



A STUDY ON THE IMPACT OF SUPPLEMENTAL BICARBONATE ON THE DEVELOPMENT OF CHRONIC KIDNEY DISEASE

Nephrology

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ABSTRACT

Background- One of the major public health issues, chronic kidney disease (CKD) is characterized by structural and functional abnormalities around the kidney. **Objectives-** To analyze the effect of oral supplementation of bicarbonate on the progression of CKD. **Methods-** A double blind Randomized controlled trial study conducted at Tertiary care centre. Patients with CKD who were visiting hospital were considered as the study subjects. A total of 60 patients participated in the study. Patients were randomly grouped into two groups through block randomization. The first group of patients received oral sodium bicarbonate, whereas the second group of patients was on standard therapy without oral sodium bicarbonate supplementation. SPSS was used for analysis. **Results-** Group 1 consisted of 31 subjects, out of which 18 (69.7%) were males and 13 (30.3%) were females. Group 2 included 29 patients, of which 16 (73.53%) were males and 13 (26.47%) were females. Among the causes for CKD, hypertension was the most common cause followed by diabetes seen in almost 50% of cases. The mean weight of groups 1 and 2 was 58.12 and 61.96 kg, respectively, whereas the mean height of groups 1 and 2 was 161.70 and 161.82 cm, respectively. The mean bicarbonate levels of groups 1 and 2 patients were 16.62 and 16.84 mEq/L, respectively. After 6 months, the bicarbonate level of group 1 significantly increased to 18.02 mEq/L, which was further increased to 19.77 mEq/L after 9 months ($p < 0.05$). The baseline eGFR values in group 1 and 2 subjects were 22.39 and 21.20 mL/min/1.73 m², respectively. The difference between these values was not significant ($P = 0.31$). Similarly, no significant difference was observed in group 1 after 6 and 9 months. **Conclusion-** Oral bicarbonate supplementation raised the participants' serum bicarbonate levels. Additionally, oral supplementation caused patients' serum albumin levels to rise and their GFR to remain constant having CKD.

KEYWORDS

chronic kidney disease, Bicarbonate supplementation, glomerular filtration rate, metabolic acidosis, renal disease

INTRODUCTION:

One of the major public health issues, chronic kidney disease (CKD) is characterized by structural and functional abnormalities around the kidney. With an 800 per million population frequency in India, CKD affects millions of individuals worldwide. [1] The two most prevalent underlying conditions linked to CKD are diabetes mellitus and hypertension, anemia, cardiovascular disease, renal osteodystrophy, and metabolic acidosis are the main side effects of CKD. [1] The higher morbidity and mortality of the condition are mostly caused by these consequences. [2] It is crucial to explore for therapeutic techniques to regulate and treat CKD as the number of people with the condition is expected to increase.

One of the initial signs of CKD is metabolic acidosis. A metabolic acidosis results from the kidney's failure to produce and eliminate ammonia ions of hydrogen. This frequently has negative consequences, including systemic inflammation, bone resorption and osteopenia, increased muscle protein catabolism, secondary hyperparathyroidism exacerbation, decreased respiratory reserve, and exhaustion of the body's buffer systems. [3,4,5] Therefore, treating metabolic acidosis is essential for reducing CKD consequences. The relevance of oral bicarbonate supplementation in treating metabolic acidosis has been proposed in earlier research. [6,7] However, we haven't made much progress in this direction. Therefore, the purpose of this study was to examine how oral bicarbonate supplementation affected the development of CKD.

MATERIALS AND METHODS

A double blind Randomized controlled trial conducted at Tertiary care centre. Patients with CKD who were visiting hospital were considered as the study subjects. A total of 60 patients participated in the study. Patients were randomly grouped into two groups through block randomization. The first group of patients received oral sodium bicarbonate, whereas the second group of patients was on standard therapy without oral sodium bicarbonate supplementation.

The inclusion criteria-

- Age: >18 years,
- Estimated glomerular filtration rate (eGFR): 15–30 mL/min/1.73 m²
- Serum bicarbonate: 10–20 mM/L
- Clinical condition: stable.

The exclusion criteria -

- Patients on steroid therapy
- Congestive heart failure
- Uncontrolled hypertension (>150/90 mmHg)

- Cognitive impairment
- Ongoing sepsis
- Morbid obesity [body mass index (BMI) ≥ 40 kg/m²]
- Malignancies.

