Hemodialysis International 2005; **9**: 296–302

The efficiency of potassium removal during bicarbonate hemodialysis

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Abstract

Background: Patients on chronic hemodialysis often portray high serum [K^+]. Although dietary excesses are evident in many cases, in others, the cause of hyperkalemia cannot be identified. In such cases, hyperkalemia could result from decreased potassium removal during dialysis. This situation could occur if alkalinization of body fluids during dialysis would drive potassium into the cell, thus decreasing the potassium gradient across the dialysis membrane.

Methods: In 35 chronic hemodialysis patients, we compared two dialysis sessions performed 7 days apart. Bicarbonate or acetate as dialysate buffers were randomly assigned for the first dialysis. The buffer was switched for the second dialysis. Serum [K^+], [HCO_3^-], and pH were measured in samples drawn before dialysis; 60, 120, 180, and 240 min into dialysis; and 60 and 90 min after dialysis. The potassium removed was measured in the dialysate.

Results: During the first 2 hr, serum [K^+] decreased equally with both types of dialysates but declined more during the last 2 hr with bicarbonate dialysis. After dialysis, the serum [K^+] rebounded higher with bicarbonate bringing the serum [K^+] up to par with acetate. The lower serum [K^+] through the second half of bicarbonate dialysis did not impair potassium removal (295.9 $\pm$ 9.6 mmol with bicarbonate and 299.0 $\pm$ 14.4 mmol with acetate). The measured serum K^+ concentrations correlated with serum [HCO_3^-] and blood pH during bicarbonate dialysis but not during acetate dialysis.

Conclusion: Alkalinization induced by bicarbonate administration may cause redistribution of K during bicarbonate dialysis but this does not impair its removal. The more marked lowering of potassium during bicarbonate dialysis occurs late in dialysis, when exchange is negligible because of a low gradient.

INTRODUCTION

Hyperkalemia remains a rather common complication in patients with end-stage renal disease being treated by chronic hemodialysis.[1] Indeed, up to 24% of the emergency dialysis procedures are performed to correct severe hyperkalemia.[2] Furthermore, 3% to 5% of the deaths in dialysis are due to hyperkalemia.[3,4] Although this dreaded complication results from excessive dietary intake in approximately 50% of the cases, other conditions such as severe azotemia, metabolic acidosis, and severe hyperglycemia in diabetics are also important.[5–8] In approximately 15% of the cases, the cause of hyperkalemia is unknown.[5]

In agreement with these latter data, we too have encountered severe hyperkalemia in some patients in whom no cause could be found even after extensive clinical, dietary, and laboratory studies. Concerned about the efficacy of potassium removal during dialysis in these patients, we speculated that bicarbonate in the dialysate could decrease potassium removal by driving potassium into the cells and hence decreasing the

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potassium gradient at the dialysis membrane. This possibility had been addressed by Dalal *et al.*[14] in a group of 12 chronic hemodialysis patients in whom potassium removal was compared utilizing three different types of dialysate buffers.[9] The authors found no differences between the three groups in serum $[K^+]$ throughout dialysis. Unfortunately, they did not correlate blood gases changes with changes in serum $[K^+]$. Nonetheless, they showed that the efficiency of potassium removal was similar no matter what buffer was used in the dialysate.

To further our understanding of potassium handling during bicarbonate dialysis, we designed a study to evaluate the effects of changing acid-base status on potassium removal during bicarbonate dialysis. Our study shows that bicarbonate dialysis, although possibly redistributing potassium into the cells, does not prevent an efficient potassium removal. We further speculated that acid-base changes, by acting slowly and late, redistribute potassium into the cells mainly during the last 2 hr of dialysis, at a time when a reduced gradient is causing negligible removal of potassium across the dialysis membrane.

