بسم الله الرحمن الرحيم

EFFECT OF ANDROGEN THERAPY ON PLASMA LIPID PATTERN

THESIS

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BY

SHERIF MONDI MOHAMED MOURAD

M.B., B., Ch.

UNDER THE SUPERVISION OF

Professor Dr.
HUSSEIN EL SAYED EL DAMASY
Prof. of Internal Medicine

Professor Dr.
SAYED MOHAMED RAAFAT
Prof. of Internal Medicine

Dr. MOHAMED FAHMY ABDEL AZIZ
Lecturer of Internal Medicine

AIN SHAMS UNIVERSITY
FACULTY OF MEDICINE
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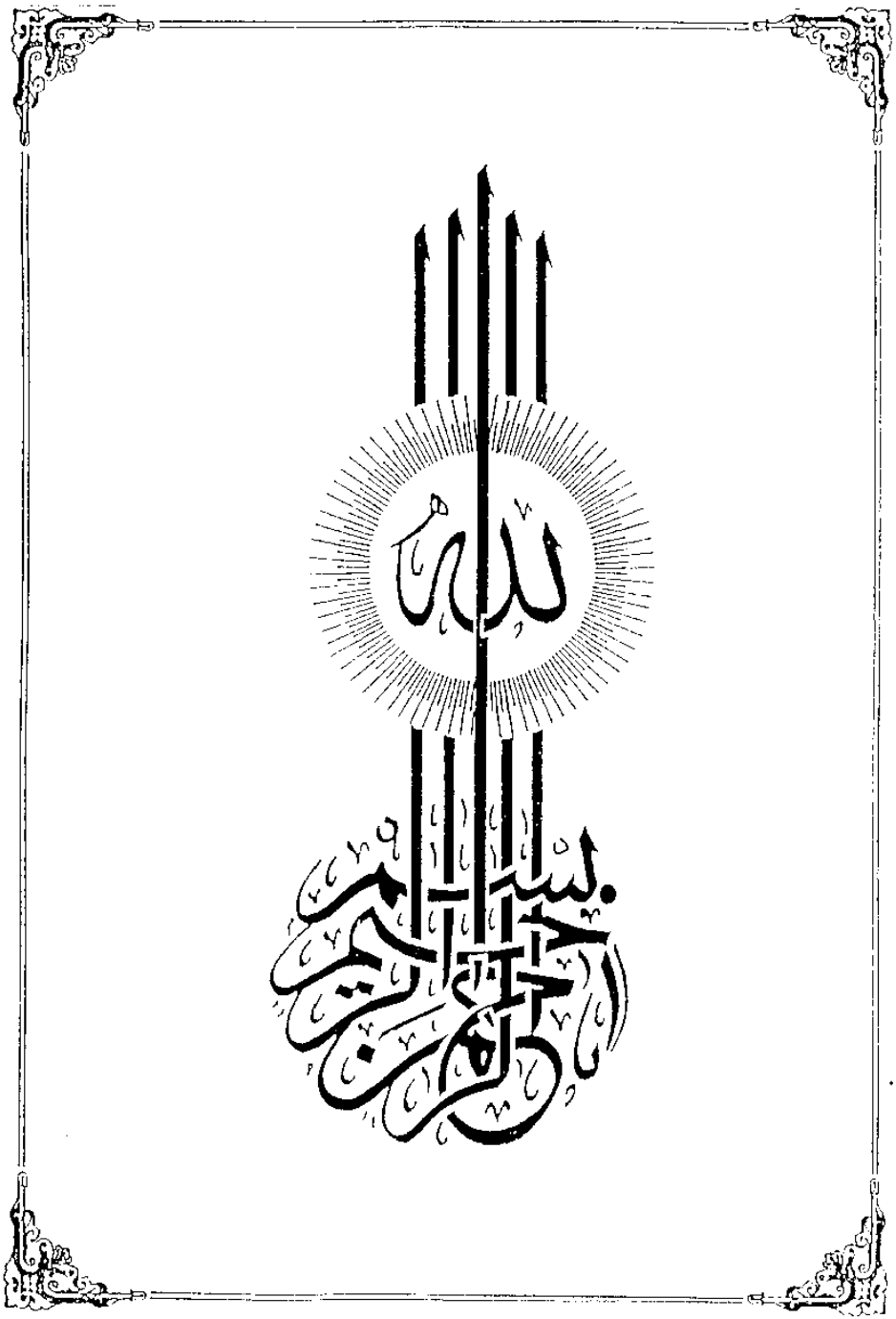

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CONTENTS

page

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INTRODUCTION AND AIM OF THE WORK

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Testosterone is one of several factors known to influence plasma lipids and lipoproteins but how the male sex hormone affects the lipoproteins is incompletely understood.

Haffner et al (1983) reported a consistent and profound reduction of high density lipoprotein cholesterol (HDLC), apolipoprotein AI and apolipoprotein AII as well as a significant increase in low density lipoprotein cholesterol (LDLC) during therapy with stanozolol, a 17- alpha methyl androgenic anabolic steroid.

