بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

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MONA MAGHRABY

Evaluation of the effect of cholecalciferol on vascular calcification in hemodialysis patients

A thesis submitted for the fulfillment of PhD degree in Pharmaceutical Sciences (Clinical Pharmacy)
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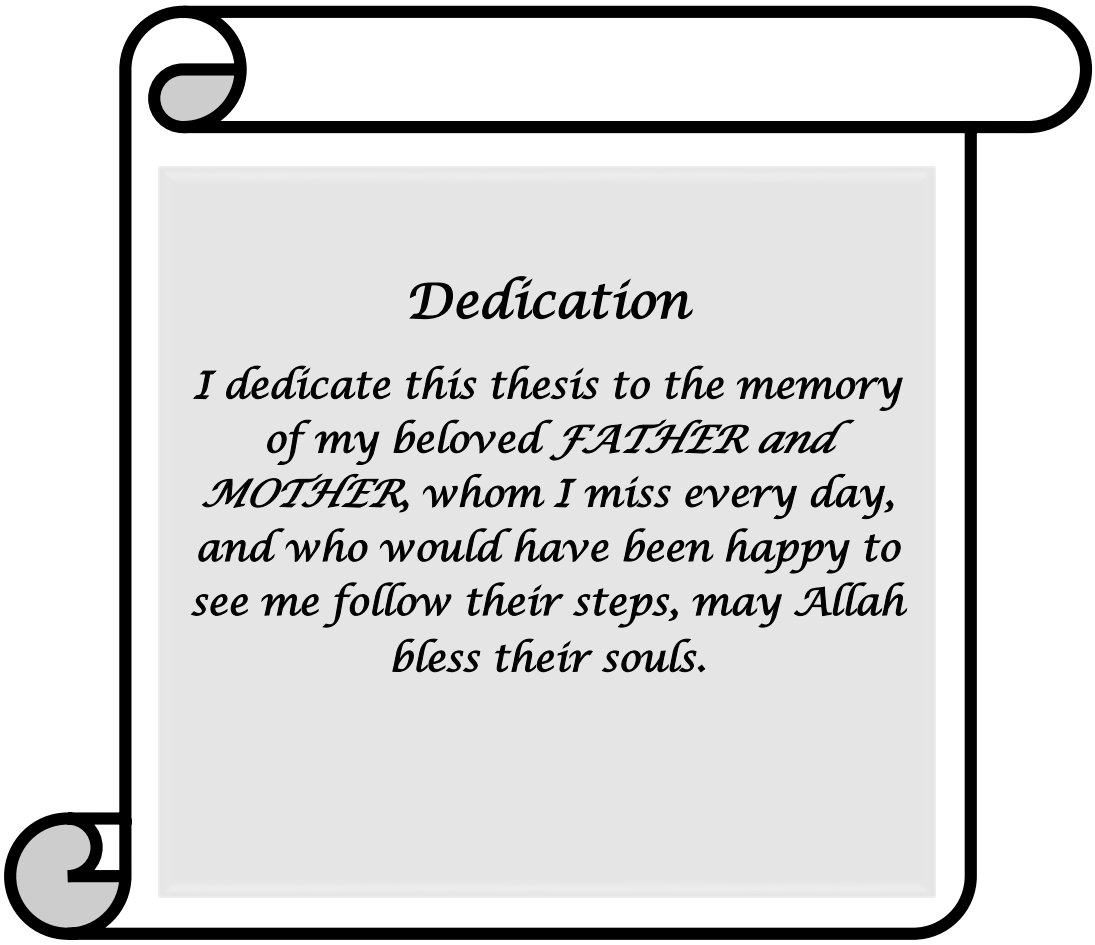

Dedication

I dedicate this thesis to the memory of my beloved FATHER and MOTHER, whom I miss every day, and who would have been happy to see me follow their steps, may Allah bless their souls.

Table of Contents

Table of Contents

List of Abbreviations

1,25 $(OH)_2D$	1,25 di-hydroxyl vitamin D
25 (OH)D	25- hydroxyl vitamin D
ACCP	American college of clinical pharmacy
ADE	Adverse drug events
ADMA	Asymmetric dimethyl arginine
AKI	Acute kidney disease
Ca	Calcium
Ca X P	Calcium Phosphate product
CCP	Calciprotein particles
CKD	Chronic renal failure
CKD-EPI	Chronic kidney disease – Epidemiology collaboration creatinine equation
CKD-MBD	Chronic kidney disease – Mineral bone disorders
CVD	Cardiovascular diseases
ECG	Echocardiography
ESRD	End stage renal disease
FGF-23	Fibroblast growth factor - 23
GFR	Glomerular filtration rate
KDa	Kilo Dalton
KDIGO	Kidney disease improving global outcome
KDOQI	Kidney disease outcomes quality imitative
L-FABP	Liver type fatty acid binding protein
MDRD	Modification of diet for renal disease equation
MGP	Matrix Gla protein

