

# The effect of hemodialysis on electrolytes and acid–base parameters

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## Abstract

**Background:** Hemodialysis patients are treated with bicarbonate dialysate to correct the metabolic acidosis, which results from the metabolism of dietary and endogenous protein. The concentration of plasma  $t\text{CO}_2$  is used to gauge the success of therapy. Reported low values in pre-dialysis blood suggest incomplete correction of acidosis in a substantial percent of the dialysis population. However, questions have been raised about the reliability of  $t\text{CO}_2$  determination in dialysis patients. **Methods:** Pre- and post-dialysis blood specimens were obtained from chronic hemodialysis patients and analyzed on-site using an OPTI Critical Care Analyzer. Results were compared with reports obtained monthly from the reference laboratory to which the samples were routinely shipped for analysis. In addition, OPTI analyzer whole blood electrolytes were compared with plasma electrolytes determined in a local laboratory. **Results:** Mid-week testing of patients dialyzed against a 40-mmol/l bicarbonate dialysate found that most patients had normal acid–base status pre-dialysis and frank metabolic alkalosis by the end of dialysis. Whole blood  $t\text{CO}_2$  values determined on the OPTI CCA were 2.4 mmol/l greater than heparin plasma  $t\text{CO}_2$  assayed on the Vitros chemistry analyzer. Small differences were also observed for  $\text{K}^+$  and  $\text{Cl}^-$ . **Conclusions:** Based on our on-site determination of acid–base and electrolyte concentrations, metabolic acidosis appears to be fully correctable in well-dialyzed renal failure patients. Metabolic alkalosis is apparent in the post-dialysis period.

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## 1. Introduction

As kidney function declines, individuals ingesting a typical Western-style diet high in protein develop metabolic acidosis with an increase in the anion gap [1]. There is evidence that metabolic acidosis leads to tissue protein catabolism [2–4], promotes loss of mineral from bone [5], and intensifies insulin resistance [6]. Many patients with end-stage kidney failure

are receiving regular hemodialysis with bicarbonate dialysate in an attempt to prevent or minimize the complications of metabolic acidosis. Dialysate bicarbonate concentrations of 35–40 mmol/l are used to provide a gradient for bicarbonate to diffuse into patients at a rate sufficiently high to titrate the accumulated acid and provide a measure of base excess to carry the patients through the next interdialytic interval. Management of metabolic acidosis is dictated by the plasma concentration of  $t\text{CO}_2$  in a pre-dialysis blood sample. From published reports as well as results from our dialysis program, current hemodi-

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alysis management appears not to normalize the bicarbonate concentration in a large percent of the dialysis population [1,2,7–9]. The reasons for this failure are not entirely clear, but data have been presented suggesting that  $t\text{CO}_2$  concentrations may be falsely low in serum samples shipped to distant laboratories and analyzed many hours after the blood was drawn [8,10].

The present study was designed to examine the changes in acid–base and electrolyte concentrations during the course of a single dialysis. We were interested in defining the frequency and magnitude of metabolic alkalosis induced in patients dialyzing against high bicarbonate dialysate defined as 40 mmol/l. We also paid particular attention to changes in blood potassium concentrations in view of alkalosis-related reduction of plasma  $\text{K}^+$  concentration and the potential arrhythmogenicity of hypokalemia in a patient population at high risk for cardiovascular disease.

## 2. Methods

Mid-week blood specimens were drawn from the arterial line into 3 ml lithium heparin plastic syringes (BD Drihep Plus, BD Vacutainer Systems) at the beginning and end of dialysis. The sealed samples were kept at room temperature and analyzed within 30–60 min. An AVL OPTI Critical Care Analyzer was used with E-CI cuvettes. The analyzer was calibrated with three reference cassettes according to the instructions of the manufacturer. The performance of each batch of cassettes was tested using three concentrations of liquid control solutions.

