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Original Article

Effects of Sodum Bicarbonate supplementation on Renal function and Nutritional status in Chronic Kidney Disease patients

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Abstract

Background: Metabolic acidosis is commonly associated with chronic kidney disease which causes progressive loss of kidney function. The diminishing ability of the kidneys to maintain acid-base homeostasis results in acid accumulation, leading to various complications such as impairment in nutritional status, worsened uremic bone disease and an association with increased mortality. Recent clinical trials have suggested that correction or prevention of metabolic acidosis by alkali administration is able to attenuate kidney damage and to slow progression of chronic kidney disease and improve nutritional status.

Methods: It was a prospective study. Out of a total of 66 CKD patients (eGFR < 60 ml/1min/1.73m,^{2} serum HCO_3- 16-22 mmol/l); 33 were in treatment group and 33 in control group were included in the study. Treatment group of the study was CKD patients who received sodium bicarbonate for 6 months to correct acidosis. Control group for the study was CKD patients who did not receive any $NaHCO_3$ supplementation; attending SSMC, Mitford Hospital for the same duration. Baseline renal function and nutritional status parameters were similar in both groups. Rate of progression of CKD was measured by calculation of eGFR (4 variable MDRD- equation) at the beginning of the study and then after 3 and 6 months. Similar dietary advice was given to both groups. Purposive sampling was done. The primary end point was denoted as rate of eGFR decline. Secondary end points were serum albumin (<3.5gm/dl) and mid-arm circumference (<24 cm) and body mass index. Nutritional status was determined by measuring mid-arm circumference, serum albumin and body mass index at the starting of the study, after 3 and 6 months.

Results: Mean age (years) was 56 ± 15 & 49 ± 15;p=0.074 in treatment and control group respectively. Mean haemoglobin concentration (gm/dl) was 9.8 ± 1.5 and 9.6 ± 0.9;p=0.477 in treatment & control group respectively. At baseline mean BMI (kg/m^2) was 21.3±5 and 23±4;p=0.138 in control and treatment group respectively. In the present study, mean systolic blood pressure was 129.6±3.8 and 131.4±5.1;p= 0.184 in control and treatment group respectively at six months of study period. . In the present study, mean diastolic blood pressure was 79.1±4.6 and 80.8±3.2; p= 0.202 in control and treatment group respectively at six months of study period. Serum bicarbonate was raised significantly in treatment group than control group at six months of study period (26.3 ± 1.6 and 21.2 ± 1.1; p<0.001). Serum potassium was reduced significantly in treatment group than control group at six months of study period (4.5 ± 0.6 and 5 ± 0.5; p=0.001). Mid-arm circumference was increased significantly in treatment group than control group at six months of study period (24.4 and 22.4 cm; p<0.001). Serum albumin (gm/dl) was increased significantly in treatment group than control group at six months of study period (3.4 and 2.8;p<0.001). Body mass index was similar in treatment group and control group at six months of study period (23.1 and 21.2; p=0.090). After six months eGFR (ml/min/m^2) was declined significantly in control group than treatment group (3.02± 2.25 and 1.13± 2.31; p=0.001).

Conclusion: Oral sodium bicarbonate supplementation in patients with metabolic acidosis slows the rate of decline of renal function in patients with advanced stages of CKD. This easily affordable and simple strategy also improved the nutritional status of advanced stages of CKD patients with metabolic acidosis.

Keywords: Bicarbonate, CKD, Metabolic acidosis Nutritional status.

Introduction

In the 21st century chronic kidney disease (CKD) is emerging as a global public health problem. About 5-10% of world populations are suffering from CKD. Approximately 1.8 million people, worldwide, are currently treated with renal replacement therapy (RRT), which consists primarily of kidney transplantation and dialysis. The vast majority of these patients cannot afford renal replacement therapy on reaching ESRD. Hence the secondary prevention of ESRD remains the primary focus of the efforts of physicians involved in care of CKD patients.