METHODOLOGY

Group 1 received 600 mg of sodium bicarbonate orally three times every day. To attain bicarbonate levels >23 mmol/L, the dosage was raised appropriately. The subjects were all adhered to 6 and nine months. All of the subjects' physical characteristics, including weight, height, and BMI, were measured. The individuals' kidney health was also examined for any underlying conditions. Venous blood was drawn from each individual while maintaining an aseptic environment and serum was also drawn. Following enzymatic methods with the help of the COBAS kit from Roche Diagnostics in Switzerland, serum bicarbonate was measured in accordance with the instructions from the manufacturer. By measuring absorbance at 340 nm on an automated analyzer (Roche Diagnostics) [8], which is proportional to the bicarbonate content in the serum, one may determine how much NADH is consumed in the process. The Roche/cobas CREJ2 test, which is based on Jaffe's method, was used to assess the levels of creatinine in serum using an automated analyzer. Using a kit created for Roche/Cobas C systems, an automated analyzer performed a photometrical estimate of albumin in serum. At pH 4.1, serum albumin and bromocresol green bond to produce a blue-green complex. This has a wavelength of 630 nm.

For nutritional assessment we used Mid arm circumference (MAC) in which subject's elbow was flexed to 90° and the midpoint between the tip of acromion and olecranon process was located. The MAC was measured with the subject standing erect by recording the arm circumference with the arm relaxed and elbow extended.

Statistical Analysis

The statistical analysis was performed using SPSS for windows version 22.0 software (Mac, and Linux). Student's t-test was used to calculate the significance between means. The findings were present in number and percentage analyzed by frequency, percent, and Chi-square test. The critical value of P indicating the probability of significant difference was taken as <0.05 for comparison.

RESULTS

Table 1: Anthropometry and etiology of CKD in study subjects

Diagnosis	Group		Total
	Group 1	Group 2	
Hypertension	7 (21.2%)	8 (23.5%)	15 (22.4%)
Hypertension and diabetes	10 (30.3%)	11 (32.4%)	21 (31.3%)

Hypertension and other causes	4 (12.1%)	6 (17.6%)	10 (14.9%)
Diabetes	3 (9.1%)	0 (0%)	3 (4.5%)
Diabetes and other causes	3 (9.1%)	4 (17.6%)	7(13.4%)
Other causes	4 (9.1%)	0 (0%)	4 (4.5%)
Total	31 (100%)	29 (100%)	60 (100%)
Gender: Males	18	16	60
Females	13	13	
Mean weight	58.12	61.96	-
Mean height	161.70	161.82	-
Mean BMI	22.32	23.44	-

As per table 1 Group 1 consisted of 31 subjects, out of which 18 (69.7%) were males and 13 (30.3%) were females. Group 2 included 29 patients, of which 16 (73.53%) were males and 13 (26.47%) were females. Among the causes for CKD, hypertension was the most common cause followed by diabetes seen in almost 50% of cases. The mean weight of groups 1 and 2 was 58.12 and 61.96 kg, respectively, whereas the mean height of groups 1 and 2 was 161.70 and 161.82 cm, respectively. The mean BMI of group 1 was 22.32 and of group 2 were 23.44. It was observed that the difference of mean values of weight, height, and BMI between both the groups was not statistically significant.

Table 2: Mean serum bicarbonate, eGFR, serum albumin, and muscle mass levels at baseline, 6 and 9 months in both groups

Parameter	Group	n	Mean	Standard deviation	P
HCO ₃ (mEq/L)	Group 1	31	16.62	3.05	<0.01
	Baseline				
	At 6 months	31	18.02	1.24	
	At 9 months	30	19.77	1.86	
	Group 2				
	Baseline	29	16.84	2.17	
eGFR (mL/min/1.73 m ²)	Group 1				0.31
	Baseline	29	16.85	1.46	
	At 6 months	29	16.32	1.80	
	At 9 months	28			
	Group 2				
	Baseline	29	21.21	4.37	
Serum albumin (g/dL)	Group 1				0.00
	Baseline	31	4.05	0.59	
	At 6 months	31	4.24	0.47	
	At 9 months	30	4.34	0.44	
	Group 2				
	Baseline	29	4.13	0.45	
Muscle mass (kg)	Group 1				0.35
	Baseline	29	4.04	0.42	
	At 6 months	29	4.02	0.54	
	At 9 months	28			
	Group 2				
	Baseline	29	21.21	4.37	
Muscle mass (kg)	Group 1				0.01
	Baseline	31	20.03	4.74	
	At 6 months	31	21.54	4.99	
	At 9 months	30	21.52	4.57	
	Group 2				
	Baseline	29	21.96	5.67	
Muscle mass (kg)	Group 1				0.04
	Baseline	29	21.25	4.40	
	At 6 months	28	20.29	4.86	
	At 9 months	28			
	Group 2				
	Baseline	29	21.96	5.67	