Blood samples assayed by the reference laboratory were drawn into 4 ml Vacuette tubes with clot activator and separator (Greiner Bio-one). After a variable time, the tubes were centrifuged and refrigerated, then packaged with Frigid Ice (TechPak, Peabody MA) and flown overnight to the reference laboratory located in Fort Lauderdale, FL for analysis the following day. The OPTI CCA calculated total bicarbonate from the measured pH and  $p\text{CO}_2$  using the Henderson–Hasselbach equation. The reference laboratory assayed  $t\text{CO}_2$  directly using either a Hitachi H 747 chemistry analyzer (Roche Diagnostics, Indianapolis, IN) or an Olympus AU 5200 analyzer (Olympus America, Melville, NY).

Body mass index (BMI) was calculated as weight (kg)/height (m)<sup>2</sup>. Percent body fat was calculated as  $1.281 \times \text{BMI} - 10.13$  for men and  $1.48 \times \text{BMI} - 7.0$  for women [11]. The formulae of Chertow and Watson were used to calculate total body water [12]. The percent change in plasma volume was calculated as  $(\text{HCT}_{\text{post}} - \text{HCT}_{\text{pre}}) \times 100 / \text{HCT}_{\text{pre}}$ . The anion gap was calculated as  $(\text{Na}^+ - \text{Cl}^- - t\text{CO}_2)$ .

Seventeen chronic hemodialysis patients provided written consent to participate in this study. There were nine men and eight women with an age range from 32 to 83 years. Six patients had diabetes. Twelve patients had blood withdrawn from arteriovenous fistulae or grafts while five samples were taken from central venous catheters. Mean weight, BMI, and percent body fat were 79.6 kg (95% CI=70.3–88.8), 27.2 (95% CI=24.7–29.7), and 28.7 (95% CI=24.6–32.7). The fat-free body mass (FFBM) averaged 56.1 kg (95% CI=49.9–62.2). The percent water of the FFBM was 78.1 (95% CI=76.9–79) and 70.4 (95% CI=69.3–71.5) by the formulae of Chertow and Watson, respectively. Patients dialyzed from 3.5 to 4.5 h, 3 days a week against a 40 mmol/l bicarbonate, 2.0 mmol/l  $\text{K}^+$  dialysate. Dialyzers were not reused. None of the patients was taking supplemental base other than calcium carbonate.

Data are presented as the mean with 95% confidence limits. Two-tailed paired and unpaired  $t$  tests were used to evaluate significance of differences among the means. Linear regression analysis was used to determine associations among variables. A  $p < 0.05$  was accepted as significant.

## 3. Results

Acid–base and electrolyte results are listed in Table 1 with separate listings for arterial and venous samples. The mean pre-dialysis pH for all samples was 7.37 (95% CI=7.34–7.43). The pH of venous samples was significantly lower than arterial blood. pH increased significantly during dialysis in both groups. The increase was associated with significant increases in  $t\text{CO}_2$  and  $\text{HCO}_3^-$ , whereas  $p\text{CO}_2$  did not change. The average  $\text{HCO}_3^-$  value in post-dialysis blood was in excess of 30 mmol/l. Among the strong ions, both  $\text{K}^+$  and  $\text{Cl}^-$  exhibited statistically significant decreases during dialysis, whereas  $\text{Na}^+$  did not

