Study of the Relation between Dyslipidemia and Parathyroid Hormone in HCV Positive Prevalent Hemodiaylsis Patients

Thesis

Submitted for partial fulfillment of master Degree
in Internal Medicine

Presented By

Amira Elsayed Ahmed Attya
M.B.B.Ch

Supervised By

Prof. Dr. Magdy Elsharkawy
Professor of Internal Medicine & Nephrology
Faculty of Medicine – Ain Shams University

Dr. Waleed Anwar Abdel Mohsen
Assistant Professor of Internal Medicine & Nephrology
Faculty of Medicine – Ain Shams University

Dr. Walid Ahmed Bichari
Assistant Professor of Internal Medicine &Nephrology
Faculty of Medicine – Ain Shams University

Faculty of Medicine
Ain Shams University
2015


وأنزل الله عليك
الكتاب والحكمة
وعلَّمَكَ مَا لَمْ تَكُن
تَعْلَمُ وكَانَ فَضْلُ
اللَّهِ عَلَيْكَ عَظِيماً
صدق الله العظيم
سورة النساء الآية (١١٣)

Acknowledgment

Praise be to **ALLAH**, The Merciful, The Compassionate for all the gifts **I** have been offered; One of the gifts is accomplishing this research work.

Words cannot adequately assure my deepest thanks and gratitude to ***Prof. Dr. Magdy Elsharkawy,*** Professor of Internal Medicine & Nephrology, Faculty of Medicine – Ain Shams University, for his continuous encouragement, constructive criticism and continuous assistance. I really have the honor to complete this work under his supervision.

I would like to express my deepest thanks and gratitude to ***Dr. Waleed Anwar Abdel Mohsen,*** Assistant Professor of Internal Medicine & Nephrology, Faculty of Medicine – Ain Shams University, for his unlimited help, valuable guidance, continuous encouragement and forwarding his experience to help me complete this work.

I can't forget to thank with all appreciation and gratitude ***Dr. Walid Ahmed Bichari,*** Assistant Professor of Internal Medicine & Nephrology, Faculty of Medicine – Ain Shams University, for his valuable assistance, kind supervision, his great efforts and time he has devoted to this work.

I can never forget to thank all patients who willingly participated in this study, as well as the physician and nurses, who were totally supportive during all steps of data collection.

Last but not least all thank and gratitude go to my Family, especially my Parents, my Husband and my children, for pushing me forward in every step in my life.

Amira Elsayed Ahmed Attya

List of Contents

List of Abbreviations

AIC : Arterial intimal calcification

AL+3 : Aluminum

AMC : Arterial medial calcification

aRR : Adjusted relative risk

Bdna : Branched-chain DNA

BMI : Body mass index

CETP : Cholesteryl ester transfer protein

CHOICE : Choices for Healthy Outcomes in Caring for ESRD

CI : Confidence interval

CKD : Chronic kidney disease

CRP : C-reactive protein

CVD : Cardiovascular disease

DOPPS : Dialysis Outcomes and Practice Patterns Study

ESRD : End-stage renal disease

GFR : Glomerular filtration rate

HCV : Hepatitis C virus

HD : Hemodialysis

HDL : High-density lipoprotein

IFN : Interferon

LCAT : Lecithin cholesterol acyl transferase

LDL : Low-density lipoprotein

MI : Myocardial infarction

NH : Nocturnal hemodialysis

List of Abbreviations *(Cont...)*

PT : Parathyroid

PTH : Parathyroid hormone

RLDT : Lombard Dialysis and Transplant Registry

SD : Standard deviation

SHPT : Secondary hyperparathyroidism (SHPT)

SPSS : Statistical analysis for social science

TG : Triglycerides

TRL : Triglyceride-rich lipoproteins

UF : Ultrafilteration

USRDS : US Renal Data System

VDRs : Vitamin D receptors

VLDL : Very-low-density lipoprotein

VLDL : Very-low-density lipoprotein

WHO : Health Organization

List of Tables

List of Tables *(Cont...)*

List of Figures

Introduction

Cardiovascular disease (CVD) is the leading cause of death in hemodialysis patients and must be prevented to improve their prognosis. Atherosclerosis is often a complication in patients of renal failure and adversely affects the prognosis of CKD patients. Dyslipidemia and vascular calcification is a cause of atherosclerosis ***(Kanda, 2013).***

Secondary hyperparathyroidism (SHPT) is a common complication of dialysis as a consequence of decreased renal function and impaired mineral metabolism. disorders of calcium, phosphate, and vitamin D homeostasis, as well as increased intact parathyroid hormone (iPTH) concentrations are associated with multiple comorbidities including renal osteodystrophy, anemia with erythropoietin resistance, vascular calcification, and cardiovascular disease. In fact, disordered calcium phosphorus homeostasis and resultant SHPT cause significant long-term morbidity and mortality in dialysis patients. Since a better control of SHPT is associated with a more favorable prognosis, optimal management of SHPT may be one of the principal goals in managing hemodialysis patients ***(Brillhart et al., 2012).***

Regardless of age, heart disease is a major cause of morbidity and mortality among patients with renal failure. The lipid profile of patients undergoing chronic hemodialysis (HD)

indicates an increase in triglycerides, elevated very low-density lipoprotein (VLDL), decreased high-density lipoprotein (HDL) and increased lipoprotein a. Total cholesterol levels may be lower in HD patients. Dyslipidemia is an established cardiovascular risk factor in the general population. In one study, dyslipidemia predicted cardiovascular disease in patients on HD. But, other studies have reported uncertainties about this.

