Normalization of Uremic Acidosis in Hemodialysis Patients With a High Bicarbonate Dialysate

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ABSTRACT

Uremic acidosis accompanies chronic renal failure in hemodialysis patients because of a retention of nonvolatile acids. Standard bicarbonate (39 mEq/L) and acetate (38 mEq/L) dialysates do not completely correct the acidosis. The acid-base and biochemical effect of a high-bicarbonate (42 mEq/L) dialysate was evaluated in 38 patients during high-efficiency and high-flux dialysis over 12 wk. All patients were dialyzed on standard bicarbonate dialysate before the study and for 8 wk after the study. In order to monitor potential excessive alkalosis, predialysis and postdialysis arterial blood gases were measured in seven patients who initially had a normal predialysis pH. Serum chemistries revealed no significant changes in predialysis BUN, calcium, ionized calcium, or phosphorus during the 12-wk study. There was no change in postdialysis ionized calcium or phosphorus. Predialysis and postdialysis serum total CO2 (STCO2) increased over the 12-wk study (P < 0.0001). By week 12, 75% of the hemodialysis patients had an STCO2 > 23 mEq/L and no patient had an STCO2 > 30 mEq/L predialysis. After the 8-wk washout, all chemistries were no different from presudy concentrations. Predialysis blood gases in seven patients with normal predialysis HCO3 revealed a significant increase (P < 0.009) in PCO2 and HCO3 over the 12-wk study; predialysis pH and PO2 did not change. There was no significant change in postdialysis blood gases. It was concluded that: (1) a high-bicarbonate dialysate corrects predialysis acidosis in 75% of hemodialysis patients without causing progressive alkalemia, hypoxia, or hypercarbia; and (2) predialysis BUN, calcium, ionized calcium, and phosphorus are unaffected by high-bicarbonate dialysate.

Key Words: Acidosis, hemodialysis, bicarbonate, blood gases, high-flux dialysis

One of the goals of hemodialysis therapy in the chronic renal failure patient is the correction of metabolic acidosis resulting from the inability to excrete hydrogen ions. The degree of acidosis present in dialysis patients can vary widely in severity depending on the length of each dialysis treatment, protein intake, frequency of dialysis treatments, and the type of buffer present in the dialysate. Persistent metabolic acidosis can have adverse consequences for bone metabolism and formation (1-3). Continued buffering of acid by skeletal carbonates may occur with only a minimal decrease in serum CO2 (4). Chronic acidosis has also been shown to adversely affect nitrogen balance and protein homeostasis in animals and humans (5-7).

Several studies using acetate or bicarbonate dialysate buffers in concentrations up to 36 mEq/L reveal that predialysis HCO3 is low, indicating that standard bicarbonate and acetate dialysates do not completely correct uremic acidosis (8-10). This study was performed to determine the ability of a high-bicarbonate dialysate (HBD) (42 mEq/L) to correct predialysis uremic acidosis in a group of stable chronic hemodialysis patients. The effect of chronic high-bicarbonate dialysate on biochemical parameters and arterial blood gases was also assessed.

MATERIALS AND METHODS

The study was approved by the Human Investigations Committee of Emory University, and 38 patients gave informed consent to participate in the study. All patients had been previously dialyzed with standard bicarbonate containing Na+ (139 mEq/L), K+ (2.0 mEq/L), Ca2+ (2.5 mEq/L), Mg2+ (1.0 mEq/L), Cl- (105.5 mEq/L), HCO3- (36 mEq/L), acetate (3 mEq/L) (total base 39 mEq/L), and glucose (100 mg/dL) dialysate for at least 6 months before the study. Acetate, as acetic acid, is added to the dialysate to react with an equimolar concentration of HCO3, leading to the generation of dissolved PO2 for pH control of the final dialysate. The resultant dialysate thus contains 36 mEq/L of HCO3 and 3 mEq/L of acetate, which is metabolized by the liver and consumes an H+ ion. High-flux dialysis was performed in 13 pa-
tients with CT-190 (Baxter Laboratory, Chicago, IL) dialyzers. High-efficiency dialysis was performed in 25 patients with CA-210 (Baxter) dialyzers. Ultrafiltration control hemodialysis machines (model 480: Drake-Willock, Portland, OR) were used for all treatments. Blood flows were 400 mL/min, and dialysate flows were 500 mL/min. Dialysis time was calculated for each patient to achieve a 55% reduction in predialysis BUN. All patients were dialyzed thrice weekly.