METHODS

We studied 35 stable end-stage renal disease patients (20 women) being treated by thrice-a-week hemodialysis. The mean age was 48.5 ± 2.4 years (range, 23 and 76 years). None of the patients were diabetics or suffering from acute catabolic or inflammatory disease. There was no clinical evidence of gastrointestinal bleeding although three patients were on long-term omeprazol therapy. None of the patients were receiving adrenergic blockers or insulin. All of the patients had normal fasting blood glucose. None showed severe metabolic acidosis ($pH < 7.20$) or very high blood urea concentrations (mean urea concentration, 163 ± 32 mg/dL). End-stage renal disease was caused by hypertensive nephrosclerosis in 15 patients, primary glomerulonephritis in 8 patients, lupus nephritis in 4 patients, chronic pyelonephritis and adult polycystic kidney disease in 2 patients each, and obstructive nephropathy in 1 patient, and in 3 patients the etiology was unknown. The prescribed potassium content of the diet was < 80 mEq per day. All of the patients had repeated nutritional evaluations to rule out excess potassium intake.

The patients were dialyzed with a delivery system (single-pass machines, Model AK95, Gambro BCT, Lakewood, CO). The type of dialyzer regularly used for each patient (either GFS-Plus 16 or GFS-Plus 20, Gambro BCT) was also used for the study. According to their regular dialysis schedule, all patients were dialyzed for 4 hr. To standardize the dialysis procedures, we did not include patients requiring more or less dialysis time. All dialysis solutions contained (in mM) potassium 2, sodium 139, calcium 2.5, magnesium 1, and chlorides 107.5. In addition they contained either 37 mM acetate or 33 mM bicarbonate plus 4 mM acetate.

Studies were done during the first dialysis of a given week (Week 1) and the first dialysis of the following week (Week 2; longest possible period without dialysis, approx. 68 hr). In this way, each patient served his or her own control. For the purpose of this study, we did not reuse dialyzers. On the day of the study in Week 1, the patients were randomly assigned to a dialysis with either bicarbonate buffer or acetate buffer and then switched 1 week later to the buffer not used in Week 1. Between these two dialysis procedures, the patients were dialyzed as regularly done with bicarbonate dialysis. There were no differences between bicarbonate and acetate dialysis procedures in UFR, weight removed during dialysis, and blood and dialysate flows. Dialysate flow was always 500 mL/min, and the mean blood flow during bicarbonate dialysis was 438 ± 12 and 437 ± 13 mL/min during acetate dialysis.

Blood samples were obtained from the arterial line immediately before dialysis; 60, 120, 180, and 240 min into dialysis; and again 60 and 90 min after ending dialysis. These samples were processed immediately after being drawn for potassium, bicarbonate, and pH measurement. At the end of dialysis, the patients were then asked to void to measure any renal potassium excretion that could have occurred during the dialysis session. As it turned out, all of the patients had no measurable urinary volume. The total volume of dialysate produced during the entire dialysis session was collected in appropriate tanks, the volume was determined, and after meticulous mixing, the potassium concentration was measured. The total potassium removed (TKR) was calculated as

$$TKR = (D_{vol} \times [K^+]_D),$$

where D_{vol} is the total dialysate volume and $[K^+]_D$ is potassium dialysate concentration.

Statistical analysis

All values are reported as means ± SEM. The significances of the differences between variables during bicarbonate versus acetate dialysis were assessed by a paired t test. The significances of the differences in serum $[K^+]$,

$[HCO_3^-]$, and blood pH obtained before, during, and after dialysis were estimated by two-way analysis of variance and then when significant, paired Student's t tests were used. The comparisons between total potassium removed, UFR, and weight removed during bicarbonate dialysis and during acetate dialysis were made by Student's t test. Spearman rank correlations were used to correlate blood pH and serum $[HCO_3^-]$ with serum $[K^+]$ during both bicarbonate and acetate dialysis.

RESULTS

Changes in serum potassium (Figure 1A)

The mean serum $[K^+]$ measured immediately before bicarbonate dialysis was slightly (but not significantly) higher than the mean $[K^+]$ before acetate dialysis. From then on, and for the first 2 hr of dialysis, the serum $[K^+]$ decreased at a similar rate with both kinds of dialysates. As a result, the mean serum $[K^+]$ remained similar with bicarbonate and acetate dialysis procedures during these first 2 hr. At the third hour, the mean serum $[K^+]$ then became significantly lower with bicarbonate dialysis ($p = < 0.05$) and remained so not only until the end of dialysis ($p = < 0.05$), but also during the initial rebound 60 min after ending dialysis. Ninety minutes after the end of dialysis, the values evened up owing to a greater rebound with bicarbonate dialysis (Figure 1B).

