EFFECT OF EGYPTIAN DIETARY PHOSPHATE ON SERUM CALCIUM AND PHOSPHOROUS LEVELS IN PATIENTS OF CHRONIC RENAL FAILURE UNDER REGULAR HEMODIALYSIS

THESIS

Submitted By

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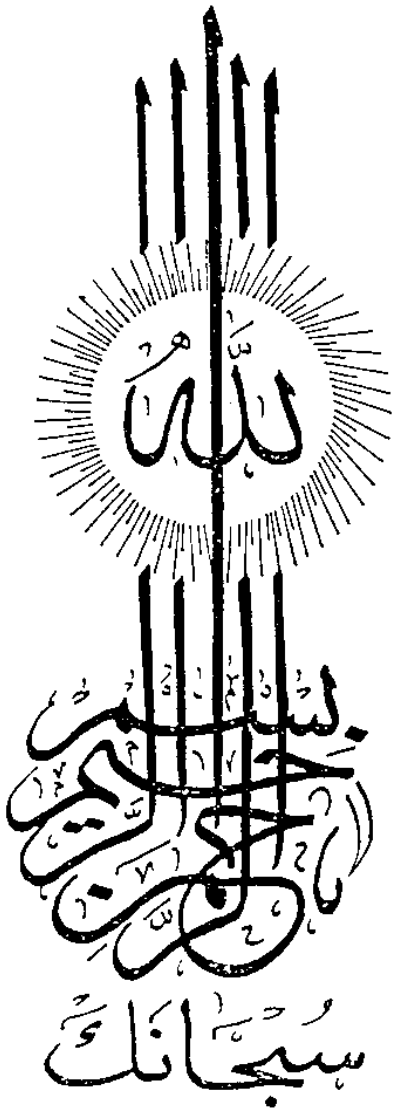

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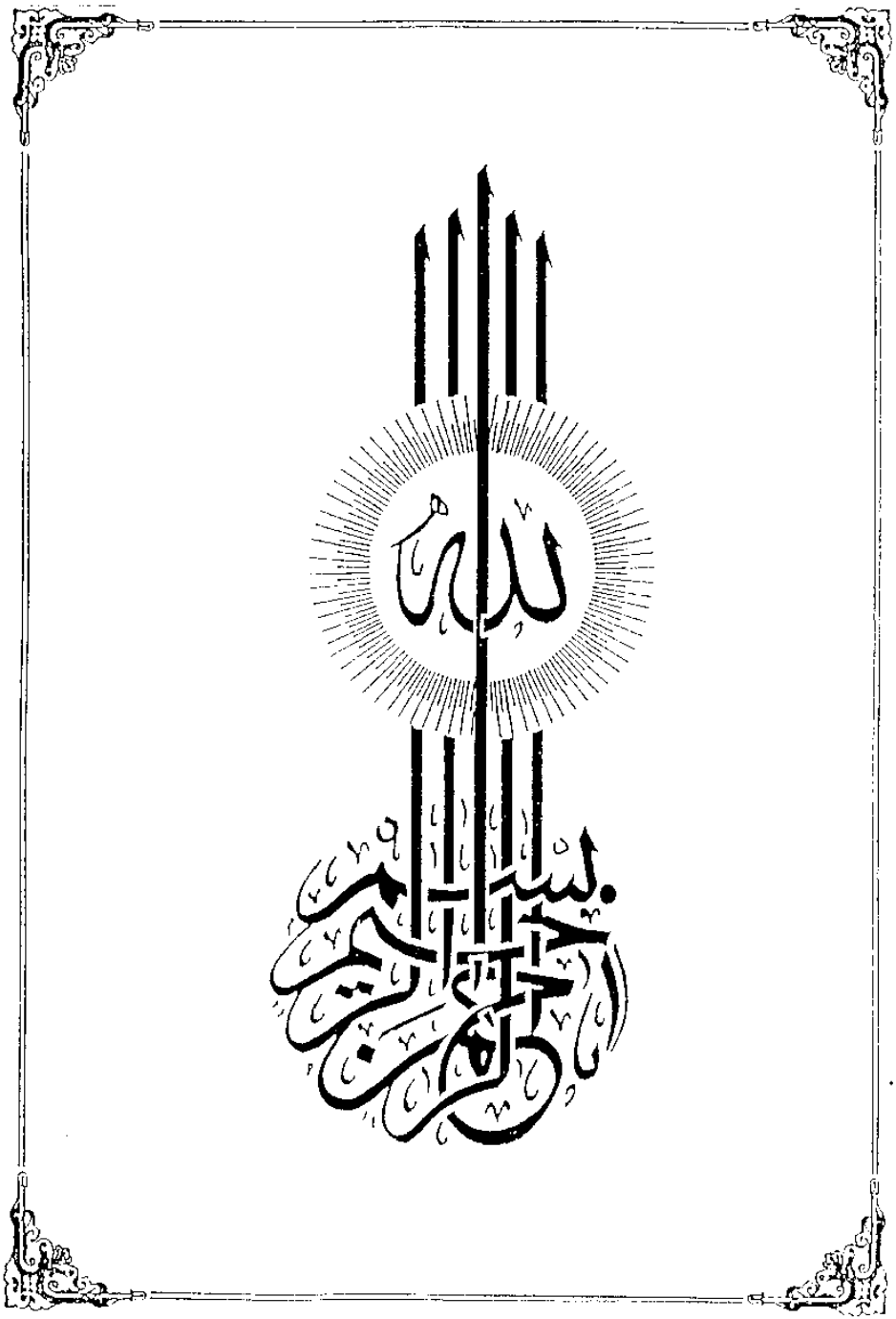

