Original Paper

Oral Bicarbonate Slows Decline of Residual Renal Function in Peritoneal Dialysis Patients

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Key Words

End-stage renal disease • Peritoneal dialysis • Continuous ambulatory peritoneal dialysis • Metabolic acidosis • Residual renal function

Abstract

Background/Aims: Metabolic acidosis is a common consequence of end-stage renal disease (ESRD) which may result in a substantial adverse outcome. The effect of oral bicarbonate on the preservation of residual renal function (RRF) in peritoneal dialysis (PD) patients has been rarely reported. **Methods:** We randomly assigned 40 continuous ambulatory peritoneal dialysis (CAPD) patients to the oral bicarbonate group or placebo group at a 1:1 ratio. All enrollments were followed for a duration of 104 weeks. We took residual creatinine clearance (CCr), a measure of residual renal function (RRF), as the primary outcome. Residual CCr was calculated as the average of urea and creatinine clearance from a 24-hour urine collection. **Results:** Thirteen patients in the placebo group and 15 patients in the treatment group completed the 104 weeks of follow-up with a comparable dropout rate (placebo group: 35% vs treatment group: 25%). Compared with the placebo group, serum bicarbonate in treatment group was significantly increased at each time point, and oral bicarbonate resulted in a slower declining rate of residual CCr ($F=5.113$, $p=0.031$). Baseline residual CCr at enrollment also had a significant effect on residual CCr ($F=168.779$, $P<0.001$). Charlson Comorbidity Index which was adopted to calculate a comorbidity score had no significant effect on residual CCr loss ($F=0.168$, $P=0.685$). **Conclusion:** Oral bicarbonate may have a RRF preserving effect in CAPD patients, and a normal to high level of serum bicarbonate (≥ 24 mmol/L) may be appropriate for RRF preservation.

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Introduction

Metabolic acidosis, which is mainly manifested as low serum bicarbonate, is common in end-stage renal disease (ESRD) and may result in a series of severe consequences including protein-wasting, inflammation, low serum albumin concentration, insulin resistance and bone disease [1-6]. Correction of acidosis is one of the primary purposes of renal replacement treatment. The National Kidney Foundation Disease Outcomes Quality Initiative (K/DOQI) guideline recommends that a bicarbonate supplement in chronic peritoneal dialysis (PD) patients with serum bicarbonate < 22 mmol/L is beneficial for bone metabolism and nutritional status [7]. However, the optimal level of serum bicarbonate or arterial pH needed to achieve the desired results is currently unknown [8, 9].

Decline of residual renal function (RRF) is an independent risk factor of adverse outcomes in chronic kidney disease (CKD) and ESRD patients [10, 11]. Maiorca et al. reported a 50% reduction in mortality of PD patients with RRF, and every 1 ml/min increase in glomerular filtration rate was associated with a 40% reduction in the risk of death in dialysis patients [12]. Similarly, another prospective observational study also reported a strong association between RRF and PD patient survival [12-14]. Several factors such as age, sex, inflammatory/nutritional status, peritonitis rate, blood pressure, hemoglobin, renal function and transport type at PD initiation, and ESRD etiology were all reported to be associated with the loss of RRF [15, 16]. However, whether or not low serum bicarbonate has an impact on RRF in PD patient is unclear [17, 18]. Some fundamental and clinical trials showed that base supplementation, either by modification of the diet or by bicarbonate administration, might slow the decline of kidney function in subjects with CKD [19-21]. A single-center randomized controlled study conducted by de Brito-Ashurst and his colleagues [22] in late stage CKD patients with acidosis demonstrated that correction of metabolic acidosis with alkali supplements slowed the progression of CKD to ESRD. Two other studies showed that alkali supplements, either sodium citrate or sodium bicarbonate, had a GFR preserving effect in CKD patients [23, 24]. A meta-analysis concluded that alkali therapy might provide a long-term favorable effect on renal function in patients with CKD [25]. Nevertheless, rare study was conducted in peritoneal dialysis patients. Furthermore, does more active base supplementation therapy have a further renal function preserving effect in peritoneal dialysis patients? Therefore, the purpose of this study was to testify the hypothesis that maintenance of a normal to high level of serum bicarbonate by administration of oral bicarbonate may slow the decline of residual renal function in peritoneal dialysis patients.

