STUDY OF THE EFFECTS OF CAPTOPRIL ON INSULIN DEPENDANT DIABETIC PATIENTS WITH DIABETIC NEPHOPATHY

THESIS
SUBMITTED FOR PARTIAL FUFILMENT FOR
THE MASTER DEGREE IN INTERNAL MEDICINE

BY

TAREK ABDEL HAMID MOSTAFA DOWOD

SUPERVISORS

DR. SAYED M. SHALABY
ASSISTANT PROFESSOR OF INTERNAL MEDICINE
FACULTY OF MEDICINE- AIN SHAMS UNIVERSITY

CO-SUPERVISORS

DR. NEHAD AMER
LECTURER OF INTERNAL MEDICINE

FACULTY OF MEDICINE
AIN SHAMS UNIVERSITY
1993

بســـم الله الرحمن الرحيم

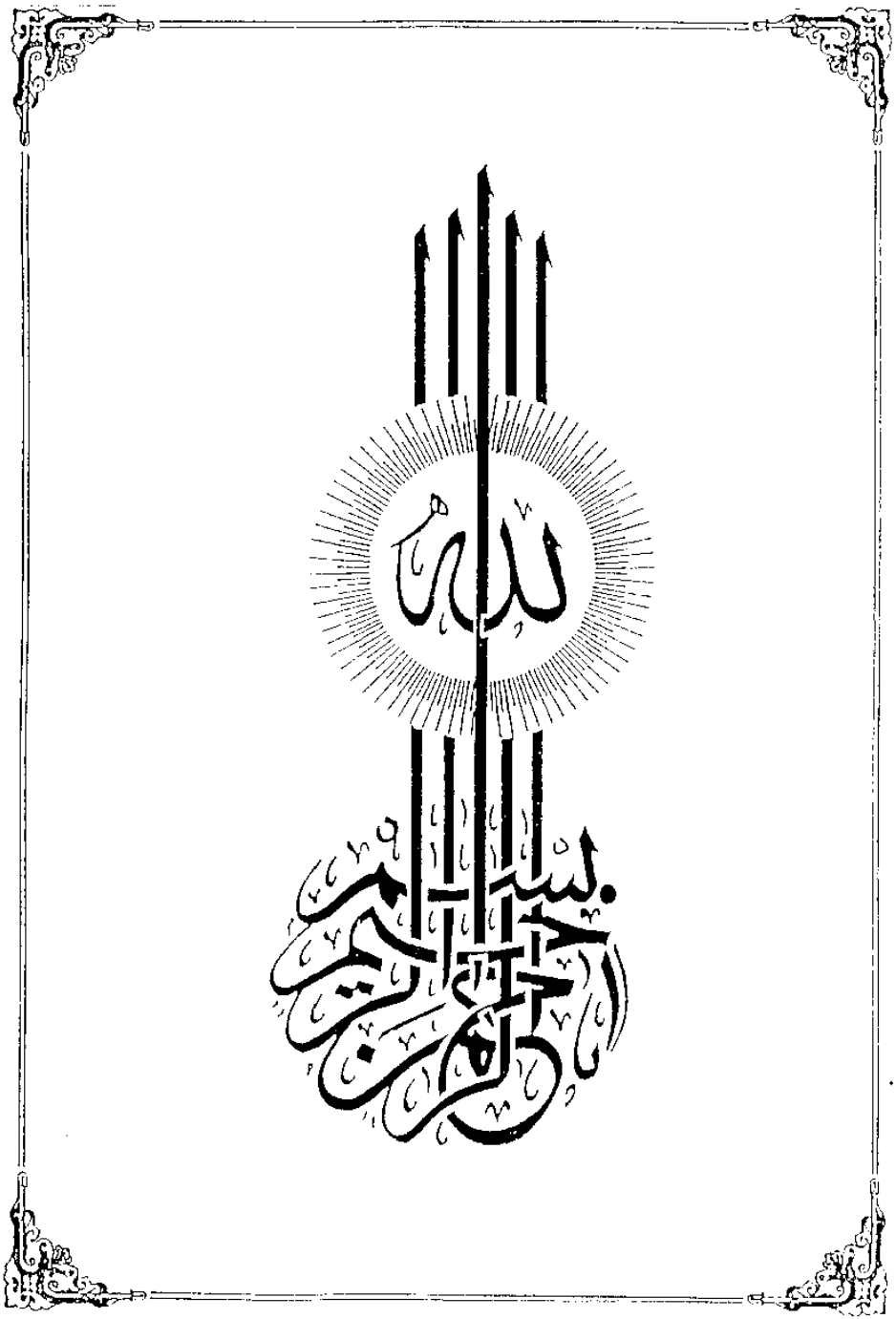
سبحانك

لا علم لنا إلا ما علمتنا
إنك أنــت العليم الحكيم

صدق الله العظيم

قرآن كريم

** سورة البقره آية ٣٢ **



ACKNOWLEDGEMENT

thanks to GOD, who can do my life in the perfect way.

I would like to express my deep gratitude to DR.SAYED M.SHALABY assistant professor of internal medicine, Ain Shams University, his planning, continuous guidance and encouragement.

I wish to extend deep sincere thanks to DR.NEHAD AMER, lecturer of internal medicine, Ain Shams University for her advice and help.

I wish to express my deep gratitude to professor DR.KHALID ZAHRANI, prof. of dermatology, professor DR.KHALID GHARIB, prof. of internal medicine and DR.AJLAL M.SH.HAMED assistant prof. of internal medicine , Alminia University for their great help and support.

THIS THESIS IS DEDICATED
TO MY WIFE WHO SUFFERS
A LOT DURING PREPARATION
OF MY THESIS

CONTENTS

LIST OF ABBERVATIONS

IDDM	INSULIN DEPENDENT DIABETES MELLITUS.
NIDDM	NON INSULIN DEPENDENT DIABETES MELLITUS.
JOD	JUVENILE ONSET DIABETES.
MOD	MATURITY ONSET DIABETES.
FBS	FASTING BLOOD SUGAR.
PPBS	POST PRANDIAL BLOOD SUGAR.
GFR	GLOMERULAR FILTRATION RATE.
