Anaesthetic induction agents in patients with severe sepsis or septic shock

An Essay

Submitted for Partial Fulfilment of Master Degree of

Anaesthesia

By

Ahmed Mohammed Refaeey Yahia

(M.B.B.CH.)

Supervision by

Prof. Dr. Nabil Mohammed Abd El Motey

Professor of Anaesthesiology and intensive care

Faculty of Medicine-Ain Shams University

Prof. Dr. Hazem Mohammed Fawzy

Professor of Anaesthesiology and intensive care

Faculty of Medicine- Ain Shams University

Dr. Niven Gerges Fahmy

Lecturer of Anaesthesiology and intensive care

Faculty of Medicine- Ain Shams University

Faculty of Medicine

Ain Shams University

2015

سورة البقرة الآية: ٣٢

Acknowledgment

- First and foremost thanks are due to **ALLAH**, we all owe every good.
- Words will never be able to express my deepest gratitude to the soul of my mother and my beloved father, who s without his sincere emotional support and pushing me forward, this work, would not have ever been completed.
- I would like to express my sincere appreciation and gratitude to **Prof. Dr. Nabil Mohammed Abd El Motey,** Professor of Anaesthesiology and Intensive Care, for his supervision and constructive guidance to accomplish this work.
- Td like also to give my cardinal thanks to **Prof. Dr. Hazem Mohammed Fawzy,** Professor of Anaesthesiology and Intensive Care, for his continuous support and direction that make realization of this work much easier.
- I owe a particular dept. of gratitude to **Dr. Niven Gerges Fahmy,** Lecturer of Anaesthesiology and Intensive Care, for her patience, dedication and encouragement throughout this work.

Ahmed Refaeey

Contents

Subjects	Page

- List of Abbreviations I
- List of Figures IV
- List of Tables V
- Introduction 1
- Aim of the Work 4
- Review of literature
  - Chapter (1): Pathophysiology of sepsis 5
  - Chapter (2): Management of sepsis. 36
  - Chapter (3): Anaesthetic considerations of septic patients 59
- Summary 83
- References 86
- Arabic summary

List of Abbreviations

ACCP	American College of Chest Physicians
AIDS	Acquired immune deficiency system
ALI	Acute lung injury
ARDS	Adult respiratory distress syndrome
ATP	Adenosine tri phosphate
AUC	Area under the curve
CD 14	Cluster of differentiation 14
CI	Cardiac index
CNS	Central nervous system
CRP	C reactive protein
CT SCAN	Computed tomography scan
CVC	Central venous catheter
CVP	Central venous pressure
CVS	Cerebrovascular system
DIC	Disseminated coagulopathy
EEG	electroencephalogram
ELISA	The enzyme-linked immunosorbent assay
ESICM	European society of intensive care medicine
FI O_2	Fraction of inspired oxygen
GABA	Gamma amminobutryic acid
GIT	Gastrointestinal tract
HB	haemoglobin
HR	Heart rate

ICU	Intensive care unit
IL 1	Interleukin 1
INR	International normalized ratio
I.V.	intravenous
K ATP	adenosine triphosphate–sensitive potassium channel
LBP	Lipopolysaccharide binding protein
LPBS	Lipopolysaccharide binding proteins
LPS	lipopolysaccharides
MAC	Minimum alveolar concentration
MAP	mean arterial pressure
MODS	Multiple organ system failure
MR-Pro-ADM	mid regional fragment of pro adrenomedullin
NMDA	N-methyl D-aspartate
NPV	negative predictive value
NR	Not reported.
PATHFAST	A compact immunoanalyzer with superior assay performance
PCT	Procalcitonin
PCWP	Pulmonary catheter wedge pressure
PEEP	Positive end expiratory pressure
PPV	positive predictive value
Pro-ADM	proadrenomedullin
PROWESS	Protein C Worldwide Evaluation in Severe Sepsis
RSI	Rapid sequence induction

RR	Respiratory rate
Sa O_2	Oxygen saturation
SBP	Systolic blood pressure
SCCM	the Society of Critical Care Medicine
SCD14	Soluble cluster of differentiation 14
ScVO_2	Central venous oxygen saturation.
SD	Standard deviation
SOAP	Sepsis Occurrence in the acutely ill patients
SIRS	Systemic inflammatory response syndrome
STREM 1	soluble triggering receptor expressed on myeloid cells-1
Su PAR	soluble urokinase-type plasminogen receptor
SV	Stroke volume
SVR	Systemic vascular resistance
T	Temperature
TFPI	tissue factor pathway inhibitor
TNF	tumour necrosis factor
TRACE	Time-Resolved Amplified Cryptate Emission
UPAR	Urokinase-type plasminogen activator receptor
US	Ultrasound
WBC	White blood cell

List of figures

Figure No.	Description	Page No.
1	Diagram showing phases of septic shock.	21
2	The cytokine cascade in response to sepsis and exercise.	26
3	Procalcitonin (PCT) increase reflects the continuous development from a healthy condition to the most severe states of disease.	29
4	Flow chart of lactate production.	32
5	Diagnosis of systemic inflammatory response syndrome (SIRS), sepsis, severe sepsis and septic shock.	44
6	C.T scans of pancreatic abscess.	45
7	Time to hemoglobin desaturation with initial F_AO_2=0.87	64

