Title: EFFECTS OF SODIUM BICARBONATE THERAPY ON COGNITIVE AND CEREBROVASCULAR FUNCTION IN MIDLIFE AND OLDER ADULTS WITH CHRONIC KIDNEY DISEASE: A PILOT RANDOMIZED TRIAL

Authors and Affiliations: Fangning Gu[1], Zhiying You[1], Nell Hawkins[1], Rachael Reddin[1], Rahaf Hamour[1], Allison Shapiro[2], Christina Coughlan[3], Douglas Seals[4], Seth Furgeson[1], Angelina Dixon[1], Kristen L Nowak[1], Jessica Kendrick [1]

[1] Division of Renal Diseases and Hypertension, University of Colorado Anschutz Medical Campus, Aurora, CO

[2]Department of Pediatrics, Section of Pediatric Endocrinology, Children's Hospital Colorado, University of Colorado Anschutz Medical Campus, Aurora, CO

[3]Department of Neurology, University of Colorado Alzheimer's and Cognition Center (CUACC), University of Colorado Anschutz Medical Campus, Aurora, CO

[4]Department of Integrative Physiology, University of Colorado Boulder, Boulder, CO

Corresponding Author: Jessica Kendrick MD MPH; Professor, Division of Renal Diseases and Hypertension, University of Colorado Denver, 12700 E. 19th Ave, C281, Aurora, CO 80045; Phone: 303-724-4837; Fax: 303-724-7499; Email: Jessica.Kendrick@cuanschutz.edu

Abstract

Introduction: Metabolic acidosis may create a pathway to cognitive impairment in chronic kidney disease (CKD) by contributing to cerebrovascular dysfunction. Trials examining the effect of sodium bicarbonate ($NaHCO_3$) on cognitive function are lacking.

Methods: We conducted a randomized, double-blind, placebo-controlled pilot study examining the effect of 12 months of $NaHCO_3$ on cognitive function in 34 patients aged 50-80 years with CKD stage 3b-4 (eGFR 15-44 ml/min/1.73m^2) with metabolic acidosis (serum bicarbonate level 16-22 mEq/L). Participants were randomized 1:1 to $NaHCO_3$ or placebo. The primary endpoint was change in overall cognition (Cognitive Function Composite score) assessed by the NIH Toolbox® Cognition Battery over 12 months. Secondary endpoints were change in cerebrovascular reactivity and pulsatility of the middle cerebral artery (MCA) assessed by Transcranial Doppler Ultrasonography over 12 months.

Results: 33 patients completed the study. After 12 months of treatment with $NaHCO_3$ therapy, the Cognitive Function Composite score increased significantly from baseline (mean ± SD, 47.3 ± 8.5 to 49.3 ± 11.0, p=0.03), however, there was no difference compared to placebo (p=0.39). $NaHCO_3$ therapy resulted in a significant reduction in time to perform the Trail Making Test-A (median [IQR], 31.3 [27.0, 36.3] to 29.0 [19.4, 38.2] seconds, p=0.02), however there was no difference compared to placebo (p=0.29). After 12 months of treatment, there was a significant increase in resting pulsatility index of the MCA in the placebo group, but there were no statistical differences between groups (p=0.71). $NaHCO_3$ treatment resulted in a significant decrease in baseline mean blood flow velocity of the MCA (p=0.03), but there was no difference from placebo (p=0.11).

Conclusions: 12 months of $NaHCO_3$ therapy did not result in significant improvements in cognitive function in patients with CKD stages 3b-4. Our results support the need for a larger, randomized controlled trial.