EFFECT OF CORRECTION OF CHRONIC METABOLIC ACIDOSIS BY ORAL SODIUM BICARBONATE THERAPY ON NUTRITIONAL STATUS IN HEMODIALYSIS PATIENTS

Thesis

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By

Wael Ramadan El-Metwally

Diploma Of Internal Medicine

Zagazig University

Under Supervision of

Prof. Dr. GAMAL ELSAYED MADI

Professor of Internal Medicine and Nephrology
Faculty of Medicine – Ain Shams University

Dr. AHMED SHABAN SERAGELDEEN

Lecturer of Internal Medicine and Nephrology
Faculty of Medicine – Ain Shams University

Faculty of Medicine
Ain Shams University
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List of Abbreviations

AE	Anion exchanger
ANG	Angiotensin
ANK	Ankylosis locus
BCG	Bromocresolgreen
BIA	Bioelectric impedance analysis
BMI	Body mass index
BUN	Blood urea nitrogen
CA II	Carbonic anhydrase II
CA IV	Carbonic anhydrase IV
CAPD	Continuous ambulatory peritoneal dialysis
CD	Collecting ducts
CHF	Congestive heart failure
CKD	Chronic kidney disease
CKD-MBD	Chronic kidney disease- mineral bone disorder
CVC	Calcifying vascular cells
CVD	Cardiovascular disease
DEXA	Dual-energy x-ray absorptiometry
DOQI	Dialysis Outcome Quality Initiative
eGFR	Estimated glomerular filtration rate
ENPP1	Ecto-nucleotide pyrophosphatase phosphodiesterase-1
ESA	Erythropoiesis Stimulating Agents
ESRD	End-stage renal disease
FFMI	Fat free mass index

FGF23	Fibroblast growth factor-23
FMI	Fat mass index
GFR	Glomerular filtration rate
GH/IGF-I	Growth hormone/ Insulin-like growth factor 1
Gla	γ-carboxyglutamate
HD	Hemodialysis
ID	interdialytic
IGF-1	Insulin-like growth factor 1
IL	Interleukin
iPTH	Intact parathyroid hormone
ISRNM	International Society of Renal Nutrition and Metabolism
KDIGO	Kidney Disease Improving Global Outcomes
MA	Metabolic acidosis
MAMC	Mid-arm muscle circumference
MGP	Matrix Gla protein
NHANES	National Health and Nutrition Examination Surveys
NHE3	Na+/H+ exchanger 3
nPCR	Normalized protein catabolic rate
nPNA	Protein equivalent of nitrogen appearance
OPG	Osteoprotegerin
PCR	Protein catabolic rate
PCT	Proximal convoluted tubules
PD	Peritoneal dialysis
PEW	Protein-energy wasting
PI3 kinase	Phosphatidylinositol 3-kinase
PPAR	Peroxisome proliferator-activated receptor
PTH	Parathyroid hormone

RCTs	Randomized controlled trials
REE	Resting energy expenditure
ROD	Renal osteodystrophy
RTA	Renal tubular acidosis
SD	Standard deviation
SGA	Subjective global assessment
SHPT	Secondary hyperparathyroidism
spKt/V	Single pool Kt/V
SPSS	statistical package for special science
TNF	Tumor necrosis factor
TSF	Triceps skin fold
UGR	Urea generation rate
UP	Uremic pruritis
USRDS	US Renal Data System
VC	Vascular calcification

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Introduction

INTRODUCTION

Metabolic acidosis (MA) slowly develops during natural evolution of renal impairment towards end-stage renal disease (ESRD). Although metabolic acidosis is worldwide recognized as a uremic toxin, its implication in chronic kidney disease (CKD) pathophysiology mechanism is still unknown. Even if it is unanimously accepted that metabolic acidosis is not fully compensated once hemodialysis (HD) therapy starts, K/DOQI Guidelines do not impose a specific therapy scheme for metabolic acidosis in CKD subjects, only suggest the need of treating acidosis when serum bicarbonate levels are below 22 mEq/L. Thus, there is evidence to support low serum bicarbonate level is associated with progression of kidney disease independent of baseline eGFR and other clinical, demographic, and socioeconomic factors. **(Shah et al., 2009).** In addition, oral bicarbonate administration in HD individuals must be performed with caution due to fluid retention. **(de Brito-Ashurst et al., 2009).**

Acidosis represents a continual threat to the metabolic integrity of the dialysis patient, and can adversely affect both protein and bone metabolism. Prolonged metabolic acidosis acts as a catabolic stimulus in experimental uraemic animals, promoting the release of amino acids from skeletal muscle, which can be reversed by alkali administration. Short term studies in uraemic patients have similarly shown that correction of acidosis can reduce muscle protein degradation and reduce urea generation rates (UGR). Improvement in long-term acid base balance in hemodialysis patients has been shown to result in an improvement in bone morphology, and a reduction in hyperparathyroidism **(Lu KC et al., 1995).**

In a comprehensive Cochrane Database of Systematic Reviews published recently, authors were able to find only three randomized, controlled trials (RCTs) of adult dialysis patients (n 117).There were insufficient data for most outcomes to perform a meta-analysis. In all three trials, correction of acidosis was achieved variably but was associated with significant improvement in nutritional parameters [body weight, nitrogen balance studies, isotope

protein turnover studies, triceps skinfold thickness and subjective global assessment (SGA)] apart from heterogeneity in serum albumin response. The conclusion of that report stated that data on benefits and risks of correcting MA is very limited with no RCTs of pre-ESRD patients and only three small RCTs of dialysis patients. **(Roderick et al., 2007).**

Aim of the Work

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To address the role of oral sodium bicarbonate therapy on nutritional parameters of prevalent hemodialysis patients.

Chapter One