EFFECT OF SOME NUTRITIONAL FACTORS ON EVOLUTION OF OSTEOPATHY IN THE ELDERLY

THESIS

Submitted By

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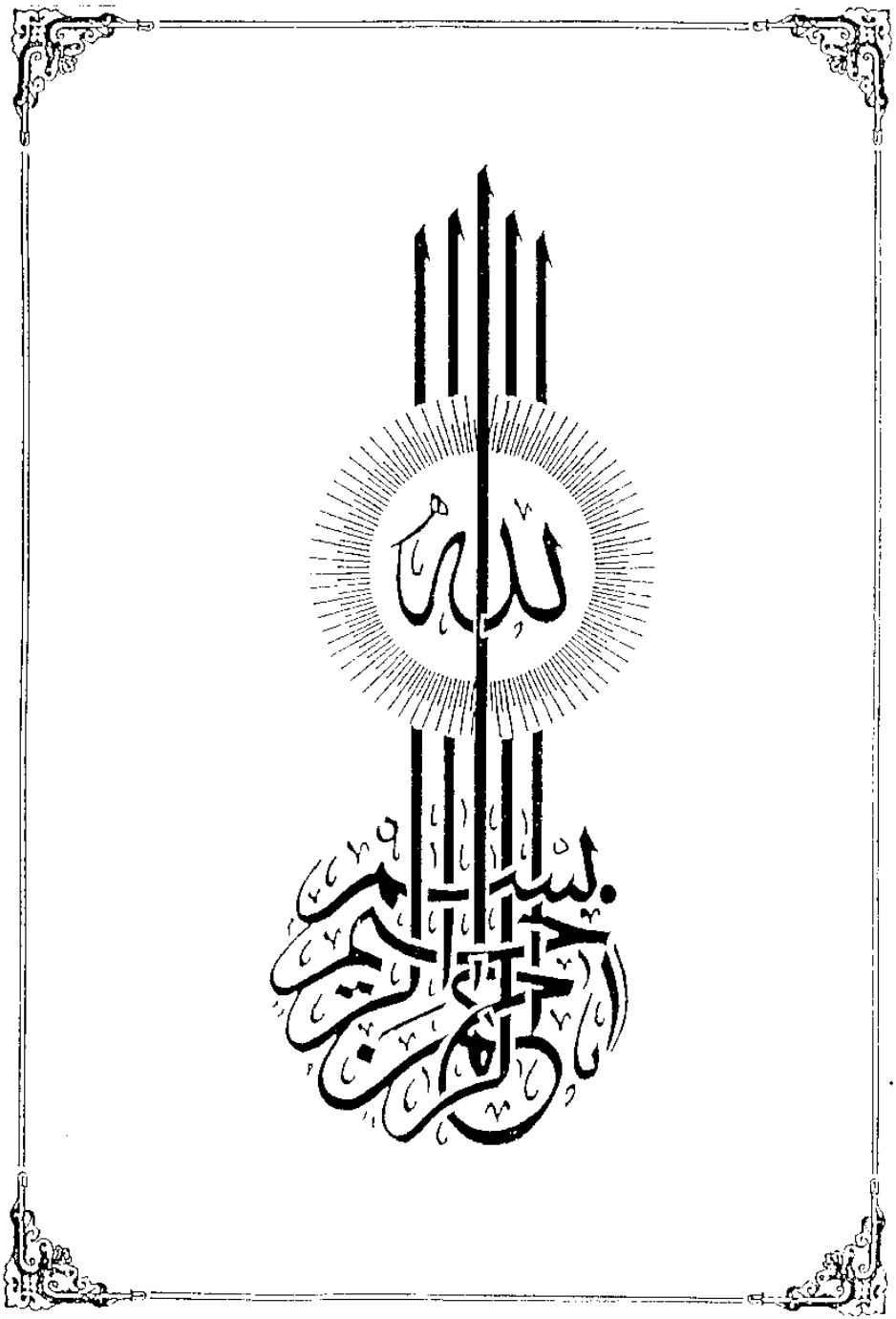
بسم الله الرحمن الرحيم

