

The Effect of Oral Sodium Bicarbonate Supplementation on Chronic Kidney Disease: a Randomised Controlled Trial

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Abstract:**Background:** Chronic kidney disease (CKD) poses serious public health concern, constituting structural and functional abnormalities in the kidney. The complications become a cause of increased morbidity and mortality in CKD patients.**Aim:** To assess the effect of oral bicarbonate supplementation on the progression of chronic kidney disease.**Material & Methods:** This prospective randomised controlled clinical trial was conducted in the Department of nephrology of our tertiary care Hospital from February 2023 till January 2024. Patients (n=70), aged more than 18 yrs, with estimated glomerular filtration rate (eGFR) of 15–30 mL/min/1.73 m² and Serum bicarbonate levels 10–20 mM/L in clinically stable condition were randomized into; Test Group - 600 mg sodium bicarbonate orally TDS; Control Group - standard therapy without oral sodium bicarbonate supplementation.

Venous samples were analysed for Serum bicarbonate, serum creatinine, serum albumin & eGFR. The patients were followed for 6 and 9 months

Results: In control group, eGFR decreased significantly at 6 months (20.24 mL/min/1.73 m²) and at 9 months (19.26 mL/min/1.73 m²) (p<0.05). In test group, serum albumin levels increased significantly, eGFR remained at par with baseline values. The serum creatinine was comparable in both the groups with no significant difference at 6 or 9 months.**Conclusions:** The present study concluded that the oral supplementation to cause improvement in the serum albumin levels & maintenance of baseline values which subsequently leads to improvement in renal function. Thus, it should be included in the management of metabolic acidosis in chronic kidney diseases patients & arrest disease progression.

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Introduction

Chronic kidney disease (CKD) poses serious public health concern, constituting structural and functional abnormalities in the kidney. Millions of people worldwide are affected by CKD with a prevalence of 8% - 10%. [1,2] In India, the prevalence rate is 4%-20%. [3,4]

Diabetes mellitus (DM) and hypertension are the most commonly associated diseases with CKD. [5] The complications associated with CKD are anaemia, cardiovascular disease (CVD), renal osteodystrophy, and metabolic acidosis. The complications become a cause of increased morbidity and mortality in CKD patients. [6] In order to curb the menace of complications, it is of utmost importance to come out with therapeutic approaches to control & manage CKD. As the prevalence of patients with CKD is predicted to rise, it is of paramount importance to look for therapeutic approaches to control and treat CKD.

Metabolic acidosis is the earliest hallmark & the most common complications chronic kidney dis-

ease patients. [7] Here the kidney is unable to synthesize ammonia and excrete hydrogen ions. This condition leads to bone demineralization, insulin resistance, secondary hyperparathyroidism, muscle protein catabolism, functional limitations in older individuals, cognitive impairment & exhaustion of body buffer systems. [8,9,10] It is also associated with cardiovascular disease in CKD patients. Unable to remove the acids from the body caused due to nephron loss or dietary acid load results in kidney tissue injury through endothelin-1 activation, the renin-angiotensin-aldosterone system, and the alternative complement pathway. [11] Low serum bicarbonate levels cause faster progression of CKD. Thus bicarbonate therapy has been advised to arrest the progression of CKD with replacement therapy. [12] Thus the present study was aimed to assess the effect of oral bicarbonate supplementation on the progression of CKD.

Material & Methods

This prospective randomised controlled clinical trial was conducted in the Department of nephrology of our tertiary care Hospital from February 2023 till January 2024. Patients (n=70), aged more than 18 yrs, with estimated glomerular filtration rate (eGFR) of 15–30 mL/min/1.73 m² and Serum bicarbonate levels 10–20 mM/L in clinically stable condition were included in the study. Patients on steroid therapy, congestive heart failure, uncontrolled hypertension (>150/90 mmHg), cognitive impairment, ongoing sepsis, morbid obesity, body mass index ≥ 40 kg/m², malignancies were excluded.

Test Group - 600 mg sodium bicarbonate orally TDS. The dosage was adjusted accordingly to achieve bicarbonate levels >23 mmol/L.

Control Group - standard therapy without oral sodium bicarbonate supplementation.

Sociodemographic parameters were recorded like height, weight, BMI. Venous samples were collected under the aseptic condition & Serum bicarbonate, serum creatinine, serum albumin were analysed in laboratory. eGFR was measured from the serum creatinine level by applying the MDRD formula (equation 1) using computer software. $eGFR = 186 \times \text{serum creatinine}^{-1.154} \times \text{age}^{-0.203} \times 0.742$ (only if female) (Equation 1). The patients were followed for 6 and 9 months.

Statistical Analysis

The tabulated data was statistically analyzed using SPSS version 22.0 for Windows (IBM Corp,

India). Quantitative data are presented as mean \pm SD or proportions. Intergroup comparisons were made using Student's paired t-test. P-value 0.05 at a 90% confidence interval was considered to be statistically significant.