Patients and Methods

Patient selection

This study was a single-center, randomized, placebo-controlled, double-blinded trial with a duration of 104 weeks. The trial was done in compliance with the protocols and principles of the Declaration of Helsinki and was approved by the Clinical Research Ethical Committee of Chinese PLA No. 254 Hospital. All patients have signed an informed consent before enrollment. Owing to the lack of similar studies, no minimal meaningful difference value and standard deviation of RRF have been reported. Therefore, sample size calculation could not be performed. We screened 168 ESRD patients who started PD in Chinese PLA No. 254 Hospital between June 2012 and December 2013. A total of 40 patients were recruited who met the following criteria: (1) under continuous ambulatory peritoneal dialysis (CAPD) for at least 6 months, and (2) stable clinical condition with serum bicarbonate < 24 mmol/L for at least two consecutive visits. Exclusion criteria: (1) < 18 years at the initiation of peritoneal dialysis; (2) history of hemodialysis (HD) or kidney transplantation; (3) initiation of PD for acute renal injury; (4) 24-hour urine output < 200 ml/day; and (5) had oral bicarbonate within 2 weeks before the enrollment. We excluded patients who either were unlikely to survive or planned to have kidney transplant, or to transfer to other renal center within 6 months.

Randomization and masking

Patients were randomly assigned at a 1:1 ratio to receive either oral bicarbonate or placebo in a double-blinded manner for 104 weeks. Random sequence was generated by computer, and the allocation programs were enclosed in coded, opaque, sealed envelopes. Both oral bicarbonate and placebo tablets (manufactured by Shanghai Yurui Biotechnology Pharmaceutical Co., Ltd.) had identical appearance, flavor, and package. Blinded to treatment allocation were study members such as nurses and patients, with exception of the designer and coordinator who initiated and distributed the tablets (oral bicarbonate or placebo). Patients in oral bicarbonate group were initiated at a dose of 1.0 g/day, with a recommendation of up-titration if serum bicarbonate was <24 mmol/L and down-titration if serum bicarbonate was >30 mmol/L. Oral bicarbonate doses could be adjusted at any time of the follow-up period. Placebo was also initiated at a dose of 1.0 g/day, and was adjusted completely according to the oral bicarbonate dosage of the last patient in treatment group.

Data collection

Demographic and baseline clinical data were collected at the start of recruitment, which included age, gender, height, body weight, body mass index (BMI), systolic pressure, diastolic pressure, primary disease, and duration of PD. Comorbidity conditions were documented covering a comprehensive list of diseases, ranging from coronary artery disease, heart failure, peripheral vascular disease, cerebrovascular disease to dementia, chronic pulmonary disease, connective tissue disease, peptic ulcer disease, liver disease, diabetes with or without complications, and from hemiplegia, leukemia, solid tumor, malignancy to AIDS. A comorbidity score was calculated using the Charlson Comorbidity Index.

Patients were followed at week -4, 0, 2, 4, 8, 26, 52, 78 and 104. Patients received diet and lifestyle counseling at each visit starting from the beginning of the placebo run-in period. Except for the trial medication, routine treatments such as antihypertensive drugs, calcitriol and erythropoietin were administrated according to the clinical needs. All the patients were treated with regular CAPD, with a lactate concentration of 35 mmol/L and calcium concentration of 1.25 mmol/L. Dialysis prescription was not changed unless there was evidence of underdialysis [26]. Trial medication tablets were counted by the investigators every month to calculate compliance. Various parameters were recorded during the follow-up visits at week 0, 4, 26, 52, 78 and 104, including body weight, systolic pressure, diastolic pressure, presence of edema (score from 0 to 3+), the number and reason for hospitalization, hemoglobin level, serum electrolytes, serum albumin, serum C-reactive protein (CRP), serum urea, serum creatinine, total weekly creatinine clearance (CCr) (adjusted by body surface), total weekly Kt/V urea, dialysis volume, PD ultrafiltration and residual CCr. We took residual CCr (a measures of RRF) as the primary outcome in this trial. Residual CCr was calculated as the average of urea and creatinine clearance from a 24-hour urine collection [27]. Residual CCr was considered null when urine output was < 200mL/d. When a patient reached a residual CCr below this level for 2 successive time points, we defined the patient as anuric from the first time point of the 2 measurements [17]. Carbon dioxide combining power, which is considered as an indirect measure of serum bicarbonate concentration, was tested using an electrode-based method (UniCel DXC 800; Beckman Coulter, Inc, CA) at week 0, 2, 4, 8, 26, 52 and 78.

