Sodium Bicarbonate Therapy of Metabolic Acidosis of Chronic Kidney Disease

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Introduction

Chronic kidney disease increase in its prevalence around the world, associated with higher mortality. Metabolic acidosis recognized by declined blood bicarbonate is a relatively common complication in chronic kidney disease. Metabolic acidosis is known to be caused by ammoniagenesis disability and dysfunction in reabsorption of bicarbonate in the kidney, and it is reported that decrease in kidney functions is led to increase in prevalence and severity of metabolic acidosis. Harmful effects by chronic metabolic acidosis in chronic kidney disease include increase in protein catabolism, uremic bone diseases, muscle wasting, accumulation of β-2 microglobulin, chronic inflammation, impaired glucose homeostasis, and impaired cardiac function, effects that adversely affect renal functions. There are some animal experiments on chronic kidney diseases reporting that metabolic acidosis may cause or aggravate proteinuria and tubulointerstitial fibrosis and accelerate declination in renal functions, but few researchers have reported changes in human renal functions by correction of metabolic acidosis. In this study, we corrected metabolic acidosis in patients with the 3, 4 stage of chronic kidney disease showing metabolic acidosis by oral administration of bicarbonate to investigate its effects on renal functions and changes in nutritional parameters additionally.

Subjects and Methods

1. Subjects

The subjects were at least 20 years old, in the 3, 4 stage of chronic kidney disease (CrCl 15~60 ml/min), showed 16 to 20 mmol/L of blood bicarbonate, and had stable clinical course. They were divided into the group who were orally administered of bicarbonate (tasna®, Nexpharm Korea) for correcting metabolic acidosis and the control group without the administration, based on their age and creatinine clearance(CrCl). Those who were less than 20 years old or had malignant tumor, severe infection, cognitive disorder, uncontrollable hypertension, congestive heart failure, steroid using, high-grade obesity were excluded from this study.

Figure 1. Patients enrollment to the study

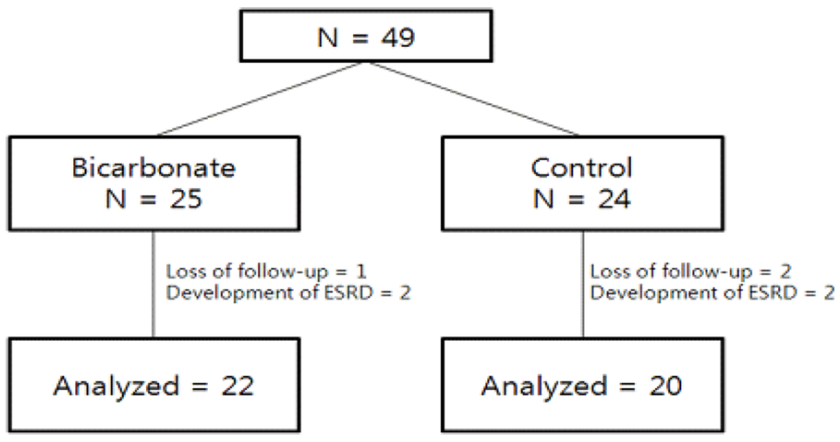


Table 1. Baseline demographic characteristics of patients

Variable	Bicarbonate(n=22)	Control(n=20)
Age	64.2 ± 8.8	63.5 ± 9.6
Male	11	11
Female	11	9
Underline disease(CRF)		
diabetes	10	8
hypertension	5	3
glomerulonephritis	6	8
unknown	1	1
Medications(n)		
calcium channel blockers	12	6
β blockers	6	10
α blockers	2	7
ACEIs/ARBs	16	15
loop diuretics	6	7

Table 2. Baseline characteristics of patients

Variable	Bicarbonate	Control	P
Weight(kg)	59.5 ± 4.8	59.5 ± 5.4	0.731
Lean body mass(kg)	45.9 ± 4.3	46.2 ± 3.5	0.919
Systolic BP(mmHg)	124.8 ± 3.4	122 ± 1.8	0.864
Diastolic BP(mmHg)	76.8 ± 3.6	74.4 ± 2.7	0.862
CrCl(ml/min per 1.73 m^2)	32.95 ± 6.35	34.87 ± 5.18	0.596
Serum creatinine(mg/dL)	2.08 ± 0.68	1.82 ± 0.46	0.161
BUN(mg/dL)	27.32 ± 9.77	28.50 ± 9.18	0.69
Urinary protein(g/24hr)	1.36 ± 0.83	1.45 ± 1.23	0.833
Plasma bicarbonate(mmol/L)	18.81 ± 1.58	18.87 ± 1.21	0.931
Plasma albumin(g/dL)	3.96 ± 0.50	4.07 ± 0.62	0.544
Urinary sodium(mmol/L)	84.5 ± 17.7	124.4 ± 60.5	0.459
Mid arm circumference(cm)	24.02 ± 3.30	24.53 ± 3.14	0.617
Triceps skin fold thickness(mm)	12.5 ± 3.60	13.7 ± 2.38	0.531
Mid arm muscle circumference(cm)	20.1 ± 1.81	20.22 ± 1.77	0.657

