RENIN-ANGIOTENSIN SYSTEM IN HYPERTENSION

Thesis

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Biochemistry

By

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CONTENTS

LIST OF ABBREVIATIONS

Ab	: Antibody
ACEA	: Angiotensin I converting enzyme activity
ACTH	: Adrenocorticotrophic hormone
Ag	: Antigen
ANOVA	: Analysis of variance
APA	: Aminopeptidase A
BP	: Blood pressure
CO	: Cardiac output
DBP	: Diastolic blood pressure
E_2	: Estrogen
ERT	: Estrogen replacement therapy
HPLC	: High performance liquid chromatography
Kg	: Kilogram
MAP	: Mean arterial pressure
mEq	: Milli equivalent
min	: Minute
Na^+/K^+	: Sodium/potassium
NaCL	: Sodium chloride
Ng	: Nanogram
NSB	: Non-specific binding
P	: Probability
Pg	: Picogram
PPH	: Postprandial hypertension
PRA	: Plasma renin activity
(r)	: Correlation coefficient
RAS	: Renin angiotensin system
RIA	: Radioimmunoassay

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SBP : Systolic blood pressure
SE : Standard error
SOHT : Sons of two hypertensive parents
SONT : Sons of two normotensive parents
SVR : Systemic vascular resistance
TPR : Total peripheral resistance
µmol : Micromole

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ABSTRACT

Hypertension is a significant risk factor for both coronary artery and cerebrovascular diseases. It is probable that a great many factors contribute to the raised blood pressure as salt intake, obesity, insulin resistance, renin angiotensin aldosterone system (RAAS) and endothelial dysfunction.

This study aimed to assess the renin-angiotensin aldosterone system as well as its correlation to arterial blood pressure (systolic and diastolic) in hypertensive patients with or without renal failure. Patients were allocated into 2 groups: GrII (essential hypertensive patients), included 28 newly discovered hypertension. GrIII: (renal hypertensive patients), included 42 hypertensive patients associated with renal failure undergoing hemodialysis. In addition 32 normal healthy subjects as control group (GrI). Serum urea, creatinine, glucose, triglycerides, cholesterol, sodium, potassium, angiotensin converting enzyme (ACE), aldosterone and plasma renin activity were determined in all groups.

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A highly significant elevations of systolic blood pressure (SBP), diastolic blood pressure (DBP) and pulse were found in GrII and GrIII in both males and females as compared to controls ($P<0.001$).

A highly significant elevation in serum ACE in both males and females or group II and group III as compared to group I ($P<0.00$).

Serum aldosterone level was significantly elevated in males and females of group III as compared to group I and group II ($P<0.001$).

Plasma renin activity in males and females of group III and females of group II was increased significantly as compared to group I ($P<0.001$).

In males, SBP and DBP were positively correlated to renin ($r=0.52$, 0.420), aldosterone ($r=0.39$, 0.32), ACE ($r=0.7$, 0.62).

In females SBP and DBP were also positively correlated to renin ($r=0.24$, 0.31), ACE ($r=0.54$, 0.31) and SBP was correlated to aldosterone ($r=0.38$).

Serum aldosterone and plasma renin activity are good discriminators between GrII (essential hypertensive patients) and GrIII (renal hypertensive patients). Serum potassium, cholesterol, ACE are the most significant biochemical markers in hypertension with or without renal failure.

Key Words:

Renin-angiotensin System-Aldosterone-Angiotensin converting enzyme-Essential hypertension-Renal failure.

I declare that this thesis has been composed by my self and the work there in has not been submitted for a degree at this or any other university.

