Relationship Between Serum Total Carbon Dioxide Concentration and Bicarbonate Concentration in Patients Undergoing Peritoneal Dialysis

Keiji Hirai¹, Susumu Ookawara¹, Momoko Matsuyama¹, Taisuke Kitano¹, Kiyonori Ito¹, Yuichiro Ueda¹, Tatsuro Watano², Shinji Fujino², Kiyoka Omoto², Yoshiyuki Morishita¹

1. Division of Nephrology, First Department of Integrated Medicine, Saitama Medical Center, Jichi Medical University, Saitama, JPN 2. Department of Laboratory Medicine, Saitama Medical Center, Jichi Medical University, Saitama, JPN

Corresponding author: Keiji Hirai, keijihirai@kfy.biglobe.ne.jp

Abstract

Background

Few studies have assessed the relationship between serum total carbon dioxide (CO_2) and bicarbonate ion (HCO_3^-) concentration in patients undergoing peritoneal dialysis. We determined the agreement between serum total CO_2 and HCO_3^- concentration and the diagnostic accuracy of serum total CO_2 for the prediction of low ($\text{HCO}_3^- < 24 \text{ mEq/L}$) and high ($\text{HCO}_3^- \geq 24 \text{ mEq/L}$) bicarbonate concentrations in patients on peritoneal dialysis.

Methods

We collected 245 samples of venous blood from 51 patients on peritoneal dialysis. Independent factors that correlated with the HCO_3^- concentration were analyzed using multiple linear regression analysis. The diagnostic accuracy of serum total CO_2 was evaluated by receiver operating characteristic (ROC) curve analysis and a 2×2 table. Agreement between serum total CO_2 and HCO_3^- concentration was assessed by Bland-Altman analysis.

Results

Serum total CO_2 was independently correlated with HCO_3^- concentration ($\beta = 0.354$, $p < 0.001$). The area under the curve of serum total CO_2 for the identification of low and high bicarbonate concentrations was 0.909. The diagnostic accuracy of serum total CO_2 for the prediction of low and high bicarbonate concentrations was: sensitivity, 91.5%; specificity, 74.7%; positive predictive value, 53.5%; negative predictive value, 96.5%; and accuracy, 78.8%. Bland-Altman analysis showed a moderate agreement between serum total CO_2 and HCO_3^- concentration.

Conclusion

Serum total CO_2 correlated closely with the HCO_3^- concentration in patients undergoing peritoneal dialysis. Serum total CO_2 might be useful for predicting low and high bicarbonate in peritoneal dialysis patients.

Categories: Nephrology

Keywords: serum total carbon dioxide, bicarbonate, peritoneal dialysis

Introduction

Metabolic acidosis is a commonly observed complication in patients with chronic kidney disease (CKD), including those undergoing peritoneal dialysis, and is associated with bone mineral loss, protein energy-wasting, insulin resistance, and higher mortality risk [1-4]. It also contributes to a rapid decline in residual renal function [5]. Therefore, early detection and accurate diagnosis of metabolic acidosis is important to preserve residual renal function and improve prognosis in patients undergoing peritoneal dialysis.

In Japan, blood-gas analyzers are available in most hospitals. Therefore, bicarbonate ion (HCO_3^-) measured using arterial/venous blood gas samples has been widely used for the assessment of metabolic acidosis in peritoneal dialysis patients [6]. A lower HCO_3^- concentration has been reported to be associated with

Review began 02/04/2021

Review ended 03/22/2021

Published 03/25/2021

© Copyright 2021

Hirai et al. This is an open access article distributed under the terms of the Creative Commons Attribution License CC-BY 4.0., which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

How to cite this article

Hirai K, Ookawara S, Matsuyama M, et al. (March 25, 2021) Relationship Between Serum Total Carbon Dioxide Concentration and Bicarbonate Concentration in Patients Undergoing Peritoneal Dialysis. Cureus 13(3): e14119. DOI 10.7759/cureus.14119

increased mortality in patients undergoing peritoneal dialysis [7]. Because the HCO_3^- concentration is an important predictor of mortality, a specific device measurement and syringe are necessary, in addition to the blood samples used for blood-gas analyses [8].

