Ringer Lactate Versus Voluven In Sepsis In Intensive Care Unit Patients

Thesis

Submitted For Partial Fulfillment of Master Degree In Critical Care

By

Raed Emad El-dain Ali

M.B.B.Ch., Faculty of Medicine, Ain Shams University

Supervised by

Prof. Dr. Mohamed Saeed Abd-Aziz

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

Dr. Mohamad Mohamad Kamal Abdallah

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

Faculty of Medicine
Ain Shams University
2019

سورة البقرة الآية: ٣٢

Acknowledgment

First and foremost, I feel always indebted to **ALLAH,** *the Most Kind and Most Merciful.*

I'd like to express my respectful thanks and profound gratitude to **Prof. Dr. Mohamed Said Abd-Aziz,** *Professor of Anesthesia and Intensive Care Faculty of Medicine, Ain Shams University for his keen guidance, kind supervision, valuable advice and continuous encouragement, which made possible the completion of this work.*

I am also delighted to express my deepest gratitude and thanks to **Dr. Mohamad Mohamad Kamal Abdallah,** *Lecturer of Anesthesia and Intensive Care Faculty of Medicine, Ain Shams University, for his kind care, continuous supervision, valuable instructions, constant help and great assistance throughout this work.*

Raed Emad El_dain Ali

List of Contents

List of Tables

List of Figures

List of Abbreviations

Abb.	Full term
ALI	Acute Lung Injury
ARDS	Acute Respiratory Distress Syndrome
AUC	Area under the curve
CVP	Central venous pressure
CVP	Central venous pressure
DVT	Deep vein thrombosis
ESICM	European Society of Intensive Care Medicine
HES	Hydroxyethyl starch
ICU	Intensive care unit
LMWH	Low-molecular weight heparin
LODS	Logistic Organ Dysfunction System
LOS	Length of stay
MAP	Mean arterial pressure
qSOFA	Quick-SOFA
rhAPC	Recombinant Human Activated Protein C
SCCM	Society of Critical Care Medicine
SDD	Selective Digestive Tract Decontamination
SIRS	Systemic Inflammatory Response Syndrome
SOFA	Sequential Organ Failure Assessment
SUP	Stress Ulcer Prophylaxis
TNF	Tumor necrosis factor
UFH	Low-dose unfractionated heparin

INTRODUCTION

Sepsis, a syndrome of physiologic, pathologic, and biochemical abnormalities induced by infection, is a major public health concern ***(Dellinger et al., 2013).***

The reported incidence of sepsis is increasing, likely reflecting aging populations with more comorbidities, greater recognition, and, in some countries, reimbursement-favorable coding. Although the true incidence is unknown, conservative estimates indicate that sepsis is a leading cause of mortality and critical illness worldwide. Furthermore, there is increasing awareness that patients who survive sepsis often have long-term physical, psychological, and cognitive disabilities with significant health care and social implications ***(Vincentet al., 2014).***

Sepsis should be defined as life-threatening organ dysfunction caused by a dys-regulated host response to infection. For clinical operationalization, organ dysfunction can be represented by an increase in the Sequential [Sepsis-related] Organ Failure Assessment (SOFA) score of 2 points or more, which is associated with an in-hospital mortality greater than 10% ***(Kaukonen et al., 2015).*** Adult patients with suspected infection can be rapidly identified as being more likely to have poor outcomes typical of sepsis if they have at least 2 of the following clinical criteria that together constitute a new bedside clinical score termed quick-SOFA (qSOFA): respiratory rate of

22/min or greater, altered mentation, or systolic blood pressure of 100 mm Hg or less ***(Vincent et al., 2015).***

Patients with severe sepsis may experience ineffective arterial circulation due to the vasodilatation associated with infection or impaired cardiac output. Poorly perfused tissue beds result in global tissue hypoxia, which is often found in association with an elevated serum lactate level. A serum lactate value greater than 4 mmol/L (36 mg/dL) is correlated with increased severity of illness and poorer outcomes even if hypotension is not yet present. As such, patients who are hypotensive or have a lactate greater than 4 mmol/L (36 mg/dL) require intravenous fluids to expand their circulating volume and effectively restore perfusion pressure ***(Dellinger et al., 2013).***

Fluid resuscitation should be commenced as early as possible in the course of sepsis. Requirements for fluid infusion are not easily determined so that repeated fluid challenges should be performed ***(Vincent and Gerlach, 2014).***

Fluid challenge is a term used to describe the initial volume expansion period in which the response of the patient to fluid administration is carefully evaluated.

During this process, large amounts of fluids may be administered over a short period of time under close monitoring to evaluate the patient's response. Fluid challenges require the definition of four components: 1) the type of fluid to be

administered; 2) the rate of fluid infusion (e.g., 500 mL to 1,000 mL over 30 minutes); 3) the end points (e.g., mean arterial pressure of >65 mm Hg, heart rate of <110 beats per minute); and 4) the safety limits (e.g., development of pulmonary edema). Maintenance fluid increases typically alter only the rate of administration of continuous fluids ***(Schierhout and Roberts, 1998).***

The Surviving Sepsis Campaign guidelines recommend the use of either colloids or crystalloids, but high-molecular-weight hydroxyethyl starch (HES) may cause acute kidney failure in patients with severe sepsis, as observed in two randomized trials. Those trials had substantial limitations, and participants received HES solutions with a molecular weight of 200 kD and a substitution ratio (the number of hydroxyethyl groups per glucose molecule) of more than 0.4. These solutions have largely been replaced by HES solutions with a lower molecular weight and a lower substitution ratio, HES 130/0.4. There are limited data about the effects of HES 130/0.4 in patients with severe sepsis, and its routine use has recently been discouraged ***(Hartog et al., 2011).***

Given the lack of efficacy data and concerns about safety, we conducted the Scandinavian Starch for Severe Sepsis/Septic Shock (6S) trial to evaluate the effects of HES 130/0.4 as compared with Ringer's lactate on the composite outcome of death or end-stage kidney failure in patients with severe sepsis ***(Reinhart et al., 2012).***

Aim of the Work

To compare between ringer lactate and voluven in resuscitation of patient with sever sepsis in intensive care unit.