RPF	RENAL PLASMA FLOW.
PRA	PLASMA RENIN ACTIVITY.
UAE	URINE ALBUMIN ECCRETION.
RF	RENAL FAILURE.
ESRF	END STAGE RENAL FAILURE.
CAPD	CONTINUOUS AMPULATORY PERITONEAL DIALYSIS.
IHD	ISCHEMIC HEART DISEASE.
CV	CARDIO VASCULAR.
LBBB	LEFT BUNDLE BRANCH BLOCK.
RBBB	RIGHT BUNDLE BRANCH BLOCK.
ACE	ANGIOTENSIN CONVERTING ENZYME.
ACE-I	ANGIOTENSIN CONVERTING ENZYME INHIBITORS.
B.P	BLOOD PRESSURE.
HBP	HYPERTENSION.
NA	SODIUM
K	POTASSIUM
PN	PERPHIERAL NEUROPATHY
SD	STANDARD DEVIATION.

INTRODUCTION AND AIM OF THE WORK

Roughly 35% of all IDDM patients develop diabetic nephropathy. This clinical syndrome is characterized by persistent albuminuria more than 300mg/24h,a relentless decline in GFR and raised arterial BP.[ANDERSEN A.R.et al 1978 and PARVING et al 1981].

The mortality in patients suffering from diabetic nephropathy is up to 100 times that of the age and sex matched background population and this is mainly due to an enormous excess of deaths from end stage renal disease. [BORCH JOHNSEN et al 1985].

Arterial HBP enhances the development of diabetic nephropathy and antihypertensive treatment reduces albuminuria and diminishes the rate of decline in the GFR. thereby postponing ESRF in patients with diabetic nephropathy. [MOGENSEN C.E. 1982 and PARVING H.H.et al 1983].Clinical studies of treatment with ACE-1 in patients with DM have shown the clinical efficacy of these agents.

Preliminary studies shown that they have no adverse effects on metabolic control of diabetes or lipids.They may also offer superior protection of renal function compared with other antihypertensive drugs. [MARSHAL S.M. 1991].

