



# Safety & Effect of Alkali Therapy on Vascular Function in Kidney Transplant Recipients: A Pilot Randomized Cross-Over Study

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## Background

- Cardiovascular disease is the leading cause of death in kidney transplant recipients (KTRs).<sup>1,2</sup>
- KTRs with lower serum bicarbonate levels have an increased risk of graft loss, cardiovascular events and mortality.<sup>3-6</sup>
- Bicarbonate administration was previously shown to slow disease progression and improve vascular function in patients with CKD.<sup>7</sup>
- We tested the hypothesis that sodium bicarbonate therapy was safe and feasible in KTRs and would improve vascular endothelial function.

## Methods

### Study Participants

- 20 adult KTRs that were  $\geq 1$  year from transplant with baseline eGFR  $\geq 45$  mL/min/1.73m<sup>2</sup> and serum bicarbonate of 20-26 mEq/L.
- All patients had to be on a stable immunosuppressive and anti-hypertensive regimen for at least 1 month.

- Exclusion Criteria:
  - BMI  $\geq 40$  kg/m<sup>2</sup>
  - Uncontrolled HTN
  - Heart Failure (NYHA Class 3-4 or known EF  $\leq 30\%$ )
  - Significant comorbidities resulting in life expectancy  $<1$  year
  - Serum potassium  $< 3.3$  or  $> 5.5$
  - Use of supplemental oxygen

### Study Design

- 18-week, randomized, double blind, placebo-controlled crossover safety and feasibility pilot study.
- Each treatment period was 8 weeks in duration with a 2-week washout period in between.
- Each patient served as his or her own control.

### Primary Outcome

- Change in brachial artery flow-mediated dilation (FMD), measured by high-resolution ultrasonography.

### Sodium Bicarbonate Dosing

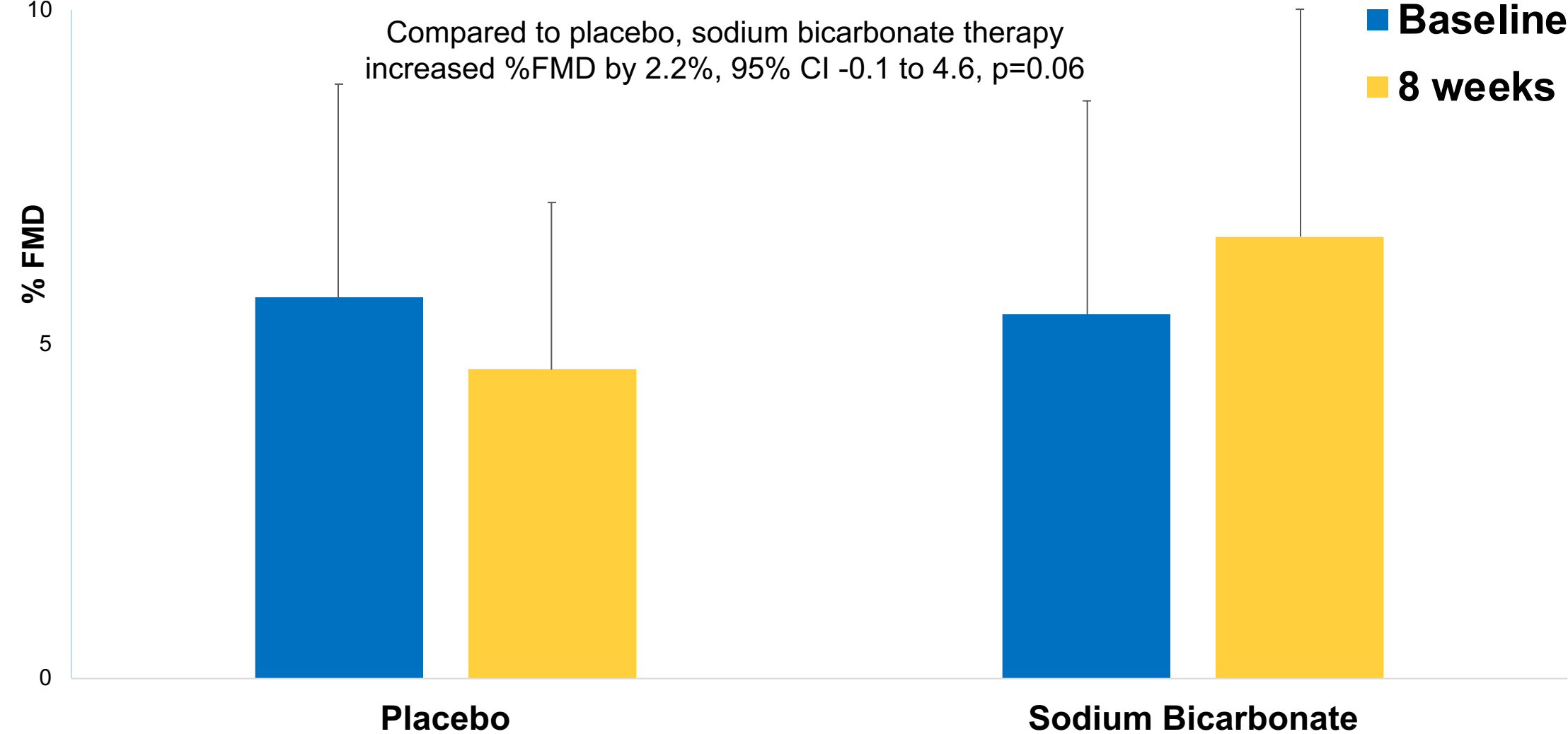
- Dose = 0.5 mEq/kg of lean body weight/day for entire 8 weeks.
- Each sodium bicarbonate tablet contained 7.7 mEq bicarbonate and 178 mg of sodium.
- Study drugs were identical in size, color, shape and taste.
- Matching placebo pill contained cornstarch.