The serum total carbon dioxide (CO_2) concentration represents the total amount of carbon dioxide in the serum. It can be readily measured, along with creatinine, urea, and electrolytes, using a biochemical analyzer in clinical settings [9]. Furthermore, serum total CO_2 has been shown to be correlated strongly with the HCO_3^- concentration in both patients with CKD not undergoing renal replacement therapy [10] and patients undergoing hemodialysis [11]. However, few studies have investigated the relationship between serum total CO_2 and the HCO_3^- concentration in patients undergoing peritoneal dialysis. We analyzed the relationship between serum total CO_2 and the HCO_3^- concentration in peritoneal dialysis patients.

Materials And Methods

Ethics approval

The study was approved by the ethics committee of Saitama Medical Center, Jichi Medical University (S17-052), and was conducted according to the principles contained within the Declaration of Helsinki. The requirement of informed consent was waived and an opt-out method was used because of the retrospective design of the study.

Participants

Inclusion criteria were: (i) age >20 years; (ii) CKD stage G5D; (iii) regular peritoneal dialysis; (iv) simultaneous measurement of serum total CO_2 and HCO_3^- concentrations. Exclusion criteria were: (i) hemodialysis and (ii) renal transplantation.

Study design

This was a single-center, retrospective, cross-sectional study. We analyzed the patient data obtained from medical records from the Division of Nephrology, Saitama Medical Center, between April 2017 and March 2019. The laboratory data of blood tests and venous blood-gas tests obtained simultaneously were used for analyses. The relationship between serum total CO_2 and the HCO_3^- concentration was analyzed using Pearson's correlation coefficient. Independent factors correlated with the HCO_3^- concentration were analyzed using multiple linear regression analysis. The diagnostic accuracy of serum total CO_2 for low and high bicarbonate was analyzed using receiver operating characteristic (ROC) curve analysis and a 2×2 table. The correlation between serum total CO_2 and HCO_3^- concentration was analyzed using Bland-Altman analysis.

Laboratory methods

Blood and urinary parameters were determined by the Department of Clinical Laboratory, Saitama Medical Center. Samples of venous blood were collected in EDTA-containing tubes from the antecubital vein in all patients and centrifuged within 15 minutes to obtain serum. Serum total CO_2 was measured within 15 minutes after centrifugation using an automated biochemical analyzer (JCA-BM6070; JEOL, Tokyo, Japan), as were biochemical parameters (hemoglobin, total protein, serum albumin, blood urea nitrogen, serum creatinine, sodium, potassium, chloride, calcium, phosphate, magnesium, and glucose). Serum total CO_2 was determined by an enzymatic method using a commercial kit (Toyobo, Osaka, Japan) in an automated biochemical analyzer. Total weekly urea clearance (Kt/V) was measured by calculating the sum of the residual renal and peritoneal clearances of urea and converting this to a weekly value [12]. Residual renal urea clearance was determined using 24-hour urine urea divided by plasma urea concentration. Total body water volume was estimated from height, weight, age, and gender using Watson's formula [13].

Samples of venous blood for gas analyses were collected in a heparinized blood-gas syringe from the brachial vein simultaneously with samples for other blood tests and analyzed within 10 minutes to obtain values for pH and the partial pressure of carbon dioxide (pCO_2). The pH and pCO_2 of blood were measured using a blood-gas analyzer (Rapidlab-1265; Siemens Healthcare Diagnostics, Tarrytown, New York). The HCO_3^- concentration was calculated from measured pH and pCO_2 using the Henderson-Hasselbalch equation [14]: $\text{pH} = 6.1 + \log([\text{HCO}_3^-]/\text{pCO}_2 \times 0.03)$.

