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Updates in management of early stage of sepsis, comparative study between hypertonic saline 7.5%and hydroxy ethyl starch 130/0.4

Thesis

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بسم الله الرحمن الرحيم

وقُلِ اعْمَلُوا فَسَيَرَى اللَّهُ عَمَلَكُمْ
ورَسُولُهُ والْمُؤْمِنُونَ

صدق الله العظيم

سورة التوبة آية (105)

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List of Abbreviations

AKI	Acute kidney injury.
APACHE	Acute Physiology and Chronic Health Evaluation.
ARDS	Acute respiratory distress syndrome.
BMNC	Bone Marrow Nucleated Cells.
Bpm	Beat per minute.
CLP	Cecal Ligation and Puncture.
CLRS	C-type lectin receptors.
CO	Cardiac output.
COP	Colloid oncotic pressure.
CRP	C-reactive protein.
CSF	Cerebro spinal fluid.
CVP	Central venous pressure.
CXR	Chest x ray.
DIC	Disseminated intravascular coagulation.
EEG	Electroencephalography.
FDA	Food and drug adminestration.
HES	Hydroxyethyl starch.
HHS	7.5%Hypertonic saline/6%hetastarch.
HR	Heart rate.
HSD	7.5 Hypertonic saline/6%dextran.
HSS	Hypertonic saline solutions.
HTS	Hypertonic saline.
IBW	Ideal body weight.
ICU	Intensive care unit.
IFN	Interferon.
IL	Interleukin.
ISS	Isotonic saline solution.
LTCCs	L-type Ca^{+2} channel.
MAP	Mean arterial pressure.
MDSCs	Myeloid-Derived Suppressor Cells.
MIF	Macrophage migration inhibitory factor.

List of Abbreviations (Cont.)

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.
NO	Nitric oxide.
NO_2-	Nitrite.
O_2	Oxygen.
OH-	Hydroxyl radical.
$ONOO^-$	Peroxynitrite.
ONOOH	Peroxynitrous.
PAI-1	Plasminogen activator inhibitor type 1.
PAR1	Protease activated receptor1.
PARS	Protease activated receptors.
PBMC	Peripheral Blood Mononuclear Cells.
PCR	Polymerase chain reaction.
PVR	Pulmonary vascular resistance.
RCT	Randomized controlled trials.
RL	Ringer lactete.
RLRS	Retionic acid inducible gene 1-like receptors.
RR	Respiratory rate.
RRT	Renal replacement therapy.
S1P1	Sphingosine 1 Phosphate receptor 1.
S1P3	Sphingosine 1 Phosphate receptor 3.
$ScvO_2$	Central venous oxygen saturation.
SD	Standard deviation.
SIRS	Systemic inflammatory response syndrome.
SMT	Standard medical therapy.
SR	Sarcoplasmic reticulum.
TIRS	Toll-like receptors.
TM	Thrombomodulin.

List of Abbreviations (Cont.)

TNF	Tumor necrosis factor.
UOP	Urine output.
VE	Vascular endothelium.
VWF	Von willebrand factor.
WBCs	White blood cells.

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Introduction

Sepsis-related mortality is a leading cause of death worldwide. Early fluid resuscitation of patients with systemic inflammatory response syndrome reduces the incidence of mortality. Aggressive intravenous fluid resuscitation is a critical component of early goal directed therapy. While there is ample evidence accumulating that colloids offer no advantage over crystalloids as the initial choice of fluid resuscitation there is an increased 90-day mortality and the need for renal replacement therapy with use of hydroxyethyl starch (HES) ***(Finfer et al., 2010).***

One of the major concerns with the use of HES as a resuscitation fluid has been the adverse effect leading to increased requirement of renal replacement therapy; this effect was overcome by the use of a lower molecular weight HES 130/0.4. A recent trial compared HES (130/0.4) with crystalloids showed no difference in renal dysfunction between the two groups and no difference in mortality up to 90 days after treatment initiation. However, significantly less volume was required to achieve hemodynamic stability for HES in the initial phase of fluid resuscitation ***(Guidet et al., 2012).***

The etiology of sepsis is based on sustained period of hypoperfusion of vital organs. The use of hypertonic saline as an early resuscitation to improve survival (initial fluid therapy), prevents circulatory failure, alleviates multiple organ dysfunction syndrome and decreases mortality rate ***(Shih et al., 2008).***

The infusion of several liters of isotonic fluids is associated with the adverse effects of extravasation into the interstial space. In sepsis this may result in peripheral and/or pulmonary edema ***(Astiz et al., 1993)***. Several

studies have been performed that used small volume resuscitation which is defined as a rapid infusion of hypertonic solution (NaCl 7.5%) at a dose of 2-4 ml/kg into a peripheral vein have some demonstrated promising beneficial effects ***(Hannemann et al., 1996).***

Most of the studies found that hypertonic saline infusion caused a rapid and significant increase in oxygen delivery, elevated cardiac output, increased oxygen extraction, redistribution of fluids from the perivascular to the intravascular space and cardiac contractility may also improve ***(Poli-de-Figueiredo et al., 2006).***

Aim of The Work

To compare the effect of early administration of hypertonic saline 7.5 % versus hydroxylethyl starch 130/0.4 on adequacy of resuscitation, progression of inflammation and outcome of septic patients**.**

Chapter I
Sepsis

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

I-Incidence:

The number of cases in the united states exceeds 750,000 per year and was recently reported to be rising ***(Lagu et al., 2012)***. Severe sepsis, which occurs when sepsis progresses to involve acute organ dysfunction, results in more than 200.000 annual fatalities, and the number of cases are projected to increase ***(Angus et al., 2001)***.

The statistics related to the incidence of sepsis are striking. The reported rates of severe sepsis average around 10 cases per 100 intensive care unit (ICU) admissions ***(Linde-Zwirble and Angus, 2004)***.

Sepsis occurs in 1-2% of all hospitalizations and is a major cause of death in intensive care units worldwide, with mortality rates that range from 20% for sepsis to 40% for severe sepsis, and to >60% for septic shock ***(Martin et al., 2003).***

Studies from other high income countries show similar rates of sepsis in the ICU. The incidence of sepsis outside modern ICUs, especially in parts of the world in