This would be an additional advantage in patients with IDDM because a third of these patients develop diabetic nephropathy. [HAFFNER S.M. et al 1990].

The aim of this work was to study the effect of ACE-1 on IDD patients with established diabetic nephropathy to find out any role in reversing, partially reversing or some recovery of the process.

REVIEW OF LITERATURE

DIABETES MELLITUS.

DM is one of the most widely distributed metabolic disorder and occurs in almost all population of the world at a variable prevalence. DM has been known from ancient times and was first reported around 1500 B.C. in the papyrus ebers found at LUXOR in EGYPT as a condition causing polyuria. the excessive indulgence of the patients in eating and drinking lead it be to described about 6 A.D. as a disease of the rich. [MOHSEN A.F. 1990].

Aretaeus of cappedocia (about 81-138 A.D.) gave the name diabetes to this condition which in GREEK mean to run through a siphon. [MOHSEN A.F. 1990].

It was in 1889 that VON MERING and MINKOWSKI produced diabetes in dogs after pancreatic extirpation and this was a great landmark since it showed that in diabetes the pancreas was the involved tissue. [MOHSEN A.F. 1990].

In 1921, BANTING and BSET produced a pancreatic extract which had a hypoglycemic effect and called it insulin. [MOHSEN A.F. 1990].

In the last 30 years great progress has been made in almost all aspects of diabetes though many questions remain un answered.

Most books define diabetes as a syndrome characterized by persistent elevation of the blood sugar above the normal range. [IRVINE W.J. 1977 and national diabetes data group 1979].

Several classification of diabetes have existed over the past 20-30 years, an earlier classification was based on the age of onset and

diabetes was classified into two main groups:

a) Juvenile onset diabetes. (JOD) and

b) Maturity onset diabetes. (MOD).

as there was several problems of grouping patients only on the basis of their age and many patients could not be fitted in either of the two groups.

IRVINE suggested a classification on the need for treatment and aetiology. This classification was adapted by the national diabetes data group (NDDG 1979).

CLASSIFICATION OF DM.

TYPE 1 DM.	TYPE 2 DM.	IMPAIRED GLUCOSE TOLERANCE.
A) ary DM.		
IDDM.	NIDDM	inherited endocrine disorders.
Main features		
IDJODM	NIDMOD with ICA negative	inborn error of metabolism.
IDMODM	NIDJODM with ICA negative	syndromes associated with pancreatic degeneration.
ICA ++ initially controlled by oral hypoglycemic agents but require insulin in late years.		syndromes associated with insulin resistance.
b) **2ndry DM:**		
gestational DM. hormonal imbalance drug induced. pancreatic disease tropical disease. liver disease.		

