ALDOSTERONE IN PATIENTS ON PROLONGED HAEMODIALYSIS

THESIS

Submitted for partial fulfillment of

Master Degree

Internal Medicine

BY

Hesham Khairat Youssef

MB. B.Ch. Faculty of Medicine

Ain Shams University 1978

SUPERVISORS

Dr. Hussein El-Damasy
Assistant Professor of
Medicine

Dr. Sayed Raafat
Assistant Professor of
Medicine

Prof. Dr. Mohamed Farid El-Asmar
Prof. Of Biochemistry

Assistant Supervisors

Dr. Badawy Labib Mahmoud
Assistant Professor of Medicine

Dr. Soheir Mohamed Gamal El-Din

Ain Shams University

(1983)

ACKNOWLEDGMENT

I wish to express my deep gratitude to Dr. Hussein El-Damasy, Ass. Prof. of Medicine and Dr. Sayed Raafat, Ass. Prof. of Medicine for their generous help and continuous guidance in supervising the thesis. In undertaking this task, they gave me incessant encouragement endowed with fatherly attitude. Sincere thanks are also due to Dr. Farid El-Asmar, Head of Biochemistry Department for his kind cooperation in supervising and evaluating the applied part of the thesis.

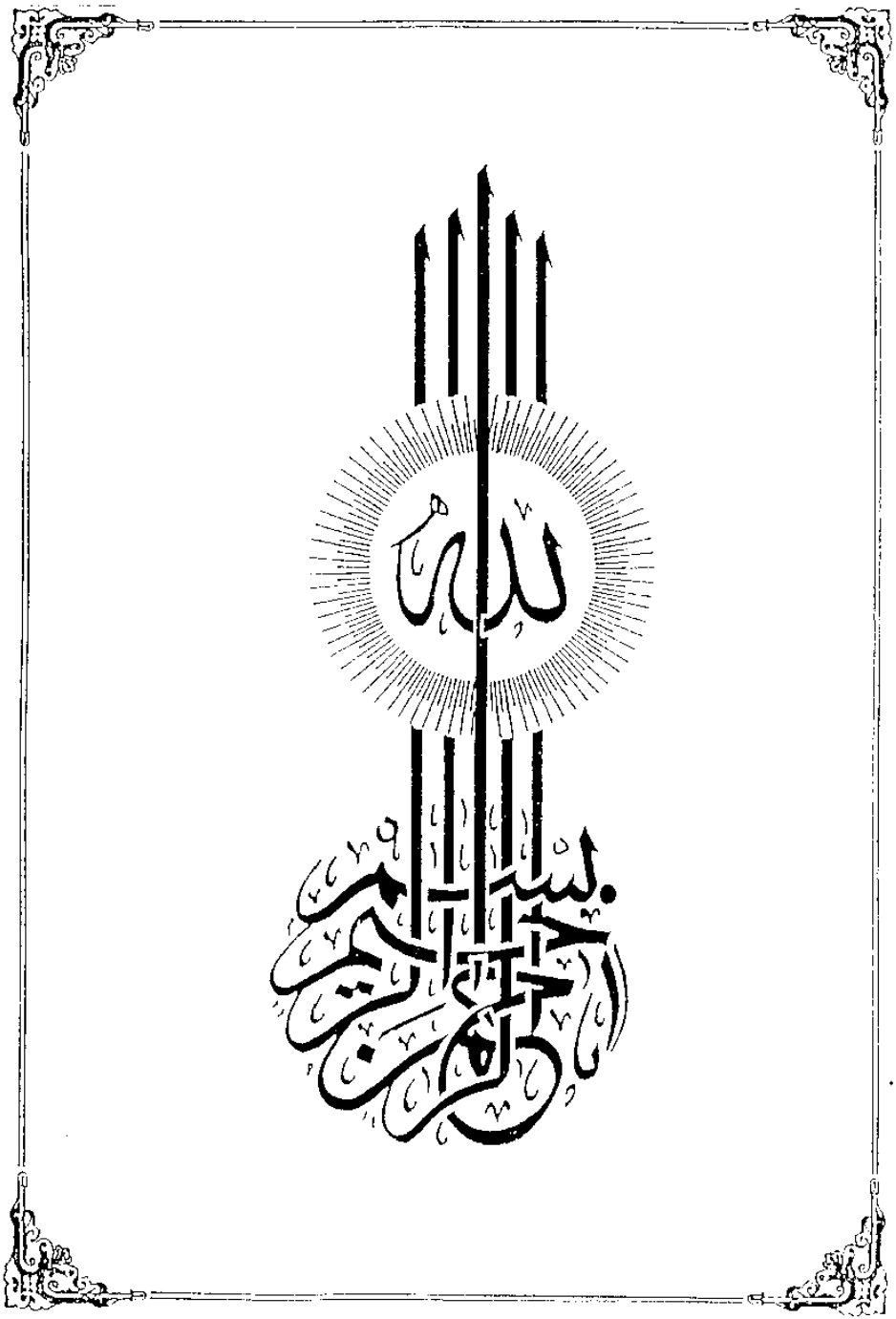
I am also greatly indebted to Prof. Dr. M. Amin Fikry, Prof. of Medicine for performing the statistical results of this work. Moral support and unfailing advice were also graciously granted by Dr. Badawy Labib, Ass. Prof. of Medicine and Dr. Soheir M. Gamal El-Din.

