

A Study of the Role of Calcium In Hypertension

Essay

Submitted for partial fulfillment
of master degree in clinical pathology

By

Manal Mahmoud Hamed

M.B., B.ch.

Supervisors

Prof. Dr. Mahmoud Sabry Sallam

Professor of clinical pathology

Faculty of Medicine

Ain Shams University

Dr. Hanzada Ibrahim Abdel Fattah

Assistant professor of clinical pathology

Faculty Of Medicine

Ain Shams University

Dr. Nashwa El Badawi

Lecturer of clinical pathology

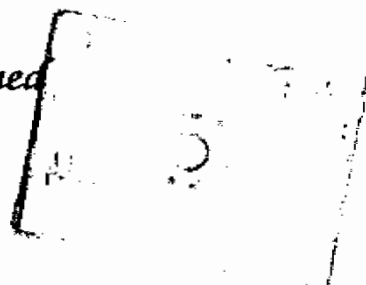
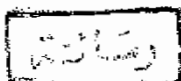
Faculty Of Medicine

Ain Shams University

1994

6/6/132

M.M



51183

Handwritten signature and notes in the bottom left corner.



بسم الله الرحمن الرحيم

"قالوا سبحانك لا علم لنا إلا ما علمتنا إنك

أنت العزيز الحكيم"

صدق الله العظيم



Acknowledgment

I would like to express my deep respect and gratitude to professor Dr / Mahmoud Sabry Sallam, professor of clinical pathology, Ain Shams University, for being encouraging, helpfull and for his kind supervision of the whole work from the start to the end.

To him goes the credit to bring this review to light, he offered me a lot of his time and experience.

Ialso would like to express my deep thanks and sincere gratitude to Ass. Prof, Dr / Hanzada Ibrahim Abdel Fattah, assistant professor of clinical pathology, Ain Shams University, for her great support, great supervision and encouragement throughout the whole work.

I am grateful to Dr / Nashwa Adel El Badawi, lecturer of clinical pathology, Ain Shams University, for her generous cooperation and constructive creticism..

To my colleagues, my family and to everyone who participated in some way or another in the planning and presentation of this study in its final form.

Dedication

*To my husband, my son,
my family for their
everlasting selfless love
and encouragement.*

Contents

Page

- List of abbreviations

i

- List of figures

ii

- List of Tables

iii

- Introduction.

iv

- Aim of the assay.

v

- Review of literature.

I- Calcium metabolism:

A- Forms of Calcium in the body.

2

B- Factors affecting calcium level.

5

C- Calcium absorption.

6

D- Calcium excretion.

7

E- Calcium requirements.

7

F- Effects of hormones on calcium metabolism.

9

1- Vitamin D.

9

2- Parathyroid hormone.

13

3- Calcitonin.

16

4- Effects of other hormones on calcium metabolism.

17

G- Cytosolic calcium metabolism.

19

H- Hypercalcemia.

23

I- Hypocalcemia.

29

II- Calcium-binding proteins:

A) Extracellular calcium-binding proteins.

31

B) Intracellular calcium-binding proteins.	32
--	----

III- Arterial hypertension.

A) Definition.	55
----------------	----

B) Classification of hypertension.	56
------------------------------------	----

C) Regulation of blood pressure.	61
----------------------------------	----

D) Mechanisms of essential hypertension,	62
--	----

E) Role of hormones in essential hypertension.	74
--	----

F) Treatment of hypertension.	81
-------------------------------	----

1- Non drug therapy	81
---------------------	----

2- Drug therapy.	84
------------------	----

G) Role of calcium in the pathogenesis of some forms of secondary hypertension.	96
--	----

IV- Calcium and hypertension:

A) Calcium metabolism in hypertension.	99
--	----

B) Calcium regulating hormones in hypertension.	112
---	-----

C) Mechanisms of blood pressure response to oral calcium.	119
--	-----

D) Cellular calcium metabolism in the pathophysiology of hypertension and related disorders.	123
--	-----

V- Methods of total calcium determination:

A) Sample collection.	128
-----------------------	-----

B) Preanalytical measures.	128
----------------------------	-----

C) Methods of analysis:	129
-------------------------	-----

1- Precipitation.	129
-------------------	-----

2- Titration.	132
3- Direct colourimetric determinations.	133
4- Spectrophotometry.	136
5- Isotope dilution mass spectrophotometry.	140
6- Dry chemistry slide method.	141

VI- Ionized calcium determination.

