The Role of Vasopressors and Inotropes In Septic Shock

Essay
Submitted for Partial fulfillment of Master Degree in
Critical Care Medicine

Presented By:
Waleed Elsayed Abdelfattah Shaheen
(M.B., B.Ch, 2007)

Under the Supervision of:

Prof. Dr. Gehan Fouad Youssef

Professor of Anesthesia and Critical Care Medicine
Faculty of Medicine, Ain Shams University

Dr. Mayar Hasan Elsersi

Lecturer of Anesthesia and Critical Care Medicine
Faculty of Medicine, Ain Shams University

Dr. Hany Ahmed Abd Elkader

Lecturer of Anesthesia and Critical Care Medicine
Faculty of Medicine, Ain Shams University

Faculty of Medicine
Ain Shams University
2014

بسم الله الرحمن الرحيم

وقُلِ اعْمَلُوا فَسَيَرَى اللَّهُ عَمَلَكُمْ
ورَسُولُهُ والْمُؤْمِنُونَ

صدق الله العظيم

سورة التوبة آية (105)

*First, thanks are all due to **Allah** for Blessing this work until it has reached its end, as a part of his generous help throughout our life.*

*My profound thanks and deep appreciation to **Prof. Dr. Gehan Fouad Youssef**, Professor of Anesthesia and Critical Care Medicine, Faculty of Medicine, Ain Shams University for her great support and advice, her valuable remarks that gave me the confidence and encouragement to fulfill this work.*

*I am deeply grateful to **Dr. Mayar Hasan Elsersi,** Lecturer of Anesthesia and Critical Care Medicine, Faculty of Medicine, Ain Shams university for her valuable supervision, co-operation and direction that extended throughout this work.*

*I would like to direct my special thanks to **Dr. Hany Ahmed Abd Elkader**, Lecturer of Anesthesia and Critical Care Medicine, Faculty of Medicine, Ain Shams University, for his invaluable help, fruitful advice, continuous support offered to me and guidance step by step till this essay finished.*

*I want also to thank **my family** for supporting me throughout my life.*

Waleed Elsayed Abdelfattah Shaheen

List of Contents

List of Abbreviations

ABP	: Arterial Blood Pressure
ACCP	: American College of Chest Physicians
ADH	: Antidiuretic hormone
aPC	: Activated form of Protein C
ATP	: Adenosine Triphosphate
ATS	: American Thoracic Society
C3 – C5	: Complement 3 - Complement 5
Ca2+	: Calcium
CAM	: Cell Adhesion Molecules
cAMP	: Cyclic Adenosine Monophosphate
CI	: Cardiac Index
CNS	: Central Nervous System
CO	: Cardiac Output
COHb	: Carboxyhaemoglobin
COMT	: Catechol-O-Methyltransferase
CPR	: Cardio-Pulmonary Resuscitation
CSF	: Cerebrospinal Fluid
CT	: Computerized Tomography
CVP	: Central Venous Pressure
CXR	: Chest X-Ray
DNA	: Deoxyribonucleic Acid
ECG	: Electrocardiographic
EGDT	: Early Goal Directed Therapy
ESICM	: European Society of Intensive Care Medicine
etCO2	: end-tidal CO2
FiO2	: Fraction Of Inspired Oxygen
FTc	: Flow time corrected
h	: Hour
HbO2	: Oxygenated Haemoglobin
HF	: Heart Failure
ICAM-1	: Intercellular Adhesion Molecule-1
ICU	: Intensive Care Unit
IgE	: Immunoglobulin E

List of Abbreviations (Cont.)

IL-1	: Interleukin-1
IM	: Intra-Muscular
IP3	: Inositol Phosphates 3
IP3 and IP4	: Inositol Phosphates (IP3 And IP4
ITBV	: Intrathoracic Blood Volume
IV	: Intra-Venous
K+	: Potassium
Kg	: Kilogram
Led	: Light Emitting Diodes
LiDCO	: Lithium Dilution Technique
LV	: Left Ventricle
MAO	: Monoamine Oxidase
MAP	: Mean Arterial Pressure
Mcg - µg	: Microgram
min	: Minute
mL	: Milliliter
mmHg	: Millimeters of mercury
MOF	: Multi-Organ Failure
NIBP	: Non-Invasive Arterial Blood Pressure
NICO	: Noninvasive Cardiac Output
NIRS	: Near Infra-Red Spectroscopy
NO	: Nitric Oxide
OPS	: Orthogonal Polarisation Spectral
PAC	: Pulmonary Artery Catheter
PaCO2	: Partial Pressure of Carbon Dioxide In Arterial Blood
PAI-1	: Plasminogen Activator Inhibitor-1
PAMPs	: Pathogen-Associated Molecular Patterns
PaO2	: Partial Pressure Of Oxygen In Arterial Blood
PARP	: Poly(ADP-ribose) Polymerase
PCR	: Polymerase Chain Reaction
PDI	: Phosphodiesterase
PEA	: Pulseless Electrical Activity

List of Abbreviations (Cont.)