Statistical analysis

The demographic and baseline clinical characteristics of the participants were compared between groups by *t*-test for continuous variables, and chi-square test for categorical variables. An intention to treat analysis, including subjects who dropped out of the trial, was adopted to avoid the effects of dropout which may break the random assignment to the treatment groups in the study. Last observation carried forward (LOCF) method was used to replace missing data to diminish the different attrition rates between the groups [28]. Overall statistical comparisons between the two groups were performed by repeated measures ANOVA. The effect of oral bicarbonate on residual CCr changes was analyzed by linear mixed models (LMMs) using treatment group (oral bicarbonate or placebo), baseline residual CCr, Charlson Comorbidity Index and patient ID as the fixed effects, and time (baseline, 26 week, 52 week, 78 week and 104 week) as the random effect. Compound symmetry covariance structure was employed for the repeated factor of time. Additionally, we employed a LMM calculation in which only subjects in each group who started and completed the follow-ups were included to improve the robustness and stability of our conclusion. An independent *t*-test was used to compare differences in the changes of hemoglobin level, serum bicarbonate, serum electrolytes,

serum albumin, serum C-reactive protein (CRP), serum urea, serum creatinine, total weekly CCr (adjusted by body surface), total weekly Kt/V urea, dialysis volume, PD ultrafiltration and residual CCr between the two groups from 0 to 104 weeks. A *p*-value of <0.05 was considered statistically significant. All probabilities were two-tailed. Statistical analyses were performed by IBM SPSS Statistics, Version 18 for Windows (SPSS Inc, Chicago IL).

Results

Among the 168 CAPD patients who were screened in our center for their eligibility of enrollment, 94 patients were ruled out owing to unwillingness to participate in the trial, and 32 patients were excluded due to the inability to meet the inclusion criteria. A total of 42 patients were randomly assigned, and

2 patients withdrew before trial started due to treatment preference. The full-analysis set consisted of 20 patients in placebo group and 20 patients in treatment group, and thus comprised the intention-to-treat group. While 13 patients in the placebo group completed the 104 weeks of follow-up, 15 patients in the treatment group completed the trial. Seven patients in the placebo group dropped out because of death (*n*=2), skin rash (*n*=1) and anuria (*n*=4), and 5 patients in the treatment group withdrew because of death (*n*=1), dyspepsia (*n*=2) and anuria (*n*=2). Flow of patients and reasons for withdrawal from the study are shown in Fig. 1.

The baseline clinical characteristics, laboratory findings, dialysis adequacy indices, residual GFR, and major comorbid conditions are shown in Table 1. There was no significant difference in any baseline parameter between the two groups. The number of anti-hypertensive drugs between the two groups was not significantly different. Serum calcium and phosphorus in placebo and treatment group was 9.27 ± 0.73 versus 9.29 ± 0.88 mg/dl (*p*=0.93), and 5.49 ± 0.82 versus 5.52 ± 0.85 mg/dl (*p*=0.94), respectively. Ten patients in placebo group and 9 in treatment group received calcium carbonate as phosphate binder. The average dose of calcium carbonate in placebo and treatment group was 1.60 ± 0.26 g/day and 1.50 ± 0.45 g/day, respectively (*p*=0.57).

Serum bicarbonate levels during the follow-up are summarized in Fig. 2. The average dose of oral bicarbonate at each time point during the follow-up is shown in Table 2. In the placebo group, there was a gradual but significant increase in serum bicarbonate level from 22.57 ± 0.89 mmol/L to 24.12 ± 0.97 mmol/L in week 4 (*P*<0.01), which peaked at 26.82 ± 0.82 mmol/L in week 8, and then almost returned to the baseline level of 22.91 ± 1.23 mmol/L

Fig. 1. Patients flow and and reasons for withdrawal.

