Update of Role of steroids therapy in septic shock

Essay

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بسم الله الرحمن الرحيم

وقُلِ اعْمَلُوا فَسَيَرَى اللَّهُ عَمَلَكُمْ
ورَسُولُهُ والْمُؤْمِنُونَ

صدق الله العظيم

سورة التوبة آية (١٠٥)

*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.*

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Samah Hassan Abutaleb Algamal

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List of Abbreviations

ACCP	: American College of Chest Physicians
ACEP	: American College of Emergency Physicians
ACTH	: Adrenocorticotrophic hormone.
AIDS	: Acquired Immuno-Deficiency Syndrome.
ALI	: Acute lung injury.
APACHE	: Acute Physiological Assessment and Chronic Health Evaluation.
APC	: Activated Protein C.
aPTT	: Activated partial thromboplastin time.
ARDS	: Acute respiratory distress syndrome.
AST	: Aspartate aminotransferase.
CARS	: Compensatory Anti-inflammatory Response Syndrome.
CBG	: Corticosteroid Binding Globulin.
CNS	: Central Nervous System.
CORTICUS	:Corticosteroid therapy of septic shock
CRP	: C-reactive protein .
CT	: Computerized Tomography.
CVP	: Central venous pressure
DAMPS	: Damage associated Molecular Patterns.
DIC	: Disseminated Intravascular Coagulopathy.
EBM	: Evidence Based Medicine.
ED	: Emergency Department.
EGDT	: Early Goal Directed Therapy.
ESCIM	: European Society of Intensive Care Medicine.
GCR	: Glucocorticoids receptor.
GCs	: Glucocorticoids.

List of Abbreviations (Cont.)

G-CSF	: Granulocyte Colony-Stimulating Factor.
GM-CSF	: Granulocyte-Macrophage Colony-Stimulating Factor.
HMGB	: High Mobility Group Box.
HPA	: Hypothalamic Pituitary Adrenal Axis.
HSP	: Heat Shock Proteins.
ICU	: Intensive care unit.
IL	: Interleukin.
IL-6	: Interleukins-6.
INF- α	: Tumor necrosis factor Alpha.
iNOS	: Isoform of nitric oxide synthase
INR	: International Normalized Ratio.
IV	: Intravenous.
LOC	: Loss of consciousness.
LPS	: Lipo-polysaccharide
MAP	: Mean Arterial Pressure.
MARS	: Mixed Antagonistic Response Syndrome.
MMIF	: Macrophage Migration Inhibitory Factor
MOF	: Multi-Organ Failure.
MRSA	: Methicilline Resistant Staph Aureus.
MVO_2	: Mixed Venous Saturation.
NE	: Norepinephrine.
NOD	: Nucleotide Oligomerization Domain.
NSAIDS	: Non-Steroidal-Anti inflammatory Drugs.
PAMPS	: Pathogen Associated Molecular Patterns.
PaO_2	: Arterial oxygen tension
PD	: Pharmaco-Dynamics.

List of Abbreviations (Cont.)

PK	: Pharmaco-Kinetic
PMNs	: Polymorphonuclear leucocytes.
PRRS	: Pattern Recognition Receptors.
PTT	: Partial Thromboplastin Time.
RCT	: Randomized Control Trial.
RDS	: Respiratory Distress Syndrome
ROS	: Reactive Oxygen Species.
SBP	: Systolic blood pressure
SCCM	: Society of Critical Care Medicine.
$ScvO_2$	: Venous Oxygen Saturation.
SD	: Standard deviation
SIRS	: Systemic Inflammatory Response Syndrome.
SOAP	: Sepsis Occurrence in Acutely ill Patients
SOFA	: Sepsis-related Organ Failure Assessment.
TAMOF	: Thrombo-cytopenia- Associated Multiple Organ Failure
TGF	: Transforming Growth Factor.
TLRs	: Toll Like Receptors.
TMA	: Thrombotic microangiopathy
TNF	: Tumor necrosis factor
TTP	: Thrombotic thrombocytopenic purpra
UOP	: Urine output
VACS	: Vasopressin and Corticosteroids in Septic Shock
WBC	: White blood cell

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Introduction

Sepsis is the systemic maladaptive response of the body to the invasion of normally sterile tissue by pathogenic, or potentially pathogenic, microorganisms. Shock may be defined as a ‘‘state in which profound and widespread reduction of effective tissue perfusion leads first to reversible, and then, if prolonged, to irreversible cellular injury.’’ ***(Kumar and Parrillo, 2008)***.