Statistics

Statistical analyses were performed using JMP v11 (SAS Institute, Cary, North Carolina). Continuous variables were expressed as mean ± standard deviation when they were normally distributed and as median

and interquartile range when non-normally distributed. Categorical variables were expressed as numbers and percentages. The peritoneal dialysis duration was not normally distributed; therefore, this variable was transformed using a natural logarithm. The relationships between two variables were evaluated using Pearson's correlation coefficient. Linear regression analysis was used to identify parameters that independently correlated with HCO_3^- concentration. The parameters that significantly correlated with HCO_3^- concentration in simple linear regression analyses were included in subsequent multiple linear regression analysis. The diagnostic accuracy of serum total CO_2 was determined using ROC curve analysis and a 2×2 table. The area under the curve (AUC), sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were calculated for the identification of low ($\text{HCO}_3^- < 24 \text{ mEq/L}$) and high ($\text{HCO}_3^- \geq 24 \text{ mEq/L}$) bicarbonate concentrations. The cut-off value for HCO_3^- was set at 24 mEq/L based on a previous study [15]. Agreement between serum total CO_2 and HCO_3^- concentration was assessed using the Bland-Altman method. $P < 0.05$ was considered to represent statistical significance.

Results

Patient characteristics

Patients' characteristics and medications are shown in Table 1. A total of 245 blood samples from 51 patients (35 males and 16 females, mean age 62.3 ± 13.6 years, mean peritoneal dialysis duration 27.5 ± 29.6 months) were obtained. Forty-one patients (80.4%) were on continuous ambulatory peritoneal dialysis (CAPD), 33 patients (64.7%) on automated peritoneal dialysis (APD), and 23 patients (45.1%) on a combination of CAPD and APD. The mean total weekly Kt/V was 1.68 ± 0.39 . Thirty-three percent of the patients had diabetes mellitus. The proportions of the patients receiving each medication were: corticosteroid, 3.9%; β -blocker, 43.1%; renin-angiotensin system inhibitor, 72.5%; aldosterone receptor antagonist, 7.8%; loop diuretic, 64.7%; thiazide diuretic, 39.2%; tolvaptan, 29.4%; potassium binder, 0.0%; phosphate binder, 82.4%; vitamin D analog, 54.9%; calcimimetic, 21.6%; and sodium bicarbonate 0.0%. Calcium concentrations of each peritoneal dialysis solution were as follows: icodextrin solution, 1.75 mmol/L; lactate-buffered solution, 1.25 mmol/L; and bicarbonate-buffered solution 1.25 mmol/L.

Number of patients		51
Number of samples		245
Age (year)		62.3 ± 13.6
Gender male (number, %)		35 (68.6)
Body mass index (kg/m ²)		22.7 ± 3.6
Peritoneal dialysis duration (month)		18.2 [9.8-33.7]
Peritoneal dialysis modality	CAPD (number, %)	41 (80.4)
	APD (number, %)	33 (64.7)
	CAPD and APD (number, %)	23 (45.1)
Peritoneal dialysis solution	Icodextrin solution (number, %)	28 (54.9)
	Lactate-buffered solution (number, %)	14 (27.5)
	Bicarbonate-buffered solution (number, %)	37 (72.5)
Diabetes mellitus (number, %)		17 (33.3)
Corticosteroid (number, %)		2 (3.9)
β-blocker (number, %)		22 (43.1)
Renin-angiotensin system inhibitor (number, %)		37 (72.5)
Aldosterone receptor antagonist (number, %)		4 (7.8)
Loop diuretic (number, %)		33 (64.7)
Thiazide diuretic (number, %)		20 (39.2)
Tolvaptan (number, %)		15 (29.4)
Potassium binder (number, %)		0 (0.0)
Phosphate binder (number, %)		42 (82.4)
Vitamin D analogue (number, %)		28 (54.9)
Calcimimetic (number, %)		11 (21.6)
Sodium bicarbonate (number, %)		0 (0.0)
4-hour dialysate/plasma creatinine		0.65 ± 0.11
Total weekly Kt/V		1.68 ± 0.39
Renal weekly Kt/V		0.69 ± 0.43
Peritoneal weekly Kt/V		1.00 ± 0.30

TABLE 1: Patient characteristics and medication

Abbreviations: APD, automated peritoneal dialysis; CAPD, continuous ambulatory peritoneal dialysis; Kt/V, urea clearance. Valuables are shown as mean ± standard deviation, median [interquartile range], or number (%).

Relationship between serum total CO₂ and HCO₃⁻ concentration

Figure 1 shows the correlation between serum total CO₂ and HCO₃⁻ concentration. Serum total CO₂ was correlated with HCO₃⁻ concentration significantly and closely ($r = 0.80$; $p < 0.001$).