Thanks are also given to the Biochemists of the endocrine laboratory, especially Miss. Azza Khedr who performed the hormone assays.

In short, to all of the above mentioned I wish to quote:

"More is thy due than more"

than all can pay.



CONTENTS

	Page
I. Aim of the Work	1
II. Review of Litzrature	2
* Embryology & Anatomy of Adrenal gland	2
* Histology of Adrenal gland	4
* Functional Anatomy of the Kidney	5
* Biosynthesis of Adrenocortical Hormones ...	7
* Functions of Mineralocorticoids	12
* Regulation of Aldosterone Secretion	20
* Measurements of Aldosterone	33
* Chronic renal failure	35
* Haemodialysis	51
* Effects of Haemodialysis on plasma Aldosterone	70
III. Materials and Methods	80
IV. Results	91
V. Discussion	105
VI. Summary and Conclusion	114
VII. References	118
VIII. Arabic Summary.	

ABBREVIATIONS

1) ACTH = Adrenocorticotrophic hormone.

2) DNA = Deoxy ribo nucleic acid.

3) DOCA = Deoxy corticosterone acetate.

4) ECF = Extra cellular fluid.

5) MCR = Metabolic clearance rate.

6) PRA = Plasma renin activity.

7) RNA = Ribonucleic acid.

AIM OF THE WORK

AIM OF WORK

Mineralocorticoids; the most important of which is aldosterone play a great role in regulation of serum sodium and potassium. They tend to increase reabsorption of sodium and increase potassium excretion. On the other hand, the level of sodium and potassium in the serum, renin-angiotensin system and ACTH play an important role in regulation of aldosterone secretion and the level of serum aldosterone. In the end-stage renal failure there is disturbance in serum potassium and sodium, and also there is loss of the nephronal mass with subsequent decrease in renin secretion.

The aim of this work is to study the level of serum aldosterone in 2 groups of patients with chronic renal failure, one group not undergoing hemodialysis and the other group undergoing regular hemodialysis for more than 8 months, in an attempt to determine the effect of long term hemodialysis on the basal level of serum aldosterone. We aimed also to determine the correlation between serum aldosterone and serum electrolytes, blood urea and creatinine in both uremic groups of patient.

REVIEW OF LITERATURE

EMBRYOLOGY OF ADRENAL GLAND

During the 4th to 6th week of foetal life, cells from coelomic mesoderm of the posterior abdominal wall near the mesonephros form a cluster between the root of the mesentery and the genital ridge to establish to foetal adrenal cortex. Some 5 weeks later, small basophilic cells appear around the foetal cortex; these are the forerunners of the permanent adrenal cortex. During the 7th week of embryonic development, the foetal adrenal cortex is invaded by cells migrating from the neural crest; these "sympathogonia" are forerunners of adrenal medulla. The foetal cortex is ACTH - dependent, and is relatively small in the absence of a functioning pituitary, Liddle (1981).

ANATOMY OF THE ADRENAL GLANDS

The suprarenal glands belong to the class of ductless glands. They are 2 small flattened bodies, of a yellowish colour, situated at the back part of the abdomen behind the peritoneum, and immediately above and in front of the upper end of each kidney. The right one is soewhat traingular in shape, bearing a resemblance to a cocked had; the left is more sewilunar, usually larger and placed at a higher level than the right. They vary in size in different individuals, being from an inch and a quarter to nearly two inches in lenght, rather less in width. Their average weight in about 5 gms each.

On making a perpendicular section, the gland is seen to consist of two substances - external or cortical, and internal or medullary. The former which constitutes the chief part of the organ, is of a deep yellow colour. The medullary substance is soft, pulpy, and of a dark brown colour. The arteries supplying the suprarenal glands are numerous and of large size; they are derived from the aorta, the phrenic, and the renal arteries; they subdivide into numerous minute branches previous to entering the

substance of the gland. The suprarenal vein returns the blood from the gland; it opens in the right side into the inferior vena cava, on the left side into the renal vein. The lymphatics terminate in the lumbar glands.