Results

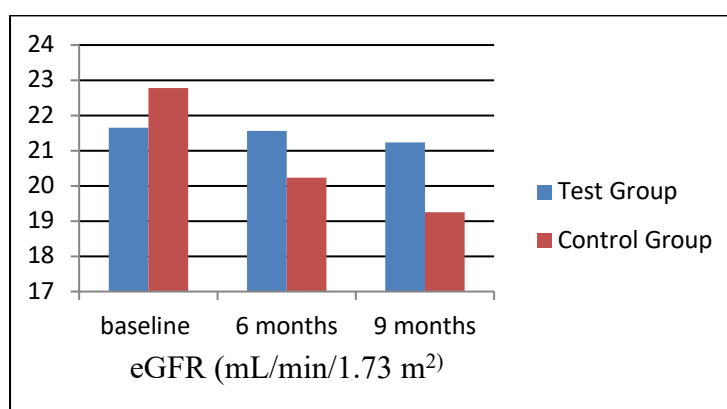
The baseline sociodemographic parameters, bicarbonate concentrations, eGFR, creatinine were comparable in both the groups with no statistically significant difference ($p < 0.05$).

In test group, bicarbonate levels at baseline, 6 months & 9 months were 16.24 mEq/L, 18.45 mEq/L and 19.55 mEq/L resp. ($p < 0.05$). The bicarbonate levels increased significantly at 6 and 9 months. In Control group, bicarbonate levels at baseline (16.94 mEq/L) were comparable with the test group and remained the same, with no statistically significant change at 6 and 9 months ($p > 0.05$).

In the test Group, serum albumin levels increased significantly at 6 and 9 months ($p > 0.05$). In the control group, serum albumin levels showed a slight decrease at 6 months (4.04 g/dL) and 9 months (4.09 g/dL) from the baseline (4.17 g/dL) which was not statistically significant ($p > 0.05$).

In the test Group, baseline eGFR values were 21.65 mL/min/1.73 m². No significant difference was observed after 6 and 9 months.

In the control Group, baseline eGFR values were 22.78 mL/min/1.73 m². The eGFR decreased significantly at 6 months (20.24 mL/min/1.73 m²) and 9 months (19.26 mL/min/1.73 m²) ($p < 0.05$). (Graph 1)



Discussion

Metabolic acidosis, is a common complication in CKD patients, wherein GFR falls below 30 ml/min. This results in a series of consequences like stunted growth in children, loss of bone and muscle mass, negative nitrogen balance & acceleration of progression of CKD. India CKD are on a rise, the morbidity & mortality associated with them puts a lot of mental & financial stress on the patients &

their families. Development of CKD occurs due to pollutants, nephrotoxins, poor sanitation, water contamination, consanguinity & genetic inbreeding. [13]

As renal function decreases, the kidneys gradually lose their capacity to synthesize ammonia & excrete hydrogen ions. Thus, in patients with low eGFR, low bicarbonate levels can be observed. Eustace JA et al 2004 observed 19 % of the CKD

patients had serum bicarbonate levels $<22\text{mmol/L}$. [14]

In the present study, In the test Group, baseline eGFR values were $21.65\text{ mL/min/1.73 m}^2$. No significant difference was observed after 6 and 9 months. Also the serum albumin levels increased significantly at 6 and 9 months. While in control group, eGFR decreased significantly at 6 months and 9 months. This is in accordance with study conducted by Alva et al 2020 which observed mean bicarbonate levels in test groups & control group patients to be 16.62 and 16.84 mEq/L, respectively. After 6 months, the bicarbonate levels in test group significantly increased to 18.02 mEq/L in 6 months & to 19.77 mEq/L in 9 months. The mean eGFR observed significant reduction with a change of about 6.2% from baseline to 9 months. Thus, supporting the fact that oral supplementation of bicarbonate reduces the metabolic acidosis during CKD condition.

Mahajan A et al 2010 had demonstrated the beneficial effects of oral bicarbonate supplementation with a slower reduction in eGFR in CKD patients. [15] Krolewski et al. has noted an eGFR reduction of $\geq 3.3\%$ per year in CKD patients. [16] Ballmer et al. study demonstrated that metabolic acidosis results in increased nitrogen excretion and decreased albumin synthesis due to increased protein degradation. Thus, the correction of metabolic acidosis is of utmost importance to prevent muscle wasting. [17]

In a systemic review and metaanalysis by Hulstijn in 2021, 15 trials including 2445 participants were followed up for 12 months. The study observed sodium bicarbonate to retard the decline in kidney function & reduced the risk of end-stage kidney failure. [18]

A study y Goraya N et al 2012 used dietary interventions with fruits and vegetables, which lowered the net dietary acid load, observed improvement in the markers of kidney injury i.e. urinary albumin, *N*-acetyl- β -D-glucosaminidase, TGF- β , and endothelin 1. GFR was maintained in patients with hypertension-associated kidney disease wherein reduction in dietary acid intake was accomplished by consuming base-inducing fruits and vegetables or bicarbonate. [19]

The positive nutritional benefits are also observed with the supplementation of sodium bicarbonate. Improved nutritional status has positive effects on the clinical outcomes in dialysis patients, whereas protein wasting & low serum albumin is associated with increased morbidity and mortality with $<35\text{ g/L}$ linked to poor outcomes. Causes of protein wasting are multifactorial, low nutrient intake, reduced protein synthesis, and increased protein catabolism. [20]

Thus, the present study supports that oral bicarbonate supplementation results in maintenance of eGFR to its baseline value whereas the eGFR degraded in patients not on oral bicarbonate supplementation. The nephrologists should manage metabolic acidosis efficiently to prevent degradation of eGFR and inturn the renal function. Sodium bicarbonate supplementation is also beneficial in improved dietary protein intake & protein anabolism.

Conclusion

The presents study concluded oral bicarbonate supplementation to cause improvement in the serum albumin levels & maintenance of baseline eGFR values which subsequently leads to improvement in renal function. Thus, it should be included in the management of metabolic acidosis in chronic kidney disease patients & arrest disease progression.

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