Methods of analysis:

A) Colourimetric methods.	145
B) The use of dry dextran gel.	145
C) Ion selective electrodes	146
- Summary and recommendations.	151
- References.	155
- Arabic summary.	

List of abbreviations

25-OHD ₃	Calcidiol (25-hydroxycholecalciferol).
1.25-(OH) ₂ D ₃	Calcitriol (1,25-dihydroxy-cholecalciferol).
PTH	Parathyroid hormone.
Ca ²⁺	Calcium.
Na ⁺	Sodium.
Mg ²⁺	Magnesium.
C cells	Parafollicular cells.
PLP	Parathyroid hormone-like protein.
OAF	Osteoclastic activating factor.
MW	Molecular weight.
CBP	Calcium binding protein.
NAD	Nicotinamide adenine dinucleotide.
CaM	Calmodulin.
ANF	Atrial natriuretic hormone.
CEBcs	Calcium entry blockers.
AAS	Atomic absorption spectrophotometry.
PIPES	1,4-piperazinediethanesulfonic acid.
IDMS	Isotope dilution mass spectrophotometry.
RBcs	red blood cells.

List of figures

	Page
Figure 1	3
Figure 2	4
Figure 3	8
Figure 4	10
Figure 5	33
Figure 6	36
Figure 7	38
Figure 8	42
Figure 9	52
Figure10	64
Figure 11	66
Figure 12	68
Figure 13	73
Figure 14	82
Figure 15	93
Figure 16	98
Figure 17	104
Figure 18	109
Figure 19	118
Figure 20	121
Figure 21	126

INTRODUCTION

An important relationship between calcium metabolism and salt sensitivity leading to hypertension is emerging and appears to be providing insights into potential mechanisms that account for the antihypertensive properties of dietary calcium in certain individuals. (Sowers et al., 1989).

Evidence has been accumulated to illustrate that calcium metabolism is deranged in a subset of population having essential hypertension. These alterations may lead to increase in intracellular calcium including smooth muscles which causes increase in peripheral resistance, the increase in calcium also occurs in RBCs, platelets and other tissues. (Erne et al., 1984).

Calcium regulatory hormones, namely parathyroid hormone, 1,25-dihydroxy cholecalciferol (Vit. D) have been observed to be elevated in a group of hypertensive population, both hormones increase the intracellular calcium influx (Linder, et al., 1986).

AIM OF ESSAY

Is to review and summarize the literature and research works suggesting abnormalities in calcium metabolism in relation to human hypertension with emphasis on the different methods of calcium determination.

Review of literature

I- Calcium metabolism

I. CALCIUM METABOLISM

Calcium plays a key role in many cellular processes. It is ubiquitously present in its free form in extracellular fluids and in bound form within the cells. Free Ca^{2+} ions in cells, imported from the outside or liberated from intracellular storage sites, is thought to be the active intracellular form.

The extracellular calcium ions is normally maintained at a concentration of about 1,200,000 nmol/L. The concentration of calcium ions in the cytosol of the resting cell is 100 nmol/L, a 5000 to 10,000 fold difference in calcium ions across the plasma membrane (Borle, 1981).

Calcium ion has a potent effect on many vital biological processes, including cell division, cell movement and muscle contraction. In endocrine system, Ca^{2+} is thought to exert its effects by first binding to a calcium-binding protein. In effect, these proteins are the intracellular receptors for Ca^{2+} . These proteins which are active only when Ca^{++} is bound, then combine with enzymes or other effector proteins and thereby modify their activity typically to activate a biochemical pathway that leads to a physiological response. The most widespread by far of the calcium binding proteins is calmodulin (Williams, 1981).