As expected, the greater portion of the changes in serum $[K^+]$ occurred during the first 2 hr with both kinds of dialysates. Indeed, 83.1% of the decrease in serum $[K^+]$ took place in the first 2 hr with bicarbonate dialysis and 86.7% with acetate dialysis. These findings suggest a strong gradient effect of serum $[K^+]$ during the first 2 hr of dialysis. By the end of dialysis, serum $[K^+]$ had decreased by 2.0 ± 0.11 and 1.7 ± 0.12 mmol/L with bicarbonate and acetate, respectively (not significantly different). These decreases in serum potassium concentration were attended by similar total removal of potassium (295.9 ± 9.6 mmol with bicarbonate and 299.0 ± 14.4 mmol with acetate). That is, potassium removal was equally efficient with either type of dialysate.

Changes in serum pH

Because changes in the acid-base status could have influenced serum $[K^+]$, we studied the behavior of both blood pH and $[HCO^-_3]$ and correlated them with the serum $[K^+]$ during bicarbonate and acetate dialysis. Predialysis blood pH values were not different between bicarbonate and acetate dialysis. With bicarbonate dialysis, blood pH increased rapidly during the first 3 hr of dialysis (Figure 2A). Each hourly pH value was significantly higher than predialysis pH value. The changes in pH during dialysis with bicarbonate took place early and

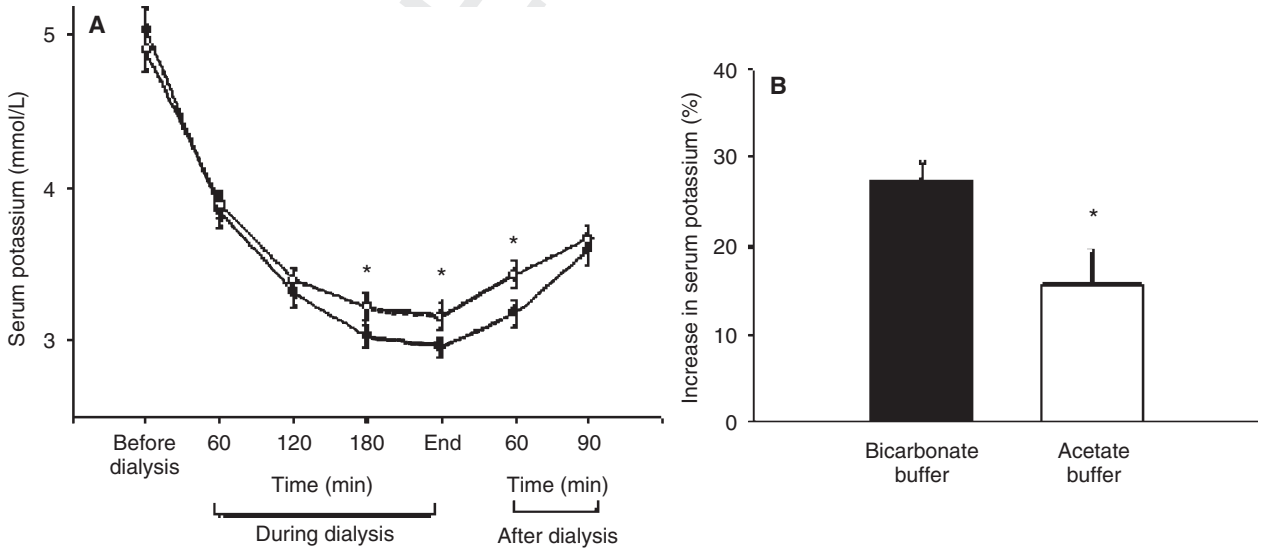

Figure 1 Serum K^+ during dialysis with HCO^-_3 or acetate in the dialysate. (A) The decrease in serum K^+ during dialysis with HCO^-_3 was greater than with acetate. Ninety minutes after the end of dialysis, mean serum potassium levels were not different. (●) Bicarbonate buffer; (○) acetate buffer. *$p < 0.05$. (B) Ninety-minute rebound in serum potassium concentration after dialysis with either HCO^-_3 or acetate as dialysate buffers. The rebound was greater after bicarbonate dialysis. *$p < 0.05$.

persisted for at least 90 min after the end of dialysis. In contrast, with acetate dialysis, blood pH did not increase until the third hour of dialysis. From then on, it remained significantly higher than predialysis pH value. These data indicate that the increase in pH induced by acetate is slow and late. Additionally, dialysis with bicarbonate brought about significantly higher blood pH values than with acetate.