Hasan et al 2012 found that overall prevalence of CKD among Bangladeshi population was 19% (Cock-Croft Gault equation) and 19.5% (MDRD equation) respectively.[1]

Metabolic acidosis is a common complication associated with progressive loss of kidney function which diminishes the ability of the kidneys to maintain acid-base homeostasis resulting acid accumulation, leading to various complications such as impairment in nutritional status, worsening uremic bone disease and an association with increased mortality. In addition to these adverse effects which are related to acid retention, metabolic acidosis may also cause kidney damage, possibly through the stimulation of adaptive mechanisms aimed at maintaining acid-base homeostasis in the face of decreasing kidney function. Recent clinical trials have suggested that correction of metabolic acidosis by alkali administration is able to attenuate kidney damage and slow progression of CKD, and may hence offer an effective, safe and affordable renoprotective strategy (Kovesdy 2012).[2] Metabolic acidosis is noted in the majority of patients with chronic renal disease(CKD) when glomerular filtration rate(GFR) decreases to less than 20% to 25%of normal, although as many as 20% of individuals can have acid-base parameters close to or within the normal range. Acidosis is generally is mild to moderate in degree, with plasma bicarbonate concentrations ranges from 12-22 Meq/L(mmol/l), and it is rare to see value less than 12mmol/l in the absence of an increased acid load. Degree of acidosis is approximately correlates severity of renal failure and usually is more severe at lower GFR.

Metabolic acidosis can develop as a result of one or more of the following patho-physiologic processes (Goodman et al 1965): increased production of nonvolatile acids, increased loss of bicarbonate and decreased renal excretion of acid.[3]

As a result, CKD leads to retention of hydrogen ions. In addition to the fall in ammonium excretion, diminished excretion of titratable acid (primarily as phosphoric acid) also may play a role in the pathogenesis of metabolic acidosis in patients with advanced kidney disease.

Chronic metabolic acidosis in patients with chronic kidney disease (CKD) may produce a variety of pathophysiologic changes: bone resorption and osteopenia, increased muscle protein catabolism, aggravation of secondary hyperparathyroidism, and exhaustion of body, endocrine disorders such as resistance to growth hormone and insulin, and hypertriglyceridemia, systemic inflammation and hypotension and malaise (www.update.com/content/pathogenesis).[4]

Another potential mechanism involves activation of the renin-angiotensin system, which is important for urinary acidification but which can also result in proteinuria, renal damage, and progressive CKD (Ng et al 2011).[5]

Uremic acidosis can increase skeletal muscle breakdown and diminish albumin synthesis, leading to muscle wasting and muscle weakness (Williams et al 1991).[6] The degree of muscle breakdown may be exacerbated by institution of a low-protein diet, which is occasionally used in an attempt to minimize progressive renal injury.

Materials and Methodology

It was a prospective study. This study was carried out from July 2013 to June 2014 among CKD patients attending to the department of nephrology of SSMC & Mitford Hospital, Dhaka fulfilling selection criteria of the study. Purposive sampling was adopted for collecting data. A written consent was taken from each patients.

Treatment group of the study was CKD patients (eGFR < 60 ml/1min/1.73m^2) who received sodium bicarbonate for 6 months to correct acidosis. Control group for the study was CKD patients (eGFR < 60 ml/1min/ 1.73 m^2) who did not receive any $NaHCO_3$ supplementation; attending for the same duration. Rate of progression of CKD was measured by calculation of eGFR (using MDRD equation) at the beginning of the study and then after 3 and 6months. Patients of both groups had taken protein 0.8-1gm/kg/day during the study period; fruits were restricted and no added salt in their diets. Patients of treatment group received $NaHCO_3$ (600 mg tablets 3 to 4 times a day,upto 2.4 gm maximum as needed) during the study period to maintain HCO_3->22 mmol/l. The primary end-point was decline in renal function by assessing changes in eGFR from baseline to the end of the study period. The secondary end-point was measurements of changes in nutritional status parameters. Nutritional status was determined by changes in body mass index, mid-arm circumference and serum albumin concentration.

