Effects of Sodium Bicarbonate Therapy on Cognitive Function in Chronic Kidney Disease

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Background

Patients with chronic kidney disease are at increased risk of cognitive impairment, which ages patients prematurely, limits engagement with cognitively intensive therapies, and can affect transplant list placement. Acid-base homeostasis becomes impaired as kidney disease progresses, and metabolic acidosis may promote dementia in CKD patients through neuronal overexcitation and imbalance, as well as cerebrovascular dysfunction. Additionally, patients with lower bicarbonate levels were found to have worsened cognition in an observational study.

Methods

Design & Setting: randomized, double-blind, placebo-controlled pilot study examining the effect of 12 months of NaHCO3 on cognitive function at University of Colorado Hospital among patients with CKD stage 3b-4 and metabolic acidosis

Population: Patients 50-80 with CKD stages 3b-4 (eGFR 15–44 ml/min/1.73 m^2) and serum bicarbonate level of 16–22 mEq/L on at least 2 separate occasions with controlled blood pressure and MOCA>24.

Exclusions: history of dementia, stroke or neurologic disease, use of chronic daily oral alkali, uncontrolled serum potassium, known ejection fraction < 30%, anticipated dialysis or kidney transplantation within 12 months, oxygen use, pregnancy, and breastfeeding

Interventions: Participants were randomized in a 1:1 ratio to either NaHCO3 or placebo through block randomization, stratified based on sex, age (matched within a 5-year range), and CKD stage. Participants were initially prescribed a dosage of study drug at 0.5 mEq/kg-lean body weight (LBW) per day. If at the 3-month follow-up visit the plasma bicarbonate level was not > 22 mEq/L, study drug dose was increased to 0.8 mEq/kg/LBW/day for the remainder of the study.

Outcomes:

Primary - Change in overall cognition (Cognitive Function Composite score) assessed by the NIH Toolbox® Cognition Battery over 12 months.

Secondary - Change in cerebrovascular reactivity and pulsatility of the middle cerebral artery (MCA) assessed by Transcranial Doppler Ultrasonography over 12 months.

Analyses: two-sample t-test was used to compare between groups the pre-post change in an outcome if there were measurements only at baseline and end of study. The paired t-test was also performed to examine the pre-post change within a group

GOAL

To evaluate the effectiveness of sodium bicarbonate therapy on improving cognitive function in patients with CKD stage 3b-4.

HYPOTHESIS

Sodium bicarbonate will improve cognitive function compared to placebo through improvement of cerebrovascular reactivity.

CONCLUSIONS

While there were trends supporting a role for sodium bicarbonate in having an effect on cognitive function, this was not significant in this underpowered study. A larger study is recommended.

Baseline Characteristics

	Placebo (n = 16)	Sodium Bicarbonate (n = 18)
Age (years)	60.6 ± 5.9	62.0 ± 7.5
Female N (%)	6 (37.5)	5 (27.8)
Race N (%)		
White	12 (75.0)	14 (77.8)
Black	0 (0)	2 (11.1)
Ethnicity N (%)		
Hispanic	4 (25.0)	4 (22.2)
Diabetes N(%)	10 (62.5)	12 (66.7)
Hypertension N (%)	16 (100.0)	16 (88.9)
Etiology of Kidney Disease N (%)		
Diabetes	6 (37.5)	8 (44.4)
Hypertension	1 (6.3)	4 (22.2)
PKD	2 (12.5)	1 (5.6)
Glomerulonephritis	3 (18.8)	1 (5.6)
Drugs/Toxins	2 (12.5)	1 (5.6)
CHF N (%)	2 (12.5)	2 (11.1)
Smoking Status N (%)		
Current	1 (6.3)	0 (0)
Former	7 (43.8)	6 (33.3)
Use of ACEi/ARB N (%)	13 (81.3)	15 (83.3)
Body mass index (kg/m^2)	31.1 ± 5.9	31.5 ± 7.2
Lean body weight (kg)	59.2 ± 12.1	59.8 ± 10.6
Systolic blood pressure (mm Hg)	124.1 ± 14.5	128.3 ± 22.0
Bicarbonate (mEq/L)	21.8 ± 1.9	23.0 ± 1.5
GFR (ml/min/1.73 m^2)	32.8 ± 10.9	36.9 ± 16.7
Study drug dose at baseline (tablets)	3.8 ± 0.8	3.9 ± 0.7

Results

Cognitive Function:
Cognitive Function Composite score increased significantly from baseline in the treatment group (p=0.03). No significant difference from placebo group

Cerebrovascular reactivity:
Significant decrease in MV_{MCA} (p=0.03) in treatment group, but there was no statistical difference from placebo (p=0.11)

Motor Function:
After 12 months of bicarbonate supplementation, there were no significant changes in dexterity, grip strength, or gait speed

Adverse Events:
There were no differences in serious adverse events between the groups. There were no deaths during the study period.

Conclusions and Limitations

Unfortunately, there were no significant differences in treatment group from placebo, though there were statistically insignificant improvements in cognitive function

Likely due to the low number of participants, the study was underpowered. COVID-19, the role of this study as a pilot study, and the time-consuming nature of the outcomes all limited participant numbers

Our research shows the need for a larger, randomized controlled trial examining the effect of bicarbonate therapy on cognitive and cerebrovascular function in patients with CKD

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