Table 1. Baseline characteristics of patients. Values for categorical variables are expressed as numbers; Values for continuous variables are expressed as mean±standard deviation. GFR, glomerular filtration rate; COPD, chronic obstructive pulmonary diseases; AIDS, acquired immunodeficiency syndrome; CRP, C-reactive protein. *Note:* There was no statistically significant difference between the two groups

	Placebo Group	Treatment Group
No. of patient	20	20
Gender (M:F)	10:10	10:10
Age (yr)	56.20±13.58	55.10±16.05
Duration of dialysis (mo)	44.60±24.68	35.55±20.21
Body height (cm)	163.25±8.58	167.50±7.54
Body weight (kg)	64.59±12.17	60.02±9.52
Body surface area (m ²)	1.8±0.2	1.8±0.2
Mean systolic pressure (mmHg)	135±18	137±19
Mean diastolic pressure (mmHg)	81±9	82±9
Urine volume (ml/24h)	780±261	781±299
Laboratory findings		
Hemoglobin (g/dl)	102.15±4.86	101.05±7.44
Serum albumin (g/dl)	35.69±4.26	36.34±3.48
Serum bicarbonate (mmol/L)	22.57±0.89	22.43±0.97
CRP (mg/dl)	0.23±0.30	0.21±0.28
Peritoneal ultrafiltration (ml/24h)	793.5±366.54	720±438.48
Total Kt/V	1.90±0.20	1.85±0.16
Residual Kt/v	0.36±0.15	0.35±0.12
Total GFR (ml/min/1.73m ²)	59.98±6.13	59.83±7.50
Residual GFR (ml/min)	1.77±0.72	1.63±0.63
Primary disease (no. of cases)		
Glomerulonephritis	7	8
Diabetic Nephropathy	6	5
Polycystic Kidney	2	2
Hypertensive Nephropathy	3	3
Other	2	2
Major comorbidity (no. of cases)		
Myocardial Infarction	4	3
Congestive Heart Failure	9	10
Peripheral Vascular Disease	6	5
Cerebrovascular Disease	4	7
Dementia	0	0
COPD	1	0
Connective Tissue Disease	1	1
Peptic Ulcer Disease	6	4
Diabetes Mellitus		
1 point uncomplicated,	2	1
2 points if end-organ damage	6	5
Moderate to Severe Chronic		
Kidney Disease (2 points)Hemiplegia (2 points)	20	20
Leukemia (2 points)	1	0
Malignant Lymphoma (2 point)	0	0
Solid Tumor (2 points, 6 points if metastatic)	0	0
Liver Disease (1 point mild, 3 points if moderate to severe)	0	0
AIDS (6 points)	0	0
Charlson Index Score	4.35±1.46	4.10±1.29

in week 104. In the treatment group, serum bicarbonate level rose dramatically from 22.43±0.97 to 30.19±0.88 mmol/L after week 8 ($P<0.01$). Although serum bicarbonate level of the treatment group gradually declined afterward, it remained significantly higher than that of the placebo group at each time point. Blood pressure and other parameters such as Ca^{2+} , P and K^{+} were also measured throughout the study (Table 2).

The baseline residual CCr, LMMs for repeated measures of time-by-group interactions and residual CCr calculated only from endogenous creatinine are all shown in Table 3. The baseline residual CCr was comparable between the two groups (1.783±0.587 vs 1.790±0.542 ml/min, $p=0.29$). Residual CCr decreased through the 104 weeks in both groups. Although it

Fig. 2. Serum bicarbonate levels (mmol/L) in treatment group (squares) and placebo group (triangles). Error bars denote SEM. * $P < 0.01$ between treatment and placebo groups.

Table 2.

	Baseline	Week 26	Week 52	Week 78	Week 104
Dose of oral bicarbonate (g)	1.0	1.5	1.5	1.5	1.5
Mean systolic pressure (mmHg)					
Placebo group	135±18	137±16	137±16	136±16	135±18
Treatment group	137±19	137±18	135±18	137±16	137±19
Mean diastolic pressure (mmHg)					
Placebo group	81±9	84±10	81±11	83±8	83±8
Treatment group	82±9	83±8	82±9	83±9	84±9
Serum Ca ²⁺ (mmol/L)					
Placebo group	2.33±0.15	2.40±0.12	2.36±0.15	2.37±0.12	2.36±1.20
Treatment group	2.32±0.17	2.41±0.14	2.35±0.13	2.38±0.14	2.37±0.13
Serum P (mmol/L)					
Placebo group	1.67±0.12	1.65±0.93	1.66±0.11	1.67±0.14	1.66±0.11
Treatment group	1.66±0.12	1.66±0.12	1.68±0.09	1.67±0.14	1.68±0.11
Serum K ⁺ (mmol/L)					
Placebo group	4.27±0.45	4.29±0.55	4.31±0.45	4.21±0.37	4.16±0.39
Treatment group	4.24±0.41	4.26±0.60	4.30±0.49	4.21±0.43	4.17±0.34

