Ain Shams University

Faculty of Medicine

Department of Anesthesia, Intensive Care

and Pain Management

Myocardial Dysfunction in Severe Sepsis

Essay

Submitted for partial fulfillment of the Master Degree in

General Intensive Care

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List of Abbreviations

ADP	Adenosine Diphosphate
APACHE II	Acute Physiology and Chronic Health Evaluation
ATP	Adenosine Triphosphate
Ca^{+2}	Calcium
cAMP	Cyclic Adenosine Monophosphate
CI	Cardiac Index
CK	Creatine Kinase
CK-MB	Creatine Kinase, MB Fraction
CO	Cardiac Output
cTnC	Cardiac Troponin C
cTnI	Cardiac troponin I
CVA	Cerebrovascular Accident
DNA	Deoxyribonucleic acid
ECG	Electrocardiography
ESC/ACC	European Society of Cardiology/American College of Cardiology Committee
ICU	Intensive Care Unit
IL	Interleukin
LV	Left Ventricle
LVEF	Left Ventricular Ejection Fraction
MEIA	Micro-particle enzyme immunoassay

MI	Myocardial Infarction
MICU	Medical Intensive Care Unit
MODS	Multiorgan dysfunction syndrome
NADPH	Nicotinamide Adenine Dinucleotide Phosphate.
NO	Nitric Oxide
NOS	Nitric Oxide Synthase
PAC	Pulmonary Artery Catheter
PAI-1	Plasminogen activator inhibitor-1
PAWP	Pulmonary Artery Wedge Pressure
SIMD	Sepsis Induced Myocardial Dysfunction
TAFI	Thrombin- activatable fibrinolysis inhibitor
TEE	Trans esophageal Echocardiograph
TNFα	Tumor Necrosis Factor α
TTE	Transthoracic Echocardiography
-ve	Negative
+ve	Positive

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Introduction

Septic shock is one of the main causes of admission and death in critically ill patients. Septic shock is a combination of hypovolemia, peripheral vascular dysfunction resulting in hypotension and abnormalities in the distribution of blood flow, cardiac failure, and cell dysfunction **(Levy et al., 2003).**

Importantly, the hemodynamic profile differs from patient to patient, at least regarding the macro circulatory disturbances. Some septic patients experience a high degree of hypovolemia, whereas others experience a high degree of impairment of vascular tone, and still others experience severe cardiac failure. A variety of combinations can thus exist **(Gustot, 2011).**

Sepsis-induced cardiac dysfunction is frequent and occurs early in the course of septic shock. It affects both the left and the right ventricles. It is reversible, and the degree of its severity is variable from patient to patient. The mechanisms responsible for its development are extra myocardial and intra myocardial **(Bouhemad et al., 2009).**

Treatment of sepsis-induced cardiac dysfunction should not be systematic and should be initiated in function of the real impact of this abnormality on tissue oxygenation. The treatment

is based on the inotrope administration. In any case, it is important to test short-term effects of inotropic drugs in terms of efficacy as well as in terms of tolerance before any prolonged administration **(Cavazzoni et al., 2010).**

Aim of the Essay

The aim of this essay was to highlight myocardial dysfunction in severe sepsis and its management.

Incidence and Pathophysiology of Sepsis Syndrome

Sepsis is the body's attempt to defend itself against an infection. In response to infection, the body releases a series of inflammatory and anti-inflammatory compounds that attack body tissues beyond the original infection **(Jane, 2001)**. Many factors contribute to the increasing incidence of sepsis as aggressive oncological chemotherapy, radiation therapy, and wide spread use of corticosteroid and immunosuppressive therapies for organ transplants and inflammatory diseases **(Ibrahim et al., 2000).**

Increased use of invasive devices such as surgical prostheses, inhalational equipment and intravenous and urinary catheter with the indiscriminate use of antimicrobial drugs that create conditions of overgrowth, colonization, and subsequent infection by aggressive antimicrobial resistant organisms increase the factors predispose to sepsis**.** Bed-ridden patients are at risk to develop bed sores which become infected and place them at risk of sepsis. There is genetic predisposition to sepsis as patients who possess the tumor necrosis factor-beta (TNF-beta) homozygous genotype have a higher incidence for

severe sepsis especially in males, above 40 years, and females, 20-45 years **(Shroder et al., 2000)**.

Pathophysiology of sepsis:

The first step in the induction of sepsis is the activation of phylogenetically conserved receptors that recognize invasion of the host by pathogenic microorganisms. This process is undertaken by receptors that recognize molecular structures, termed pathogen associated molecular patterns (PAMPs), that are shared by many pathogens, but not expressed by hosts. These receptors trigger intracellular signaling pathways that lead to activation of nuclear factor-kB (NF-kB) and other transcriptional regulators that in turn, lead to the transcription of a large number of genes involved in inflammation **(Zhang and Ghosh, 2001)**.

The sepsis cascade:

Multiple levels of mediators, receptors, and activation states at both cellular and molecular levels afford precise regulation of a response that is primarily intended to flood a site of microbial contamination or tissue injury with highly efficient effector cells. Inflammation is “tailored” to deal with a range of tissue injury states, from single cell death to extensive infections such as peritonitis; however, this highly potent system can overwhelm the host and can result in death from multisystem organ failure **(Brun-Buisson et al., 2000)**.

The acute phase reaction is the body's first-line inflammatory defence system, functioning without specificity and memory, and in front of, and in parallel with, the adaptive immune system. The antigen presenting cells (APCs) produce cytokines, which stimulate the synthesis of acute phase proteins [*e.g.,* C-reactive protein (CRP)] by the hepatocytes. C-reactive protein, bound to the antigen, increases the phagocytosis of the antigen either by binding to specific CRP receptors on phagocytic cells or via complement receptors **(Roitt et al., 2001)**.

Most inflammatory stimuli are controlled by a normal immune system. The human immune system is divided into two parts which constantly and closely collaborate, the innate and the adaptive immune system **(Roitt et al., 2001)**. The innate system reacts promptly without specificity and memory. Phagocytic cells are important contributors in innate reactivity together with enzymes, complement activation and acute phase proteins. When phagocytic cells are activated, the synthesis of different cytokines is triggered. These cytokines are not only important in regulation of the innate reaction, but also for induction of the adaptive immune system **(Roitt et al., 2001)**.

Complement is attached to the CRP-antigen complex. Antigen presenting cells process and present antigens in the context of human leucocytic antigen (HLA) class II for T-cell receptors (TcR) on T-lymphocytes. Cytokines from activated T-