Dyslipidemia in renal failure patients may be due to increased synthesis, decreased catabolism or a combination of both process. Suggested underlying mechanisms of the reduced lipolytic activity include depletion of lipoprotein lipase (LPL) stores by repeated adminstration of heparin, the existence of LPL inhibitors in uremic plasma and increased levels of apolipoprotein (apo) CIII ***(Prichard, 2012).***

Although several studies have reported that hyperparathyroidism might play a role in dyslipidemia in dialysis patients, others have found no relation between dyslipidemia and PTH serum level. Thus, the relationship between dyslipidemia and iPTH serum levels seems to be controversial. We undertook this study with the purpose to examine the relationship between lipid profile and serum levels of iPTH in chronic kidney disease (CKD) patients undergoing HD treatment ***(Prichard, 2012).***

Hepatitis C virus (HCV) infection remains very frequent in patient receiving long-term dialysis both in developed and less-developed countries. The natural history of HCV infection in dialysis patients remains incompletely understood. Defining the natural history of HCV remains difficult for several reasons: the disease has a very long duration, it is mostly asymptomatic, and determining its onset may be difficult. Because treatment is widely used, future natural history studies of chronic HCV may not be possible as easily documented onset of infection, that is, posttransfusion HCV, no longer occurs ***(Fabrizi et al., 2012).***

Hepatitis C virus (HCV) is a leading cause of chronic liver disease, including chronic hepatitis, fibrosis, cirrhosis, and hepatocellular carcinoma. Hepatitis C infection associates with lipid and lipoprotein metabolism disorders such as hepatic steatosis, hypobetalipoproteinemia, and hypocholesterolemia. Furthermore, virus production is dependent on hepatic very-low-density lipoprotein (VLDL) assembly, and circulating virions are physically associated with lipoproteins in complexes termed lipoviral particles ***(Dai et al., 2013).***

Aim of the Work

The aim of the study is to assess the possible relation between dyslipidemia and parathyroid hormone In HCV positive prevalent hemodiaylsis patients.

Dyslipidemia in CKD and Hemodialysis Patients

Approximately 50% of hemodialysis (HD) patients die from cardiovascular events. One of the main risk factors for cardiovascular events is hyperlipidemia. Progressive renal failure is associated with lipoprotein abnormalities and dyslipidemia ***(Alabakavsk, 2002).***

Dyslipidemia may not appear as hyperlipidemia (a rise in plasma cholesterol and/or low-density lipoprotein (LDL)) in the majority of HD patients. Uremic dyslipidemia has an abnormal apolipoprotein profile and composition. It is characterized by reduced concentrations of apo A-containing lipoproteins in high-density lipoprotein (HDL) and increased concentrations of intact or partially metabolized triglyceride-rich apo B-containing lipoproteins in very-low-density lipoprotein (VLDL), intermediate-density lipoprotein (IDL) and LDL. Common lipid abnormality in HD patients is hypertriglyceridemia ***(Baigent, 2005).***

Other lipid abnormalities seen in HD patients are high serum lipoprotein levels and a decrease in HDL levels. Hypertriglyceridemia is caused by increased production of Apo B protein and a marked decrease in the metabolism of VLDL, primarily as a result of decreased endothelial cell debilitation of VLDL ***(Ulusoy and Özkan, 2012).***

The lipoprotein abnormalities in HD patients are thought to be a significant factor in increased atherosclerosis. Serum total cholesterol, and particularly LDL-cholesterol, is known to be correlated with increased cardiovascular mortality in the general population. A similar correlation has also been reported in dialysis patients. However, it is today generally agreed that in the HD patient group, a low LDL cholesterol level is correlated with malnutrition and increased mortality ***(Block et al., 2007).***

Until recently, the treatment of hyperlipidemia in the HD patient group was based on adult hyperlipidemia guidelines, and it was generally thought that the approach to treatment and results in the general population would yield similar results in the HD patient group. However, in the same way that lipid abnormalities in the HD patient group differ from the general population, there are also various differences in terms of medical treatment ***(Ulusoy and Özkan, 2012).***

Treatment of hypertriglyceridemia, the most frequently observed lipid abnormality in this patient group, is advised since at above 500 mg/dl it can give rise to complications such as pancreatitis ***(Ulusoy and Özkan, 2012).***

Lifestyle changes plus fibrate or nicotinic acid are recommended for treatment of hypertriglyceridemia. However, medical treatment must be provided on the basis of a profit and