The primary end point was denoted as rate of eGFR decline, the proportion of patients with rapid decline of eGFR (>3ml/min/1.73m^2/year). Secondary end points were serum albumin (<3.5gm/dl) and mid-arm circumference(<24 cm) and body mass index. Nutritional status was determined by measuring mid-arm circumference, serum albumin and body mass index at the starting of the study and after 3 and 6 months. All the data were checked and edited after collection. Then the data were entered into computer and statistical analysis of the result obtained by using windows based computer software devise with Statistical Packages for Social Sciences (SPSS.v-14.0; SPSS inc, Chicago, IL USA).

Results

Total 70 patients were enrolled in this study; but during data collection 4 patients (2 in each group) were excluded from the study because of their death. So in this study total 66 patients (33 patients in treatment group and 33 patients in control group) were included. Mean age (years) was 56 ± 15 & 49 ± 15 in treatment and control group respectively. They were matched for haemoglobin, BMI(kg/m2), MAC(cm), s.albumin (gm/dl) and systolic and diastolic blood pressure. In the present study causes of CKD were as follows: glomerulonephritis (37%), diabetis mellitus (25%), hypertension (10%), undetermined cause (9%), obstructive uropathy (9%), systemic lupus erythematosus (4%) and autosomal dominant polycystic kidney disease (3%). In the present study co-disease was as follows: hypertension (87%), ischemic heart disease (10%) and cerebrovascular disease (2%).

Table I: Baseline charactertics of study population.

Variables	Group		P value
	Group I (Control) n=33	Group II (Treatment) n=33	
1Age (Years)	1649 ± 15	56 ± 15	0.074
Systolic BP	129±4	131±5	0.210
Diastolic BP	79±4	80±3	0.353
BMI(kg/m^2)	21±5	23±4	0.137
MAC(cm)	23.7±2.2	23.7±1.7	0.927
Hb%(gm/dl)	9 ± 0.9	9 ± 1	0.477
Serum albumin (gm/dl)	3±0.4	2.9±0.49	0.666
Serum HCO_3-	20.6±0.7	20.3±1	0.334
Serum K+	4.8±0.5	4.7±0.5	0.619
Serum Creatinine(mg/dl)	2.4±0.9	2.4±0.75	0.975
eGFR(ml/min/1.73m^2)	27±10	25±9	0.290

Note: Hb% - haemoglobin%; BP-blood pressure; BMI-body mass index; MAC-mid-arm circumference; HCO_3^- - bicarbonate; K^+-potassium; eGFR - estimated glomerular filtration rate.

Table II: Serum HCO_3 - of the study subjects at different time interval

Time	Group		P value
	Control group (Mean ± SD) n=33	Treatment group (Mean ± SD) n=33	
Baseline	20.6 ± 0.70	20.3 ± 1.06	0.334
After 3 months	21.3 ± 1.1	24.4 ± 1.3	0.001
After 6 months	21.2 ± 1.1	26.3 ± 1.6	0.001

Serum bicarbonate (HCO_3^-) of study subject at baseline in treatment and control group was similar.

Serum HCO_3^- of study subjects increased in treatment group at 3 months than control group (P<0.001) and also at 6 months (P<0.001).

Table III: Serum K+ of the study subjects.

Time	Group		P value
	Group 1 (Control) (n=33	Group 2 (Treatment) n=33	
Baseline	4.8 ± 0.5	4.7 ± 0.5	0.619
After 3 months	4.9 ± 0.4	4.5 ± 0.5	0.002
After 6 months	5.0 ± 0.5	4.5 ± 0.6	0.001

At baseline serum potassium (K^+) level was similar in control and treatment group. After 3 and 6 months serum K^+ level was reduced significantly in the treatment group than control group.

