposal (2). Sugarman and Brown (79) studied the effect of chronic mineralocorticoid administration on the disposal of an acute potassium load in hemodialysis patients. The prior exogenous administration of the mineralocorticoid deoxycorticosterone acetate for 60 h blunted the increase in plasma potassium after an acute potassium load. Conversely, the prior administration of the aldosterone antagonist spironolactone augmented the hyperkalemic response to the potassium load. These intriguing observations suggest that exogenous mineralocorticoids may be a useful modality for the prevention of hyperkalemia in hemodialysis patients.

In summary, clinical investigations performed in the past few years have enhanced our understanding of

![Figure 6. Time course of change in plasma potassium concentration in dialysis subjects during exercise alone (open circles), exercise plus propranolol (closed circles), and exercise plus metoprolol (closed triangles). All values represent mean ± SE. *P < 0.05 versus control study. P < 0.05 versus metoprolol study. Reproduced with permission from Ref. 75.](image)

**Table 1. Changing concepts in the management of hyperkalemia in dialysis patients**

<table>
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<tr>
<th>Conventional Wisdom</th>
<th>&quot;New&quot; Wisdom</th>
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<tr>
<td>Bicarbonate decreases plasma potassium acutely.</td>
<td>Bicarbonate is not effective for acute therapy of hyperkalemia.</td>
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<tr>
<td>Albuterol decreases plasma potassium acutely.</td>
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<tr>
<td>Insulin decreases plasma potassium acutely.</td>
<td>Insulin decreases plasma potassium acutely, and albuterol has an additive effect.</td>
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<tr>
<td>Hyperkalemia is due to dietary excess.</td>
<td>Hyperkalemia may be due to dietary excess, but fasting and β-blockers are also important factors.</td>
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**Table 2. Treatment and prevention of hyperkalemia in dialysis patients: specific guidelines**

**Acute treatment of severe hyperkalemia**

1. Calcium gluconate, 10% solution, 10- to 20-mL iv bolus. May be repeated every 5 min, if electrocardiographic appearance does not improve.
2. Regular insulin, 10 U + 50 mL of 50% dextrose, as iv bolus, followed by 10% dextrose @ 50 mL/min until dialysis initiated.
3. Albuterol (5 mg/mL), 10 to 20 mg, nebulized over 10 min.
4. Acute hemodialysis against a low potassium bath.

**Prevention of hyperkalemia**

1. Dietary potassium restriction, 40 to 50 mmol/day or 1.5 to 2.0 g/d.
2. Avoidance of nonselective β-blockers. If β-blockers are clinically indicated, use β-1-selective blockers, e.g., atenolol or metoprolol.
3. During prolonged fasting in diabetic dialysis patients, infuse: 10% dextrose + 10 U of regular insulin/L @ 50 mL/h. During prolonged fasting in nondiabetic dialysis patients, infuse: 10% dextrose @ 50 mL/h.
the mechanisms of hyperkalemia in ESRD patients. As a result, the guidelines for the acute treatment and prevention of hyperkalemia in hemodialysis patients may need to be revised (Tables 1 and 2). The utility of intravenous calcium and insulin for acute hyperkalemia associated with electrocardiographic abnormalities remains unchallenged. In contrast, the efficacy of intravenous bicarbonate for the treatment of hyperkalemia is not supported by prospective studies. Albuterol, either intravenous or nebulized form, appears to be a useful adjunct to the potassium-lowering action of intravenous insulin. Finally, whereas dietary potassium restriction remains an important measure for the prevention of hyperkalemia, we have become more aware of non-dietary factors contributing to hyperkalemia, including prolonged fasting and nonselective β-blockers.

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