FIGURE 1: Relationship between serum total CO2 and HCO3⁻ concentration

CO2: carbon dioxide; HCO3⁻: bicarbonate ion

Factors correlated with HCO3⁻ concentration

Simple linear regression analyses showed that HCO3⁻ concentration was significantly negatively correlated with gender male, body mass index, serum albumin, blood urea nitrogen, creatinine, uric acid, sodium, potassium, chloride, phosphate, and magnesium, and with the use of a bicarbonate-buffered solution, phosphate binder, and vitamin D analog. HCO3⁻ concentration was also significantly positively correlated with diabetes mellitus, four-hour dialysate/plasma creatinine, total weekly Kt/V, peritoneal weekly Kt/V, total calcium, and serum total CO2, and with the use of CAPD, CAPD and APD, icodextrin solution, lactate-buffered solution, loop diuretic, thiazide diuretic, and tolvaptan. Multiple linear regression analysis was performed using the variables that showed significant correlations with HCO3⁻ concentration in simple linear regression analyses (Table 2). This analysis revealed that total weekly Kt/V (standard coefficient [β] = 0.119, p = 0.027), serum albumin (β = -0.171, p = 0.007), blood urea nitrogen (β = -0.138, p = 0.011), sodium (β = 0.352, p < 0.001), chloride (β = -0.629, p < 0.001), total calcium (β = 0.204, p < 0.001), phosphate (β = -0.155, p = 0.006), and serum total CO2 (β = 0.354, p < 0.001) were independently correlated with HCO3⁻ concentration.

Parameter	Simple linear regression analysis		Multivariate linear regression analysis	
	Standard coefficient	P value	Standard coefficient	P value
Age (year)	0.083	0.20		
Gender male (yes vs. no)	-0.235	<0.001	0.084	0.09
Body mass index (kg/m ²)	-0.194	0.002	-0.006	0.91
Log-peritoneal dialysis duration (month)	0.018	0.78		
CAPD (yes vs. no)	0.353	<0.001	0.007	0.91
APD (yes vs. no)	-0.114	0.08		
CAPD and APD (yes vs. no)	0.189	0.003	0.087	0.11

Icodextrin solution (yes vs. no)	0.242	<0.001	-0.122	0.06
Lactate-buffered solution (yes vs. no)	0.242	<0.001	0.002	0.97
Bicarbonate-buffered solution (yes vs. no)	-0.242	<0.001	0.000	---
Diabetes mellitus (yes vs. no)	0.214	<0.001	0.072	0.15
Corticosteroid (yes vs. no)	0.112	0.08		
β-blocker (yes vs. no)	0.058	0.37		
Renin-angiotensin system inhibitor (yes vs. no)	0.012	0.85		
Aldosterone receptor antagonist (yes vs. no)	0.013	0.84		
Loop diuretic (yes vs. no)	0.289	<0.001	0.052	0.43
Thiazide diuretic (yes vs. no)	0.256	<0.001	0.016	0.76
Tolvaptan (yes vs. no)	0.165	0.010	-0.070	0.22
Potassium binder (yes vs. no)	0.000	---		
Phosphate binder (yes vs. no)	-0.131	0.041	0.040	0.46
Vitamin D analog (yes vs. no)	-0.173	0.007	0.049	0.22
Calcimimetic (yes vs. no)	0.075	0.24		
Four-hour dialysate/plasma creatinine	0.293	<0.001	0.008	0.88
Total weekly Kt/V	0.138	0.031	0.119	0.027
Renal weekly Kt/V	-0.031	0.63		
Peritoneal weekly Kt/V	0.160	0.012	-0.092	0.05
Total protein (g/dL)	-0.112	0.08		
Serum albumin (g/dL)	-0.206	0.001	-0.171	0.007
Hemoglobin (g/dL)	-0.040	0.54		
Blood urea nitrogen (mg/dL)	-0.481	<0.001	-0.138	0.011
Creatinine (mg/dL)	-0.134	0.037	-0.014	0.83
Uric acid (mg/dL)	-0.295	<0.001	-0.016	0.71
Sodium (mEq/L)	-0.185	0.004	0.352	<0.001
Potassium (mEq/L)	-0.301	<0.001	0.025	0.66
Chloride (mEq/L)	-0.550	<0.001	-0.629	<0.001
Total calcium (mg/dL)	0.283	<0.001	0.204	<0.001
Phosphate (mg/dL)	-0.514	<0.001	-0.155	0.006
Magnesium (mg/dL)	-0.180	0.005	-0.014	0.76
Blood glucose (mg/dL)	0.094	0.14		
Serum total CO ₂ (mmol/L)	0.805	<0.001	0.354	<0.001