Mohamed Abdullah Mahmoud Atwa


To My Dear Parents

RENIN-ANGIOTENSIN SYSTEM IN HYPERTENSION

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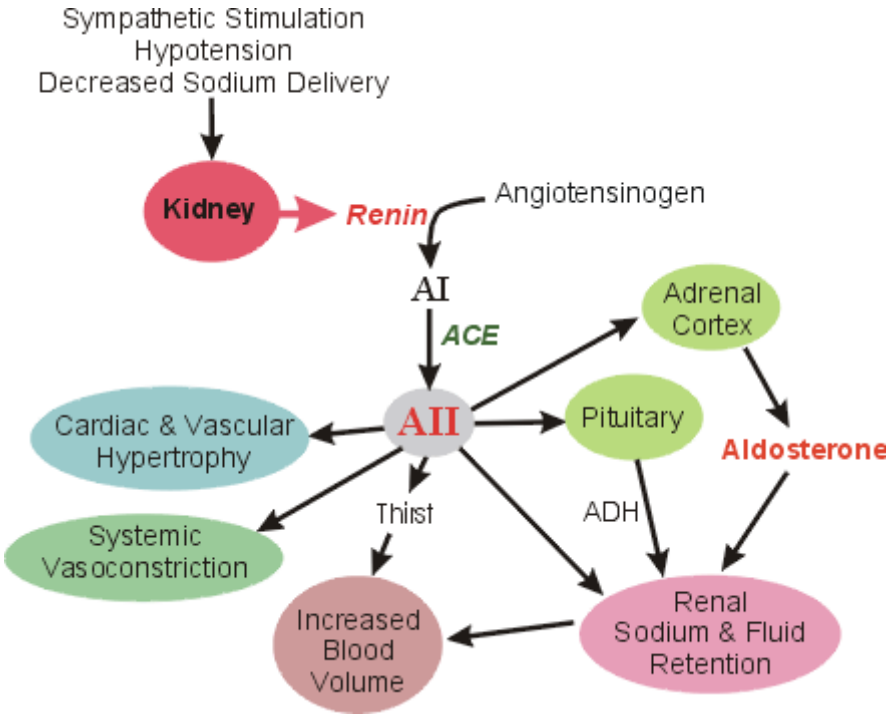
INTRODUCTION AND AIM OF THE WORK

Renin-angiotensin system:

Renin is an acid protease synthesized and secreted by juxtglomerular cells of the kidney in response to a variety of stimuli. Renin is initially synthesized as preprorenin, which is converted in Kidney and in the plasma to the active enzyme . Renin is secreted when pressure falls and sodium delivery decrease and directly inhibited by angiotensin II. Once elaborated into the circulation, renin acts on its substrate angiotensinogen A hepatically synthesized alpha Z-globulin, to generate the decapeptide angiotensin I. Angiotensin I appears to be physiologically inactive. However, is convertion by angiotensin converting enzyme (angiotensin converting enzyme is found in most tissue in the body and circulate in plasma). Thus, theoretically, the conversion of angiotensin I to angiotensin II could take place anywhere in the circulatory system. However, the activity of the enzyme in the lung is particularly high,(70-80 % of angiotensin I is converted to angiotensin II) to the octa peptide angiotensin II. Angiotensin II is an extremely potent vasopressor and also stimulate aldosterone secretion by the

adrenal gland. Additionally, the peptide has some direct sodium retaining effect in the kidney. Angiotensin II does partially suppress renin secretion by a direct action on the juxtaglomerular cells. In some tissue, angiotensin II is converted to the heptapeptide angiotensin III, which is also biologically active **(Sayago and Beierwaltes, 2001)**.

The renin-angiotensin system is activated in states characterized by volume depletion and/or hypotension and is suppressed in states characterized by volume depletion and hypertension **(Tan et al., 2000)**.



Angiotensin II acts directly on the adrenal cortex to stimulate aldosterone secretion, and in most situations it is the most important regulator of aldosterone secretion. It thus plays a central role in regulating sodium balance for example, during dietary sodium depletion, extracellular fluid volume is reduced owing to osmotic transfer of water to the intracellular fluid compartment. subsequent stimulation of the renin-angiotensin system is important in two ways. Its vasoconstrictor actions help to maintain blood pressure in the face of reduced extracellular fluid volume, whereas its action to stimulate aldosterone secretion and thus sodium retention allows volume to be conserved **(Cholewa and Mattson, 2001)**.

The intrarenal actions of angiotensin II also promote sodium retention. Angiotensin II preferentially constricts efferent arterioles, thus maintaining the glomerular filtration rate during hypovolemia and arterial hypotension. The subsequent fall in peritubular capillary hydrostatic pressure aids proximal tubule reabsorption of sodium and water. Angiotensin II also stimulates proximal tubule sodium reabsorption . reduced loop of Henle flow-due to reduced glomerular filtration rate and increased proximal reabsorption-and reduced vasa recta flow aid countercurrent multiplication and urinary concentration