Table 3: Comparison of serum bicarbonate, eGFR, serum albumin, and muscle mass levels between groups

Parameter	Timeline	Group	Mean	Standard Deviation	P
HCO ₃	Baseline to 6 months	Group 1	2.157	0.553	0.06
		Group 2	0.04	0.255	
	Baseline to 9 months	Group 1	3.330	0.567	0.00
		Group 2	0.414	0.375	
	6 to 9 months	Group 1	1.173	0.299	0.00
		Group 2	0.418	0.277	
eGFR	Baseline to 6 months	Group 1	0.096	0.704	0.14
		Group 2	0.705	0.704	
	Baseline to 9 months	Group 1	0.211	0.680	0.05
		Group 2	2.117	0.694	
	6 to 9 months	Group 1	0.307	0.563	0.10
		Group 2	1.412	0.633	
Serum albumin	Baseline to 6 months	Group 1	0.217	0.066	0.00
		Group 2	0.039	0.040	
	Baseline to 9 months	Group 1	0.283	0.084	0.01
		Group 2	0.096	0.070	
	6 to 9 months	Group 1	0.067	0.046	0.01
		Group 2	0.057	0.076	
Muscle mass	Baseline to 6 months	Group 1	1.757	0.375	0.00
		Group 2	0.725	0.544	
	Baseline to 9 months	Group 1	1.394	0.569	0.01
		Group 2	1.219	0.452	
	6 to 9 months	Group 1	0.364	0.346	0.01
		Group 2	0.494	0.504	

Serum albumin	6 to 9 months	Group 2	2.117	0.694	0.10
		Group 1	0.307	0.563	
	Baseline to 6 months	Group 2	1.412	0.633	0.00
		Group 1	0.217	0.066	
	Baseline to 9 months	Group 2	0.039	0.040	0.01
		Group 1	0.283	0.084	
Muscle mass	6 to 9 months	Group 2	0.096	0.070	0.01
		Group 1	0.067	0.046	
	Baseline to 6 months	Group 2	0.057	0.076	0.00
		Group 1	1.757	0.375	
	Baseline to 9 months	Group 2	0.725	0.544	0.01
		Group 1	1.394	0.569	
Muscle mass	6 to 9 months	Group 2	1.219	0.452	0.01
		Group 1	0.364	0.346	
	Baseline to 6 months	Group 2	0.494	0.504	0.01
		Group 1	1.757	0.375	
	Baseline to 9 months	Group 2	0.725	0.544	0.01
		Group 1	1.394	0.569	

As per table 2 the mean bicarbonate levels of groups 1 and 2 patients were 16.62 and 16.84 mEq/L, respectively. After 6 months, the bicarbonate level of group 1 significantly increased to 18.02 mEq/L, which was further increased to 19.77 mEq/L after 9 months ($p < 0.05$). The baseline eGFR values in group 1 and 2 subjects were 22.39 and 21.20 mL/min/1.73 m², respectively. The difference between these values was not significant ($P = 0.31$). Similarly, no significant difference was observed in group 1 after 6 and 9 months. Interestingly, group 1 patients displayed increased serum albumin levels compared with baseline ($P = 0.00$). In patients with bicarbonate supplementation, significant improvement in muscle mass was observed after a period of 6 and 9 months.