TABLE 2: Simple and multiple linear regression analyses of the parameters correlating with HCO₃⁻ concentration

Abbreviations: APD, automated peritoneal dialysis; CAPD, continuous ambulatory peritoneal dialysis; CO₂: carbon dioxide; HCO₃⁻, bicarbonate ion; Kt/V, urea clearance; Log, logarithm

Diagnostic accuracy of serum total CO₂ for the prediction of low and

high bicarbonate concentrations

The ROC curve of serum total CO₂ for detecting low (HCO₃⁻ <24 mEq/L) and high (HCO₃⁻ ≥24 mEq/L) bicarbonate concentrations is shown in Figure 2. The AUC was 0.909, and the optimal cut-off value was 23.7 mmol/L. The 2×2 tables, stratified according to serum total CO₂ and HCO₃⁻ concentration for low and high bicarbonate, are shown in Table 3. The diagnostic accuracy measures of serum total CO₂ for the prediction of low and high bicarbonate concentrations were as follows: sensitivity (91.5%), specificity (74.7%), positive predictive value (53.5%), negative predictive value (96.5%), accuracy (78.8%), pre-test probability (24.1%), positive post-test probability (53.5%), and negative post-test probability (3.5%).

FIGURE 2: ROC curve of serum total CO₂ for detecting low bicarbonate (HCO₃⁻ <24 mEq/L) and high bicarbonate (HCO₃⁻ ≥24 mEq/L) concentrations

AUC: area under the curve; CO₂: carbon dioxide; HCO₃⁻: bicarbonate ion; ROC: receiver operating characteristic

		HCO ₃ ⁻		Total
		Low bicarbonate (HCO ₃ ⁻ <24 mEq/L)	High bicarbonate (HCO ₃ ⁻ ≥24 mEq/L)	
Serum total CO ₂	Low serum total CO ₂ (Serum total CO ₂ <24 mmol/L)	54	47	101
	High serum total CO ₂ (Serum total CO ₂ ≥24 mmol/L)	5	139	144
Total		59	186	245

TABLE 3: 2×2 table stratified according to serum total CO₂ and HCO₃⁻ concentration for low and high bicarbonate

Abbreviations: CO₂, carbon dioxide; HCO₃⁻, bicarbonate ion

Correlation between serum total CO₂ and HCO₃⁻ concentration

Bland-Altman analysis showed moderate agreement between serum total CO₂ and HCO₃⁻ concentration. The mean difference was -1.64 ± 3.66, and 95.1% of the points were included within the limits of agreement (the mean difference between the two methods ± 2 standard deviation [95% confidence interval]) (Figure 3).

FIGURE 3: Bland-Altman plot comparing serum total CO₂ and HCO₃⁻ concentration

CO₂: carbon dioxide; HCO₃⁻: bicarbonate ion; SD: standard deviation

Discussion

In the present study, we investigated the relationship between serum total CO₂ and HCO₃⁻ concentration in

peritoneal dialysis patients and found that serum total CO_2 closely correlated with HCO_3^- concentration. We also found that serum total CO_2 has high diagnostic accuracy for predicting low bicarbonate and high bicarbonate in peritoneal dialysis patients.

Serum total CO_2 is a total concentration of all forms of CO_2 in a serum sample, including HCO_3^- , carbonate, and dissolved CO_2 . Serum total CO_2 value is known to be approximately equivalent to HCO_3^- concentration because most of CO_2 exists as HCO_3^- in blood [9]. In fact, serum total CO_2 has been reported to have a close correlation with HCO_3^- concentration in both pre-dialysis CKD patients [10] and hemodialysis patients [11]. However, a discrepancy between serum total CO_2 and HCO_3^- concentration is sometimes observed, and temperature and acidity [16] are considered one of the causes of discrepancy in patients without renal impairment [17]. In the present study, serum albumin, calcium, chloride, sodium, phosphate, blood urea nitrogen, and total weekly Kt/V in addition to serum CO_2 were independently correlated with HCO_3^- concentration in serum.