MRI	Magnetic resonance imaging
OC	Osteocalcin
ON	Osteonectin
OPG	Osteoprotegerin
OPN	Osteopontin
PO4	Phosphate
PPM	Patient per million
PTH	Parathyroid hormone
RANK	Receptor activator nuclear kappa – B
RANKL	Receptor activator nuclear kappa – B ligand
RRT	Renal replacement therapy
SHPT	Secondary hyperparathyroidism
TNF	Tumor necrosis factor
TRP	Treatment related problems
VDR	Vitamin D receptor
VSMCs	Vascular smooth muscles cells

List of Figures

List of Tables

Abstract

Background: Vascular calcification is an independent risk factor for cardiovascular diseases and all-cause mortality in end stage renal disease, and particularly in hemodialysis patients. Vitamin D deficiency has been shown to be associated with vascular calcification among this category of patients. Cholecalciferol or vitamin D3; the native inactivated 25-hydroxy vitamin D [25(OH)D], has been proposed to have a good impact on vascular calcification and vitamin D deficiency. However, clinical data is still limited.

Methods: A prospective, randomized, placebo-controlled study was carried out to evaluate the effect of oral cholecalciferol on vascular calcification and 25(OH)D levels in hemodialysis patients. A total of sixty eligible hemodialysis patients were randomly assigned to either a treatment group (Oral 200.000IU Cholecalciferol per month) or a placebo group, for 3 months. Serum 25-hydroxy vitamin D (25(OH)D), fetuin-A, fibroblast growth factor (FGF-23), osteoprotegerin (OPG), calcium, phosphorus, their product (CaXP) and parathyroid hormone (PTH) levels were all assessed at baseline and at the end of the study.

Results: Cholecalciferol significantly increased serum levels of 25(OH)D and fetuin-A in the treatment group (p-value < 0.001), while no significant difference was observed in the placebo group. Cholecalciferol administration showed no effect on either FGF-23 or OPG. None of the treatment group patients experienced any adverse effects.

Conclusion: Cholecalciferol was shown to be an effective, tolerable, inexpensive pharmacotherapeutic option to overcome vitamin D deficiency, with a possible modulating effect on vascular calcification regulators, among hemodialysis patients.

Aim of the Work

The aim of this work was to evaluate the effect of cholecalciferol on vascular calcification in hemodialysis patients, through:

a- Evaluation of Cholecalciferol efficacy by assessment of:

- ✓ Serum 25(OH)D
- ✓ Serum Fetuin-A
- ✓ Serum FGF-23
- ✓ Serum OPG
- ✓ Serum PTH

b- Evaluation of Cholecalciferol safety by assessment of:

- ✓ Serum 25(OH)D.
- ✓ Serum Ca.
- ✓ Serum PO4.
- ✓ CaXPO4 Product

c- Monitoring tolerability and adverse effects.

Review of Literature

Renal Failure

Classification of renal failure can be divided into acute kidney injury (AKI) and chronic kidney disease (CKD). AKI can be characterized by fast disease progression, while a gradual deterioration (in the range of years) of kidney functions occurs in the chronic type ***(Chawla et al., 2014).***

Chronic kidney disease and acute kidney disease can both cause a total loss of kidney functions. Afterwards, it can lead to either total or partial dependence on renal replacement therapy (RRT); dialysis (hemodialysis and peritoneal dialysis), or kidney transplantation ***(Tammen et al., 2014).***

Acute Kidney Injury (AKI):

This type can be characterized by the rapid loss of the kidneys' excretory function. It can be typically diagnosed by detecting the accumulated end products of nitrogen metabolism (urea and creatinine), or by the decreased urine output, or both ***(Bellomo et al., 2012)***. AKI's popular definition is the elevation of creatinine of ≥ 0.3 mg/dl within 48 hours, or ≥ 50% above baseline within 7 days ***(Khwaja, 2012).***

Chronic Kidney Disease (CKD):

This type can be described by a life-threatening progressive and irreversible loss of kidney functions ***(Gansevoort et al., 2013).*** It can be defined by a decrease in kidney function with a glomerular filtration rate (GFR) of less than 60 mL/min per 1.73 m^2, or markers of kidney damage, or both, for at least 3 months' period, regardless of the underlying cause ***(Webster et al., 2016).***