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## List of Abbreviations

<b>AA</b> .....	Arachidonic acid
<b>ACE</b> .....	Angiotensin Converting Enzyme
<b>Ach</b> .....	Acetylcholine
<b>ADMA</b> .....	Asymmetric Dimethyl-Arginine
<b>AGEs</b> .....	Advanced Glycation End Products
<b>AMP</b> .....	Adenosine Monophosphate
<b>Ang II</b> .....	Angiotensin II
<b>Ang II</b> .....	Angiotensin II
<b>ARBs</b> .....	Angiotensin 2 Receptor Blockers
<b>AT</b> .....	Acceleration Time
<b>AVV</b> .....	Adeno-Associated Virus
<b>BPH</b> .....	Benign Prostatic Hyperplasia
<b>CAD</b> .....	Coronary Artery Disease
<b>Camp</b> .....	Cyclic Adenosine Monophosphate
<b>CASOP</b> .....	Cavernous Artery Systolic Occlusion Pressure
<b>CC</b> .....	Corpora Cavernosa
<b>CDUS</b> .....	Color Doppler Ultrasonography
<b>cGMP</b> .....	Cyclic Guanosine Monophosphate
<b>CIMT</b> .....	Carotid Intima-Media Thickness
<b>COX</b> .....	Cyclooxygenase
<b>CVD</b> .....	Cardiovascular Disease
<b>DAG</b> .....	1, 2-diacylglycerol
<b>DDAH</b> .....	Dimethylarginine Dimethylaminohydrolase
<b>DICC</b> .....	Dynamic Infusion Pharmacocavernosometry and Cavernosography
<b>ED</b> .....	Erectile Dysfunction
<b>EDV</b> .....	End Diastolic Velocity

## List of Abbreviations

<b>eNOS</b>	.....	Endothelial Nitric Acid Synthase
<b>ER</b>	.....	Endoplasmatic Reticulum
<b>ERK1/2</b>	.....	Extracellular-Signal-Regulated Kinase 1/2
<b>ET-1</b>	.....	Endothelin-1
<b>FMD</b>	.....	Flow-Mediated Dilatation
<b>GDP</b>	.....	Guanosine Diphosphate
<b>GS</b>	.....	Guanylate Cyclase
<b>GTP</b>	.....	Guanosine Trisphosphate
<b>iNOS</b>	.....	Inducible NOS
<b>IP3</b>	.....	Inositol Trisphosphate
<b>LNMA</b>	.....	NG-Monomethyl-L-Arginine
<b>LUTS</b>	.....	Lower Urinary Tract Symptoms
<b>MAP Kinase</b>	..	Mitogen-Activated Protein Kinase
<b>MFR</b>	.....	Maintenance Flow Rate
<b>MLCK</b>	.....	Myosin Light-Chain Kinase
<b>MLCP</b>	.....	Myosin Light-Chain Phosphatase
<b>MRI</b>	.....	Magnetic Resonance Imaging
<b>NADPH</b>	.....	Nicotinamide Adenine Dinucleotide Phosphate
<b>NANC</b>	.....	Non-Adrenergic Non-Cholinergic Nerves
<b>nNOS</b>	.....	Neuronal NOS
<b>NO</b>	.....	Nitric Oxide
<b>PDE</b>	.....	Phosphodiesterase
<b>PE</b>	.....	Penile Erection
<b>PGE1</b>	.....	Prostaglandin E1
<b>PI3</b>	.....	Phosphatidyl-Inositol 3
<b>PIP2</b>	.....	Phosphatidylinositol 4, 5-biphosphate
<b>PKA</b>	.....	Protein Kinase A

## List of Abbreviations

<b>PLC</b> .....	Phospholipase C
<b>PO2</b> .....	Partial Pressure of Oxygen
<b>PPDU</b> .....	Pharmaco-Penile Duplex Ultrasonography
<b>PRMT</b> .....	Protein Arginine Methyltransferase
<b>PSV</b> .....	Peak Systolic Velocity
<b>PTGIS</b> .....	Prostacyclin Synthase
<b>QoL</b> .....	Quality of Life
<b>RAS</b> .....	Renin-Angiotensin System
<b>RhoA</b> .....	Ras Homolog Gene Family, member A
<b>RI</b> .....	Resistive Index
<b>ROCK</b> .....	Rho-Associated Protein Kinase
<b>ROS</b> .....	Reactive Oxygen Species
<b>SCF</b> .....	Slow Coronary Flow
<b>SDMA</b> .....	Symmetric Dimethyl-arginine
<b>TIMI</b> .....	Thrombolysis in Myocardial Infarction
<b>TNF-<math>\alpha</math></b> .....	Tumor Necrosis Factor Alpha
<b>WKY</b> .....	Wistar-Kyoto

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## 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 demonstrate the 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 dyslipidemic 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*).

## *Introduction and Aim of the Work*

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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