Comparison between Crystalloid Versus Colloid in Septic Shock

Systematic Review / Meta-Analysis for Partial Fulfillment of Master Degree in General Surgery

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List of Abbreviations

Abb.	Full term
AKI	Acute kidney injury
ALBIOS	Albumin Italian Outcome Sepsis
ARDS	Acute respiratory distress syndrome
CHEST	Crystalloid vs. Hydroxy-Ethyl Starch Trials
CIs	Confidence intervals
EGDT	Early goal-directed therapy
FDA	Food and Drug Administration
HES	Hydroxyethyl starch
ICU	Intensive Care Units
IRAK	IL-1 receptor-associated kinase
IVIg	Intravenous immunoglobulins
LBP	LPS-binding protein
LR	Lactated ringer’s
MD-2	Myeloid differentiation protein-2
NF-κB	Nuclear factor kappa B
NS	Normal saline
OR	Odds ratio
QSOFA	Quick sepsis related failure assessment
RCTs	Randomized control trials
SAFE	Salaine versus alumin fluid evaluation
SIRS	Systemic inflammatory response syndrome
SOFA	Sepsis related organ failure assessment
SSC	Surviving sepsis campaign
TLRs	Toll-like receptors
TRAF6	TNF receptor-associated factor-6
VISEP	Volume Substitution and Insulin Therapy in Severe Sepsis

Introduction

Shock can be split in to four categories:

Hypovolemic shock: from blood loss or excessive fluid loss (e.g., major burn).

Cardiogenic shock: the heart is unable to circulate enough blood volume to maintain adequate tissue perfusion. This can happen after heart attack or acute episode of heart failure.

Distributive shock: occurs as a result of poor distribution of blood to the tissue, leading to inadequate tissue perfusion (e.g., spinal, septic and anaphylactic shock) also known as relative hypovolaemia.

Septic shock can be associated with both absolute and relative hypovolaemia. Large fluid deficits can exist as a consequence of external (e.g., diarrhea, sweating) or internal (e.g., edema, peritonitis) losses. Relative hypovolemia in sepsis is related to the maldistributive defect with vasodilation and peripheral blood pooling. Relative (Hypovolemia) can lead to reduced circulating blood volume, diminished venous return, and in severe cases, arterial hypotension. Hypovolemia may also contribute to microcirculatory compromise, leading to organ dysfunction and, ultimately, multiple organ failure. Adequate fluid resuscitation is, therefore, one of the keystones in the management of shock. The aims being to preserve intravascular fluid volume, restore effective tissue perfusion, and re-establish and maintain a balance between tissue oxygen demand and supply. Volume repletion in patients with septic shock produces significant increases in cardiac output and systemic oxygen delivery, and although vasopressor agents are common adjuncts to fluid resuscitation, fluids alone are sometimes sufficient to reverse hypotension and restore hemodynamic stability ***(Haupt et al., 1985; Vincent and Gerlach, 2004).***

Fluid resuscitation may consist of natural or artificial colloids or crystalloids. There is no evidence-based support for one type of fluid over another ***(Packman and Rackow, 1983).***

Crystalloids and colloids are the two major categories of resuscitative fluid therapy. There has been an on-going debate in the literature as to which of the two is the safer and more effective resuscitative fluid. Colloids have been used as volume expanders for acute fluid resuscitation in trauma, preoperatively and in shocked ICU patients ***(Severs et al., 2015).***

The crystalloid family includes isotonic and hypertonic solutions that are also categorized into nonbuffered (eg, isotonic saline) and buffered solutions (eg, Ringer lactate, acetate, maleate)

The colloid family includes hypooncotic (eg, gelatins, 4% or 5% of albumin) and hyperoncotic (eg, dextrans, hydroxyethyl starches, and 20% or 25% of albumin) solutions. Generally, colloid solutions are thought to be more efficient than crystalloids in terms of the amount of fluid that remains in the intravascular space and so less fluid is required when using colloids vs crystalloids to achieve similar hemodynamic goals ***(Sugerman et al., 1971; Annane et al., 2013; Perel et al., 2013; Myburgh et al., 2017).***

Commonly used infusion fluids include semisynthetic colloids and crystalloids; the latter comprises both normal saline (NaCl 0.9%) and the more chloride-restricted 'balanced' crystalloids. Despite their significantly greater intravascular persistence, semisynthetic colloids have an importantly adverse safety profile and are associated with greater incidence of renal failure and increased mortality; To date, evidence for clinical benefits associated with albumin solutions is generally lacking; its merits in specific clinical situations are the subject of further investigation. Infusion of normal saline, with its supra physiological chloride content, is associated with higher serum chloride concentrations and metabolic acidosis, as well as renal vasoconstriction in animal and human models. Infusion of 'balanced' crystalloids is not linked to such changes ***(Zarychanski et al., 2013).***

This is because colloids are thought to have longer intravascular persistence and therefore a longer volume replacement effect, resulting in lower volume requirements and less extravascular oedema. However, colloids are costly, may cause anaphylaxis and have possible adverse renal and coagulation effects. Recent large trials and subsequent meta-analyses have concluded that there is no significant mortality benefit from resuscitation with colloids ***(Cortés et al., 2015; Guidet et al., 2017).***