## Acknowledgements

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- No conflicts of interest to disclose

## Results

**Figure 1. Percent FMD at baseline and 8 weeks after sodium bicarbonate administration**



**Table 1. Baseline Characteristics of Study Population**

Characteristic	
Age (years)	52 $\pm$ 17
Gender N(%)	
Male	16 (80.0)
Female	4 (20.0)
Race N (%)	
Non-Hispanic White	15 (75.0)
Non-Hispanic Black	0 (0.0)
American Indian	1 (5.0)
Asian	1 (5.0)
Multiple races	1 (5.0)
Unknown/not provided	2 (10.0)
Etiology of Kidney Disease N (%)	
Diabetes	3 (15.0)
Hypertension	4 (20.0)
Glomerulonephritis	2 (10.0)
Polycystic Kidney Disease	4 (20.0)
Other	7 (35.0)
Diabetes N (%)	6 (30.0)
Hypertension N (%)	20 (100)
Cardiovascular Disease N (%)	2 (10.0)
Obstructive Sleep Apnea N (%)	5 (25.0)
eGFR (ml/min/1.73m <sup>2</sup> )	75 $\pm$ 22
Serum Bicarbonate (mEq/L)	23.4 $\pm$ 2.0
Blood Pressure Medication N (%)	
ACEi/ARB	4 (20.0)
Diuretic	1 (5.0)
Calcium Channel Blocker	6 (30.0)

All values are mean  $\pm$  SD unless otherwise specified. eGFR= estimated glomerular filtration rate.

**Table 2: Safety Data with use of Sodium Bicarbonate Therapy in KTRs**

Safety Parameter	Placebo	Sodium Bicarbonate	P-value
Systolic Blood Pressure, mmHg			
Baseline	125 $\pm$ 10	129 $\pm$ 19	
8 weeks	127 $\pm$ 16	124 $\pm$ 14	
$\Delta$ from baseline	2.1 $\pm$ 11	-4.4 $\pm$ 14	0.17
Diastolic Blood Pressure, mmHg			
Baseline	72 $\pm$ 7	75 $\pm$ 9	
8 weeks	77 $\pm$ 9	73 $\pm$ 9	
$\Delta$ from baseline	4.6 $\pm$ 8	-1.6 $\pm$ 9	0.02
Weight, kg			
Baseline	77.7 $\pm$ 12.2	78.2 $\pm$ 13.0	
8 weeks	77.8 $\pm$ 11.6	77.7 $\pm$ 11.7	
$\Delta$ from baseline	0.1 $\pm$ 1.7	-0.6 $\pm$ 2.3	0.40
Serum Bicarbonate, mEq/L			
Baseline	23.4 $\pm$ 2.1	24.1 $\pm$ 1.5	
8 weeks	23.6 $\pm$ 1.7	24.54 $\pm$ 1.7	
$\Delta$ from baseline	0.2 $\pm$ 1.7	0.3 $\pm$ 1.5	0.93
Serum Potassium, mg/dL			
Baseline	4.0 $\pm$ 0.2	4.0 $\pm$ 0.3	
8 weeks	3.9 $\pm$ 0.2	3.9 $\pm$ 0.3	
$\Delta$ from baseline	-0.1 $\pm$ 0.3	-0.1 $\pm$ 0.3	0.95

All values are mean  $\pm$  SD unless otherwise specified..

- The mean (SD) age, eGFR, and serum bicarbonate of study participants were 52 (17) years, 74.7 (22.4) mL/min/1.73m<sup>2</sup>, and 23.4 (2.0) mEq/L respectively (Table 1).
- Serum bicarbonate levels increased by 0.3 mEq/L with sodium bicarbonate therapy (Table 2).
- There is a trend towards improved FMD with sodium bicarbonate therapy when compared to control (Figure 1).
- 24-hour urine NH<sub>4</sub> excretion decreased significantly with sodium bicarbonate therapy (mean change -9.1 (11.0) mmol/day, p=0.002).

## Conclusions

- Sodium bicarbonate therapy is safe and feasible in KTRs.
- There is a trend towards improvement in FMD with sodium bicarbonate therapy, strengthening the need for larger RCTs to evaluate the effects of sodium bicarbonate therapy in KTRs.

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