Table 3: Comparison of serum bicarbonate, eGFR, serum albumin, and muscle mass levels between groups

Parameter	Timeline	Group	Mean	Standard Deviation	P
HCO ₃	Baseline to 6 months	Group 1	2.157	0.553	0.06
		Group 2	0.04	0.255	
	Baseline to 9 months	Group 1	3.330	0.567	0.00
		Group 2	0.414	0.375	
	6 to 9 months	Group 1	1.173	0.299	0.00
		Group 2	0.418	0.277	
eGFR	Baseline to 6 months	Group 1	0.096	0.704	0.14
		Group 2	0.705	0.704	
	Baseline to 9 months	Group 1	0.211	0.680	0.05
		Group 2	2.117	0.694	
	6 to 9 months	Group 1	0.307	0.563	0.10
		Group 2	1.412	0.633	
Serum albumin	Baseline to 6 months	Group 1	0.217	0.066	0.00
		Group 2	0.039	0.040	
	Baseline to 9 months	Group 1	0.283	0.084	0.01
		Group 2	0.096	0.070	
	6 to 9 months	Group 1	0.067	0.046	0.01
		Group 2	0.057	0.076	
Muscle mass	Baseline to 6 months	Group 1	1.757	0.375	0.00
		Group 2	0.725	0.544	
	Baseline to 9 months	Group 1	1.394	0.569	0.01
		Group 2	1.219	0.452	
	6 to 9 months	Group 1	0.364	0.346	0.01
		Group 2	0.494	0.504	

The highest difference in the bicarbonate levels was found between baseline and 9 months' subjects. Furthermore, when both the groups were compared, the difference in the serum bicarbonate value at different time points is highly significant. Post hoc analysis corroborated that in patients without bicarbonate supplementation

(group 2), a significant reduction in the eGFR with a change of about 6.2% from baseline to 9 months was observed. In group 1, statistically significant difference in the serum albumin levels between different time intervals was observed wherein baseline to 9 months was highly significant ($P=0.006$). When both the groups' subjects were compared, the difference in the serum bicarbonate value at different time points was found to be highly significant. When compared between time points, significant improvement in the muscle mass was observed from baseline to 6 months (7.54%) and baseline to 9 months (7.46%) in group 1. However, no significant improvement was found between 6 and 9 months. In group 2, a significant decrease in muscle mass was observed from baseline to 9 months (7.64%). But no significant changes were noticed between baseline and 6 months, as well as between 6 and 9 months subjects. Furthermore, when compared between the groups at all time points, the muscle mass was significantly different ($P=0.001$).

DISCUSSION-

In addition to diabetes and hypertension, nephrotoxins, poor sanitation, contaminated water, consanguinity, and pollution are some of the factors that cause CKD in India. The management of CKD has grown in importance as the number of patients with diabetes and hypertension in India is increasing. Changing a few of the linked factors can slow the disease's course. The early management of CKD centered on such controllable variables as hypertension, hyperglycemia, proteinuria and control.[9,10] Metabolic acidosis has been identified as one of the potential causes contributing to the disease's progression in studies conducted over the past ten years.

We investigated the role of bicarbonate supplementation in relieving disease complications in patients with CKD. Time-dependent significant increase in the mean bicarbonate levels of group 1 was observed, while no change was reported in group 2. Thus, it was very clear that oral supplementation of bicarbonate decreases the metabolic acidosis during CKD condition, which was also suggested by earlier report.[11,12]

It is generally recognized that people with CKD frequently have a decline in eGFR. In fact, eGFR rate is a marker used to assess illness severity and track the response to treatment.[13] An eGFR decline of 3.3% each year in CKD has been verified in a prior studies done [14,15] In our study, bicarbonate administration caused eGFR to be maintained at its starting point, but eGFR declined in the group not receiving bicarbonate supplementation. This is consistent with a previous study that also demonstrated a slower drop in eGFR following bicarbonate administration[16].

Ballmer et al.'s study [17] confirmed that increased protein breakdown in metabolic acidosis leads to increased nitrogen excretion and decreased albumin production. Consequently, to avoid protein (muscle) wasting in these patients, metabolic acidosis must be corrected. According to findings [17], supplementing with sodium bicarbonate was linked to enhanced dietary protein intake, lower protein catabolism, and increases in serum albumin and lean body mass.

CONCLUSION-

Oral bicarbonate supplementation raised the participants' serum bicarbonate levels. Additionally, oral supplementation caused patients' serum albumin levels to rise and their GFR to remain constant having CKD. Additionally, bicarbonate supplementation increased the muscle mass in CKD patients. All of these points to bicarbonate's potential function in the therapy of CKD development by alleviating metabolic acidosis.

Conflict of Interest- None declared

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