Changes in serum HCO_3^-

The serum $[HCO_3^-]$ response was very similar to the pH changes for both types of dialysates (Figure 2B). Predialysis procedure $[HCO_3^-]$ values were not significantly different and, as expected, increased rapidly with bicarbonate dialysis but not with acetate dialysis. Until the end of dialysis, each hourly serum $[HCO_3^-]$ was significantly higher than the value measured in the previous hour with bicarbonate dialysis. Compared to predialysis levels, serum $[HCO_3^-]$ remained higher throughout the postdialysis period. These data indicate that during bicarbonate dialysis, the changes in serum $[HCO_3^-]$ occur rapidly and persist at least 90 min after dialysis. In contrast, acetate dialysis caused very slow changes in serum $[HCO^-_3]$ (hourly increments in $[HCO^-_3]$ were never significant when compared to the $[HCO_3^-]$ measured the previous hour). All the same, at 2 hr the mean serum $[HCO_3^-]$ became significantly higher than predialysis level and remained so during the postdialysis periods.

Correlation between serum $[K^+]$ and pH and serum $[K^+]$ and $[HCO_3^-]$

During dialysis with bicarbonate, the decreasing level of serum $[K^+]$ correlated inversely with the rising blood pH ($r = 0.639$) and serum $[HCO_3^-]$ ($r = 0.642$). In contrast, during acetate dialysis, the serum $[K^+]$ correlated poorly with blood pH ($r = 0.339$) and not at all with serum $[HCO_3^-]$ ($r = 0.066$; Figure 3).

DISCUSSION

Our study shows that serum $[K^+]$ decreases more during bicarbonate dialysis than during acetate dialysis and, yet, potassium removal through the dialysis membrane is the same with both types of dialysates. Thus, the greater decrease in serum $[K^+]$ during the last 2 hr of bicarbonate dialysis suggests that potassium may have shifted into the cells at a higher rate than during dialysis with acetate. This notion is relevant because redistribution of potassium into the cells by changes in serum $[HCO_3^-]$ is generally accepted.[9] According to this view, bicarbonate administration through the dialysis bath could have caused potassium to move into the cell. In contrast, other studies suggest that bicarbonate-induced potassium translocation does not occur in organic or anion gap acidosis.[10–12]

Hence, because most forms of acidosis in chronic renal failure are associated with high anion gap, it seems unlikely that bicarbonate administration through the dialyzer would cause potassium redistribution. Moreover,