HBD contained the following electrolytes: Na⁺ (139 mEq/L), K⁺ (2.0 mEq/L), Ca²⁺ (2.5 mEq/L), Mg²⁺ (1.0 mEq/L), Cl⁻ (102.5 mEq/L), HCO₃⁻ (39 mEq/L), acetate (3 mEq/L) (total base 42 mEq/L), and dextrose (100 mg/dL). Serum chemistries measured during the study included BUN, total calcium (Ca), ionized calcium (ICa), phosphorus (P), and serum total carbon dioxide (STCO₂). Serum chemistries were obtained predialysis initially, every 2 wk during the study, and after the 8-wk washout. Postdialysis serum chemistries were obtained 10 min after dialysis on weeks 0 and 12.

Seven patients with normal prestudy predialysis values of pH and Pco₂ had repeated blood gas measurements predialysis and postdialysis to assess the maximum effect of HBD on pH and Pco₂. If progressive alkalalemia occurred, it would be present in the group of patients who began the study with normal blood gas status. Blood gas measurements for pH, Pco₂, and PO₂ were measured, within 5 min of sampling, in heparinized whole blood with a Corning Model 168 Arterial Blood Gas Analyzer (Ciba-Corning, Medfield, MA); samples were obtained predialysis and 10 min postdialysis on weeks 0, 4, and 12.

All data were analyzed with the general linear models (GLM) program from SAS* version 5.18 (SAS Institute Inc, Cary, NC) for paired samples. The t test procedure was used to compare changes after the washout. P ≤ 0.05 was considered significant.

RESULTS

All 38 patients completed the study. pH, Pco₂, and PO₂ analysis of the dialysate solutions used during the study revealed: (mean ± SE, [N = 24]) pH = 7.31 ± 0.008; Pco₂ = 79.1 ± 1.3 mm Hg, PO₂ = 114.9 ± 3.9 mm Hg, HCO₃⁻ = 39.7 ± 0.23 mEq/L, and TCO₂ = 42.1 ± 0.25 mEq/L. The overall prerruction to post reduction in BUN was 54% at the beginning of the study and 58% at week 12. There were no changes in the dialysis prescription for any patient during the study. Predialysis and postdialysis STCO₂ concentrations observed during the study are shown in Figure 1. There were significant (P < 0.0001) increases in both predialysis and postdialysis STCO₂ over 12 wk with HBD. STCO₂ decreased significantly (P < 0.009) to prestudy concentrations after the 8-wk washout when standard bicarbonate dialysate was used. Seventy-five percent of the patients had a predialysis STCO₂ > 23 mEq/L by week 12 of the study, whereas only 8% of the patients had a predialysis STCO₂ > 23 mEq/L before the study. There were no patients in whom predialysis STCO₂ exceeded 30 mEq/L. STCO₂ concentrations postdialysis were > 30 mEq/L in 10 out of 38 patients (26%) but did not exceed 34 mEq/L in any patient.

Arterial blood gas data from seven patients with normal prestudy pH and Pco₂ are listed in Table 1. There was no significant change in predialysis pH or PO₂ over the study. There was a small but significant (P < 0.009) increase in predialysis Pco₂ (mean Δ < 3.6 mm Hg) over the study. There were no significant changes in any postdialysis blood gas parameter over 12 wk with HBD.

Predialysis and postdialysis serum biochemical parameters are listed in Table 2. There was no significant change in predialysis BUN either during the study or after the washout. Predialysis ICa data from weeks 2 and 4 were not used in the analysis because of incomplete sample collection. Predialysis ICa, Ca, and P were unchanged over the study; however, Ca and P decreased significantly (P < 0.05) after the washout. Postdialysis ICa and P were unchanged over 12 wk, whereas postdialysis Ca increased (P < 0.05) significantly. There was no difference in predialysis or postdialysis STCO₂, BUN, Ca, ICa, P, or %Δ BUN in high-flux compared with high-efficiency dialysis.