Table 3. Baseline, 26-week follow-up, 52-week follow-up, 78-week follow-up, and 104-week follow-up outcome measures of patients in each group. * Calculated as (Clc+Clu)/2. ** Calculated as Clc

	Baseline	Week 26	Week 52	Week 78	Week 104	P
Total CCr (ml/min/1.73m ²)						
Placebogroup	57.17±5.54	56.97±8.20	55.48±6.58	53.89±4.92	53.80±9.60	0.91
Treatment group	55.89±6.99	55.68±5.20	54.37±4.99	53.43±5.14	53.00±8.44	
Residual CCr(ml/min)*						
Placebo group	1.78±0.59	1.63±0.51	1.32±0.48	1.11±0.44	1.00±0.48	0.03
Treatment group	1.79±0.54	1.68±0.58	1.50±0.56	1.32±0.45	1.24±0.47	
Residual CCr(ml/min)**						
Placebo group	2.25±0.74	2.20±0.51	1.76±0.64	1.52±0.61	1.50±0.73	0.04
Treatment group	2.27±0.83	2.29±0.58	1.99±0.78	1.78±0.60	1.80±0.70	
Total Kt/V						
Placebo group	1.83±0.20	1.75±0.18	1.74±0.18	1.73±0.19	1.71±0.22	0.76
Treatment group	1.81±0.15	1.74±0.14	1.73±0.19	1.71±0.13	1.70±0.17	

seemed that residual CCr decreased at a faster rate in the placebo group than the treatment group starting at week 26, no significant difference was found between the two groups in each time point (for week 26, 1.626±0.509 vs 1.683±0.576 ml/min, $p=0.742$; for week 52, 1.331±0.483 vs 1.503±0.556 ml/min, $p=0.306$; for week 78, 1.088±0.426 vs 1.324±0.454 ml/min, $p=0.098$; for week 104, 0.985±0.468 vs 1.241±0.471 ml/min, $p=0.093$). Overall statistical comparisons by repeated measures ANOVA also showed a more rapid but

insignificant decline of RRF in the placebo group ($F=0.902$, $P=0.348$). LMMs for repeated measures showed a significant difference between placebo and oral bicarbonate groups ($F=5.683$, $p=0.023$). No significant interaction of group*time in RRF change was detected in our trial ($F=2.024$, $P=0.095$). Time and baseline RRF also had significant effects on RRF change ($F=42.365$, $P=0.000$; $F=168.360$, $P=0.000$, respectively) but not on the Charlson Comorbidity Index score ($F=0.163$, $P=0.689$). Similar results were found when only subjects who completed the follow-up were included in the calculation (data not shown).

Discussion

Although high-lactate dialysate could improve nutritional status and reduce hospitalization of patients, it has limitations, such as the inability to adjust lactate concentration in dialysate when needed, and the possibility of alkalosis in some patients who extensively use high-lactate dialysate [29]. Citrate-based therapy was more effective on changes in serum calcium, magnesium and PTH [30], though more costly. Several observational studies have found that higher bicarbonate concentration may be associated with an improvement of kidney measures and survival for patients with CKD. For example, Kovesdy et al. reported lower CKD progression at bicarbonate concentrations of less than 28 mEq/L in veterans [31], and a similar conclusion was drawn in AASK (African American Study of Kidney Disease and Hypertension) [32]. In our study, oral sodium bicarbonate was demonstrated as a convenient and safe method for correcting acidosis. In the treatment group, serum bicarbonate level reached its peak in week 8, and then decreased gradually until the end of the study. Significant differences were found in all time points between the placebo and the bicarbonate groups. Interestingly, a transient elevation of serum bicarbonate in the placebo group was found during the first 8 weeks. We attributed this phenomenon to a “trial effect” which has been described in another study [33]. Diet and lifestyle counseling of the enrolled participants at each visit changed their diet and behavior and resulted in an increase of serum bicarbonate [33]. Moreover, the baseline therapy of calcium bicarbonate may have also influenced the level of serum bicarbonate. Increased serum $[\text{HCO}_3^-]$ in the placebo patients might have been due to the short-term higher compliance with their previously prescribed CaCO_3 . After 8 weeks, gradual decline in serum bicarbonate level was detected in both groups, possibly due to the loss of RRF [33] and reduction in patients’ compliance. This suggests that the addition of base-producing fruits and vegetables may transiently achieve the same outcome as oral bicarbonate, but the effect was not sustainable. At the same time, side effects such as hypercalcemia and ectopic calcification have limited the long-term usage of high dose calcium carbonate in the patients.