However, although the word, sepsis, has been used for more than 2700 years, it is only relatively recently that they have begun to understand the pathophysiology of sepsis in any depth ***(Vincent and Abraham, 2006)***.

Severe sepsis is defined as sepsis complicated by organ dysfunction, and septic shock is severe sepsis with acute circulatory failure characterized by persistent arterial hypotension unexplained by other causes ***(Levy et al., 2003)***.

Septic shock is sepsis-induced hypotension that persists despite adequate fluid resuscitation associated with elevated blood lactate levels beyond the normal limits that reflects prognosis of degree of shock ***(Dellinger et al., 2008)***, Sepsis reflects the delicate balance between defense mechanisms against invading micro -organisms and both direct and indirect effect of those micro-organisms and their product. Sepsis may not be attributable solely to an “immune system gone haywire” but may indicate an immune system that is severely compromised and unable to eradicate pathogens. Mechanisms of organ failure and death in patients with sepsis remain unknown ***(Richard et al, 2003).***

Effective antimicrobial administration within the first hour of documented hypotension was associated with increased survival in adult patients with septic shock. Despite a

progressive increase in mortality rate with increasing delays ***(Kumar et al, 2006).***

Despite the frequent focus of sepsis management within the critical care community, such management should not be limited to within the walls of intensive care or acute medical units. Surgical causes for sepsis are myriad and early treatment of sepsis is vital if the pathophysiological process is to be obtunded and the outcome improved, so it is vital that anaesthetists, surgeons and intensivists should consider all aspects of sepsis management early on in the care of patients undergoing source control surgery. One of the most challenging therapies to consider in this context (or any other relating to sepsis) is the role for supplementary steroid therapy ***(Grover and Handy, 2012)***

The rationale for the use of corticosteroids stems from two main properties: their permissive role in maintaining vasomotor tone; and their immunomodulatory effect, being either anti-inflammatory or immunosuppressive. Each of these is complex and warrants consideration in turn ***(Grover and Handy, 2012)***

Aim of the work

This essay will present the pathophysiological process & body response to sepsis, clinical parameters for patient assessment, discussing both classic ways of management of sepsis & septic shock passing to the new modalities in therapy especially steroid therapy focusing in its controversial role in sepsis.

Chapter 1

Definition and diagnosis

Introduction:

Clear definitions of sepsis are important clinically in facilitating accurate diagnosis and appropriate treatment. Clear definitions are also important for the purposes of clinical trials, insuring that only patients who do have sepsis are enrolled, reducing the risks of misclassification bias. New markers specific for infection rather than inflammation need to be developed, but currently physicians must rely on the presence of a number of signs and markers of sepsis in their diagnosis; no one variable alone is sufficient**(Cavaillon and Adrie, 2009)**.

The word ‘‘sepsis’’ comes from the Greek word ‘‘sepo" meaning decay or putrefaction, and its original usage described the decomposition of organic matter in a manner that resulted in decay and death ***(Geroulanos and Douka, 2006)***

In the Hippocratic model of health and disease, living tissues broke down by 1 of 2 processes. Pepsis was the process through which food was digested, leading to health. Sepsis, however, denoted tissue breakdown that resulted in disease. Hippocrates used this term to describe the process of abnormal tissue breakdown that resulted in a foul odor, pus-formation, and sometimes dead tissue ***(Vincent and Abraham, 2006).***

The term ‘‘shock’’ comes from the French word choquer meaning ‘‘to collide with,’’ and aptly describes the body’s response to invading microbes and, to a large extent, its disruptive effect on normal physiology. Initially used in the medical literature in the 1700s ***(Kumar et al, 2006).***

Sepsis is the systemic maladaptive response of the body to the invasion of normally sterile tissue by pathogenic, or potentially pathogenic, microorganisms. Shock may be defined as a ‘‘state in which profound and widespread reduction of effective tissue perfusion leads first to reversible, and then, if prolonged, to irreversible cellular injury.’’ ***(Kumar and Parrillo, 2008)***.