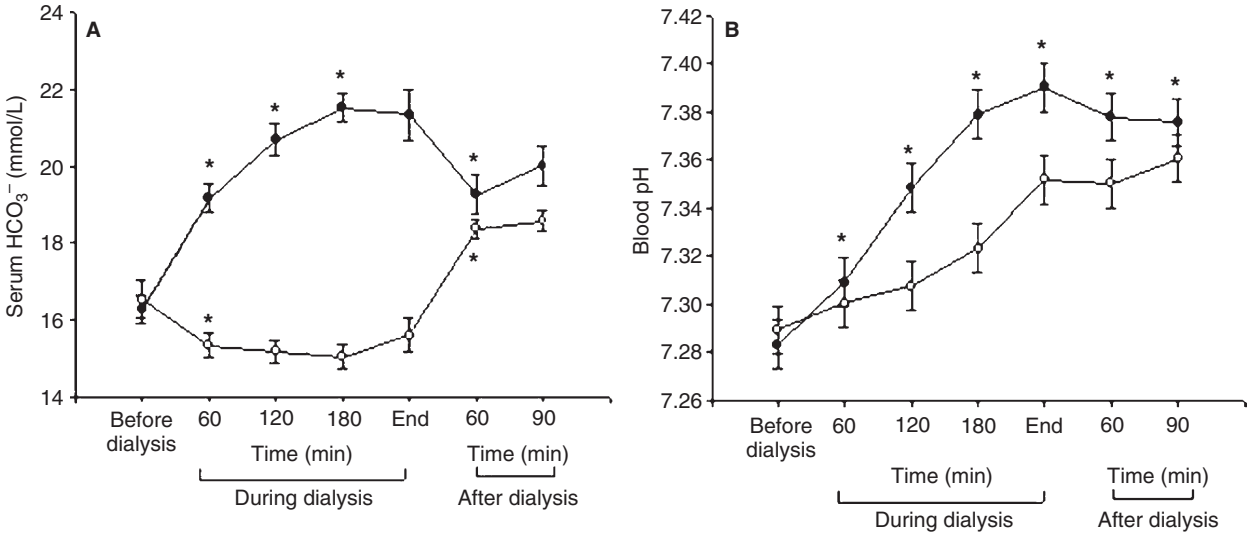

Figure 2 Blood pH and serum $[HCO^-_3]$ during bicarbonate (●) and acetate (○) dialysis.

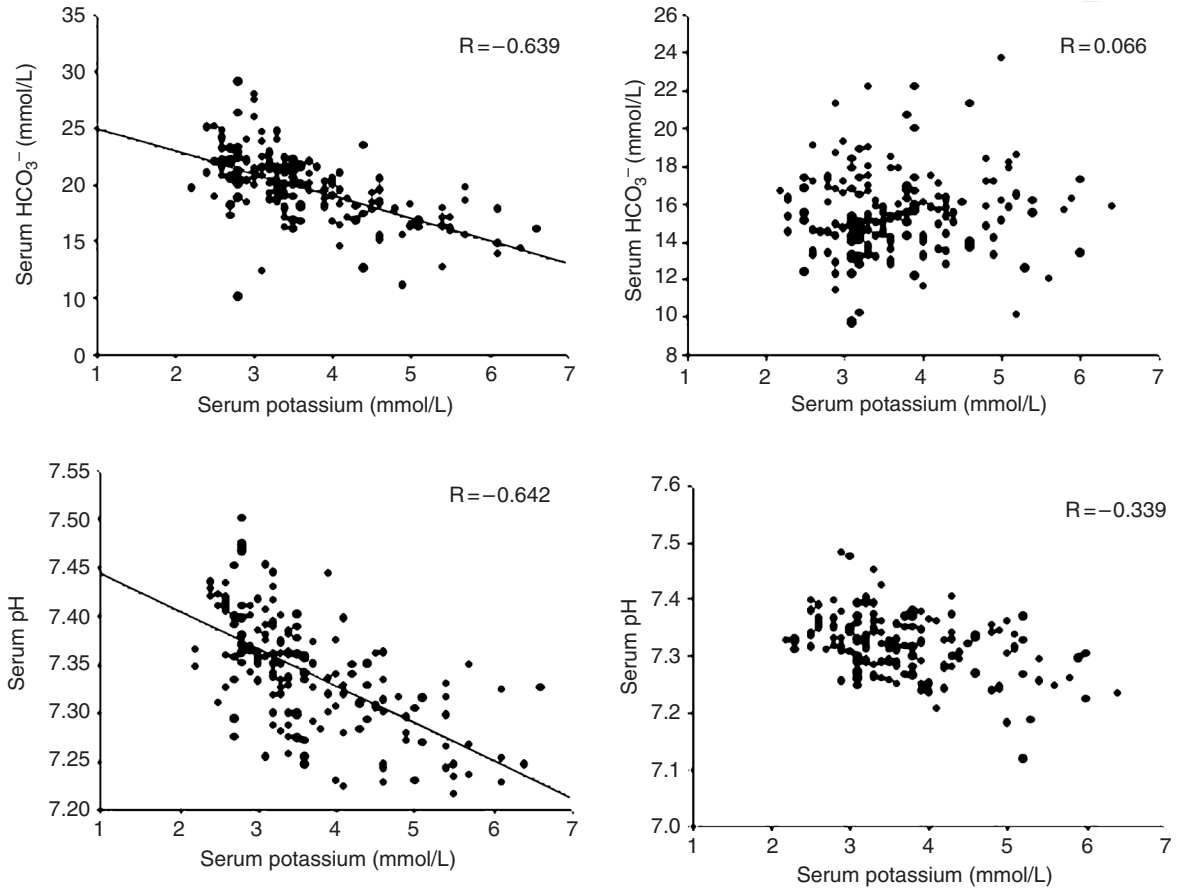

Figure 3 Correlations between serum potassium and serum [HCO_3^-] (top row) and serum potassium and blood pH (bottom row) during bicarbonate (left column) and acetate (right column) dialysis.

