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Updates of Early Goal Directed Therapy In Management Of Sepsis Syndrome In Critically Ill Burn Patients

Essay
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Contents

List of Abbreviations

(ABCDE)……..airway, breathing, circulation, disability and exposure
ALI ……..……..…Acute lung injury
APC……..…….……..……activated protein C
ARDS……...…... Adult respiratory distress syndrome
AVPU…….Alert, Voice, Pain and Unresponsive
BMZ.…….……the basement membrane zone
BNP……..……B – type Natriuretic Peptide
COPD…….…..…….chronic obstructive pulmonary disease
CORTICUS……... The Corticosteroid Therapy of Septic Shock study
CPAP……..…….. Continuous positive air way pressure
CRP…….. ...…..C-reactive protein
CVP ……...Central venous pressure
CXC……..chemokines
CXCR2……..…. chemokines receptors 2
DIC…….…...……disseminated intravascular coagulation
ED.……...……..…….Emergency Department
EGDT……..…… Early Goal-directed therapy
EPCR…….…..…..…..the endothelial cell protein C receptor
GAGs…….…… Glycosaminoglycans
G-CSF……..…..…..……granulocyte colony-stimulating factor
GFR ……..…….……..Glomerular filtration rate
GM-CSF……..……...granulocyte macrophage colony-stimulating factor
Hct ……..…….……..Hematocrit
HR…….…….…….....heart rate
ICU ……..…….…….……. Intensive care unit
IL-1…….…….…….…….……Interleukin-1
IL-1β…….……..…….……interleukin -1 beta
(IL-6)……..…….…….…….. Interleukin-6
(IL-8)……..……..……interleukin-8
(IL-10)……..…….. Interleukin-10
IVF…….……..…….…..... Intra venous fluid
MAP ……..……..… mean arterial pressure
MIF……..……..…..…Macrophage Migration Inhibitory Factor
MODS……..……..…...multiorgan dysfunction syndrome.

NIV……..……**noninvasive ventitlation**
NT-proBNP…….……..…….... **N terminal –pro-BNP**
PCT…….……..…… **procalcitonin**
PIRO ……..... (**Predisposition, infection, response, organ dysfunction)**
PLA2……..…….…..…….……. ***Phospholipase A2***
PRBC ……..…….……..…..….. ***packed red blood cells***
Pro…….....…….…….……... **prothrombin**
(rhAPC)…….…..…. **Human recombinant activated protein C**
RR……..…….……...…….***respiratory rate***
SBP……..……..***systolic blood pressure***
ScvO2 ……..……..……..… ***Central venous oxygen saturation***
SIRS……..….. ***Systemic Inflammatory Response Syndrome.***
SOAP……..…the Sepsis Occurrence in Acutely ill Patients
SSC…….....…….....…….***the Surviving Sepsis Campaign***
(s TREM)…..... Soluble Triggering Receptors Expressed on Myeloid Cells
SVR…….…..……. ***systemic vascular resistance***
TF ……..…..……. ***Tissue factor***
TNF – RA…….…..……...***TNF – receptor antagonist***
(TNF-α) ……..……..……***Tumer Necrotic Factor α***
TM……..……..……..***thrombomodulin***
TLR-2 or TLR-4 ……..……..……...***Toll-like receptors 2-4***
UO……..……..……..….….***urinary output***
US ……..…..…..……..…..…..……. ***The United States***
UV……..……..……..…..……***ultraviolet***

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INTRODUCTION

Sepsis, especially severe sepsis and septic shock are difficult healthcare problems all over the world. It has high mortality rates. Until recently outcomes remained relatively static and the incidence is increasing. The optimal treatment strategy is constantly evolving and including initial resuscitation, rapid diagnosis, timely administration of appropriate antibiotics, source identification and control and meticulous emergency department (ED) and intensive care unit (ICU) management***(Burdette et al.,2010).***

The systemic inflammatory response syndrome can be self-limited or can progress to severe sepsis and septic shock. The transition to serious illness occurs during the critical "golden hours", when definitive recognition and treatment provide maximal benefit in term of outcome. These golden hours may elapse in the emergency department, hospital ward or the intensive cares unit***. (Burdette et al., 2010).***

Sepsis is often lethal, with mortality of 25% to 30% and 40% to 70% in severe sepsis and septic shock, respectively. It is the second leading cause of death among patients in non-coronary ICUs. Furthermore, sepsis also substantially reduces the quality of life of those who survive. Despite availability of potent antibiotic the mortality with sepsis is very high. There is ongoing effort to

find out and try strategies which would improve outcome of this population**. *(Annane et al., 2003).***

A more definitive resuscitation strategy involves goal oriented manipulation of cardiac preload, after load and contractility to achieve a balance between systemic oxygen delivery and oxygen demand. End points include normalized values of mixed venous oxygen saturation, arterial lactate concentration, base deficit and pH***.(Alspach,2006).***

During the first 6 h, the goal of initial resuscitation of sepsis-induced hypoperfusion should include all of the following as one part of the treatment protocol:

- Central venous pressure (CVP) 8-12 mmHg.
- Mean arterial pressure (MAP) ≥ 65mmHg.
- Urine output ≥ 0.5ml/kg/h.
- Central venous (ScvO2) or mixed venous oxygen (SvO2) saturation≥70%.