DISCUSSION

This study demonstrates that: (1) HBD normalizes predialysis serum bicarbonate in over 75% of chronic hemodialysis patients; (2) predialysis BUN, Ca, ICa, and P were not changed by HBD; (3) increasing postdialysis alkalalemia was not evident in arterial blood.
TABLE 1. Predialysis and postdialysis arterial blood gas data in seven patients with normal prestudy blood gases

<table>
<thead>
<tr>
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<td></td>
<td>0</td>
<td>4</td>
<td>12</td>
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<tr>
<td></td>
<td>Predialysis</td>
<td>Postdialysis</td>
<td>Predialysis</td>
<td>Postdialysis</td>
<td>Predialysis</td>
<td>Postdialysis</td>
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<tr>
<td>pH</td>
<td>7.39 ± 0.04</td>
<td>7.53 ± 0.01</td>
<td>7.41 ± 0.01</td>
<td>7.51 ± 0.01</td>
<td>7.41 ± 0.01</td>
<td>7.52 ± 0.01</td>
</tr>
<tr>
<td>Pco₂ (mm Hg)</td>
<td>39.0 ± 0.58</td>
<td>38.9 ± 0.86</td>
<td>42.6 ± 1.47</td>
<td>40.6 ± 0.73</td>
<td>41.4 ± 1.10</td>
<td>41.3 ± 0.75</td>
</tr>
<tr>
<td>P₀₂ (mm Hg)</td>
<td>77.5 ± 6.30</td>
<td>87.2 ± 3.70</td>
<td>73.1 ± 5.80</td>
<td>78.3 ± 5.90</td>
<td>73.9 ± 4.50</td>
<td>79.2 ± 2.60</td>
</tr>
<tr>
<td>HCO₃ mM</td>
<td>23.7 ± 0.39</td>
<td>32.9 ± 1.01</td>
<td>26.8 ± 0.58</td>
<td>32.1 ± 0.50</td>
<td>26.5 ± 0.30</td>
<td>33.5 ± 0.59</td>
</tr>
<tr>
<td>TCO₂ mM</td>
<td>24.9 ± 0.41</td>
<td>34.4 ± 0.93</td>
<td>28.1 ± 0.62</td>
<td>33.3 ± 0.53</td>
<td>27.8 ± 0.30</td>
<td>34.8 ± 0.56</td>
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*P < 0.009 over the study.

**P < 0.0002 over the study.

TABLE 2. Biochemical analysis in all patients during the study²

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<tr>
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<td>0</td>
<td>12</td>
<td>20</td>
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<tr>
<td>BUN pre</td>
<td>73.2 ± 2.2</td>
<td>71.0 ± 3.2</td>
<td>69.6 ± 2.1</td>
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<tr>
<td>BUN post</td>
<td>33.6 ± 1.4</td>
<td>29.3 ± 1.3³</td>
<td>ND</td>
<td></td>
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<td></td>
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<tr>
<td>ICA pre</td>
<td>2.32 ± 0.04</td>
<td>2.32 ± 0.05</td>
<td>2.30 ± 0.04</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICA post</td>
<td>2.23 ± 0.04</td>
<td>2.17 ± 0.04</td>
<td>ND</td>
<td></td>
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<tr>
<td>Ca pre</td>
<td>9.71 ± 0.18</td>
<td>9.74 ± 0.10</td>
<td>9.2 ± 0.13³</td>
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<tr>
<td>Ca post</td>
<td>9.26 ± 0.11</td>
<td>9.52 ± 0.07³</td>
<td>ND</td>
<td></td>
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<tr>
<td>P pre</td>
<td>5.60 ± 0.38</td>
<td>5.93 ± 0.38</td>
<td>4.8 ± 0.27³</td>
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<tr>
<td>P post</td>
<td>3.06 ± 0.18</td>
<td>3.25 ± 0.19</td>
<td>ND</td>
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</tbody>
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* Values are mean ± SE. Data are reported as milligrams per deciliter; ICA is reported as milliequivalents per liter. Pre, predialysis; post, postdialysis; ND, not determined.

* P < 0.05 from weeks 0 to 12.