"وقل رب زدني علما"

صدق الله العظيم



DEDICATION

To my husband *who made this work possible with his encouragement and tolerance,*
To my daughters *who are my hope for brighter future.*

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LIST OF ABBREVIATIONS

μCi	micro Curie
μM	Micro mole
1,25 $(OH)_2$ D_3	1,25 dihydroxycholecalciferol
^{125}I	Iodine-125
25 OH D	25 dihydroxycholecalciferol
^{45}Ca	Calcium-45
ACTH	Adenocorticotropic hormone
ADP	Adenosine diphosphate
Alk. Ph.	Alkaline phosphatase
ATP	Adenosine triphosphate
BMD	Bone mineral density
c.p.m.	Count per minute
Ca	Calcium
Ca/Cr	Urinary calcium/creatinine
Ca^{2+}	Calcium ion
$CaFl_2$	Calcium fluoride
cAMP	Cyclic adenosine monophosphate
CPC	Cresolphthaline complex
Cr	Creatinine
CT	Calcitonin
D vit	Vitamin D
DNA	Deoxyribonucleic acid

DPO	2,4 diphenyloxazole
EDTA	Ethylene diamine tetra acetic acid
EGTA	Ethylene glycol bis - (2-aminoethyl ether) tetra acetic acid
GC	Group-specific component
GF	Glomerular filteration
IU	International Unit
IU/ml	International unit per millilitre
L	Litre
Mg	Magnesium
$MgCl_2$	Magnesium chloride
mRNA	Messenger ribonucleic acid
N	Normality
NADP	Nicotinamide adenine dinucleotide phosphate
NaF	Sodium fluoride
NcAMP	Nephrogenous cyclic adenosine monophosphate
ng/ml	Nanogram per millilitre
P	Phosphorus
PEG	Polyethylene glycol
pg/ml	Picrogram per millilitre
PO_4^{3-}	Phosphate ion
PTH	Parathyroid hormone
r.p.m.	Revolution per minute
RDA	Recommended dietary allowances
RIA	Radioimmunoassay

RNA	Ribonucleic acid
S.D.	Standard deviation
S.E.	Standard error
T	Thoracic
TSH	Thyroid stimulating hormone
ttt	Treatment
ucAMP	Urinary cyclic adenosine monophosphate
UHP/Cr	Urinary hydroxyproline/creatinine
USA	United States of America

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AIM OF THE WORK

Osteoporosis is one of the most common, serious and expensive health problems in the elderly. It may be defined as a disorder in which not enough bone is present to maintain skeletal strength, with the result that fractures occur with minimal stress. The bone itself appears normal in most respects, although study of bone cell activity has indicated that the rate of osteoclastic bone resorption may be greater than normal and greater than the rate of new bone deposition. The ideal therapeutic program for osteoporosis is based not on slowing the rate of bone loss but rather on making positive the bone tissue balance. This would add bone to such an extent that the amount of bone becomes higher than the fracture threshold. Although many therapeutic agents have been investigated, very few can increase bone mass.

Our aim is to assess the short term effect (i.e. 3 months) of nutritional role of calcium supplementation, calcium and vitamin D intake and combination of calcium and fluoride on the process of osteoporosis in osteoporotic males.

The effect of adding fluoride to calcium supplementation and vitamin D combination on restoration of the bone mass will also be determined.

Introduction

INTRODUCTION

Aging is a basic characteristic of all living matters. The proportion of aging population is steadily increasing and so are problems of their health care, family relations, housing, income security, employment and use of leisure time (Khan, 1988).

From a biologic stand point, there is a limited knowledge of the process of aging. The general biologic process extends over the entire life span and is considered by experiences that have gone on before. In the later ages, however, there is a cell loss and reduced cell metabolism (Watkin, 1964).