Severe sepsis was defined as two or more systemic inflammatory response syndrome criteria: temperature< 36ºC or >38ºC, heart rate >90 beats /min, respiratory rate>20breath/min or PaCO2<35mmHg and white blood cell count <4000/mm3,>12000mm3 or 10%band, a presumed or documented source of infection, and at least one organ dysfunction; including change in mental status, acute renal dysfunction, platelets <

100/mm3, lactate>3mmol/L and total bilirubin>4 mg/DL***.(Alspach,2006).***

Septic shock was defined as two or more systemic inflammatory response syndrome criteria, a presumed or documented source of infection and a systolic blood pressure (SBP)≤90 mmHg after a fluid challenge of 20 to30 ml/kg over 30 minutes. A patient was also considered to be in septic shock if there SBP remained at least 40 mmHg below a well documented base line SBP after 20-30 ml/kg fluid challenge over 30 minutes, conversely; if a patient had a well documented base line low SBP (between 75 and 90mmHg), then they were not considered to be in septic shock if there blood pressure was in this range***.(Russell,2011).***

A critical burn injury is a unique trauma that often is accompanied by significant metabolic disturbances as well as perturbation of innate and adaptive immunity. Human skin is not only a barrier against environmental insults and against colonization of pathogenic microbes but, more importantly, it is an immune organ with significant surveillance and thermoregulatory functions***. (Schwacha, 2003).***

Patients with critical burns as defined by the American Burn Association {partial-thickness burns of greater than 10 % of total body surface area, third degree burns, electrical burns, including, lightning injury, chemical burns, inhalation injury and

burns with concomitant trauma}, should be transferred to specialized burn center as soon as possible after their initial assessment and resuscitation. A community general and plastic surgeon with an interest in burns could manage moderate burns that do not involve functionally significant body sites**. *(Michael et al., 2010).***

The diagnosis of sepsis is the first of the challenges which confront the clinician or intensive care specialist, specially because its identification, when not sufficiently early to allow intervention, may result in shock, organ failure or even patient death .Early sepsis diagnosis continues to be one of the most difficult tasks whether because the first clinical manifestation may pass unnoticed or because they can be confused with those of other non infectious processes. Further more the indirect laboratory indications (coagulation studies, glycemia, etc), usually employed to reach diagnosis of sepsis individually have little sensitivity and less specificity. Similarly the results of bacteriological examination collected on the occasion of first suspicion are not immediately available to guide specific therapy***.(Paulo el al., 2003).***

Sepsis syndrome is a complex condition that occurs as a result of the systemic manifestation of infection. It is associated with high mortality and morbidity risks for critically ill patients. Assessment and monitoring aimed at early recognition and treatment on the basis of evidence based guidelines which are evocated for patients with severe sepsis. Awareness of risk factors, clinical symptoms, signs, pathophysiology and updates of management of sepsis to promote the best practices for sepsis care in intensive care unit. ***(Angus et al., 2001).***

Sepsis remains a major cause of death in burn victims today. Many patients are susceptible to the development of systemic infections as burn patients. Severe dysfunction of the immune system, the possibility of a prolonged hospitalization and invasive diagnostic and therapeutic procedures, all contribute to sepsis.***(Roberts et al., 2001).***

Sepsis incidence:

Sepsis syndrome is a frequent cause of intensive care unit (ICU) admission and may also develop in patients admitted to the ICU for other reasons. In addition, the incidence of sepsis has increased over the past few decades despite advances in supportive care and the hospital case fatality rate for patients with sepsis remains high. Patients with sepsis are also at risk for

complications such as acute lung injury and multisystem organ failure. ***(Rivers and Ahrens, 2008).***

Sepsis is the leading cause of mortality in critically ill patients. Delay in diagnosis and treatment often results in rapid progression to circulatory collapse, multiple organ failure and eventually death. Therefore, accurate and early diagnosis will limit morbidity, reduce costs and improve patients' outcome**.** It remains a leading cause of death both worldwide and in the United States (US). It is estimated that nearly 1,000,000 cases of sepsis occur each year, with 750,000 of these falling into the high-risk group of severe sepsis and septic shock. This group carries mortality rates that range from 20% for sepsis to 40% for sever sepsis and to > 60% for septic shock**.** ***(Martin et al., 2003).***

