Correlation between parathyroid function abnormalities and lipid profile In haemodialysis patients

Protocol for thesis
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Abbreviations:

ABCA1	ATP-Binding Cassette transporter type A1
ACAT	Acyl-CoA cholesterol Acyltransferase
Apo	apoproteins (apolipoproteins)
APTT	Activated Partial Thromboplastin Time
AREs	AU-rich elements
ATGL	adipocyte triglyceride lipase
AUF1	AU-rich binding factor 1
BALP	bone alkaline phosphatase isoenzyme
BMP	bone morphogenic proteins
Ca	calcium
$[Ca^{2+}]i$	cytosolic calcium
cAMP	cyclic adenosine monophosphate
CaSR	calcium -sensing receptor
CE	esterified cholesterol (cholesteryl esters)
CETP	cholesteryl ester transfer protein
CKD	chronic kidney disease
CKD-MBD	CKD-associated mineral and bone disorder
CM	chylomicron
CRF	chronic renal failure
CRI	chronic renal insufficiency
CUA	calcific uremic arteriolopathy
CV	coefficients of variation
DBP	vitamin D-binding protein
DGAT	acyl-CoA diglycerol acyltransferase
DPD	deoxypyridinoline
ESRD	end-stage renal disease
FA	fatty acid
FFA	free fatty acids
FGF-23	Fibroblasts Growth Factor-23
FGFR1	fibroblast growth factor receptor 1
GFR	glomerular filtration rate
HD	hemodialysis
HDL	high-density lipoprotein
HL	hepatic lipase

HSL	hormone-sensitive lipase
IDL	intermediate density lipoproteins
IGF	insulin-like growth factor
IP_3	inositol(1,4,5)trisphosphate
iPTH	intact PTH
IRMA	immunoradiometric assay
IVS	intervening sequences
KSRP	K-homology splicing regulator protein
LCAT	lecithin cholesteryl acyl transferase
LDL	low-density lipoprotein
LDL-R	low density lipoprotein receptor
Lp(a)	Lipoprotein (a)
LPL	lipoprotein lipase
LPLa	LPL activity
LRP	low density lipoprotein receptor-related protein
M-CSF	macrophage colony-stimulating factor
mRNA	messenger RNA
NKF KDOQI	National Kidney Foundation Kidney Disease Outcomes Quality Initiative
NSB	non-specific binding
OFC	osteitis fibrosa cystica
OPG	Osteoprotegerin
ox-LDL	Oxidized LDL
PD	peritoneal dialysis
Pin1	peptidyl-prolyl isomerase
PIP_2	phosphatidylinositol(4,5)bisphosphate
PKC	protein kinase C
PL	phospholipids
PLC	phospholipase C
PLD	phospholipase D
PPARa	alpha-type peroxisome proliferator-activated nuclear receptor
PTH	parathyroid hormone
PTH-R1	PTH receptor
PTHrp	parathyroid hormone related peptide
PTx	parathyroidectomy

RANKL	receptor activator of nuclear factor-kappa B ligand
ROD	renal osteodystrophy
RRT	renal replacement therapy
RXR	retinoic acid receptor
sdLDL	small dense LDL
SHPT	Secondary hyperparathyroidism
SR-B1	scavenger receptor class B, type1
T3	tri-iodothyronin
T4	thyroxin
TC	Total Cholesterol
TG	triglycerides
TNF	tumor necrosis factor
TRAP	tartrate-resistant acid phosphatase
TRL	triglyceride-rich lipoproteins
VLDL	very-low-density lipoproteins
VLDL-R	very low density lipoprotein receptor
VDR	vitamin D receptor
VDRE	specific DNA response element

Introduction And Aim of the work

INTRODUCTION

CKD disturbs calcium and phosphate homeostasis. This occurs mainly because of decreased renal excretion of phosphate and diminished renal hydroxylation of 25-hydroxyvitamin D to calcitriol **(Lund, 2007).**

Circulating calcitriol levels begin to fall when the GFR is less than 40ml/min and are severely reduced in subjects with end-stage kidney disease. Progressive kidney dysfunction results in hyperphosphatemia and calcitriol deficiency. These result in hypocalcaemia. These abnormalities directly increase PTH levels **(Lund, 2007).**

Patients with chronic renal failure display type IV lipoproteinemia. They have elevated serum levels of very-low-density, intermediate-density, and low-density lipoprotein. Serum cholesterol levels are usually normal and those of high-density lipoprotein are low **(Massry and Akmal, 1989).**

It is generally accepted that hypertriglyceridemia is due to decreased removal from the blood secondary to reduced activity of lipoprotein lipase and hepatic lipase. Secondary hyperparathyroidism and elevated blood levels

of parathyroid hormone (PTH) may play an important role in the pathogenesis of the triglyceridemia of chronic renal failure **(Massry and Akmal, 1989).**

This defect was apparently due to the rise in calcium content of the liver mediated by the state of secondary hyperparathyroidism of CRF. An increase in calcium content of the liver may reflect an elevation in cytosolic calcium of hepatocytes. The elevation in Ca of hepatocytes in CRF downregulates the mRNA of hepatic lipase (**Klin et al, 1996).**

Excess PTH suppresses insulin release from pancreatic islets and the insulin deficiency results in carbohydrate intolerance. Insulin deficiency also causes decreased synthesis of lipoprotein lipase and hence abnormal lipid metabolism. Thus, the hyperparathyroidism of chronic renal failure may play a paramount role in the genesis of the abnormal metabolism of both carbohydrates and lipids **(Massry and Akmal, 1989).**

The aim of work:

To study the correlation between parathyroid dysfunction and dyslipidemia in patients with CRF under regular HD.

Review of literature

Chapter (1)

Parathyroid Dysfunction in ESRD

Parathyroid hormone (PTH):

The parathyroid glands are four pea-sized glands located on the thyroid gland in the neck. The parathyroid glands secrete parathyroid hormone (PTH), a polypeptide that helps maintain the correct balance of calcium and phosphorous in the body **(Tomasello, 2008).**

PTH, an 84 amino acid polypeptide, is synthesized in a precursor form, pre-pro-PTH of 115 amino acids. Post-translational cleavages yield a 90 amino acid polypeptide (pro-PTH) and then the active 1-84 PTH, which is stored within intracellular secretory granules. The half-life of intact 1-84 PTH is short (< 10 minutes) due to effective enzymatic cleavage in the liver (Kupffer cells) and the kidney (tubular cells) **(Monier-Faugere et al., 2000).**

The principal actions of PTH are:

(1) PTH activates osteoblasts and, subsequently, osteoclasts, which leads to increased bone turnover and mobilisation of calcium and phosphorus from bone **(Haas, 2007).**

(2) PTH decrease renal excretion of calcium and increase urinary excretion of phosphorus.This phosphaturic effect of PTH facilitates the disposal of