Endogenous creatinine clearance is an inaccurate determinant of the GFR because of the tubular secretion of creatinine. Urea clearance is lower than the inulin clearance because of the reabsorption of urea by the proximal tubules. Therefore, we adopted the mean of endogenous creatinine and urea clearance rate to approximate the RRF [34]. Our study showed that compared with placebo, oral administration of bicarbonate slowed down the rate of RRF decrease.

RRF plays an important role in maintaining fluid balance, phosphorus control, and removal of uremic toxins, and has a major impact on the outcome of PD [29, 35]. Metabolic acidosis is a common complication of CKD, and correction of acidosis is one of the primary purposes of renal replacement treatment. Our study showed that increasing serum bicarbonate to a relatively high level ($>24\text{mmol/L}$) by oral administration of bicarbonate has a favorable effect on preserving RRF in PD patients. Although the underlying mechanism of metabolic acidosis in accelerating the deterioration of RRF in CKD patients is not clear, probable principles may involve endothelin, aldosterone, and angiotensin II caused by acid load [36-38]. Previous clinical studies had shown that oral carbonate or fruits and vegetables have a RRF-preserving effect during correction of metabolic acidosis [39, 40].

However, all of the above studies were conducted on participants in CKD stage 1-4 without dialysis, and the effect of oral bicarbonate on RRF in CAPD patients has not been reported. A 3-year observational study from Tae Ik Chang et al. [16] has reported that after adjusting for multiple potentially confounding covariates, the rate of RRF decline was significantly greater in patients with time-averaged serum bicarbonate (TA-Bic) <24 mEq/L than those with TA-Bic >24 mEq/L. In addition, patients with TA-Bic <24 mEq/L also had a 2.62-fold higher risk of becoming anuric. Nevertheless, whether correction of metabolic acidosis to the level of TA-Bic >24 mEq/L provides additional protection for RRF in these patients is unknown. A randomized controlled trial which was aimed to detect the effect of oral bicarbonate on nutritional status and hospitalization of CAPD patients showed a tendency of slower decrease of RRF in the oral bicarbonate group [28]. Though, the absence of significant difference between the placebo and oral bicarbonate groups was probably due to the relative short follow-up.

Compared with previous studies, this study has several characteristics that strengthen the reliability of our findings. First, this is the first randomized controlled trial to our knowledge which was designed to investigate the effect of oral bicarbonate on RRF in CAPD patients. The random design guaranteed the balance of baseline characteristics of all participants and reduced bias from enrollment. Previous observational study only drew an association between oral bicarbonate and a decrease in RRF loss without determining the causal relationship. This interventional trial further examined the causality relationship and demonstrated that administering oral bicarbonate and maintaining a normal to high level of serum bicarbonate may have a positive effect on RRF preservation. Second, the 104 weeks of follow-up time warranted the ability to detect the long-term effect of oral bicarbonate on RRF. As mentioned previously, a similar effect of oral bicarbonate was also detected in another trial [33], but because of its relative short observation period, no significant difference was detected between the two groups.

We acknowledge that there are some limitations in our study. First, the study was a single-center study which included only a small number of patients, but we increased the sample size by using repeated measures ANOVA. Large-scale prospective studies are required to further testify the conclusion. Second, the drop-out rate was high owing to the poor health condition and low baseline RRF of the enrolled patients [41], though we adopted the LMMs to take advantage of all the available data. Third, all the participants in our study accepted diet counseling at each visit, but protein intake and nutritional status were not assessed and was introduced to the analysis as a covariate. Modification of Diet in Renal Disease (MDRD) study has reported a potential benefit of dietary protein restriction to slow the progression of CKD [42]. Hence, diet protein intake and nutritional status should be taken into account in our subsequent studies. Fourth, patient-focused outcomes such as quality of life and physical function were not recorded, necessitating further research. At last, though we have found the causality between base supplement and the slowed decline of RRF, to what extent oral bicarbonate could decrease the mortality or morbidity of CAPD patients is still unknown. More long-term prognostic studies are required to answer this question.

Conclusion

Oral bicarbonate may have a RRF-preserving effect in CAPD patients, and an increase of serum bicarbonate to a normal or high level may slow the decline of RRF. Large-scale prospective studies are needed to confirm our findings.

Disclosure Statement

The authors declare that they have no conflicts of interest.

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