Table IV: Nutritional status at 0,3months in control group (n=33)

Variables	Baseline	After 3 months	P value
BMI (Kg/m^2)	21.3 ± 5.0	21.2 ± 5.0	0.320
MAC (cm)	23.7 ± 2.2	23.0 ± 2.2	0.001
S.albumin (gm/dl)	3.00 ± 0.4	2.8 ± 0.4	0.001

In control group body mass index (BMI) of study subject of was similar at baseline and after 3 months.

In the same group mid- arm circumference (MAC) of study population decreased after 3 months (P<0.001).

In the control group serum albumin (s.albumin) decreased from baseline to 3 months (P<0.001).

Table V: Nutritional status at 0, 6 months in control group (n=33)

Variables	Baseline	After 6 months	P value
BMI (Kg/m^2)	21.3 ± 5.0	21.2 ± 5.1	0.145
MAC (cm)	23.7 ± 2.2	22.4 ± 2.3	0.001
S. albumin (gm/dl)	3.0 ± 0.4	2.8 ± 0.5	0.005

In control group body mass index (BMI) of study subject was similar at baseline and after from 6 months (P=0.145)

In the above group mid-arm circumference (MAC) of study population was higher at baseline than after 6 months (P<0.001).

In control group serum albumin (s.albumin) was higher at baseline than after 6 months (P<0.005).

Table VI: Nutritional status at 0, 3 months in treatment group (n=33)

Variables	Baseline	After 3 months	P value
BMI (Kg/m^2)	23.01 ± 4.04	23.03 ± 4.02	0.487
MAC (cm)	23.7 ± 1.7	24.0 ± 1.7	0.007
S. albumin (gm/dl)	2.9 ± 0.4	3.1 ± 0.4	0.001

In the treatment group body mass index (BMI) of study subject was similar at baseline and after 3 months (P=0.487).

In the same group mid-arm circumference (MAC) of study population was higher after 3 months than that of baseline (P<0.007). In the treatment group serum albumin (s.albumin) was higher after 3 months than from baseline (P<0.001).

Table VII: Nutritional status at 0, 6 months in treatment group (n=33)

Variables	Baseline	After 6 months	P value
BMI (Kg/m^2)	23.0 1± 4.04	23.16 ± 4.07	0.044
MAC (cm)	23.7 ± 1.7	24.4 ± 1.9	0.001
S. albumin (gm/dl)	2.9 ± 0.4	3.4 ± 0.4	0.001

In the treatment group body mass index (BMI) of study subject of was higher after 6 months than baseline (P=0.044).

In the same group mid-arm circumference (MAC) of study population was raised after 6 months from baseline (P<0.001).

In the treatment group serum albumin (s.albumin) increased after 6 months (P<0.001).

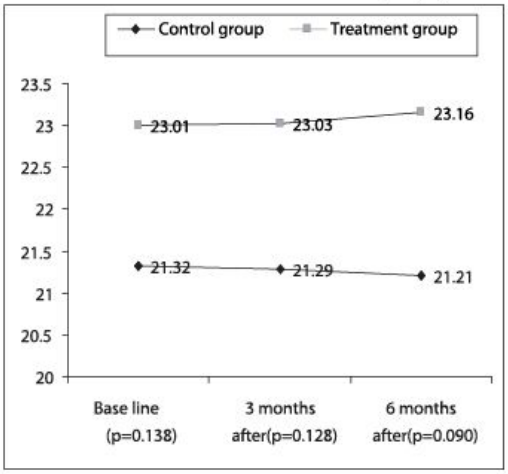

Fig 1: Body mass index (BMI) of the study subjects at 0,3,6 months

There was no difference of BMI between treatment group and control group at 0, 3 and 6 months.