PiCCO	: Pulse-induced continuous cardiac output
PLC-β	: Phospholipase C-β
PMNs	: Polymorphonuclear Leukocytes
PRRs	: Pattern Recognition Receptors
PVR	: Pulmonary Vascular Resistance
PVV	: Pulse Pressure Variation
rhAPC	: Recombinant Activated Protein C (drotrecogin alfa)
RNS	: Reactive Nitrogen Species
ROS	: Reactive Oxygen Species
RV	: Right Ventricle
SaO2	: Arterial Oxygen Saturation
SBP	: Systolic Arterial Pressure
SCCM	: Society of Critical Care Medicine
ScvO2	: Central Venous Oxygen Saturation
SDF	: Sidestream Dark Field
SIRS	: Systemic Inflammatory Response Syndrome
SIS	: Surgical Infection Society
SpO2	: Pulse Oximetry
StO2	: Tissue Oxygen Saturation
SV	: Stroke Volume
SVI	: Stroke Volume Index
SvO2	: Mixed Venous Oxygen Saturation
SVR	: Systemic Vascular Resistance
SVR	: Stroke Volume Resistance
SVT	: Supra-Ventricular Tachycardia
SVV	: Stroke Volume Variation
TEB	: Thoracic Electric Bioimpedance
TED	: Transesophageal Doppler
TF	: Tissue Factor
TLRs	: Toll-Like Receptors
TNF α	: Tumor Necrosis Factor Alpha
TTE	: Transthoracic Echocardiography

List of Abbreviations (Cont.)

V1	: Vasopressin 1
VASST	: Vasopressin and Septic Shock Trial
VCAM-1	: Vascular Cell Adhesion Molecule-1
VF	: Ventricular Fibrillation
VO2	: Oxygen Consumption
VT	: Ventricular Tachycardia
Wbcs	: White Blood Cells
α	: Alpha
β	: Beta

List of Figures

List of Tables

Introduction

Severe sepsis is among the most common reason for admission to intensive care units (ICUs) throughout the world. The increasing use of immunosuppressive agents, and the aging of the population have contributed to the exponential increase in the incidence of sepsis. Despite dramatic improvements in diagnostic and treatment procedures, mortality rates among septic patients remain high **(Gaieski et al., 2010).**

Sepsis is the clinical syndrome that results from a dysregulated inflammatory response to infection. Severe sepsis occurs when sepsis is accompanied by either organ dysfunction or evidence of hypoperfusion or hypotension **(Marik and Lipman, 2007).**

Septic shock results when infectious agents or mediators induced by these agents circulate in the bloodstream and produce hemodynamic decompensation. Its pathogenesis is critically dependent on activation of the innate immune response. The innate response is triggered by activation of cells that secrete inflammatory mediators including cytokines (most importantly, tumor necrosis factor [TNF], interleukin [IL]-1, and IL-6), chemokines (such as IL-8), prostaglandins, and histamine. These mediators act on vascular endothelial cells to cause systemic vasodilatation, increased vascular permeability, and neutrophil recruitment into tissues **(Annane et al., 2005).**

The initial priority in managing septic shock is to maintain a reasonable mean arterial pressure and cardiac output while the source of infection is identified and addressed, and measures to interrupt the pathogenic sequence leading to septic shock are undertaken **(Steven, 2009).**

Hemodynamic monitoring is a cornerstone in the care of the hemodynamically unstable septic patient. Its main goal is to detect cardiovascular insufficiency and give a baseline to judge the effectiveness of any applied treatment. Monitoring technologies progress from the most simple, non-invasive and intermittent to the most complex, highly invasive and continuous. However, there has been a steady trend toward less invasive monitoring to reduce the complications associated with invasive techniques **(Trzeciak et al., 2006).**

