

## Background

- Acid retention is common in patients with chronic kidney disease as the kidneys progressively lose the ability to synthesize ammonia and excrete hydrogen ions. Lower serum bicarbonate levels are associated with kidney disease progression in patients with chronic kidney disease. Whether serum bicarbonate levels are associated with kidney disease progression in patients with polycystic kidney disease (PKD) is unknown.
- We tested the hypothesis that lower bicarbonate levels are associated with kidney function decline, and that increased serum bicarbonate are associated with decreased total kidney volume in patients with PKD.

## Methods

### Study Population

- Multicenter, randomized, double-blind, placebo-controlled HALT-PKD trials studied 1018 patients. HALT A included individuals (n=395) with early ADPKD and HALT B included individuals (N=379) with moderately advanced ADPKD. All were included with baseline serum bicarbonate levels and at least three measurements of eGFR.

### Exposure Variables

- Bicarbonate was examined as a continuous variable and in categories ( $\leq 24$ , 25-28 and  $>28$  mEq/L, with 25-28 mEq/L as the reference group).

### Outcome/Analyses

- The outcome was yearly change in slope of total kidney volume (TKV) and eGFR. Multiple linear regression models were used to examine association between serum bicarbonate and change in slope of eGFR/TKV. Covariates in the fully adjusted model: age, race/ethnicity, sex, treatment randomization, smoking status, cardiac history, BMI, systolic blood pressure, baseline eGFR and urine albumin.

## Results

- Mean (SD) age was  $43 \pm 10$  years. Mean (SD) serum bicarbonate and eGFR at baseline was  $26.7 \pm 2.4$  mEq/L and  $69.6 \pm 25.5$  ml/min/1.73m<sup>2</sup>, respectively.
- Participants with serum bicarbonate  $\leq 24$  mEq/L had lower eGFR, BMI, and systolic blood pressure (SBP) than those with bicarbonate levels  $>24$  mEq/L.
- In the fully adjusted model, each 1 mEq/L increase in serum bicarbonate level was associated with a 0.1 ml/min/1.73m<sup>2</sup> increase in annual slope of eGFR ( $\beta$  0.1 ml/min/1.73m<sup>2</sup>, 95% CI 0.002 to 0.15,  $p=0.04$ ), Table 1.
- A serum bicarbonate level  $\leq 24$  mEq/L was associated with a yearly decline in eGFR slope in unadjusted analysis and in partially adjusted analysis, but only trended towards significance in the fully adjusted model ( $p=0.09$ ), Table 1.
- Table 2 shows the association of serum bicarbonate with change in eGFR in HALT A and HALT B separately. There was no significant association between serum bicarbonate and eGFR in HALT A. In HALT B, each 1 mEq/L increase in serum bicarbonate level was associated with a 0.11 increase in annual slope of eGFR ( $\beta$  0.11 ml/min/1.73m<sup>2</sup>, 95% CI 0.02 to 0.20,  $p=0.02$ ). Baseline eGFR in HALT A and HALT B was  $90 \pm 17$  ml/min/1.73m<sup>2</sup> and  $48.4 \pm 11.6$  ml/min/1.73m<sup>2</sup>, respectively.

Table 1. Association of Bicarbonate with Annual Change in eGFR in All Participants

Bicarbonate Level (mEq/L)	$\beta$ (95% Confidence Interval)		
	Unadjusted	Model 1	Model 2
$\leq 24$	-0.7 (-1.22 to -0.16)	-0.5 (-1.06 to -0.04)	-0.4 (-0.93 to 0.07)
25-28	REF	REF	REF
$\geq 28$	0.3 (-0.15 to 0.78)	0.2 (-0.20 to 0.69)	0.2 (-0.26 to 0.64)
Per 1 mEq/L increase	0.1 (0.05 to 0.2)	0.1 (0.02 to 0.18)	0.1 (0.002 to 0.15)

Model 1: adjusted for age, gender, race, treatment randomization

Model 2: adjusted for model 1 plus smoking, cardiac history, BMI, SBP, baseline eGFR and urine albumin

Table 2. Association of Bicarbonate with Annual Change in eGFR in HALT A and HALT B

Bicarbonate Level (mEq/L)	$\beta$ (95% Confidence Interval)		
	Unadjusted	Model 1	Model 2
<b>HALT A</b>			
$\leq 24$	-0.24 (-1.12 to 0.64)	-0.33 (-1.21 to 0.54)	-0.3 (1.20 to 0.55)
25-28	REF	REF	REF
$\geq 28$	-0.10 (-0.78 to 0.57)	0.10 (-0.60 to 0.76)	-0.04 (-0.73 to 0.64)
Per 1 mEq/L increase	0.01 (-0.11 to 0.13)	0.05 (-0.07 to 0.17)	0.03 (-0.1 to 0.15)
<b>HALT B</b>			
$\leq 24$	-0.69 (-1.29 to -0.09)	-0.66 (-1.22 to -0.09)	-0.51 (-1.07 to 0.05)
25-28	REF	REF	REF
$\geq 28$	0.71 (0.10 to 1.32)	0.41 (-0.17 to 0.99)	0.44 (-0.13 to 1.00)
Per 1 mEq/L increase	0.18 (0.08 to 0.27)	0.13 (0.04 to 0.22)	0.11 (0.02 to 0.20)

Model 1: adjusted for age, gender, race, treatment randomization

Model 2: adjusted for model 1 plus smoking, cardiac history, BMI, SBP, baseline eGFR and urine albumin

- Participants with lower serum bicarbonate ( $\leq 24$  mEq/L) were more likely to be younger, female, and have higher systolic blood pressure than those with serum bicarbonate levels  $> 28$  mEq/L.

- Per 1 mEq/L increase of serum bicarbonate, the unadjusted model showed a total of 3.6 increase in TKV ( $\beta$  3.6 mL, 95% CI -0.9 to 8.1), model 1 showed a 0.3 total increase ( $\beta$  0.3 mL, 95% CI -4.0 to 4.6), and model 2 showed a 1.1 increase ( $\beta$  1.1 mL, 95% CI -3.1 to 5.4).

## Conclusions

- Lower serum bicarbonate levels are associated with an increased risk of decline in eGFR in patients with PKD.
- The association between bicarbonate and eGFR was only significant in participants from the HALT B cohort. This suggests serum bicarbonate plays a significant role in progression in moderately to advanced ADPKD but not in early ADPKD.
- Serum bicarbonate levels are not associated with TKV in patients with PDK when analyzed as continuous variable or in categories.

## Implications

- Future studies are needed to determine how sodium bicarbonate may be associated with the mechanisms of PDK progression
- Future studies are needed to determine if bicarbonate administration slows progression of kidney disease in patients with PKD.

## Disclosures

- The study team has no disclosures