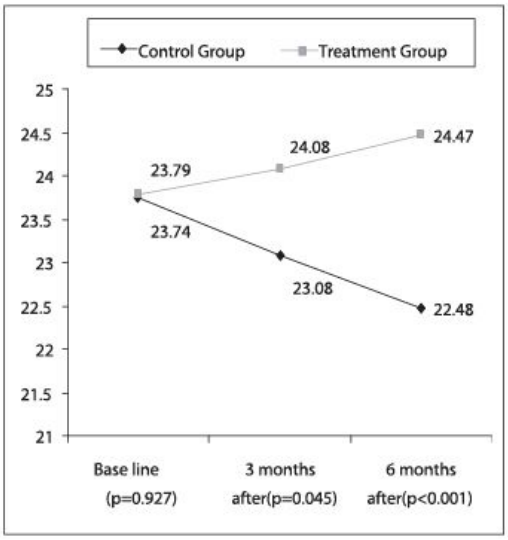

Fig 2: Mid-arm circumference (MAC) of the study subjects at 0,3,6 months.

In the above figure the values of MAC were similar at baseline in two groups. Improvement of MAC in treatment group than control group was significant at 3and 6 months.

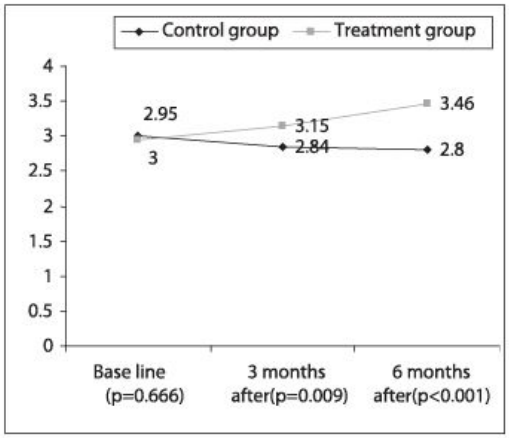

Fig 3: Serum albumin status of the study subjects at 0,3,6 months.

In the above figure baseline serum albumin was similar in two groups; there was significant improvement of serum albumin at 3 and 6 months in treatment group than the control group.

Table VIII: Status of eGFR in control group at 0,3,6 months.

Variables	Baseline	Time interval	P value
eGFR ml/min/1.73m2	27.9± 10	After 3 months 26 ± 8	0.003
eGFR ml/min/1.73m2	27.9 ± 10	After 6 months 24.9 ± 8.9	0.001

Estimated glomerular filtration rate (eGFR) reduced at 3 and 6 months from baseline.

Table IX: Status of eGFR in treatment group at 0,3,6 months.

Variables	Baseline	Time interval	P value
eGFR ml/min/1.73m2	25.3 ± 9.9	After 3 months 24.3 ± 9.3	0.061
eGFR ml/min/1.73m2	25.3 ± 9.9	After 6 months 24.1 ± 10.1	0.008

Estimated glomerular filtration rate (eGFR) reduced at 6 months from baseline.

Table X: Changes in eGFR between control and treatment group at 6 months.

Variables	Group		P value
	Group I (Control) (Mean ± SD) n=33	Group II (Treatment) (Mean ± SD) n=33	
Change of eGFR at 6 months	3.02 ± 2.25	1.13 ± 2.31	0.001

Changes in reduction of estimated glomerular filtration rate (eGFR) was significantly low at 6 months in treatment group than the control group.

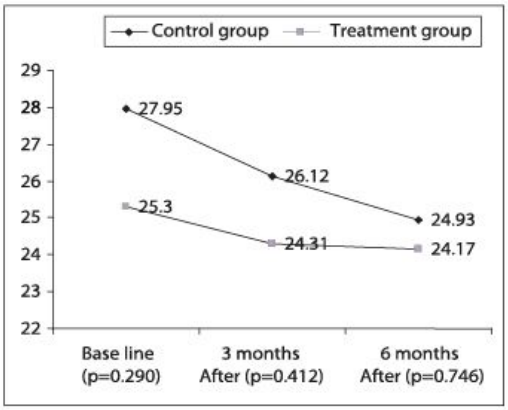

Fig 4: Estimated glomerular filtration rate (eGFR) status of the study subjects at 0,3,6 months.