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CONTENTS

LIST OF ABBREVIATION

$25(OH)D_3$	: 25 hydroxy cholecalciferol
$1,25(OH_2)D_3$	: 1,25 dihydroxy chole calciferol
2,3-DPG	: 2,3 diphosphoglycerate
ATP	: Adenosine triphosphate
PTH	: Parathyroid hormone
cAMP	: 2',3' cyclic adenosine monophosphate.
Tm	: Maximum tubular reabsorption
E.C.G.	: Electro Cardio Graph.
C_aBP	: Calcium binding protein.
CT	: Calcitonine
ECF	: Extracellualr fluid
GFR	: Glumeruler filteration rate
% TRP	: Percentage tubular reabsorption of phosphate.
TmP/GFR	: Maximum tubular reabsorption of phosphate/ glumeruler filteration rate.
α	: Alpha
B	: Beta
γ	: Gama
MHD	: Maintenance haemodialysis
RDT	: Regular dialysis treatment
Hb	: Haemoglobin
Ht%	: Haematocrit
M.C.V.	: Mean corpuscular volume
M.C.H.	: Hean corpuscular haemoglobin
M.C.H.C	: Hean corpuscular haemoglobuin concentration.
U.U.G.	: Micro, microgram.
G.P.T.	: Glutamic Pyruvic Transaminase
G.O.T.	: Glutamic Oxaloacetic Transaminase

AIM OF THE WORK

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Aluminium salts are extensively used as theraputic binders in the management of hyperphosphatemia in chronic renal failure at its various stages to prevent renal osteodystrophy and to protect the kidney. The efficiency of these binders depends on the pharmaceutical processing

Aluminium containing gels available in the local market are usually used as antacid, our aim is to assess the acute effect of Egyptian dietary phosphate on the serum calcium and phosphate tolerance before and after taking aluminium hydroxide gel. This will be carried out by analysing the calcium, and phosphorous content of some Egyptian diet components and following the serum calcium and phosphorous changes before and after one and three hours eating this experimental diet by normal, and chronic renal failure cases with and without dialysis.

The finding may be of help in better administration of the phosphate binder depending on the phosphate content of each meal.