2. Methods

The 49 patients were selected according to the selection standards and were divided into the bicarbonate group (n=25) and the control group (n=24). All the patients were explained of open label, prospective study and showed consent. The research period was 12 months. Based on the basic clinical data of the subjects were investigated sex, age, height, basal & concomitant diseases of chronic kidney diseases, and medicines in use. The subjects visited outpatiently per month for follow-up observation. At the baseline, weight, lean body mass(LBM), blood urea nitrogen(BUN), blood creatinine(Cr.), creatinine clearance calculated from urine collected for 24 hours, urine protein, urine sodium, and arterial blood gas analysis were investigated to measure blood bicarbonate, pH, mid arm circumference(MAC), triceps skinfold thickness(TSF), mid arm muscle circumference(MAMC), blood cholesterol, albumin, blood pressure, heartbeat count, hemoglobin(Hb.), hematocrit(Hct.), and electrolytes at intervals of six months (at 0, 6, and 12 month). The MAC and the TSF were measured by one nurse for maintaining consistency, measured three times per visit to calculate mean values for record. At every outpatient visit, the subjects had their blood pressure taken, and their history of drug administration and adverse effects were investigated. The lean body mass was measured by using body composition analysis (Biospace Salus). The creatinine clearance was calculated from urine collected for 24 hours, and MAMC was calculated by the Bishop Formula15) (MAMC (cm) = MAC (cm) - TSF (mm) x 0.314) based on the MAC and the TSF. The oral bicarbonate was initially administered at 500 mg for a dose, twice a day, and then was increased in dose by the month to maintain blood bicarbonate at 23 mmol/L or more.

Results

Oral bicarbonate was initially administered of 1g/day (500mg bid) and then was increased by month to maintain 23mmol/L and more of blood bicarbonate, with mean 1.86 0.43g/day.

The creatinine clearance was decreased by mean 3.47ml/min/yr in the control group without oral bicarbonate but was rather increased by 7.19ml/min/yr in the bicarbonate-administered group. The lean body mass was increased by mean 0.95kg/yr in the bicarbonate group but was decreased by mean 2.83kg/yr accompanied with decreased in the weight in the control group. The MAMC was increased by mean 1.07cm/yr in the bicarbonate group but was decreased by mean 0.35cm/yr in the control group.

During this study changes in blood pressure by bicarbonate administration was not observed, and the agents for blood pressure in use were continually used without noticeable changes. There was almost no edema by bicarbonate administration or adverse effects such as gastrointestinal disorders by agents.

Figure 2. Plasma bicarbonate level during the study period. Urinary sodium excretion per day. Creatinine clearance. Serum creatinine. Urinary protein excretion per day. Data are means SE)