Table 1  
Blood gas and electrolyte values pre- and post-dialysis

Parameter	Pre-dialysis			Post-dialysis		
	All	CVC	Graft	All	CVC	Graft
pH	7.37 (7.34–7.43)	7.30 (7.26–7.33)	7.40 (7.38–7.43)	7.49 (7.45–7.57)	7.40 (7.33–7.46)	7.52 (7.50–7.55)
pCO <sub>2</sub>	42.5 (40.2–47.3)	46.7 (41.6–51.8)	40.7 (39–42.5)	43.0 (38.1–53.2)	53.6 (43.2–64)	38.6 (35.6–41.6)
tCO <sub>2</sub>	25.5 (23.7–29.1)	23.8 (21.2–26.4)	26.2 (24–28.2)	32.5 (31.1–35.3)	33.3 (30.8–35.9)	32.1 (30.5–33.7)
HCO <sub>3</sub> <sup>-</sup>	24.2 (22.5–27.8)	22.3 (19.8–24.8)	24.9 (22.8–27)	31.1 (29.9–33.8)	31.7 (29.4–34)	30.9 (29.4–32.5)
BE	-1.1 (-3.1–3.0)	-4.2 (-6.6–1.8)	0.1 (-2.1–2.4)	7.0 (5.8–9.5)	5.4 (3.6–7.2)	7.7 (6.3–9.0)
Na <sup>+</sup>	138 (136–144)	135 (128–142)	140 (138–142)	139 (139–141)	140 (137–142)	139 (138–140)
K <sup>+</sup>	4.5 (4.2–5.1)	4.6 (3.7–5.5)	4.4 (4.2–4.6)	3.2 (3–3.4)	3.1 (2.7–3.5)	3.2 (3.1–3.3)
Cl <sup>-</sup>	103 (101–108)	101 (94–108)	104 (103–105)	100 (99–101)	99 (97–101)	100 (99–101)
AG	15.8 (14.4–18.8)	16.9 (14.4–19.3)	15.3 (13.6–17.1)	11.7 (11–13)	12 (10.9–13.1)	11.6 (10.8–12.4)
HCT	32.8 (31.3–36)	36.3 (33.7–38.9)	31.3 (30.2–32.5)	37.6 (34.8–43.6)	41.5 (35–48)	36 (33.3–38.6)

Mean and 95% confidence limits are presented. Units are mm Hg for blood gases, mmol/l for electrolytes and anion gap, percent for hematocrit. CVC refers to central venous catheters.

change. The K<sup>+</sup> concentration fell by 1.3 mmol/l (95% CI 1.1–1.6), and all post-dialysis K<sup>+</sup> concentrations were below 3.5 mmol/l. As a result of these changes, there was a decrease in the anion gap of 4 mmol/l. On average, plasma volume decreased by 14.6% (95% CI= 11.2–14.6).

No correlation was observed between the change in plasma bicarbonate and change in plasma volume or body weight, BMI, total body water by either formula, fat-free body mass, or percent water of the FFBM. No correlation was seen between the post-dialysis HCO<sub>3</sub><sup>-</sup> and any of the parameters related to body or water mass. The water volumes calculated with the formula of Chertow were statistically larger than those using the Watson formula.

Results reported from the reference laboratory for these same 17 patients were as follows (mmol/l): Na<sup>+</sup> 139 (95% CI= 137–142), K<sup>+</sup> 5.0 (95% CI= 4.7–5.3), Cl<sup>-</sup> 99 (95% CI= 96–102), tCO<sub>2</sub> 18.4 (95% CI= 16.8–19.9). Of 17 tCO<sub>2</sub> values, 16 were ≤ 21 and 9 of 17 ≤ 19 mmol/l. The calculated anion gap

was 22.2 (95% CI= 20.4–24.0). It should be noted that these values were obtained after a 3-day interval from the last dialysis. Based on published values, tCO<sub>2</sub> concentrations obtained after a 3-day interval are expected to average < 1.0 mmol/l lower than after a 2-day interval [9]. Among our patients, the 2-day on-site values were 7.1 mmol/l higher than the 3-day central laboratory results. This discrepancy in tCO<sub>2</sub> values accounted entirely for the 6.4 mmol/l difference in the anion gap between the two sets of samples.

Nine specimens were drawn into sterile, lithium heparin vacuum tubes. An aliquot of whole blood was withdrawn by puncturing the rubber stopper with a needle but without exposing the blood to room air. The whole blood sample was assayed immediately using the OPTI analyzer. The heparinized tube was then delivered to the Clinical Chemistry Laboratory at The Medical College of Virginia Hospital and processed for routine plasma electrolytes using a Vitros 950 analyzer (Ortho Clinical Diagnostics, Raritan, NJ). These results are shown in Table 2. Small but statistically significant differences between whole blood and plasma K<sup>+</sup> and Cl<sup>-</sup> were found. The difference in tCO<sub>2</sub> was also significant, with the mean whole blood concentration 2.4 mmol/l greater than for plasma.