Serum albumin represents the nutritional status of patients and is reportedly associated with dietary protein intake in peritoneal dialysis patients [18]. Protein intake is associated with metabolic acidosis because amino acids into which dietary proteins are broken down release hydrogen ions [19]. Increased serum albumin was reported to be associated with metabolic acidosis in pre-dialysis CKD patients [20]. The weak acidity of albumin has also been considered as the cause of this phenomenon [21]. These findings are consistent with our result, showing a negative correlation between serum albumin and HCO_3^- concentration.

It has been reported that HCO_3^- was positively correlated with calcium concentration in hemodialysis patients [22]. In the present study, HCO_3^- concentration was positively correlated with calcium concentration in peritoneal dialysis patients. These findings suggest that serum HCO_3^- concentration might be positively correlated with calcium concentration in patients with end-stage renal disease. There were differences in calcium concentrations among peritoneal dialysis solutions used in the present study. The possibility remains that these differences might affect the results of our study.

HCO_3^- concentration has been shown to decrease along with an increase in chloride concentration through following equilibrium with HCl and NaHCO_3 : $\text{H}^+ + \text{Cl}^- + \text{Na}^+ + \text{HCO}_3^- = \text{Na}^+ + \text{Cl}^- + \text{H}_2\text{CO}_3$ [23]. In the present study, chloride concentration was negatively correlated with HCO_3^- concentration, which is consistent with the findings of previous reports [10-11].

A cross-sectional study of peritoneal dialysis patients reported that sodium concentration was lower in patients with $\text{HCO}_3^- < 22 \text{ mEq/L}$ than in patients with $22 \leq \text{HCO}_3^- < 28 \text{ mEq/L}$ [24]. In the present study, sodium concentration was positively correlated with HCO_3^- concentration. These results suggest that sodium concentration is positively associated with HCO_3^- concentration in peritoneal dialysis patients.

Phosphate and blood urea nitrogen were shown to be associated with daily protein intake in patients with end-stage renal disease [25]. Protein intake is negatively associated with bicarbonate, as the amino acids into which dietary proteins are broken down release hydrogen ions [19]. Phosphate and blood urea nitrogen were reported to be negatively correlated with bicarbonate in peritoneal dialysis patients [24], which is consistent with the findings of our study.

Currently available peritoneal dialysis fluids contain alkaline anions of 35-40 mmol/L as lactate or/and bicarbonate [6]. The influx of alkaline anions from the peritoneal dialysis fluid into the blood occurs during peritoneal dialysis because the alkaline anion concentration in serum is usually lower than that in peritoneal dialysis fluid [24]. A previous study reported that dialysis adequacy assessed by daily Kt/V was positively correlated with serum bicarbonate level [26]. In the present study, the total weekly Kt/V was positively correlated with HCO_3^- concentration. These results suggest that peritoneal dialysis dose-dependently increases serum HCO_3^- concentration caused by the influx of bicarbonate from the peritoneal dialysis fluid into the blood.

In the present study, serum total CO_2 was closely correlated with HCO_3^- concentration and showed high accuracy for the differentiation of low or high bicarbonate concentrations. Therefore, serum CO_2 may be a good predictor of bicarbonate concentration and useful to predict whether this is low or high. However, the correlation between serum total CO_2 and HCO_3^- concentration in the present study ($\beta = 0.323$) was weaker as compared with that of hemodialysis patients ($\beta = 0.858$) [11]. The number of clinical parameters

correlated with HCO_3^- concentration was greater in the present study than in the previous one [11] (eight vs three), which might explain the lower correlation between serum total CO_2 and HCO_3^- in this study. The correlation between serum total CO_2 and HCO_3^- concentration might be attenuated in peritoneal dialysis patients. Further studies are necessary to confirm the close correlation between serum total CO_2 and HCO_3^- concentration and the usefulness of serum total CO_2 for the diagnosis of low or high bicarbonate concentrations in peritoneal dialysis patients.