In the United States(US), 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. ***(Burn et al., 2004).***

Infectious complications and sepsis are still the most important reasons of mortality in burn centers. Therefore not only bacterial infections should be considered as the source of infection, fungal colonization and infection gain a rising

importance in the management of sepsis in burn patients. Burn patients are at the highest risk for mycoses even more than oncologic and transplant patients. Due to compromised immune defense and large wound surfaces burn patients are predisposed for acquiring fungal organisms. The broad use of topic and systemic antibiotic agents either as prophylaxis or in case of confirmed bacterial infection further facilitates the development of mycoses .***(Ballard et al ., 2008).***

The skin dysfunction or total loss may cause infection, loss of body heat and increased evaporative loss of water. The systemic effect of burn injuries includes the release of inflammatory cytokines. The patients may develop sepsis based on these alterations. It is reported that sepsis patients after burn injury may develop multiple organ failure on 8th day of admission on average***. (Maike et al., 2009).***

Sepsis can be a response to any class of microorganism. Microbial invasion of the blood stream is not essential for the development of sepsis. Local or systemic spread of microbial signal molecules or toxins can also elicit a response. The occurrence of gram-negative sepsis has diminished over the years to 25-30% in year 2000. Gram-positives account for the majority of cases up to 30-50%. In 11-19% cases, the etiology is polymicrobial in nature. Fungi, Viruses and parasites account for 1- 4% but their frequency could be underestimated. Lastly cultures

may be negative in 30% of cases, mainly in patients with community-acquired sepsis who are treated with antibiotics before admission. (***Figure 1***). ***(Annane et al., 2003).***

The source of infection is usually endogenous. Infections of the chest, abdomen, genitourinary system and primary blood stream cause more than 80% of sepsis. Rates of pneumonia, bacteremia and multiple site infection have steadily increased over time whereas abdominal infections have remained unchanged and genitourinary infections have decreased**.** ***(Alberti et al., 2002).***

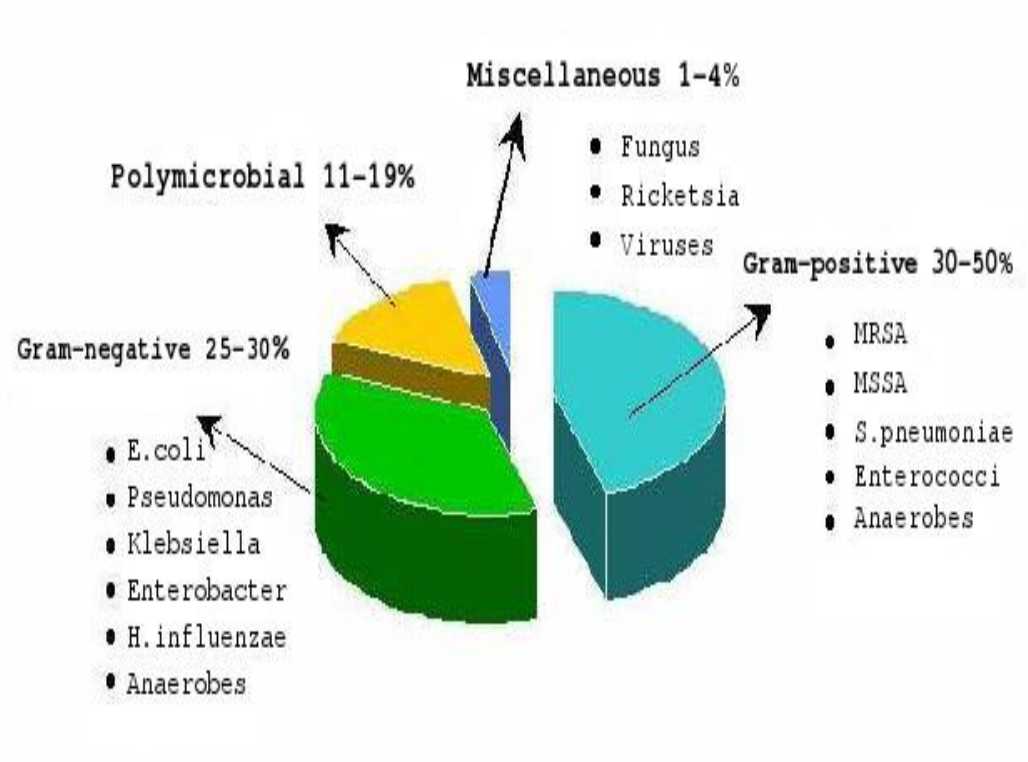

Figure (1): *Etiology of Sepsis.* ***(Annane et al., 2003).***