List of Tables

table No.	Description	Page No.
1	Sepsis definitions by the American college of chest physicians (ACCP) and the society of critical care medicine.	8
2	Epidemiology of pathogenic organisms.	10
3	Etiology of severe sepsis	12
4	Description of clinical goals of selected biomarkers of sepsis.	23
5	Clinical manifestations of sepsis.	41
6	Treatment guidelines of sepsis.	47
7	Goal-directed therapy: a summary of clinical targets.	49

Introduction

Sepsis, a high mortality syndrome is a substantial health burden. In the United States, sepsis kills about 250,000 people annually, Killing more people than breast cancer, prostate cancer and AIDS combined ***(Amir Baluch et al., 2007).***

Because varying definitions of sepsis and septic shock were used in the past, standardized definitions were produced by The American College of Chest Physicians and the Society for Critical Care Medicine Consensus Conference on Standardized Definitions of Sepsis in 1991. Sepsis is defined as an infection-induced syndrome involving 2 or more manifestations of systemic inflammatory response syndrome: (1) temperature > 38 degrees or < 36 degrees; (2) heart rate > 90 beats/min; (3) respiratory rate > 20 breaths/min or PaCO2 < 32 mmHg; and (4) white blood cell count > 12000/microliter, < 4000/microliter or > 10% immature (band) forms. Septic shock is an increasingly severe complication of sepsis involving hypotension despite adequate fluid resuscitation as well as the presence of perfusion abnormalities or organ dysfunction. The latter are evident in resultant lactic acidosis, oliguria, obtundation, and so forth ***(Amir Baluch et al., 2007).***

Severe sepsis may have infective and non-infective causes. Infections is common and amenable to treat; therefore, in patients presenting with clinical signs of systemic inflammation (SIRS), an infective cause should be actively sought. Community-acquired infections in previously well patients are easier to recognize than nosocomial infections in debilitated hospitalized patients ***(Eissa et al., 2010).***

Septic patients portray instable hemodynamic states because of hypotension or cardiomyopathy, caused by vasodilation, thus, impairing global tissue perfusion and oxygenation threatening functions of critical organs. Therefore, it has become the primary concern of anaesthesiologists in conducting anaesthesia (induction, maintenance, recovery, postoperative care). The anaesthesiologist must have a precise anaesthetic plan based on a thorough pre anaesthetic evaluation ***(Seok Hwa Yoon, 2012).***

Emergent endotracheal intubation is a common procedure performed for the stabilization of critically ill patients and the majority of these patients will require an induction agent for rapid-sequence intubation (RSI). Etomidate and midazolam are the most popular drugs among the induction agents ***(Tae Yun Kim et al., 2008).***

Most intravenous anaesthetics have anti-inflammatory effects, so they respond well to septic patients. However, it may be useful to use drugs, such as ketamine or etomidate, which carry less cardiovascular instability effects than propofol, thiopental, and midazolam ***(Seok Hwa-Yoon, 2012).***

Sepsis, severe sepsis and septic shock constitute an on-going disease process of increasing severity. The patient with sepsis, severe sepsis and septic shock is at high risk patient whose underlying pathology should not be taken lightly careful planning and management of the patient is required ***(Radford, 2002).***

Aim of the work

The main goal of this work is to spot light on the pathophysiology of sepsis, management and discuss the effect of the anaesthetic induction agents on the hemodynamic of the severely septic patient.

Pathophysiology of sepsis

Sepsis is a life-threatening condition caused by an inappropriate immune response to an infection and is a major cause of death globally. Normally, when bacteria or other microbes enter the human body, the immune system efficiently destroys the invaders. In sepsis the immune system goes into overdrive, and the chemicals it releases into the blood to combat the infection trigger widespread inflammation that can ravage the entire body ***(Recknagel, 2012).***

Definitions:

Bacteremia: Is the presence of viable bacteria in the blood.

Infection: Is a microbial phenomenon in which an inflammatory response to the presence of microorganisms or the invasion of normally sterile host tissue by these organisms is characteristic.

Systemic inflammatory response syndrome (SIRS): SIRS is defined as two or more of the following variables:

- Temperature of more than 38˚C or less than 36˚C.
- Heart rate of more than 90 beats per minute.

- Respiratory rate of more than 20 breathe per minute or a PaCO2 level of less than 32mmHg.
- Abnormal white blood cell count (> 12,000/uL or < 4000/uL).

When two or more of systemic inflammatory response syndrome criteria are met without evidence of infection, patients may be diagnosed simply with SIRS ***(Amir Baluch et al., 2007).***

Severe sepsis: Is sepsis plus at least one of the following signs of organ hypo perfusion or dysfunction. Areas of mottled skin, capillary refilling requires three seconds or longer, urine output <0.5 mL/kg for at least one hour, or renal replacement therapy, Lactate >2 mmol/L, abrupt change in mental status, abnormal electroencephalographic (EEG) findings, platelet count <100,000 platelets/mL, disseminated intravascular coagulation, acute lung injury or acute respiratory distress syndrome (ARDS), and cardiac dysfunction, as defined by echocardiography or direct measurement of the cardiac index ***(Balk, 2000).***

Sepsis-induced hypotension: is defined as a systolic blood pressure SBP < 90 mmHg or mean arterial pressure MAP < 70 mm Hg or a SBP decrease > 40 mm Hg in the absence of other causes of hypotension ***(Dellinger, 2013).***