However, although the word, sepsis, has been used for more than 2700 years, it is only relatively recently that they have begun to understand the pathophysiology of sepsis in any depth ***(Vincent and Abraham, 2006)***.

With this new insight into the mechanisms underlying sepsis has came the potential for new and improved therapeutic interventions, and simultaneously a realization that the available terminology and definitions of sepsis were confusing and inadequate. In this chapter, I will outline progress in the field of sepsis definitions, and discuss possible approaches for the diagnosis.

Sepsis Syndrome:

In ***1989, Roger Bone*** proposed the term ‘‘sepsis syndrome’’, defining it as hypothermia (temperature less than 96 ◦F (35.5 ◦C)) or hyperthermia (greater than 101 ◦F (38.3 ◦C)), tachycardia (greater than 90 beat/min), tachypnea (greater than 20 breaths/min), clinical evidence of an infection site, and at least one end-organ demonstrating inadequate perfusion or dysfunction. This terminology was somewhat redundant as sepsis was already a known syndrome, and is no longer used, having being replaced by the term ‘‘severe sepsis’’ ***(Cavaillon and Adrie, 2009)***.

Systemic Inflammatory Response Syndrome:

In 1991, a Consensus Conference was held by the American College of Chest Physicians (ACCP) and the Society of Critical Care Medicine (SCCM) to *Sepsis and Non-infectious Systemic Inflammation.* Edited by J.-M. Cavaillon and C. Adrie Copyright create a ‘‘set of definitions that could be applied to patients with sepsis and its sequelae’’ ***(ACCP-SCCM Consensus Conference, 1992)***. The goal of the conference was to provide a ‘‘framework’’ to define the systemic inflammatory response to infection, and by so doing to improve the early diagnosis of sepsis, thus allowing earlier therapeutic intervention. It was realized that the lack of a single definition for sepsis created difficulties in identifying patients, particularly for clinical trials, and it was believed that having a single, universally accepted definition would facilitate ongoing research in this field ***(ACCP-SCCM Consensus Conference, 1992)***.

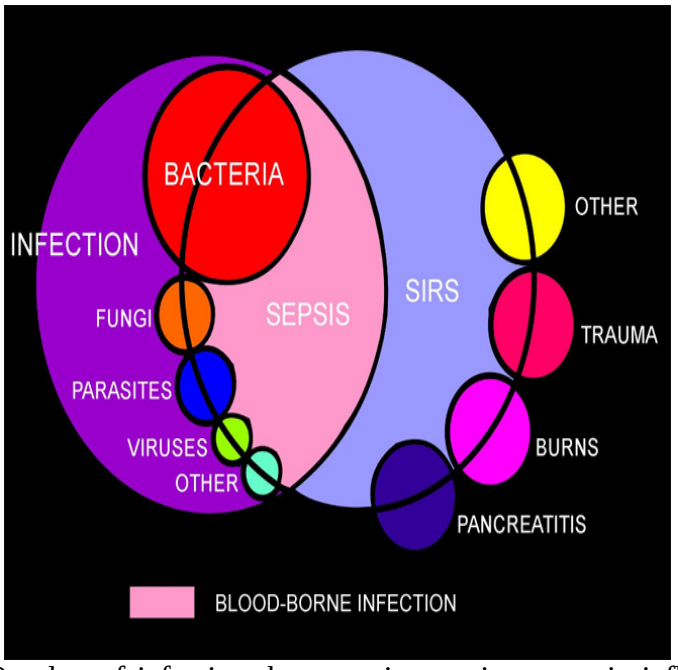

Fig. (1): Overlap of infection, bacteremia, sepsis, systemic inflammatory response syndrome (SIRS), and multiorgan dysfunction**.** ***(Bone et al, 1992)***.