In the above figure there was similar reduction of eGFR at 3 and 6 months in both treatment group and control group.

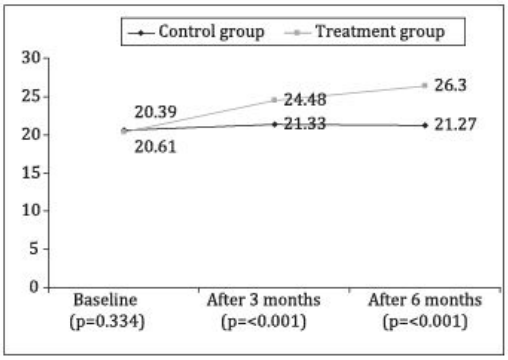

Fig 5: Serum bicarbonate (HCO_3-) of study subjects at different time interval

At baseline serum HCO_3^- was similar in treatment and control group. There was significant improvement in serum HCO_3^- level at 3 and 6 months from baseline between treatment and control group.

Table XI: Serum creatinine of the study subjects.

Time	Group		P value
	Group I (Control) (Mean ± SD) n=33	Group II (Treatment) (Mean ± SD) n=33	
Baseline	2.44 ± 0.96	2.45 ± 0.75	0.975
After 3 months	2.51 ± 0.83	2.54 ± 0.79	0.881
After 6 months	2.67± 0.99	2.57 ± 0.81	0.660

There was no difference in serum creatinine level between treatment and control group at baseline and at 3 and 6 months interval.

Discussion

Metabolic acidosis is a common complication associated with progressive loss of kidney function. In this prospective trial oral sodium bicarbonate supplementation was associated with positive effects in both primary and secondary end points in patients with CKD. Sodium bicarbonate supplementation slowed decline of renal function in treatment group as assessed by eGFR (ml/min/1.73m^2) to 1.13 in treatment group and 3.02 in in control group in six months. This finding is similar to the study of Mahajan et al 2010[7] which was carried out for 5 years,the decline was 1.4 in the treatment group versus 2.1 in placebo group. They used oral $NaHCO_3$ supplementation of 0.5mEq/kg. In another study the rate of decline of Kidney function in sodium bicarbonate treated group was similar to the normal age-related decline (Bankhead 2009).[8] In the study of De Brito-Ashurat et al 2009, that was conducted over two years, eGFR reduced to 1.88 ml/min/1.73m^2 in treatment group who received $NaHCO_3$ and 5.93ml/min in control group without supplementation.[9] The present study had shown a higher decline in eGFR in both control and treatment group over 6 months period. Many factors might influence it: poor nutritional status, poor socio-economic condition and poor drug compliance.

Lim et al 1998 had revealed that acidotic milleu in CKD was associated with muscle wasting and impaired albumin synthesis; which was consistent with present study where treatment group showed higher serum albumin level following sodium bicarbonate supplementation than control.[10] This has been shown in other studies (Movilli et al 1998,[11] Ballmer et al 1995).[12] De Brito-Ashurit et al 2009 also found significantly higher albumin levels in the treatment group than control group at 12 and 24 months interval of study period. In the present study decreased serum albumin level at baseline was found in both case and control group which also seen in study of Eustace et al 2004.[13]

Uremic acidosis can increase skeletal muscle breakdown and diminished albumin synthesis, leading to muscle wasting and muscle weakness. The presenting study has shown that mid-arm circumference was below cut-off point for determination of chronic energy deficiency (Chokraborty et al 2011).[14] The mid-arm circumference improved significantly in treatment group than the control group after six months. A similar result was also found in a previous study (De Brito Ashurst et al 2009).[9] The decreased level of mid-arm circumference in control group of presenting study could be explained by the studies done earlier Bailey et al 1996[15] and Boirle et al 2000;[16] but contrary to the study of Garibotto et al 1994 which concluded that change in protein synthesis and degradation were well balanced and net proteolysis was not augmented in patients with chronic renal failure.[17]