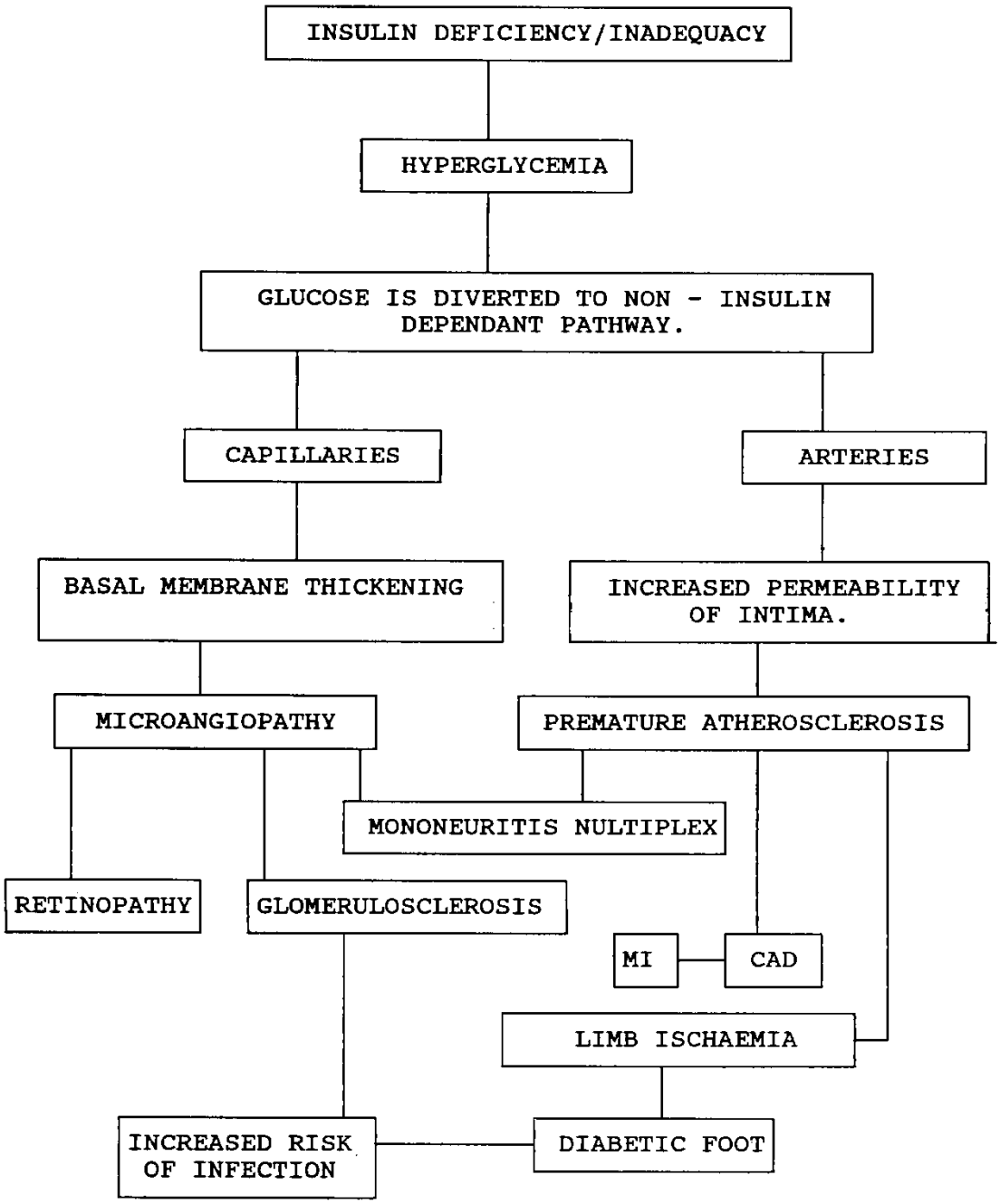
ICA = ISLET CELL ANTIBODY.
IDJODM = INSULIN DEPENDANT JUVENILE ONSET DIABETES.
NIDMOD = NON INSULIN DEPENDANT MATURITY ONSET DIABETES.
type 2 DM is the commonest cause of impaired glucose tolerance.

CHARACTERISTIC OF DIFFERENT TYPES OF IDIOPATHIC DM.

[TSUJU S., et al 1971].

	type 1	type 2
age of onset (years).	any age but mainly <35 years.	any age mainly >35 year
genetic susceptibility to organ specific autoantibody.	++	-
viral infection of islets.	+	-
HLA DR3/DR4	+++	-
ICA in serum	persistent	absent
associated clinical organ specific auto immune disease.	++	-
cell mediated immunity to islets.	++	-
treatment type	insulin and diet control	diet with or without oral hypoglycemic agents.

PATHOPHYSIOLOGY AND CLINICAL MANIFESTATIONS.



An outline of the pathophysiological features leading to chronic complications of DM. [MOHSEN A.F. 1990].

MAJOR COMPLICATIONS OF DM.
[MOHSEN A.F.1990]

a) ACUTE :

1) coma/precoma
   ketoacidosis.
   hyperosmolar non ketotic coma.
   lactic acidosis.
   hypoglycemia

2) infections.

3) acute neuropathy.

b) CHRONIC :

1) DIABETIC NEUROPATHY.

2) DIABETIC NEPHROPATHY.

3) DIABETIC RETINOPATHY.

4) ATHEROMA FORMATION.

5) PEDOPATHY. (DIABETIC FOOT).