CARDIOVASCULAR RESPONSES TO INCREASED INTAKE OF SODIUM CHLORIDE IN RATS

THESIS
Submitted In Partial Fulfillment
For The Degree Of M.D.
(PHYSIOLOGY)

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1994

بسم الله الرحمن الرحيم

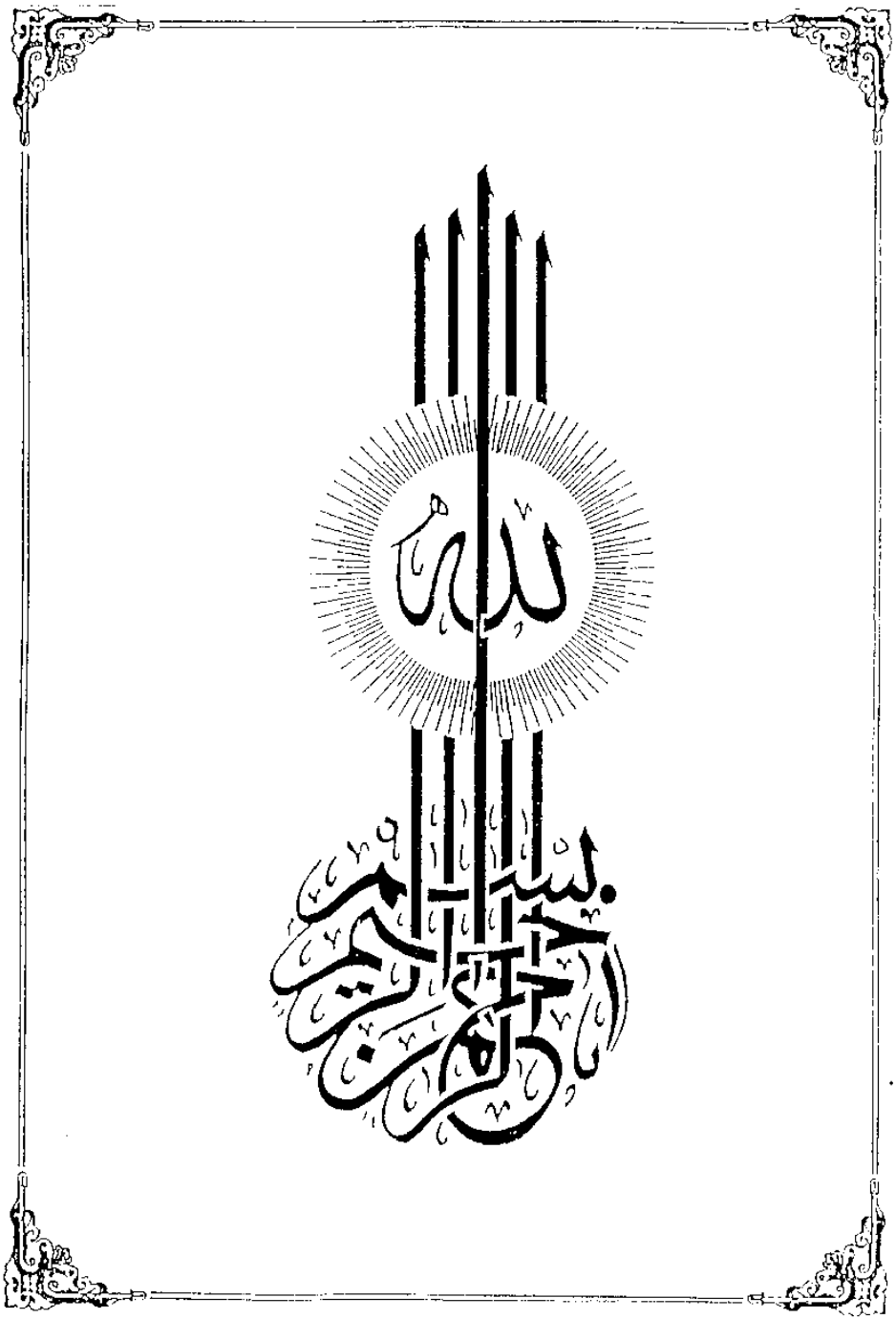
اقْرَأْ بِاسْمِ رَبِّكَ الَّذِي خَلَقَ

خَلَقَ الْإِنسَانَ مِنْ عَلَقٍ

اقْرَأْ وَرَبُّكَ الْأَكْرَمُ الَّذِي عَلَّمَ بِالْقَلَمِ

عَلَّمَ الْإِنسَانَ مَا لَمْ يَعْلَمْ

العلق ١-٥



TO MY PARENTS , MY WIFE AND MY DAUGHTER

ACKNOWLEDGEMENT

*I am deeply grateful to Professor **AHMED MOHAMED KAMEL** , Head Of Physiology Department , for his support , encouragement and generous cooperation .*

*I wish to express my special thanks and deep gratitude to Professor **MAHMOUD HANY AYOBE** , for suggesting and planning this study , and for his help in solving problems met with throughout the entire work .*

*Deepest gratitude must be expressed to Professor **MOHAMED RIFAAT A. RIFAAT** , for his precious guidance and keen supervision as well as for his stimulating remarks and sharp interest throughout this study .*

*I am deeply indebted to **Dr.HOSSAM EL-DIN A. AWAD** , Assist.Professor Of Physiology , for initiating this line and for continuous close supervision , and for his help and support .*

*I wish to express my cordial appreciation to Professor **NABIL A. EL-DAMARAWY** , for unfailing enthusiasm and invaluable efforts in conducting and presenting this work .*

*I would like also to express my thanks to my colleague **Dr.ASHRAF A. TOURKEY** , Lecturer Of Physiology , for his support and kind help .*

Finally , I would like to thank all members of Physiology Department , for their interest .