Table 2  
Comparison of whole blood and plasma electrolytes

	Whole blood		Plasma		p-value
	Mean	95% CI	Mean	95% CI	
Na <sup>+</sup>	142	140–145	143	142–145	0.07
K <sup>+</sup>	4.2	3.9–4.5	4.3	4.0–4.7	<0.001
Cl <sup>-</sup>	103	101–106	101	98.8–103	<0.001
tCO <sub>2</sub>	29.6	27.8–31.4	27.2	25.5–28.9	<0.001

Whole blood electrolytes were assayed on the OPTI critical care analyzer, plasma electrolytes on the Vitros chemistry analyzer.

#### 4. Discussion

Among the many changes in dialysis therapy of end-stage kidney failure over the years has been the switch to bicarbonate dialysate and an increase in the

concentration of bicarbonate in an attempt to treat metabolic acidosis. Despite a 40 mmol/l dialysate, very few of the dialysis patients in our chronic program had achieved normal plasma bicarbonate values in their pre-dialysis blood samples. A prior study [8] raised concern about artifactual lowering of the  $t\text{CO}_2$  (test used to define acid–base status). The escape of  $\text{CO}_2$  from the blood sample in the laboratory after prolonged exposure to room air has been postulated to cause erroneously low values [13,14]. This error may be exaggerated in plasma or serum samples that are shipped over long distances and analyzed many hours after being drawn, though proof of this assertion is lacking. There is concern as well about the possible leakage of  $\text{K}^+$  from cells during the interval between blood sampling and analysis since the high cellular concentration of  $\text{K}^+$  could increase plasma concentrations. Accurate  $t\text{CO}_2$  and  $\text{K}^+$  values are critically important for the management of patients with little or no residual kidney function.

Our results, obtained on-site using a portable blood gas-electrolyte analyzer, provide a more positive view of acid–base regulation by current dialysis technique and indicate that metabolic alkalosis, not acidosis, may be the predominant metabolic abnormality among adequately treated dialysis patients. Most of our patients had normal acid–base parameters pre-dialysis and frank metabolic alkalosis immediately post-dialysis based on the OPTI CCA results. In fact, 14 of 17 patients had  $t\text{CO}_2 \geq 30$  mmol/l. Although the on-site and reference laboratory electrolyte concentrations cannot be directly compared, it seems clear that the latter values provide a far different picture of the state of acid–base management compared to the on-site values. A similar though less marked discrepancy was observed in the case of potassium concentrations, which were always higher in the blood sent to the reference laboratory in comparison to the OPTI CCA values. These  $t\text{CO}_2$  findings are in disagreement with an unpublished study carried out by the reference laboratory that its values for  $t\text{CO}_2$  did not differ from those measured by a local laboratory<sup>1</sup> and with letters to the Editor written by the managers of two large laboratories servicing dialysis units [13,14].

<sup>1</sup> Personal communication to Dr. Anton Schoolwerth from Gambro Healthcare Laboratory Services, Fort Lauderdale, FL.

The on-site OPTI CCA and reference laboratory electrolyte concentrations reported in this paper were obtained on whole blood and serum, respectively. Analytical methods also differed. To approximate how much of the discrepancy in results could reasonably be attributed to differences in technology, we compared OPTI analyzer whole blood to heparinized plasma electrolytes, the latter measured on a Vitros chemistry analyzer in the Clinical Chemistry Laboratory of The Medical College of Virginia Hospital [8]. The mean value for the OPTI  $t\text{CO}_2$  was 2.4 mmol/l greater than the Vitros, a statistically significant difference but not large enough to account for the discrepancy with the reference laboratory values. Small though significant differences were found for both  $\text{K}^+$  and  $\text{Cl}^-$ .

Whereas some of the potential adverse effects of chronic metabolic acidosis have been reported [2–6], there is much less known about the toxicity, if any, of chronic metabolic alkalosis in the dialysis population. Should other studies of hemodialysis patients confirm the widespread prevalence of metabolic alkalosis, its effect on a host of risk factors for cardiovascular and bone disease will need to be defined.

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