There was higher increase in HCO_3^- in the treatment group than the control group after six months in this study; similar result was also found in a previous study of Goraya et al 2013.[18] In the present study serum K^+ level was reduced significantly in treatment group than control group. Possible reason could be due to correction of acidosis resulted in influx of extracellur excess k^+ to intracellular and thereby reduction its serum level. In the study of De Brito Ashurst et al 2009, a significant reduction of serum potassium was also found in the treatment group than the control group following $NaHCO_3$ supplementation.[9]

Summary

The present prospective trial was conducted in the department of nephrology, Sir Salimullah Medical College and Mitford Hospital, Dhaka, during July 2013 to June 2014. The CKD patients (eGFR<60/ml/min/1.73m^2) were included in the study. A total of 66 such subjects were included in the study and were given sodium bicarbonate in treatment group (n=33) but control group (n=33) did not receive any sodium bicarbonate supplementation. There were no significant difference in age, sex, serum bicarbonate, blood pressure and nutritional parameters between treatment and control group at the beginning of study.

There was significant increase in HCO_3^- in the treatment group than the control group (26.3±1.6 and 21.2±1, mmol/L; p <0.001) after six months of study period. Serum potassium levels decreased more (4.5 ± 0.6 and 5.0 ± 0.5, mmol/L; p<0.001) in treatment than control group respectively after six months. In control group at 0, 3 and 6 months mid-arm circumference was and 23.7 ± 2.2 to 23.0±2.2, (p<0.001), then 22.4 ± 2.3,cm,(p<0.001); serum albumin was 3.0 ± 0.4 to2.8 ± 0.4,(p< 0.001) then to 2.8 ± 0.5,gm/dl,(p<0.005) and estimated glomerular filtration rate was 27±10 to

26±8,(p<0.003) then to 24±8.9,ml/min/1.73m^2, (p<0.001) respectively showing significant decrease. But at 0, 3 and 6 months BMI was similar 21.3 ± 5.0 to 21.2 ± 5.0, (p=0.320), then to 21.2 ± 5.1, kg/m^2,(p=0.145).

In treatment group at 0, 3, and 6 months there was progressive increase of mid-arm circumference from baseline 23.7±1.7 to 24.0±1.7, (p<0.007) then 24.4±1.9, cm(p<0.001) and serum albumin 2.9 ± 0.4 to 3.1 ± 0.4, (p<0.001) then 3.4±0.4 gm/dl,(p<0.001) respectively. But body mass index and estimated glomerular filtration rate was similar at 0 and 3 months 23.01 ± 4.04 to 23.03 ± 4.02kg/m^2,(p=0.487) and 25.3 ± 9.9 to 24.3 ± 9.3, ml/min/1.73m^2, p=0.061) respectively. At six months there was some decrease in estimated glomerular filtration rate (ml/min/1.73m^2) from baseline 25.3 ± 9.9 to 24.1 ± 10.1, (p< 0.008).

Estimated glomerular filtration rate (ml/min/1.73m^2) declined 3.02 and 1.13 in control and treatment group respectively (p<0.001) after 6 months. There was no significant difference in serum creatinine concentration between control and treatment group after six months of study period (2.6±.9 and 2.5±.8 mg/dl; p =0.660).

Conclusion & Recommendation

Supplementation of oral sodium bicarbonate had increased serum bicarbonate level significantly and was associated with slower deterioration of renal function and improvement of nutritional status in the treatment group than that of control group without sodium bicarbonate. Oral sodium bicarbonate should be prescribed in CKD patients with low serum bicarbonate level.

Further study should be conducted with long term follow up period to see the sustained effect.

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