Memorandum

This work was carried out using the facilities and funds of the Cardiovascular Research Unit Physiology Department .

CONTENTS

INTRODUCTION

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Excess dietary sodium has been incriminated in the development of hypertension . According to this concept , dietary salt restriction and / or natriuresis have gained position as important lines in treatment of hypertension .Although ,the evidences in favor of such theory are attractive,many authorities remain skeptical against it.

Although , experimental studies have documented that high sodium intake induces hypertension in rats , dogs and baboons , yet , such evidences are not conclusive in humans .

In this respect , some investigators have found a positive relationship between sodium intake (estimated by urinary sodium excretion) and blood pressure , others have found no relationship or even reported a lower sodium excretion in hypertensives than in normotensives .

No one doubts that , very high intake of salt is harmful , however , the question is whether hypertension could be developed and maintained with the sort of salt intake that exists nowadays in civilized societies .

It was important , therefore , to study the cardiovascular risks induced upon increasing the salt intake but in low doses . Such a model was developed in rats , in a preliminary study *(Ayobe , et al , 1992a)* , by substituting their drinking water with isotonic saline .

AIM OF WORK

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This work was planned in order to study the cardiovascular changes in rats allowed to drink only isotonic saline (0.9 % sodium chloride) instead of tap water .

In the intact rat , the effect of saline intake for 2 , 4 & 8 weeks , was assessed on cardiovascular parameters such as arterial blood pressure , ECG & cardiac mass . Also , alterations in cardiac functions such as chronotropy , inotropy and coronary flow were investigated in vitro in a Langendorff preparation of isolated heart perfusion , both under baseline conditions and in response to beta-adrenergic stimulation .

The relationship of plasma sodium levels to changes induced by saline in vivo and in vitro , was also investigated .

REVIEW OF LITERATURE

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I-Physiological Regulatory Mechanisms Triggered By Increased Sodium Chloride Intake

The interrelationship between high salt intake and serum sodium level was investigated by *Kirkendal , et al , (1976)* who showed significant elevation in serum sodium when subjects consumed high salt intake . In agreement with these results , *Kawasaki , et al , (1987)* demonstrated marked increases in plasma sodium in all subjects receiving high salt diet , as also documented by *Hayek , et al , (1983) ; Sagnella , et al , (1985) and Kohno , et al , (1987)* .

Also , *Kawano , et al , (1992)* showed significant elevation in serum sodium concentration in rats after 7 days of high salt intake (16-18 g / day) , as also proved by *Fenwick , (1992)* . Moreover , *Morita , et al , (1993)* added that administration of sodium chloride in diet for dogs resulted in significant increase in plasma sodium concentration .

On the other hand , *Perera and Blood (1947)* showed no significant alterations in serum sodium either on salt restriction or increased salt intake in man . Also , *Luft , et al , (1979)* reported no significant changes in plasma sodium levels following sodium

administration at 6 levels (10 - 1500 mEq / L) for 7 days in human , as also demonstrated by *Weidmann , et al , (1986)* .

Whether the plasma sodium level increased significantly or insignificantly in response to sodium chloride administration in previous literatures , nearly all of the investigators proved that sodium excretion in urine was significantly elevated in all diet regimens containing high sodium . In *1985 , Sagnella , et al ,* attributed the augmented sodium excretion after saline loading in dogs to the decreased tubular reabsorption of sodium rather than to increased filtration , and they concluded that neither increased filtered sodium nor decreased aldosterone secretion can account for the increase in sodium excretion . Part of the increase must result from the action of another factor , which is the natriuretic hormone , 3 types of the natriuretic factor have been identified , atrial natriuretic factor (ANP) which is released from the cardiac atrium in response to stretch , brain natriuretic peptide (BNP) and C-type natriuretic peptide (C-typeNP) . Also , 3 different natriuretic receptors have been demonstrated , ANP-RGC(A) and ANP-RGC(B) mediating biologic actions and ANP-RC which principal function is to remove the natriuretic peptides from the circulation , that is , to regulate plasma levels of the natriuretic peptides . However , ANP-RC may also mediate a biologic effect *(Jaimson , et al , 1992)* . The specific ANP receptors have been also identified in the kidneys , and the density of ANP receptors were decreased on a high sodium diet in

rats , concluding finally that ANP mechanism may be involved in the pathogenesis of salt-induced hypertension in spontaneously hypertensive rats *(Hedner , et al , 1987)*.The atrial natriuretic polypeptide hormone (ANP) exerts a potent , rapid but short-lived diuretic and natriuretic effect by specifically decreasing tubular reabsorption of sodium and the magnitude of this effect apparently increases with progressive saline loading . These data were supported by the findings of *Salazar , et al , (1986) ; Khono , et al , (1987) ; Gradin and Persson (1987)* .

While , *Gradin , et al , (1987)* showed that on high salt diet , the decreased natriuretic and diuretic responses to ANP were attributed to the fact that ANP may act as a functional antagonist to nor adrenaline and angiotensin II , also it could be a down regulation of renal ANP receptors since chronic salt loading would be expected to raise at least intermittently circulating ANP levels .

Moreover , *Morita , et al , (1992)* found out that intravenous infusion of brain natriuretic peptide (BNP) increased urinary fluid and electrolyte excretion and decreased jejunal fluid and electrolyte absorption , while C-type natriuretic peptide (CNP) has a similar effect on jejunal absorption as BNP , however , CNP has no significant effect on renal fluid or electrolyte excretion .

De-Bald , et al , (1981) showed that the diuretic and natriuretic effect were accompanied by regional vasorelaxation ,