The Effect of Hemodiafiltration on Sclerostin level and bone specific alkaline phosphatase in Comparison to High Flux dialysis

Thesis
submitted for partial fulfillment of the MD degree in internal medicine

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2018

بسم الله الرحمن الرحيم

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم الحكيم

صدق الله العظيم

سورة البقرة الآية: ٣٢

Acknowledgement

*First of all, all gratitude is due to **God** almighty for blessing this work, until it has reached its end, as a part of his generous help, throughout my life.*

*Really I can hardly find the words to express my gratitude to **Prof. Dr. Hesham Mohamed El Sayed and Prof. Dr. Magdy Mohamed El Sharkawy;** Professors of Internal Medicine, faculty of medicine, Ain Shams University, for their supervision, continuous help, encouragement throughout this work and tremendous effort they had done in the meticulous revision of the whole work. It is a great honor to work under their guidance and supervision.*

*I owe much to **Dr. Walid Taha** head of nephrology department at Maadi Military Hospital for his continues help, valuable suggestions and patience throughout the whole work.*

*I owe much to **Dr. Cherry Reda kamel and Dr. Hussein Sayed Hussein;** Assistant Professors of Internal Medicine faculty of medicine, Ain Shams University, for their continues help, valuable suggestions and patience throughout the whole work.*

*I owe much to **Dr. Mostafa Abdel Nasier Abdel Gawad;** Lecturer of Internal Medicine faculty of medicine, Ain Shams University, for his continues help throughout the whole work.*

*Last but not least, I dedicate this work to my **family** and **friends** whom without their sincere emotional support, pushing me forward this work would not have ever been completed.*

Contents

List of Abbreviations

1, 25-OH2-D3	: 1, 25-dihydroxyvitamin D
AGE	: Advanced glycation end products
ALP	: Alkaline phosphatase
BFR0	: Bone formation rate
BMD	: Bone mineral density
BMI	: Body mass index
BS-AP	: Bone specific alkaline phosphatase
Ca	: Calcium
CatK	: Cathepsin K
CKD	: Chronic kidney disease
CKD-MBD	: Chronic kidney disease-mineral and bone disorder
CRP	: C-reactive protein
CVD	: Cardiovascular disease
DA	: Dialysis amyloidosis
DEXA	: Dual-energy X-ray absorptiometry
DF	: Dialysate flow
Dkk-1	: Dickkoph -1
DPD	: Deoxypyridinoline
ELISA	: Enzyme-linked immunosorbent assay
ESRD	: End-stage renal disease
FGF-23	: Fibroblast growth factor 23
FGFR1	: Fibroblast growth factor receptor one
GFR	: Glomerular filtration rate
GPI	: Glycosylphosphatidylinositol
HCV	: Hepatitis c virus
HD	: Hemodialysis
HDF	: Hemodiafiltration
HGB	: Hemoglobin

List of Abbreviations (Cont.)

ICTP	:	C-terminal telopeptides of type I collagen
IQR	:	Interquartile range
JIA	:	Juvenile idiopathic arthritis
LMWP	:	Low-molecular-weight protein
LRP	:	Lipoprotein receptor-related protein
LVH	:	Left ventricular hypertrophy
M	:	Male
MiRNAs	:	Micro RNAs
OA	:	Osteoarthritis
OC	:	Osteocalcin
OL-HDF	:	Online hemodiafiltration
OPG	:	Osteoprotegerin
PICP	:	Procollagen type I carboxy-terminal extension peptide
Po4	:	Phosphorus
PTH	:	Parathyroid hormone
PYD	:	Pyridinoline
RA	:	Rheumatoid arthritis
RLS	:	Restless legs syndrome
ß2-m	:	Beta2-microglobulin
sScl	:	Serum sclerostin
SsRNAs	:	Single-stranded RNAs
TIBC	:	Total iron binding capacity
TMP	:	Transmembrane pressure
TNFa	:	Tumor necrosis factor alpha
TRAP	:	Tartrate-resistant acid phosphatase
U test	:	Mann Whitney Test
UF	:	Ultra filtration
Wnt pathway	:	Wingless pathway

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INTRODUCTION

Chronic kidney disease (CKD) is a pandemic affecting >10% of the Western population. CKD is associated with high rates of cardiovascular mortality. CKD also confers an increased fracture risk. Patients with an estimated glomerular filtration rate of <60ml/min had a twofold increased risk of hip fracture. The risk for fractures further increases up to four fold in dialysis patients as compared with age and gender matched non-CKD individuals **(Naylor et al., 2014).**

Vascular calcification and bone disorders are entitled chronic kidney disease-mineral and bone disorder (CKD-MBD) which contributes to increased morbidity and mortality in CKD patients. The mechanisms causing the CKD-MBD syndrome are associated with the stimulation of osteocyte secretion **(Kooman et al., 2014).**

Although several biomarkers of CKD-MBD, such as calcium, phosphate, parathyroid hormone (PTH predict outcome in end-stage renal disease (ESRD), there is a need of a biomarker that could predict the presence and extent of vascular calcification and bone disorders **(Drechsler et al., 2011).**

Sclerostin is a new and potentially important player in the well-known bone–vascular axis in chronic kidney disease (CKD) and end-stage renal disease. Sclerostin, a 22-kDa protein secreted by osteocytes and chondrocytes. Sclerostin was found to be a potent inhibitor of bone formation.

Osteocytes effectively act as mechanoreceptors for bone formation, and sclerostin was shown to play a key role in the development of osteoporosis **(Pierre et al., 2015).**

Sclerostin is the product of the SOST gene, which was discovered in 2001. Inactivating mutations of the SOST gene have been associated with sclerosteosis, a high bone mass phenotype. Sclerostin is a Wnt signaling pathway antagonist that results in negative regulation of bone formation by repressing differentiation and proliferation of osteoblasts **(Rochefort et al., 2010)**.

Sclerostin, an osteocyte-derived glycoprotein acts as a soluble inhibitor of the Wnt signaling pathway and its physiological role is to reduce bone formation. The serum sclerostin levels increase with the progression of CKD (**Fang et al., 2014)**.

In patients undergoing maintenance dialysis, sclerostin has been reported to be increased and associated with bone quality impairment **(Cejka et al., 2012).**

Circulating sclerostin levels correlate negatively with serum PTH levels in both the general population and dialysis patients. High levels of PTH and sclerostin coexist in CKD. This observation raises the suspicion that sclerostin contributes to the well-known PTH resistance in CKD **(Cejka et al., 2011).**

As sclerostin expression is decreased by mechanical loading of the skeleton, low physical activity in patients with