* P < 0.05 from weeks 12 to 20.

Gas measurements; (4) there was no postdialysis hypoxemia or hypercarbia with HBD.

Numerous studies with both acetate and bicarbonate in concentrations from 29 to 39 mEq/L have failed to normalize predialysis STCO₂ (8–11). Kobrin and Raja studied the effects of a dialysate bicarbonate of 40 mEq/L over a 2-wk period (12). The mean predicted predialysis serum bicarbonate obtained with a 40-mEq/L bicarbonate bath was ~23.7 mEq/L. However, the use of this system requires a concomitant reduction or increase in dialysate sodium for the adjustment of the dialysate bicarbonate concentration. Ahmad et al. also reported normalization of predicted predialysis serum bicarbonate with the use of a 40-mEq/L bicarbonate dialysate after two to five dialyses (13).

A potential complication of long-term HBD may be the development of chronic metabolic alkalosis postdialysis. Kobrin and Raja reported arterial blood gases observed with a 40-mEq/L bicarbonate dialysate in seven patients (12). Postdialysis TCO₂ averaged 29 mEq/L, whereas postdialysis pH was nearly 7.50. They observed no significant changes in Pco₂ or P₀₂ over the study. Our results obtained in seven patients who began the study with a normal pH and Pco₂ agree with those of Kobrin and Raja. Although postdialysis TCO₂ increased in these seven patients from 24.3 to 28.9 mEq/L after 12 wk, the postdialysis pH remained unchanged. Thus, progressive alkalosis did not develop in those patients who began the study with normal acid-base parameters. The lack of progression of alkalosis indicates the attainment of a new steady state for bicarbonate transfer during dialysis. These data indicate that the postdialysis alkalosis observed with HBD was no different than what is normally observed with standard bicarbonate dialysate. If progressive metabolic alkalosis did occur, a compensatory hypercarbia would be observed. However, the increase in Pco₂ postdialysis over the study was minimal. A slight compensatory predialysis increase in Pco₂ of 3.6 mm Hg was well within the normal range for Pco₂. The predicted HCO₃⁻ and TCO₂ obtained during the study from blood gas data are higher than the STCO₂ concentrations measured by titrametric methods. However, it is well documented in studies by Trenchard et al. (14), Santoro et al. (15), and Natelson and Nobel (16) that shifts in the pK⁺ of bicarbonate in patients with chronic renal disease leads to erroneous results when the Henderson-Hasselbalch equation is used to predict HCO₃⁻ and TCO₂. These reports recommend the use of serum titrametric methods for the measurement of CO₂.

The correction of metabolic acidosis in hemodialysis patients may result in improvements in both bone and protein metabolism. Chronic metabolic acidosis has been shown to decrease bone carbonate, calcium, and phosphate stores, which may lead to osteomalacia or osteopenia (1–4,17–19). The correction of sustained metabolic acidosis with alkali therapy has been shown to produce a significant rise in bone mineralization rate and a positive trend in cal-

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cium balance (3). The relationship observed was approximately 1 nEq of Ca$^{2+}$ efflux for 16 to 21 nEq of proton influx. In addition, long-term ingestion of bicarbonate salts has been shown to prevent the development of osteopenia due to an increase in bone formation (20). The normalization of acid-base balance observed during HBD may improve bone formation rates as well as decrease the progression of secondary hyperparathyroidism in patients with high bone turnover rates (21).

Another potential benefit in correcting acidosis in dialysis patients may be to decrease protein degradation. Studies in experimental animals and in vitro observations have demonstrated increased protein breakdown in response to metabolic acidosis (5–7, 22). However, whether normalizing acid-base balance in patients on dialysis has a protein-sparing effect has not been studied.

These data demonstrate that HBD is effective in ameliorating the predialysis acidosis in the majority of chronic hemodialysis patients without producing progressive alkalosis. The potential benefit to bone mineralization may help to alleviate the osteopenia and osteodystrophy associated with chronic renal failure. In addition, improvements in nitrogen balance and protein homeostasis may be observed after the normalization of predialysis uremic acidosis. The long-term effects of the normalization of $\text{HCO}_3^{-}$ on protein and bone metabolism require further study.

ACKNOWLEDGMENTS

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