short-term (60 min) effects of bicarbonate infusions on serum [K^+] are exceedingly small or altogether absent.[13] This lack of effect from bicarbonate is supported by studies of Dalal *et al.*[14] showing equal lowering of serum [K^+] and equal potassium removal with both bicarbonate and acetate dialysis. Likewise, Williams *et al.*[15] found no evidence of potassium shifting in eight patients dialyzed against either bicarbonate or acetate buffers.

Unfortunately, the authors did not report postdialysis serum [K^+] and, thus, a rebound that could have taken place immediately after dialysis as a result of a reverse cell-to-blood K^+ shifting could not be appreciated. Be that as it may, it appears anyway that bicarbonate infusion could bring about shifting of potassium into the cell but only 3 to 4 hr after bicarbonate administration, as proposed by Blumberg *et al.*[16] Concurring with this notion, our findings suggest potassium redistribution toward the end of bicarbonate dialysis. That is, potassium could have moved out of the extracellular compartment, over and beyond any shifting that could have taken place during acetate dialysis. This notion is further sustained by the larger rebound observed 90 min after ending dialysis with bicarbonate.

The reasons for such redistribution seem unrelated to changes in blood glucose[8] because we excluded diabetics and did not allow glucose in dialysis baths. In addition, redistribution by catecholamine release because of fluid contraction seems unlikely as we held similar ultrafiltration rate and total fluid removals during both kinds of dialysis.[17] This also should have ruled out differences in K^+ removal by solute drag. Thus, because dialysate buffers were the only differences allowed, the mechanisms for potassium redistribution must be searched in the changes in blood pH and [HCO_3^-]. In fact, the increases in blood pH and [HCO_3^-] were swifter and more striking with bicarbonate dialysis than with acetate dialysis. This early changes in blood pH and in serum [HCO_3^-] could then account for a shifting of potassium into the cells as

shown in the literature[10–12] and thus the differences observed in serum $[K^+]$ after the second hour of dialysis. Studies in normal subjects have shown that bicarbonate-induced shifting of potassium is a late effect.[16] Supporting this alkalinization-induced redistribution, the serum $[K^+]$ in our study showed a strong inverse correlation with both blood pH and serum $[HCO_3^-]$ during dialysis with bicarbonate, but not during dialysis with acetate. Actually, acetate also increased serum $[HCO_3^-]$ but, if any K^+ redistribution took place, it must have been an insignificant event.

Alternatively, the lower serum $[K^+]$ during the last 2 hr of bicarbonate dialysis could have resulted from a dilutional effect. Such a dilution could have taken place if bicarbonate from the bath had entered the blood compartment at a rate that would drive water from the cells and dilute the serum K^+. In contrast to bicarbonate, acetate buffering is slow and incomplete (approx. one-half enters alternative metabolic pathways).[18,19] Thus, significant shifting of water would not be expected during acetate dialysis. In support of this notion, in our study serum $[HCO_3^-]$ during bicarbonate dialysis increased much earlier than with acetate dialysis. The idea of dilution, however, to explain the differences in serum potassium after the second hour suffers from a counternotion. That is, if indeed serum $[K^+]$ was lowered by dilution, the potassium gradient would also be lower, and therefore, the total potassium removal should have been decreased. Be that as it may, neither dilution nor shifting of serum potassium into the cells diminished the efficiency of potassium removal during bicarbonate dialysis. A reason for this undisturbed removal may rest in a slow and late process that took place too late in dialysis when the gradient had already decreased and the dialysance was negligible.[16]

In summary, our data suggest that internal K^+ redistribution occurs during bicarbonate dialysis. These effects are late, when most of the K^+ had already been removed and the transmembrane K^+ gradient had shrunk to minimal levels. In this manner, total K^+ removal is unaffected during bicarbonate dialysis.

Manuscript received October 2004; revised January 2005.

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