However, recent trials have challenged this theory owing to certain variables in administration. Studies have found that positive fluid balance is associated with worsened outcomes in hospitalized patients, and knowing the differences in the amounts of infused fluids has critical implications ***(Seymour and Angus, 2013; Van Haren and Zacharowski, 2014).***

There has been considerable debate about the type of fluid that is most appropriate for resuscitation of patients with septic shock. Advocates of colloids point to their perceived selective ability to expand the intravascular space owing to the oncotic pressure they generate from the large molecular weight solutes in which they are suspended. This advantage in theory will allow smaller volumes of fluid to be administered, which in turn reduces the risk of volume overload and tissue edema. However, colloids are expensive and immunogenic and are associated with an increased risk of renal impairment when compared with crystalloids ***(Begg and Mazumdar, 1994).***

Furthermore, their ability to selectively expand the intravascular space may be lost in endothelial Leakage states such as sepsis. Data from recent fluid-related clinical trials1 have challenged the physiological concept of selective intravascular expansion with colloids since they report no large differences in the volumes of crystalloid or colloid used ***(Egger et al., 1997).***

Aim of the Work

To systematically review the effects of colloids compared with crystalloids in fluid resuscitation for septic shock.

Chapter 1

SEPTIC SHOCK

▪ Introduction

Sepsis and septic shock are life-threatening conditions caused by a dysregulated immune response to infections, which may lead to tissue and organ injures and finally to death. Despite advances in management, sepsis and septic shock still represent major healthcare problems worldwide leading to a substantial consumption of health-care resources. New guidelines and bundles have recently been published ***(Bone et al., 1992; Levy et al., 2003; Singer et al., 2016).*** In this study we review the epidemiology, the history of definitions, the diagnostic and therapeutic approaches of sepsis and septic shock.

▪ New Definition

The European Society of Intensive Care Medicine and the Society of Critical Care Medicine convened a new panel of 19 experts to update definitions of sepsis and septic shock, which were characterized by limited specificity and inadequate sensibility. The most relevant changes were the elimination of the term severe sepsis, considered redundant, and the deleting of the concept of SIRS, which may simply reflect an appropriate host response to several non-infectious diseases (such as pancreatitis and ischemic reperfusion syndromes) ***(Singer et al., 2016).***

- **Sepsis Related Organ Failure Assessment (SOFA)**

The results of the third international consensus conference, published in 2016, allow to define the following conditions: Organ dysfunction is represented by an increase in the Sequential [Sepsis-related] Organ Failure Assessment (SOFA) score of 2 points or more (Table 1). Sepsis is defined as life threatening organ dysfunction caused by a dysregulated host response to infection. Septic shock is defined as a subset of sepsis in which circulatory, cellular or metabolic abnormalities are associated to increased risk of mortality. Clinical parameters to identify patients with septic shock are: vasopressor requirement to maintain a mean arterial pressure of 65 mm Hg or greater and serum lactate level greater than 2 mmol/L (>18 mg/dL) in the absence of hypovolemia ***(Gotts and Matthay, 2016; Singer et al., 2016).***

- **Quick Sepsis Related Failure Assessment (QSOFA)**

The same group of experts elaborated a simplified version of the SOFA score, the quick SOFA Score (quick SOFA or qSOFA), incorporating systolic blood pressure of 100 mmHg or less, respirator rate of 22/min or greater and altered mentation (any Glasgow coma scale score different from 15). The qSOFA score is based on clinical criteria but does not requir-e laboratory tests, thus it provides a simple and quick evaluation of patients with suspected infection who are more likely to have poor outcomes ***(Singer et al., 2016).***

Table (1): Sequential [Sepsis-related] Organ Failure Assessment (SOFA) score.

Parameters	Score				
	0	1	2	3	4
PaO_2/FiO_2(mmHg)	≥400	<400	<300	<200	<100
MAP (mmHg) and catecholamine doses[b] need	MAP ≥ 70	MAP < 70	Dopamine <5 or dobutamine (any dose)	Dopamine 5.1-15 or epinephrine ≤0.1 or norepinephrine ≤0.1	Dopamine >15 or epinephrine >0.1 or norepinephrine >0.1
Platelets (×10^3/μL)	≥150	<150	<100	<50	<20
Bilirubin (mg/dL)	<1.2	1.2-1.9	2.0-5.9	6.0-11.9	>12.0
Glasgow coma scale	15	13-14	10-12	6-9	<6
Creatinine (mg/dL)	<1.2	1.2-1.9	2.0-3.4	3.5-4.9	>5.0
Urine output (mL/d)				<500	<200

Abbreviations: PaO2 = partial pressure of oxygen; FiO2 = fraction of inspired oxygen; MAP = mean arterial pressure.

a Adapted from ***(Singer et al., 2016).***

b Catecholamine doses are calculated as mg/kg/min for at least 1 h.

- **Stages of sepsis**

i. Systemic inflammatory response syndrome (SIRS)

Two or more the following:

- Temperature more than 38 or less than 36
- Heart rate more than 90