INTRODUCTION

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The role of phosphorous retention in the development of secondary hyperparathyroidism in chronic renal disease is well established (Slatopolsky et al., 1971). If phosphorous absorption is decreased, according to the decrease in renal function, hyperparathyroidism and its adverse effects can be prevented (Slatopolsky et al., 1972). There is also another idea that phosphorous retention interferes with Vit D metabolism by decreasing the convertion of 25-hydroxycholecalciferol 25(OH) D_3 to 1,25 dihydroxy chole calciferol 25 $(OH)_2$ D_3 (Tanaka et al., 1974).

The control of the intestinal absorption of phosphorous is important to patients with compromised renal function. Unfortunately there is no nutritionally complete, palatable, low phosphorous diet. Consequently, phosphorous-binding gels have been prescribed with food to control phosphorous absorption in order to prevent secondary hyperparathyroidism. The most effective phosphorous-binding agents such as aluminium-containing gels are poorly soluble, many patients find them unpalatable and others suffer from nausea and vomiting following ingestion.

REVIEW OF LITERATURE

Another problem in treatment with aluminium-containing gels is the potential development of aluminium toxicity. The possibility of aluminium toxicity in chronic renal failure patients under regular haemodialysis as a consequence of antacid ingetion has been raised by (Alfrey et al., 1976), who described a fetal encephalopathic syndrome in dialysis patient who were subsequently found to have high concentrations of aluminium in their brains.

REVIEW OF LITERATURES

Phosphte Homeostasis

Phosphorous is an important constituent of all body tissue. It is an essential element in phospholipid cell membranes, nucleic acids, phosphoprotein required for mitochondrial function.

A normal man (70 kg) contains approximately 712 gm of phosphorous. About 80% of this is in bone; 9% in skeletal muscle. The bulk of phosphorous in skeletal muscle and viscera is inside the cell, where its average concentration in cell water is 100 m moles/liter(Krebs et al., 1959).

The intracellular phosphate pool is involved in the regulation of the intermediary metabolism of proteins. In addition, intracellular phosphate may directly regulates several prominent enzymtic reactions including glycolysis. (Tsuboi **et al.,** 1965) and ammoniagenesis (O'Donovan **et** al., 1966).

Lichtman et al., (1971) reported that another critical enzymatic process that is tightly regulated by phosphate is red cell 2,3 diphosphoglycerate (2,3-DPG) synthesis which modulates the oxygen, carrying capacity of haemoglobin.

Most important phosphorous is found in the high energy phosphate bonds of ATP (adenosine triphosphate). The energy stored in ATP is used for a wide variety of physiological proccesses, including muscle contractility, neurological function and electrolyte transport, as well as a large number of important biochemical reactions. Further more phosphorous is important constitutent in a number of other essential intracellular compounds including cyclic adenine and guanine mucleotides and enzymatic co-factors such as nicotinamide diphosphate(Jeffrey , 1982).

Dietary intake of phosphorous amounts to about 800-1200 mg/day, some 80 % of the ingested phosphate is absorbed principally in the jejunum (Wilkinson et al., 1976), and is under the control of vitamine D_3 and several of its principle metabolitis(Walling, 1977).

Since an amount equivalent to 30 - 40 % of intake is excreted in the stool, it follows that intestinal phosphate secretion contributes in part to fecal excretion. Despite the ubiquity of phosphate in the diet (especially red meat, fish, poultry eggs, milk products and legumes),

maintenance of normal phosphate balance requires an efficient renal conservation mechanism.

Mobilization of phosphate from bone contributes little to the maintenance of the serum phosphate concentration, while the kidney is clearly the single most important organ for the steady-state serum phosphate level (Jeffery et al., (1982).

Although the precise mechanism of renal phosphate transport along the nephron remains controversal (Knox et al., (1977), important factors have been elucidated:-

1. Variation in dietary phosphate intake lead to marked changes in tubular reabsorption of phosphate (Foulks (1955). He found that phosphate disappears from urine in dogs after short term fasting, while the same animals have high phosphate in the urine when they are fed normal diet.

Lotz et al., (1968) reported that in man oral taking of phosphate results in a progressive increase in urinary phosphate with decrease in the fraction of filtered load that is reabsorbed. On