The nerves are exceedingly numerous, and are derived from the solar "epigastric" and renal plexuses, and form the phrenic and pneumogastic "vagus" nerves. They enter the lower and inner part of the capsule, traverse the cortex, and terminate round the cells of the medulla, Gray (1977).

HISTOLOGY OF ADRENAL CORTEX

The adrenal cartex is divided into 3 zones of variable distinctness. The outer zona glomerulosa is made up of whorls of cells that are continuous with the columns of cells which form zona fasciculata. These columns are separated by venous sinuses. The inner portion of the zona fasciculata merges into the zona reticularis, where the cell columns become interlaced in a network. The cells contain abundant lipids, especially in the outer portion of the zona fasciculata. All 3 cortical zones secrete cortecosterone, but the enzymatic mechanism for aldosterone biosynthesis is limited to the zona glomerulosa, while the enzymatic mechanism for forming cartisol and sex hormones is found in the 2 inner zones. The cells of adrenal cartex contain large amounts of smooth endoplasmic reticulum, which seems to be involved in the steroid forming process. Other steps in steriod biosynthesis occur in the mitochondria, Ganong. (1979).

FUNCTIONAL ANATOMY OF THE KIDNEY

Each individual renal tubule and its glomerulus is a unit, or nephron which is the functional unit of the kidney. There are approximately 1 million nephrons in each human kidney. The glomerulus, is about 200 um in diameter, is formed by invagination of a tuft of capillaries into the dilated blind end of the nephron (Bowman's capsule). The capillarics are supplied by an afferent arteriole and drained by a slightly smaller efferent arteriole. There are 2 cellular layers separating the blood from the glomerular filterate in Bowman's capsule: the capillary endothelium and the epithelium of the glomerulus. These layers are separated by a basal lamina. The endothelium is fenestrated, with pores that are approximately 100 nm in diameter. The pseudopodia of the epithelial cells (podocytes) form slits along the capillary wall that are approximately 25 nm wide. The basal lamina does not contain visible gaps or pores. Functionally, the glomerular membrane permits the free passage of neutral substances up to 4 nm in diameter and almost totally excludes those with diameters greater than 8 nm. However, the charges on molecules as well as their diameters affect their passage into

Bowman's capsule. The human proximal convoluted tubule is about 15 mm long and 55 um in diameter. Its wall is made up of a single layer of cells, the luminal edge of which have a brush border due to the presence of microvilli. The convoluted portion of the proximal tubule drains into the straight portion, which forms the first part of the loop of Henle. The proximal tubule terminates in the thin segment of the descending limb of the loop of Henle, which has an epithelium made up of flat cells. The nephrons with glomeruli in the outer portion of the renal cortex have short loops of Henle, whereas those with glomeruli in the juxtamedullary region of the cortex have long loops extending down into the medullary pyramides. In humans, only 15% of the nephrons have long loops. The total length of the thin segment of the loop varies from 2 - 14 mm in length. It ends in the thick segment of the ascending limb, which is about 12 m.m in length. The thick ascending limb of the loop of Henle reaches the glomerulus of the nephron from which the tubule arose and passes close to its afferent arteriole, the wall of which contains the renin secreting juxtaglomerular cells. At this point, the tubular epithelium is modified histologically to form the macula

densa. The macula densa is arbitarily designated as the point where the loop of Henle ends and the distal convoluted tubule begins. The juxtaglomerular cells, the macula densa, and a few granulated cells between them are known collectively as the juxtaglomerular apparatus. The distal convoluted tubule is about 5 mm long. Its epithelium is lower than that of the proximal tubule, and although there are a few microvilli, there is no distinct brush border. The distal tubules coalesce to form collecting ducts that are about 20 mm long and pass through the renal cortex and medulla to empty into the pelvis of the kidney at the apexes of the medullary pyramids. The total length of the nephrons, including the collecting ducts, ranges from 45 to 65 mm. Ganong, (1979).

Biosynthesis of Adrenocortical Hormones:

The hormones of the adrenal cortex are derivatives of cholesterol. The contain the cyclopentanoperhydrophenanthrene nucleus. The adrenocortical steroids are of 2 structural types: those that have a 2 - carbon side chain attached at position 17 of the D ring and Contain 21 carbon atoms ("C 21 steroids"), and those that have a keto or