Shock (1963) has shown that during the ages 30 to 60 years there is gradual reduction in the performance capacity of most organ systems. For example, the speed of conducting a nerve impulse diminishes by 15%, the rate of blood flow through the kidney is reduced 65%, and the resting cardiac output is reduced by 30%. The pulmonary function (the maximum voluntary ventilatory capacity) is reduced 60%.

Age-related bone loss is a universal phenomenon. Many older individuals who have an unusually low bone mass initially or lose bone faster with age will develop clinically apparent osteoporosis, with skeletal fractures, deformities and pains.

Other bone diseases occur with increased frequency in the elderly, including osteomalacia, in which bone mineralization is impaired, and primary hyperthyroidism and malignancy involving the skeleton, in which there is increased bone destruction. There are less common forms of osteoporosis that

occur in younger individuals, in which glucocorticoid excess, alcoholism, liver disease and immobilization may be contributing factors (Lawrence, 1982).

Swanson and Pearl (1959) reported that bony tissue in the adult cannot be considered as static material. It is a dynamic substance, which constantly remodels itself. Formation of new bone and destruction of old bone go on simultaneously. These processes approximately balance each other in the healthy adult. As a person grows older, however, the process of bone destruction may overbalance that of bone building.

STRUCTURE OF BONE

Bone is a living tissue with a collagenous protein matrix that has been impregnated with mineral salts, especially phosphates of calcium. It supports the body, provides a store house of Ca^{2+} and other minerals that aids in maintaining mineral homeostasis, and aids the lungs and kidneys in the maintenance of acid-base balance by providing additional phosphate and carbonate buffers. The protein in the collagen fibers that form bone matrix is complex (Junqueira and Carneiro, 1983). Adequate amounts of both protein and minerals must be available for the maintenance of normal bone structure. Mineral in bone is mostly in the form of hydroxy-apatites, which have the general formula

$$Ca_{10-x}^{2+}(H_3O^+)_{2x}(PO_4^{3-})_6(OH^-)_2.$$

Sodium and small amounts of magnesium carbonate are also present in bone. It is interesting that bone contains a protein with a large number of ϒ-carboxyglutamic acid residues, and these residues bind Ca^{2+}. Furthermore, a high content of this protein correlates with ongoing calcification. However, ϒ-carboxylation is catalyzed by vitamin K and vitamin K deficiency only causes skeletal abnormalities in the fetus.

The cells in bone that are primarily concerned with bone formation and resorption are the osteoblasts, the osteocytes and the osteoclasts. Osteoblasts are the bone forming cells that secrete collagen, forming a matrix around themselves which then calcifies. Osteocytes are bone cells surrounded by calcified matrix. They send processes into the canaliculi that ramify throughout the bone. Osteoclasts are multinuclear cells that erode and resorb previously formed bone (Junqueira and Carneiro, 1983).

Two major forms of bone exist; *compact cortical bone* forms the external envelops of the skeleton, *trabecular or medullary bone* forms plates that traverse the internal cavities of the skeleton. The proportions of cortical and trabecular bone vary at different sites. Vertebral bodies contain predominantly trabecular bone, while the proximal femur contains predominantly cortical bone. The responses of the two forms of bone to metabolic influences and their susceptibility to fracture differ (Consensus Conference, 1984).

Bone undergoes continuous remodelling (turnover) throughout life. Osteoclasts resorb bone in microscopic cavities; osteoblasts then reform the bone surfaces, filling the cavities. Normally, bone resorption and formation are linked closely in space, time and degree. Mechanical and electrical forces, hormones and local regulatory factors influence remodelling.

Peak bone mass is achieved at about 35 years of age for cortical bone and earlier for trabecular bone. Sex, race, nutrition, exercise and overall health influence peak mass. Bone mass is approximately 30% higher in men than in women and approximately 10% higher in blacks than in whites. In each group, bone mass varies among individuals.

After reaching its peak, bone mass declines throughout life because of an imbalance in remodelling. Bone loses both mineral and organic matrix but retains their basic organization. In women, bone mass decreases rapidly for three to seven years after menopause. Bone loss also is enhanced in a variety of diseases (Consensus Conference, 1984).