The measurement of serum total CO_2 has two advantages as compared with blood-gas analyses. First, the cost of a blood gas-syringe can be saved and the amount of blood required will be reduced using serum total CO_2 instead of a blood-gas test. Second, serum total CO_2 can be used to predict low bicarbonate and high bicarbonate without the use of a blood-gas analyzer. Therefore, the measurement of serum total CO_2 could reduce some of the burden on peritoneal dialysis patients and laboratory staff.

Our study had four limitations. First, it was a retrospective, observational study; therefore, selection bias could not be completely eliminated. Second, the study was performed at a single center, which limits the external validity of the results. Third, the study cohort was small, which restricts the generalizability of our findings. Fourth, we used venous blood samples for the analyses. The results might have been different if arterial blood samples had been used. Therefore, further prospective, large-scale, multicenter studies are necessary to confirm our findings.

Conclusions

Serum total CO_2 correlated closely with HCO_3^- concentration in peritoneal dialysis patients. Serum total CO_2 might be useful for predicting low and high bicarbonate in peritoneal dialysis patients.

Additional Information

Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. Ethics committee of Saitama Medical Center, Jichi Medical University issued approval S17-052. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

Acknowledgements

We thank all staff members of the Department of Clinical Laboratory (Saitama Medical Center, Jichi Medical University, Saitama, Japan) for their excellent work and support.

References

1. Cochran M, Wilkinson R: Effect of correction of metabolic acidosis on bone mineralisation rates in patients with renal osteomalacia. *Nephron*. 1975, 15:98-110. [10.1159/000180501](#)
2. Stein A, Moorhouse J, Iles-Smith H, et al.: Role of an improvement in acid-base status and nutrition in CAPD patients. *Kidney Int*. 1997, 52:1089-95. [10.1038/ki.1997.433](#)
3. Garibotto G, Sofia A, Russo R, et al.: Insulin sensitivity of muscle protein metabolism is altered in patients with chronic kidney disease and metabolic acidosis. *Kidney Int*. 2015, 88:1419-1426. [10.1038/ki.2015.247](#)
4. Chang TI, Oh HJ, Kang EW, et al.: A low serum bicarbonate concentration as a risk factor for mortality in peritoneal dialysis patients. *PLoS One*. 2013, 8:e82912. [10.1371/journal.pone.0082912](#)
5. Liu XY, Gao XM, Zhang N, et al.: Oral bicarbonate slows decline of residual renal function in peritoneal dialysis patients. *Kidney Blood Press Res*. 2017, 42:565-574. [10.1159/000479641](#)
6. Nakayama M, Kawaguchi Y, Akiba T, et al.: A new peritoneal dialysis fluid for Japanese patients: a randomized non-inferiority clinical trial of safety and efficacy. *Clin Exp Nephrol*. 2017, 21:895-907. [10.1007/s10157-016-1346-9](#)
7. Raikou VD, Kyriaki D: Mortality and low serum bicarbonate level in patients on hemodiafiltration versus peritoneal dialysis. *Indian J Nephrol*. 2018, 28:105-112. [10.4103/ijn.ijn_232_16](#)
8. O'Leary TD, Langton SR: Calculated bicarbonate or total carbon dioxide?. *Clin Chem*. 1989, 35:1697-1700. [10.1093/clinchem/35.8.1697](#)
9. Dobson GP, Veech RL, Hoeger U, Passonneau JV: Enzymatic determination of total CO_2 in freeze-clamped animal tissues and plasma. *Anal Biochem*. 1991, 195:232-237. [10.1016/0003-2697\(91\)90322-k](#)
10. Hirai K, Minato S, Kaneko S, et al.: Approximation of bicarbonate concentration using serum total carbon dioxide concentration in patients with non-dialysis chronic kidney disease. *Kidney Res Clin Pract*. 2019, 38:326-335. [10.23876/j.krcp.19.027](#)

