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A comparative study on the use of human albumin 4%, versus hydroxyethyl starch 6%; 130/0.4 versus normal saline 0.9%, regarding the Impact of fluid resuscitation type on survival rate, and organ dysfunction in severe sepsis.

Thesis

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بسم الله الرحمن الرحيم

وقُلِ اعْمَلُوا فَسَيَرَى اللّهُ عَمَلَكُمْ
ورَسُولُهُ والْمُؤْمِنُونَ

صدق الله

العظيم

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(105)

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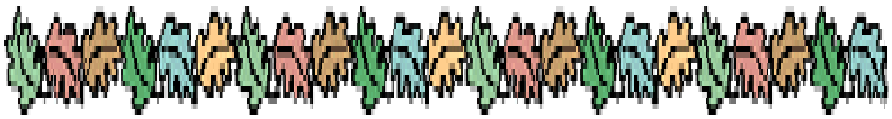

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List of Abbreviations

ALBIOS	Albumin Italian Outcome Sepsis
AKI	Acute kidney injury.
ARDS	Acute respiratory distress syndrome.
bpm	Beat per minute.
CCR	chemokine receptor
CHEST	Crystalloids versus HydroxyEthylStarch Trial
CLP	Cecal Ligation and Puncture
CLRS	C-type lectin receptors.
CRISTAL	CRISTALoid vs. colloids in resuscitation of critical ill patients
CRP	C-reactive protein.
CSF	Cerebro spinal fluid.
CVP	Central venous pressure.
CXR	Chest x ray.
DCs	Dendertic cells
DIC	Disseminated intravascular coagulopathy.
EEG	Electroencephalography.
EARSS	Early Albumin Resuscitation for Sepsis and Septic shock
FDA	Food and drug administration.
GPL	Glycosylphosphatidylinositol
GSK-3	Glycogen Synthase Kinase-3
HES	Hydroxyethyl starch.
HMG-B1	High mobility group box-1
HR	Heart rate
IBW	Ideal body weight.
ICAM-1	Intercellular Adhesion Molecule-1
ICU	Intensive care unit.
IFN	Interferon.
IL	Interleukin.
IRAK	IL-1Receptor associated kinase.
LFA-1	Leucoc yte function associated antigen -1
LPS	Lipopolysaccharides
LRRS	Leucine rich repeat
LTA	Lipoteichoic acid
MAP	Mean arterial pressure.

MDL-1	Myeloid associating lectin-1.
MDSCs	Myeloid-Derived Suppressor Cells
MIf	Macrophage migration inhibitory factor.
MV	Mechanical Ventilation.
NaCl	Sodium chloride.
NET	Neutrophil extracellular traps.
NF-κ B	Nuclear factor kappa-light-chain-enhancer of activated B cells.
NLRS	Nucleotide-binding oligomerization domain like receptors.
NOD	Nucleotide-binding oligomerization
PAI-1	Plasminogen activator inhibitor type 1.
PAR1	Protease activated receptor1.
PARS	Protease activated receptors.
PAMP	pathogen-associated molecular patterns
PRRs	Pattern Recognition Receptors
PCR	Polymerase chain reaction.
PGN	Peptidoglycan.
PVR	Pulmonary vascular resistance.
RA	Ringer acetate
RAGE	Receptor for advanced glycation end products.
RCT	Randomized clinical trails
RL	Ringer lactete.
RLRS	Retionic acid inducible gene 1-like receptors.
RR	Respiratory rate.
RRT	Renal replacement therapy.
6 S	Scandinivian Starch for Severe Sepsis and Septic Shock
S1P1	Sphingosine 1 Phosphate receptor 1.
S1P3	Sphingosine 1 Phosphate receptor 3.
SAFE	Saline versus Albumin Fluid Evaluation
$ScvO_2$	Central venous oxygen saturation.
SD	Standard deviation.
SIRS	Systemic inflammatory response syndrome.
SMT	Standard medical therapy.
SOFA	Sequential organ failure assessment
SR	Sarcoplasmic reticulum.
TAK-1	Transforming growth factor- associated kinase-1
TIRS	Toll-like receptors.
TREM-1	Triggering receptor expressed on myeloid cells
TM	Thrombomodulin.

TNF	Tumor necrosis factor.
UOP	Urine output.
VISEP	Volume substitution and Intensive insulin therapy in SEPsis
vWF	von Willebrand factor.
WBCs	White blood cells.

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Introduction

Fluid resuscitation has long been a fundamental component in the management of septic patients and choice of fluid has been a standing issue of debate.

Despite the evidence regarding a limited benefit with colloid use, surveys suggest that they are frequently the preferred choice for fluid resuscitation. (**Delaney et al., 2011)**

With their higher molecular weight, colloids remain in the intravascular space longer, and, therefore, provide more rapid hemodynamic stabilization than crystalloids, which extravasate to a greater degree so that more fluids are required to achieve the same end points. However, colloids are more expensive than crystalloids, in particular albumin, so that other colloids have been developed, including gelatins, dextrans, and hydroxyethyl starch (HES) solutions**.(Vincent et al., 2007)**

SAFE Study provides evidence that; albumin and saline should be considered clinically equivalent treatments for intravascular volume resuscitation in a heterogeneous population of patients in the ICU. **(Finfer et al.,2011)**

At the same time, several studies have questioned the safety of HES in critically ill patients, with particular concern that its use increases the risk of acute kidney

injury. Most concern has focused on the use of concentrated HES solutions (10%) with a molecular weight of more than 200 kD and a molar substitution ratio (the number of hydroxyethyl groups per glucose molecule) of more than 0.5.(**Perner et al.,2012)**

Additional concern arouse from a recent Scandinavian trial reporting that the use of 6% HES (130/0.42) significantly increased mortality in patients with severe sepsis and septic shock. **(Perner et al .,2012**)

Also CHEST trial a recent large randomized trial suggested that the use of HES was associated with increase in acute kidney injury , purities, hepatic failure and increased rate of blood products use. **(Myburgh et al. ,2012).**

So, where does this leave us in the big fluid debate? The present results are interesting and add another little piece to the big puzzle, but much more work is needed before we will be able to see the full picture and to better determine where each fluid fits. Although we use these fluids every, we still know surprisingly little about them**.(Vincent et al., 2007)**

Aim of the work

To compare, and determine the effect of resuscitation fluids type on patients with severe sepsis with crystalloids i.e.; saline 0.9% versus colloids i.e.; HES 6% 130/0.4 or H. albumin 4% on survival rate and organ functions during ICU course.

Review of literature

Chapter 1

Sepsis review

Introduction

Sepsis is one of the oldest and most elusive syndromes in medicine. ***(Majno, 1991)***

In 1992, an international consensus panel defined sepsis as a systemic inflammatory response to infection, noting that sepsis could arise in response to multiple infectious causes, and that septicemia was neither a necessary condition nor a helpful term. Instead, the panel proposed the term "severe sepsis" to describe instances in which sepsis is complicated by acute organ dysfunction, and they codified "septic shock" as sepsis complicated by either hypotension that is refractory to fluid resuscitation or by hyperlactatemia. **(Bone et al., 1992)**

In 2003, a second consensus panel endorsed most of these concepts, with the caveat that signs of a systemic inflammatory response, such as tachycardia or an elevated white-cell count, occur in many infectious and noninfectious conditions and therefore are not helpful in distinguishing sepsis from other conditions. Thus, "severe sepsis" and "sepsis" are sometimes used