List of Contents

List of Contents

List of Contents

List of Abbreviations

AA..... Arachidonic acid

ACE ..... Angiotensin Converting Enzyme

Ach..... Acetylcholine

ADMA ..... Asymmetric Dimethyl-Arginine

AGEs..... Advanced Glycation End Products

AMP..... Adenosine Monophosphate

Ang II ..... Angiotensin II

Ang II ..... Angiotensin II

ARBs..... Angiotensin 2 Receptor Blockers

AT..... Acceleration Time

AVV ..... Adeno-Associated Virus

BPH ..... Benign Prostatic Hyperplasia

CAD ..... Coronary Artery Disease

Camp..... Cyclic Adenosine Monophosphate

CASOP..... Cavernous Artery Systolic Occlusion Pressure

CC ..... Corpora Cavernosa

CDUS..... Color Doppler Ultrasonography

cGMP..... Cyclic Guanosine Monophosphate

CIMT ..... Carotid Intima-Media Thickness

COX..... Cyclooxygenase

CVD ..... Cardiovascular Disease

DAG..... 1, 2-diacylglycerol

DDAH ..... Dimethylarginine Dimethylaminohydrolase

DICC..... Dynamic Infusion Pharmacocavernosometry and Cavernosography

ED ..... Erectile Dysfunction

EDV ..... End Diastolic Velocity

List of Abbreviations

eNOS ..... Endothelial Nitric Acid Synthase

ER ..... Endoplasmatic Reticulum

ERK1/2 ..... Extracellular-Signal-Regulated Kinase 1/2

ET-1 ..... Endothelin-1

FMD ..... Flow-Mediated Dilatation

GDP ..... Guanosine Diphosphate

GS ..... Guanylate Cyclase

GTP ..... Guanosine Trisphosphate

iNOS ..... Inducible NOS

IP3 ..... Inositol Trisphosphate

LNMMA ..... NG-Monomethyl-L-Arginine

LUTS ..... Lower Urinary Tract Symptoms

MAP Kinase .. Mitogen-Activated Protein Kinase

MFR ..... Maintenance Flow Rate

MLCK ..... Myosin Light-Chain Kinase

MLCP ..... Myosin Light-Chain Phosphatase

MRI ..... Magnetic Resonance Imaging

NADPH ..... Nicotinamide Adenine Dinucleotide Phosphate

NANC ..... Non-Adrenergic Non-Cholinergic Nerves

nNOS ..... Neuronal NOS

NO ..... Nitric Oxide

PDE ..... Phosphodiesterase

PE ..... Penile Erection

PGE1 ..... Prostaglandin E1

PI3 ..... Phosphatidyl-Inositol 3

PIP2 ..... Phosphatidylinositol 4, 5-biphosphate

PKA ..... Protein Kinase A

List of Abbreviations

PLC..... Phospholipase C

PO2 ..... Partial Pressure of Oxygen

PPDU ..... Pharmaco-Penile Duplex Ultrasonography

PRMT ..... Protein Arginine Methyltransferase

PSV..... Peak Systolic Velocity

PTGIS ..... Prostacyclin Synthase

QoL..... Quality of Life

RAS ..... Renin-Angiotensin System

RhoA ..... Ras Homolog Gene Family, member A

RI ..... Resistive Index

ROCK ..... Rho-Associated Protein Kinase

ROS ..... Reactive Oxygen Species

SCF..... Slow Coronary Flow

SDMA ..... Symmetric Dimethyl-arginine

TIMI ..... Thrombolysis in Myocardial Infarction

TNF-α ..... Tumor Necrosis Factor Alpha

WKY ..... Wistar-Kyoto

List of Tables

List of Tables

List of Tables

List of Tables

List of Figures

ABSTRACT:

Background: Erectile dysfunction (ED), the inability to achieve and/or maintain an erection sufficient to permit satisfactory intercourse, is a highly prevalent disease whose aetiology is mostly vasculogenic**.** It is associated with subclinical coronary artery disease (CAD) and is nowadays considered a marker of future cardiovascular events. The higher prevalence of ED in patients with cardiovascular risk factors(CVRF) reflects the underlying endothelial dysfunction**.**

ADMA is a naturally occurring amino acid that exists as a result of proteolysis of methylated proteins. Several factors, such as oxidative stress and increased levels of low-density lipoproteins (LDLs), are responsible for induced production of ADMA in endothelial cells.