11. Hirai K, Ookawara S, Morino J, et al.: Relationship between serum total carbon dioxide concentration and bicarbonate concentration in patients undergoing hemodialysis. *Kidney Res Clin Pract.* 2020, 39:441-450. [10.23876/j.krcp.19.126](https://doi.org/10.23876/j.krcp.19.126)
12. Lysaght MJ, Pollock CA, Hallet MD, Ibels LS, Farrell PC: The relevance of urea kinetic modeling to CAPD. *ASAIO Trans.* 1989, 35:784-790.
13. Watson PE, Watson ID, Batt RD: Total body water volumes for adult males and females estimated from simple anthropometric measurements. *Am J Clin Nutr.* 1980, 33:27-39. [10.1093/ajcn/33.1.27](https://doi.org/10.1093/ajcn/33.1.27)
14. Ramsay AG: Clinical application of the Henderson-Hasselbalch equation. *Appl Ther.* 1965, 7:730-736.
15. Vashistha T, Kalantar-Zadeh K, Molnar MZ, Torlén K, Mehrotra R: Dialysis modality and correction of uremic metabolic acidosis: relationship with all-cause and cause-specific mortality. *Clin J Am Soc Nephrol.* 2013, 8:254-264. [10.2215/CJN.05780612](https://doi.org/10.2215/CJN.05780612)
16. Maas AH, van Heijst AN, Visser BF: The determination of the true equilibrium constant (pK_1) and the practical equilibrium coefficient (pK_1') for the first ionization of carbonic acid in solutions of sodium bicarbonate, cerebrospinal fluid, plasma and serum at 25 and 38. *Clin Chim Acta.* 1971, 33:325-343. [10.1016/0009-8981\(71\)90490-6](https://doi.org/10.1016/0009-8981(71)90490-6)
17. Kim Y, Massie L, Murata GH, Tzamaloukas AH: Discrepancy between measured serum total carbon dioxide content and bicarbonate concentration calculated from arterial blood gases. *Cureus.* 2015, 7:e398. [10.7759/cureus.398](https://doi.org/10.7759/cureus.398)
18. Sarwar S, Sherman RA: How well does serum albumin correlate with dietary protein intake in dialysis patients? *Kidney Int Rep.* 2017, 2:90-93. [10.1016/j.ekir.2016.09.004](https://doi.org/10.1016/j.ekir.2016.09.004)
19. Halperin ML, Jungas RL: Metabolic production and renal disposal of hydrogen ions. *Kidney Int.* 1983, 24:709-713. [10.1038/ki.1983.217](https://doi.org/10.1038/ki.1983.217)
20. Raphael KL, Zhang Y, Ying J, Greene T: Prevalence of and risk factors for reduced serum bicarbonate in chronic kidney disease. *Nephrology (Carlton).* 2014, 19:648-654. [10.1111/nep.12315](https://doi.org/10.1111/nep.12315)
21. Rossing TH, Maffeo N, Fencel V: Acid-base effects of altering plasma protein concentration in human blood in vitro. *J Appl Physiol* (1985). 1986, 61:2260-2265. [10.1152/jappl.1986.61.6.2260](https://doi.org/10.1152/jappl.1986.61.6.2260)
22. Wu DY, Shinaberger CS, Regidor DL, McAllister CJ, Kopple JD, Kalantar-Zadeh K: Association between serum bicarbonate and death in hemodialysis patients: is it better to be acidotic or alkalotic? *Clin J Am Soc Nephrol.* 2006, 1:70-78. [10.2215/CJN.00010505](https://doi.org/10.2215/CJN.00010505)
23. Nagami GT: Hyperchloremia - why and how. *Nefrologia.* 2016, 36:347-353. [10.1016/j.nefro.2016.04.001](https://doi.org/10.1016/j.nefro.2016.04.001)
24. Mujais S: Acid-base profile in patients on PD. *Kidney Int Suppl.* 2003, 64:S26-36. [10.1046/j.1523-1755.2003.08803.x](https://doi.org/10.1046/j.1523-1755.2003.08803.x)
25. Raja RM, Ijelu G, Goldstein M: Influence of Kt/V and protein catabolic rate on hemodialysis morbidity. A long-term study. *ASAIO J.* 1992, 38:M179-M180. [10.1097/00002480-199207000-00014](https://doi.org/10.1097/00002480-199207000-00014)
26. Tattersall JE, Dick C, Doyle S, Greenwood RN, Farrington K: Alkalosis and hypomagnesaemia: unwanted effects of a low-calcium CAPD solution. *Nephrol Dial Transplant.* 1995, 10:258-262. [10.1093/ndt/10.2.258](https://doi.org/10.1093/ndt/10.2.258)