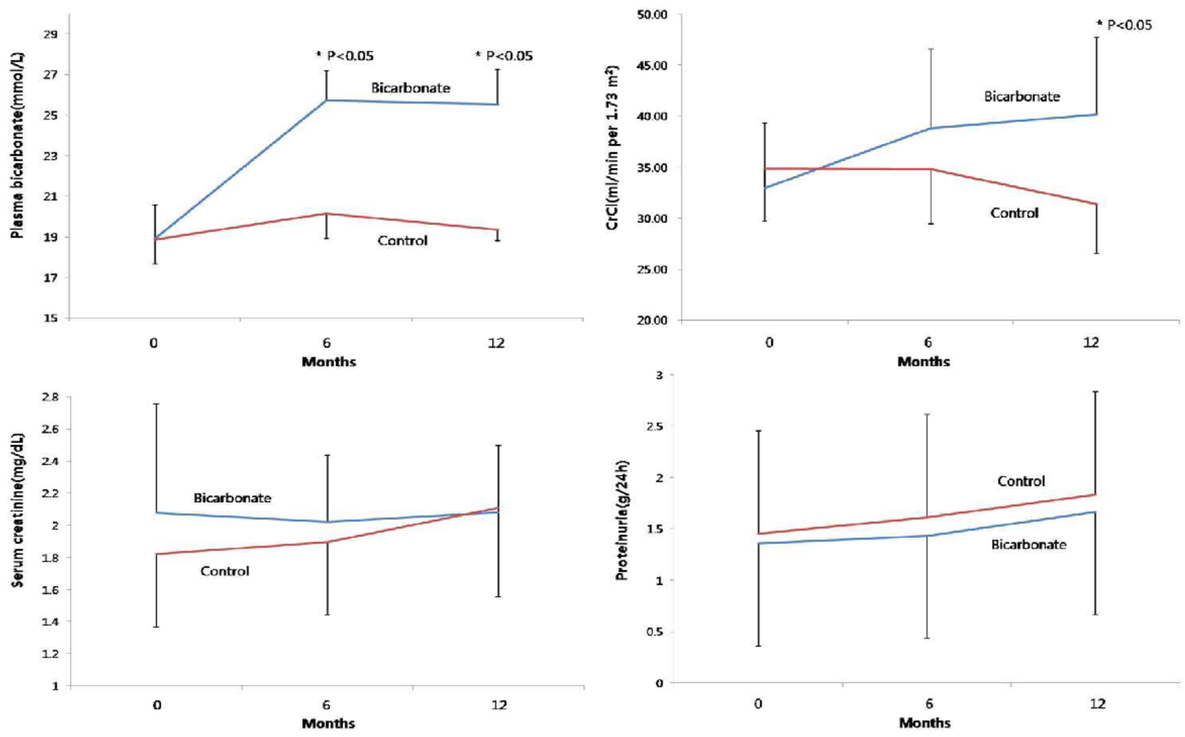
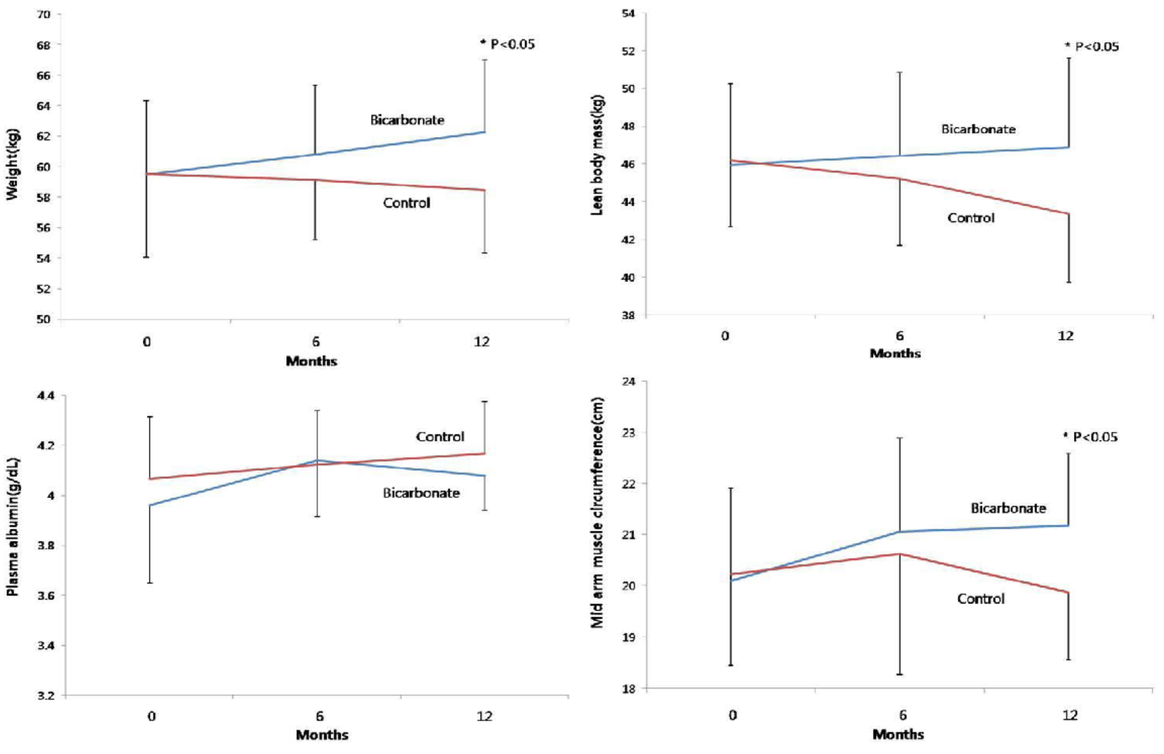


Figure 3. Body weight during the study period. Lean body mass. Mid arm muscle circumference. Plasma albumin. Serum potassium. Data are means SE



Conclusion

Oral administration of bicarbonate to chronic kidney disease patients accompanied with metabolic acidosis may contribute to preservation of renal functions and induce positive results in nutritional parameters. It is needed to initially apply active treatment to chronic kidney disease patients showing metabolic acidosis from repetitive blood test, and further long-term and randomized controlled trials are needed to verify effects of bicarbonate administration.

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