EFFICACY AND SAFETY OF ATORVASTATIN IN SEPTIC PATIENTS

Thesis

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By

Dr. Hanaa Mohamed Abd Allha Ahmed El Gendy
M.B.B.Ch., M.Sc., M.D. of Anesthesia

Under Supervision of

Prof. Dr. Alaa El din Abd Elwahab Koraa
Professor of Anesthesia and Intensive Care
Faculty of Medicine - Ain Shams University

Prof.Dr. Gamal El din Mohammad Ahmed Elewa
Professor of Anesthesia and Intensive Care
Faculty of Medicine - Ain Shams University

Dr. Mohamed Mohamed Nabil El Shafei
Assistant Professor of Anesthesia and Intensive Care
Faculty of Medicine – Ain Shams University

Faculty of Medicine
Ain Shams University
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ABBREVIATIONS

ALT ..... Alanine aminotransferase

APACHE ..... Acute Physiology and Chronic Health Evaluation

APC ..... Activated protein C

ARDS ..... Acute respiratory distress syndrome

AST ..... Aspartate aminotransferase

ATP ..... Adenosine triphosphate

BUN ..... Blood Urea Nitrogen

CD ..... Cluster of differentiation

CPK ..... Creatine phosphokinase

CRP ..... C- reactive protein

CRRT ..... Continous renal replacement therapy

CVP ..... Central venous pressure

CYP ..... Cytochrome P

DIC ..... Disseminated Intravascular Coagulopathy

DNA ..... Deoxyribonucleic acid

DO2 ..... Oxygen delivery

DVT ..... Deep venous thromboembolism

EGDT ..... Early Goal directed therapy

FiO2 ..... Fraction of inspired oxygen

GAGs ..... Glycosaminoglycans

G-CSF ..... Granulocyte colony-stimulating factor

GM-CSF Granulocyte macrophage colony-stimulating factor

HIV Human Immune Deficiency Virus

HMGB1 High-mobility group box 1

HMG-CoA 3-hydroxy-3-methylglutaryl-coenzyme A

HO Heme oxygenase

HR Heart rate

ICAM Intercellular adhesion molecule

ICU Intensive care unit

IL Interleukin

INF Interferon

LDL Low density lipoprotein

LFA Lymphocyte function-associated antigen

LPS Lipopolysaccharide

LVEF Left ventricular ejection fraction

MABP Mean Arterial Blood Pressure

MAPK Mitogen-activated protein kinase

MCP1 Monocytic chemoattractant protein

MDR Multi Drug Resistant

MHC Major Histocompatibility Complex

MIF Macrophage inhibitory factor

NO Nitric oxide

PAF Platelet activating factor

PAI-1 Plasminogen activator inhibitor-1

PaO2 Arterial O2 tension

PGE2 Prostaglandin E2

PGI2 Prostaglandin I2

POAP Pulmonary artery occlusion pressure

PPAR Peroxisome proliferator-activated receptor gama

PT Prothrombin time

PTT Partial thromboplastin time

SaO2 Arterial oxygen saturation

SBP Systolic Blood Pressure

SIRS Systemic inflammatory response syndrome

SOFA Sequential organ failure assessment

Scvo2 Central venous O2 saturation

Svo2 Mixed venous O2 Saturation

TF Tissue factor

Th cell T helper cell

TLR Toll like receptor

TNF Tumour necrosis factor

VO2 Oxygen uptake

WBC White blood cell

INTRODUCTION

Sepsis is considered one of the leading causes of mortality in the hospital setting. Although some advances have been made in treating patients with sepsis, the mortality of patients with sepsis remains extremely high **(Stephen et al., 2011).**

Sepsis is a process consisting of numerous inflammatory cascades and it is initiated by the presence of bacterial toxins and results in systemic inflammation and multiple organ and tissue damage. Cytokines have a prominent role in the defense mechanisms of the host. Their production is mediated by numerous metabolic pathways, which are independent from each other. In order to treat sepsis effectively, intervention should be made at multiple levels, as controlling just one or two pathways does not impede the overall process **(Terblanche et al., 2007).**

Inhibitors of 3-hydroxy-3-methylglutaryl coenzyme A reductase, namely statins, are a class of drugs used for their ability to lower cholesterol levels. Their primary indication is the prevention of cardiovascular disease. Recently statins have been attributed to have anti-inflammatory and immunomodulatory pleiotropic effects. They inhibit the synthesis of products of mevalonate pathway such as isoprenoids and geranyl-geranylpyrophosphate **(Gao et al., 2008).**

They also modify the intercellular interactions and the cellular chemotaxis of the immune system. Furthermore, statins reduce the release of cytokines and acute-phase proteins. They demonstrate antioxidant properties and an anti-apoptotic action,

contributing to the stabilization of the atheromatic plaque, modifying cell activity by inhibition of the expression of certain genes and participate in various other mechanisms of the inflammatory response **(Gao et al., 2008).**

Having all these properties, statins have been suggested as an adjunct in the treatment of patients with sepsis. Thus, we sought to examine the efficacy and safety of atorvastatin in the treatment of patients with sepsis.

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