Vasoactive drugs are the mainstay of hemodynamic management of septic shock when fluids fail to restore adequate tissue perfusion. Vasoactive drugs are a group of bioactive chemicals, which change vasomotor tone through their influence on various peripheral receptors. So they largely improve perfusion pressure and preserve regional distribution of cardiac output through an increase in mean arterial pressure above autoregulatory thresholds. Most of these drugs have inotropic effects that improve oxygen delivery and cardiac output through increasing heart rate and contractility. So, understanding the pharmacological action of these drugs is crucial **(Holmes and Walley, 2009).**

Aim of The Work

Evaluating the role of vasopressors and inotropes in septic shock in intensive care unit.

Incidence, Terminology and Pathophysiology of Septic Shock

Incidence:

The incidence of sepsis varies among the different racial and ethnic groups, but appears to be highest among African-American males. The estimated annual incidence of severe sepsis over the years from 2004 to 2009 ranges from 300 to 1031/100,000. Epidemiological studies of the incidence of severe sepsis showed that incidence increased by approximately 13% each year with mortality rates ranging from 15% to 30% and more than 60% in septic shock **(Gaieski et al., 2013)**.

In the United States, sepsis is the second leading cause of death in non-coronary ICU patients, and the tenth most common cause of death overall according to data from the Centers for Disease Control and Prevention (the first being multiple organ failure). Sepsis is common and also more dangerous in elderly, immunocompromised, and critically-ill patients. It occurs in 1-2% of all hospitalizations and accounts for as much as 25% of intensive care unit (ICU) bed utilization **(Martin et al., 2003)**.

Definitions and Terminology:

Adequately defining sepsis has been an ongoing problem for many years till the the American College of Chest Physicians (ACCP) and the Society of Critical Care Medicine (SCCM) organized and held a consensus conference in 1991. It was the hope of this committee that if standardized definitions existed, earlier detection of sepsis would provide for earlier therapeutic intervention and improved outcomes **(Bone et al., 1992)**.

The committee created the new term systemic inflammatory response syndrome (SIRS). This acronym is intended to encompass the initial inflammatory process seen in sepsis as well as other non-infective processes; such as pancreatitis, major trauma and tissue injuries, hemorrhagic shock, and burn injuries. The relationship between non-infective and infective processes and SIRS is presented in **(Figure 1.1) (Bone et al., 1992)**.

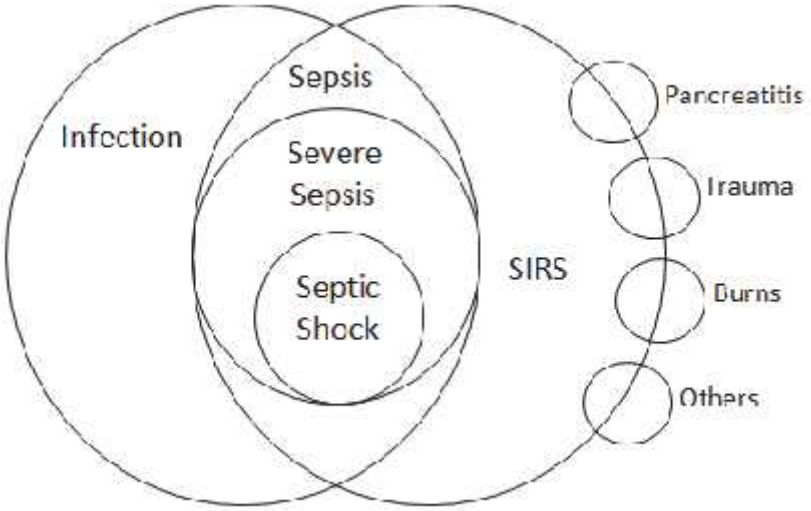

Figure 1.1: Relationship of Infective and Non-infective Processes and the Systemic Inflammatory Response Syndrome (SIRS) (Bone et al., 1992).

In 2001 during an International Sepsis Definitions Conference that included representatives from the ACCP, SCCM, American Thoracic Society (ATS), European Society of Intensive Care Medicine (ESICM), and Surgical Infection Society (SIS), and again in 2012 by the SCCM and ESICM, a practical modification of SIRS has been published, and developed an expanded view of sepsis after revisiting the literature **(Dellinger et al., 2013)**.

This conference developed the concept of a staging system for sepsis based on four separate characteristics designated by