Chapter 1

SEPSIS

1. SIRS and new sepsis definition:

A 2016 task force convened by national societies including the Society of Critical Care Medicine (SCCM) and the European Society of Intensive Care Medicine (ESICM) proposed a new definition of sepsis, termed Sepsis-3 ***(Singer et al., 2016).***

The new proposal defines sepsis as life-threatening organ dysfunction caused by a dysregulated host response to infection ***(Singer el al., 2016; Seymour et al., 2016).***

The new definition abandoned use of host inflammatory response syndrome criteria (SIRS) in identification of sepsis and eliminated the term severe sepsis. An earlier sepsis definition, Sepsis-1, was developed at a 1991 consensus conference ***(Bone et al., 1998***) in which SIRS criteria were established. Four SIRS criteria were defined, namely tachycardia (heart rate >90 beats/min), tachypnea (respiratory rate >20 breaths/min), fever or hypothermia (temperature >38 or <36 °C), and leukocytosis, leukopenia, or bandemia (white blood cells >1,200/mm3, <4,000/mm3 or bandemia ≥10%).

Patients who met two or more of these criteria fulfilled the definition of SIRS, and Sepsis-1 was defined as infection or

suspected infection leading to the onset of SIRS. Sepsis complicated by organ dysfunction was termed severe sepsis, which could progress to septic shock, defined as "sepsis-induced hypotension persisting despite adequate fluid resuscitation." A 2001 task force ***(Levy et al., 2003)*** recognized the limitations with these definitions, but did not offer alternatives due to a lack of supporting evidence. However, they did expand the list of diagnostic criteria, resulting in the introduction of Sepsis-2. Therefore, in order to be diagnosed with sepsis under the Sepsis-2 definition, as with Sepsis-1, an individual must have at least 2 SIRS criteria and a confirmed or suspected infection ***(Bone et al., 1998; Peach, 2017).*** In effect, the definitions of sepsis and septic shock remained unchanged for more than two decades.

As part of the 2016 SCCM/ESICM evaluation of criteria for identifying septic patients, the task force compared traditional SIRS criteria to other methods, including the Logistic Organ Dysfunction System (LODS) and Sequential Organ Failure Assessment (SOFA) scoring ***(Seymour et al., 2016).*** Based on this analysis, the authors recommended use of SOFA scoring to assess the severity of organ dysfunction in a potentially septic patient.

2. Pathophysiology

Sepsis remains a critical problem with significant morbidity and mortality even in the modern era of critical care

management. Multiple derangements exist in sepsis involving several different organs and systems although controversies exist over their individual contribution to the disease process ***(Bombín et al., 2008).***

Septic patients have substantial, life-threatening alterations in their coagulation system, and currently, there is an approved therapy with a component of the coagulation system (activated protein C) to treat patients with severe sepsis. Previously, it was believed that sepsis merely represented an exaggerated, hyper inflammatory response with patients dying from inflammation-induced organ injury. More recent data indicate that substantial heterogeneity exists in septic patients' inflammatory response, with some appearing immuno-stimulated, whereas others appear suppressed ***(Alberti et al., 2005).***

Cellular changes continue the theme of heterogeneity. Some cells work too well such as neutrophils that remain activated for an extended time. Other cellular changes become accelerated in a detrimental fashion including lymphocyte apoptosis ***(Alberti et al., 2005).***

Metabolic changes are clearly present, requiring close and individualized monitoring. At this point in time, the literature richly illustrates that no single mediator/ system/ pathway/ pathogen drives the pathophysiology of sepsis. This review will briefly discuss many of the important alterations that account for the pathophysiology of sepsis ***(Bombin et al., 2008).***

A. Dysregulated Coagulation

Normal hemostasis exists as a finely tuned balance where the blood typically remains liquid to allow free flow within the vessels yet clots appropriately to control bleeding. Under normal conditions the clotting cascade is extremely complex ***(Ryan et al., 1992).*** During inflammatory situations such as sepsis, significant alterations occur at multiple levels within both the coagulation system and the cells that regulate this system ***(Baron et al., 2006).***

Septic patients frequently manifest disseminated intravascular coagulation with consumption of platelets and prolongation of clotting times. In addition, the altered hemostasis allows blood to clot when it should not, clogging blood vessels and reducing blood flow ***(Levi et al., 2001).***

Although the coagulopathy is systemic, the bleeding typically occurs in select sites, where dysfunctional vasculature provides the necessary environment for bleeding to occur at that site. The interaction between the clotting system, circulating white blood cells and platelets, and the endothelium adds another layer to an already multifaceted picture. Although several of these abnormalities have been documented in septic patients, the underlying cause of the coagulopathy almost certainly remains multifactorial ***(Lorente et al., 1993).***