

Chronic Metabolic Acidosis and its Adverse Effects in CKD and Bone Density

Snehil Chilkamari¹, Prakash Dasari¹, Rupesh Raina^{1,2}

¹Department of Nephrology/Cleveland Clinic Akron General Medical Center, Akron, OH

²Department of Nephrology, Akron Children’s Hospital, Akron, OH

Introduction

- Metabolic Acidosis in the setting of Chronic Kidney Disease (CKD) is the build-up of acid in the blood due to impaired excretion of bicarbonate by the kidney [1].
- The prevalence of metabolic acidosis increases in later stages of CKD as kidney function declines and is seen in over 30% of stage 4 and 5 CKD patients [1].
 - Stage 3a CKD patients with metabolic acidosis, numbering 1.4 million in the US, account for 9.4% of that population.
 - Stage 3b CKD patients with metabolic acidosis in the US stands at 1.1 million, or 18.1%,
 - Stage 4 and 5 CKD patients with metabolic acidosis in the US stands at 31.5%, or 600,000 [1,3].
- Metabolic acidosis is defined as a serum bicarbonate (HCO3-) of <22 mEq/L (106, 107, 108). A normal range of serum bicarbonate is 22-29 mEq/L (mmol/L) [1-4].
 - Metabolic acidosis is considered mild to moderate from 12-22 mEq/L and severe when less than 12 mEq/L.
- Metabolic Acidosis has been shown to have harmful effects throughout the body, one of which is bone degradation associated with Bone Mineral Disorder (BMD)
 - Low levels of serum bicarbonate is associated to lower BMD[1].
- Pathophysiology of BMD is complex, and our understanding is evolving [2]. A deeper understanding of BMD can lead to reliable treatments to prevent underlying conditions in the latter stages of CKD, such as hypocalcemia.

Objective

- By assessing the current clinical data on metabolic acidosis in this literature review, we aim to:
 - Establish a comprehensive review of the various interventional trials of alkali therapy in CKD
 - Evaluate their associations with clinical outcomes like mortality.

Preliminary Results

- Roughly only 2.7% of patients with CKD stages 2-4 received alkali therapy to treat their metabolic acidosis [4].
- Chronic metabolic acidosis (CMA) adversely impacts the musculoskeletal system, especially muscle strength.
 - CMA increases protein degradation and decreases protein synthesis that results in skeletal muscle degradation and impairment of muscle formation.
- Insulin resistance is induced in CKD patients with metabolic acidosis as they need to release insulin at higher than normal levels to inhibit proteolysis in fed states.

Methodology

Research Design: Retrospective literature review of chronic metabolic acidosis in patients with chronic kidney disease (CKD) irrespective of age and gender

Study Selection: Literature search utilizing CINAHL (2005 - 2021), Cochrane (2017 - 2021), Medline/PubMed (1986 - 2021), and Web of Science (1965 - 2021) was directed. Keywords used in search included “Metabolic Acidosis” AND each additional keyword separately: “Osteoporosis”, “Bone Density”, “Chronic Kidney Disease”, “CKD”, and “Alkali”. No restriction on time or geographic location. Study was narrowed to the English language.

Study Variables: Patient demographics (age, sex, weight), Interventions, Handgrip Strengths, Bone Mass Density, BMI, Biomarkers (Blood Urea, SBP, DBP, PTH, Calcium, Albumin, Creatine, Haemoglobin, Phosphorus, Bicarbonate, pH, Cholesterol, Potassium)

Data Collection: Data regarding metabolic acidosis in patients with CKD irrespective of age and gender is recorded and data analysis will follow

Discussion

- Low levels of serum bicarbonate is linked to lower BMD [1].
 - Sodium bicarbonate as intervention may lead to reduced progression of CKD [3].
- A study using the nationally representative database of hemodialysis patients, showed strong associations between serum phosphorus and calcium and an increased risk of death [4].
- KDIGO’s clinical practice guidelines recommend treatment of metabolic acidosis in patients with CKD with oral bicarbonate supplementation until serum bicarbonate is within normal range (22-29 mEq/L), unless contraindicated
- Treatment of severe acidosis is typically administered to prevent further progression of CKD and other harmful effects on the body [4,5].
- Further research in the form of double-blinded, placebo-controlled, randomized trials is needed to corroborate current data. Additionally, research should focus on establishing new recommendations to supplement current guidelines in that the alkali therapy is selectively applied.

References

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