While other studies by Hill et al (1980) and Nordoy et al (1979) in normal men suggested that endogenous plasma testosterone levels are closely related to lipids and lipoproteins.

It was also reported by Nordoy et al (1979) that serum testosterone levels in normal men had been positively correlated with high density lipoprotein cholesterol and total cholesterol.

In our work we used testosterone enanthate for two months to study its effect on plasma lipids of young (aged between 30 and 40 years) fertile normolipaemic males complaining of erectile failure.

We hope that this study enable us to overcome the contradictory concerning the effect of androgens on plasma lipids and lipoproteins and its relation to atherosclerosis.

The aim of this work is to study the effect of androgen therapy on plasma lipids and lipoproteins.

REVIEW OF LITERATURE

PLASMA LIPIDS AND LIPOPROTEINS

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The total lipids in human serum fall into the following fractions: triglycerols, phospholipids, cholesterol and cholesteryl esters, and , in addition , the existence of a much smaller fraction of unesterified long chain fatty acids (free fatty acids, FFA) that account for less than 5% of the total fatty acids present in the plasma (Harper et al., 1979).

Table (1)

Lipids of the blood plasma in man:

Lipid	mg/ dl Mean	Range
- Total lipids	570	360-820
- Triglycerol	142	80-180
- Total phospholipid	215	123-390
- Lecithin		50-200
- Cephalin		50-130
- sphyngomyelins		15-35
- Total cholesterol	200	107-320
- Free cholesterol(nonesterified)	25	26-106
- Free fatty acids (non esterified)	12	6- 16

(Quoted from Harper, 1979).

Practically all of the lipids of the plasma are present as lipoprotein complexes which provide the body

with a transport system for the insoluble lipids, and all lipids except for fatty acid and lysolecithin circulate in the plasma from their site of origin to their site of utilization in association with these lipid-protein complexes (Eisenberg and Levy,1975).

Lipoprotein molecule composition and apolipoproteins:

Each lipoprotein particle contains a non polar core, in which many molecules of hydrophobic lipid are packed to form an oil droplet. This hydrophobic core accounts for the most of the mass of the particle. It consists of triglycerides and cholesteryl esters in varying proportions. Surrounding the core is a polar surface coat of phospholipids that stabilize the lipoprotein particle so that it can remain in solution in the plasma. In addition to phospholipids the polar coat contains small amounts of unesterified cholesterol. Each lipoprotein particle also contains specific proteins (apoprotein) that are partly exposed at the surface(Sata et al., 1972).

The apoproteins are polypeptides. According to the ABC nomenclature, the apoproteins are classified into : A (AI & AII), B, C (C I, C.II & C. III) and E. They are prepared by delipidation of isolated lipoproteins(Harper et al.,1979).

Five groups of lipoprotein having major roles in the transport and metabolism of lipids are present in plasma: (1) Chylomicrons derived from intestinal absorption of triglycerols, (2) very low density lipoproteins (VLDL or pre- β lipoproteins) also formed to a lesser extent from dietary lipids but mainly derived from the liver for the export of triglycerol (TG), (3) low density lipoproteins (LDL or β- lipoproteins), representing a final stage in catabolism of VLDL and possibly chylomicrons, (4) high density lipoproteins (HDL or β - lipoproteins) ; involved in VLDL and chylomicron metabolism and also in cholesterol metabolism, and (5) free fatty acids (FFA) not generally classified with the other plasma lipoproteins, since their structure is different, consisting of long chain fatty acids attached to serum albumin.(Morrisset, et al.,1976).

The protein moiety of lipoproteins is known as an apolipoprotein or apoprotein, constituting nearly 60% of some HDL and as little as 1% of chylomicrons. Many lipoproteins contain more than one type of apoprotein polypeptide. They differ in their amino acid content and may be identified from their terminal amino acid residues by polyacrylamide gel electrophoresis and by immunochemical methods.(Mayes, 1977).

The two major groups of apoproteins of HDL are AI and AII. The main apoprotein of LDL is apoprotein B, which is found also in VLDL and chylomicrons. Apoprotein C-I, C-II & C-III are smaller polypeptides found in the VLDL, HDL and chylomicrons. The C apoproteins are freely transferable between VLDL and chylomicrons on the one hand and HDL on the other (Soutar et al., 1982).

The apoprotein binds to specific enzymes or transport proteins on the cell membranes, thus directing the lipoprotein to its sites of metabolism (Berman et al., 1978).

Classification and methods of separation of lipoproteins :

Lipoproteins are classified in several fractions which differ from one another in the following aspects:

- Composition of the carrier protein.
- Distribution pattern of the lipids transported by these carriers.
- Density (VLDL, LDL , HDL).
- Electric charge and antigenic property.

Use is made of these differences to separate the lipoprotein fractions (Brown et al., 1981).

There are two methods for separation of the different fractions of plasma lipoproteins: ultracentrifugation and electrophoresis (Smith et al., 1978).