In our study, atorvastatin administration resulted in a significant decrease in ADMA levels and improvement of erectile function

Aim: To demonstratethe effect of Atorvastatin on ADMA level and erectile function in patients with normal or high LDL level vasculogenic erectile dysfunction.

Patients and Methods: The study will include 30 patients aged 30-60 years old with vasculogenic erectile dysfunction.The patients will be collected from The Andrology Outpatient Clinic – Ain-Shams University Hospitals.

Results: Among the study group 10 subjects showed moderate elevation of plasma ADMA (33.3%), 10 subjects with high level (33.3%) and 10 subjects with normal level (33.3%), while in control group only 5 subjects had high ADMA level, one subjects with moderate elevation and 24 subjects had normal level (80%)

There was high significant reduction in both ADMA and LDL level after atorvastatin treatment and significant improvement in IIEF score, However no significant change in Testosterone level

CONCLUSIONS

We demonstrated that short-term treatment with atorvastatin has great influence on plasma ADMA levels with marked improvement in lipid profile (LDL) and erectile function in both normolipidemic and dyslipidenic patients.

Keywords: erectile dysfunction, ADMA, LDL, IIEF, Testosterone, penile duplex

1. INTRODUCTION

Erectile dysfunction (ED), the inability to achieve and/or maintain an erection sufficient to permit satisfactory intercourse, is a highly prevalent disease whose aetiology is mostly vasculogenic ***(Brunner et al., 2005).***

Damage to the endothelial lining of the arterial walls impairs the nitric oxide (NO) pathway and the ability for vasodilation. Endothelial dysfunction is an important pathophysiologic factor underlying both vasculogenic erectile dysfunction (ED) and atherosclerosis in other vascular beds ***(Vlachopoulos et al., 2009).***

The presence of increased levels of ADMA in many conditions associated with ED ***(Vlachopoulos, 2008)*** as well as in men with CAD and ED ***(Elesber, 2006)*** has led to the hypothesis that elevated levels of this compound may inhibit penile NO synthesis.

Functionally, statins reverse endothelial dysfunction by decreasing the action of oxidized low-density lipoprotein (LDL) on endothelial cells, resulting in an increase of NO activity ***(McFarlane et al., 2002).*** Several studies found that statins could rapidly improve endothelial function, even before changing the lipid profile ***(Masumoto et al., 2001).***

Previous studies showed improvement of erectile function after statins administration ***(El-Sisi et al., 2013).***

Aim of the Work:

To demonstrate the effect of Atorvastatin on ADMA level and erectile function in patients with normal or high LDL level vasculogenic erectile dysfunction.

2.1. Vasculogenic Erectile Dysfunction

2.1.1. Penile Anatomy

The penis is composed of three bodies of erectile tissue running in parallel; the corpus spongiosum, encompassing the urethra and terminating in the glans penis; and the two corpora cavernosa (CC) which function as blood-filled capacitors providing structure to the erect organ ***(Andersson and Wagner, 1995)***. The penile CC are highly specialized vascular structures that are morphologically adapted to their function of becoming engorged during sexual arousal. The trabecular smooth muscle constitutes approximately 40-50% of tissue cross-sectional area, as assessed by histo-morphometric analysis ***(Nehra et al., 1998)***. There are three main arteries in the penis: cavernosal, dorsal, and bulbourethral. All three arise from a shared branch of the internal pudendal artery and provide an extensive anastomotic network ***(Yiee and Baskin, 2010)***.

Some studies performed *in vitro* experiments using the pudendal artery instead of cavernosal tissue to investigate pathophysiological aspects of ED since this artery is the major resistance to penile engorgement during sexual stimulation. Novel findings suggest that the