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Hydroxyethyl Starch In Severe Sepsis

Essay

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Tamer Mohamady Abuelhassan

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LIST OF ABBREVIATIONS

ACTH	Adreno Cortico Trophic Hormone
AKI	Acute Kidney Injury
AKIN	Acute Kidney Injury Network
APC	Activated Protein C
ARDS	Adult Respiratory Distress Syndrome
ARF	Acute Renal Failure
AUC	Area Under the Curve
BNP	B type Nantriuretic Peptide
CARS	Compensatory Anti-inflammatory Response Syndrome
CHEST	Crystalloid versus Hydroxyethyl Starch Trial
CL(cr)	Creatinine Clearance
CMDh	The Coordination Group for Mutual Recognition and Decentralised Procedures
COP	Colloid Osmotic Pressure
CORTICUS study	The Corticosteroid Therapy of Septic Shock study
CRF	Chronic Renal Failure
CRYSTMAS study	6%Hydroxyethylstarch(130/0.4) vs 0.9% NaCl fluid replacement in patients with severe sepsis
CVP	Central Venous Preesure
CXC	Chemokines
CXCR2	Chemokines Receptor 2
DAMPs	Damage Associated Molecular Patterns
DIC	Disseminated Intravascular Coagulopathy
ED	Emergency Department
EGDT	Early Goal Directed Therapy
EMA	European Medicines Agency
EPCR	Endothelial Cell Protein C Receptor
FiO_2	Fraction of inspired Oxygen

GCS	Glasgow Coma Scale
G-CSF	Granulocyte Colony-Stimulating Factor
GD	Goal Directed
GM-CSF	Granulocyte Macrophage Colony-Stimulating Factor
Hct	Hematocrit
HDS	Hemodynamic Stabilization
HES	Hydroxylethyl Starch
HR	Heart Rate
ICU	Intensive Care Unit
IL	InterLeukin
kDa	kilo Daltons
LPS	Lipopolysaccharide
MAP	Mean Arterial Blood Pressure
MARS	Mixed Antagonistic Response Syndrome
MODS	Multi Organ Dysfunction in Sepsis
MS	Molar Substitution
MW	Molecular Weight
NAG	Beta-N-acetyl-beta-D-glucosaminidase
NaCl	Sodium chloride
NGAL	neutrophil gelatinase-associated lipocalin
PAMPs	Pathogen-Associated Molecular Patterns
$PaCO_2$	Carbon Dioxide Tension in the Arterial Blood
PaO_2	Oxygen tension in the Arterial Blood
PLA_2	Phospholipase A_2
PIRO	predisposition, infection, response, organ dysfunction
PRAC	Pharmacovigilance Assessment Committee
PRBCs	packed red blood cells
rhAPC	recombinant human Activated Protein C
RIFLE score	Risk, Injury, Failure, Loss, and End-stage kidney disease

RRT	Renal Replacement Therapy
6S Study	Scandinavian Starch for Severe Sepsis/Septic Shock
SBP	Systolic Blood Pressure
$SCVO_2$	Central venous oxygen saturation
SIRS	Systemic Inflammatory Response Syndrome
SOFA score	Sequential Organ Failure Assessment score
SSCG	Surviving Sepsis Campaign Guidlines
STREM	Soluble Triggering Receptors Expressed on Myeloid Cells
T	Thrombin
TF	Tissue Factor
TLR	Toll-like receptors
TM	Thrombodulin
TNF	Tumour Necrosis Factor
TNF-RA	Tumor Necrosis Factor – receptor antagonist
tPO_2	Partial pressure of oxygen at tissues

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INTRODUCTION

Sepsis syndrome in adults is a disease spectrum that ranges from an inflammatory response to sepsis, severe sepsis and septic shock. Sepsis is defined as an inflammatory response with a presumed or identified source of infection. Severe sepsis is defined as sepsis with one or more organ system dysfunction. Septic shock is defined as hypotension (mean arterial pressure(MAP) <65mmHg or systolic blood pressure(SBP) <90mmHg) despite adequate fluid resuscitation ***(Levy et al., 2003).***

Mortality from sepsis ranges from 25% to 30% in severe sepsis and 40% to 70% in septic shock despite the availability of potent antibiotic. There is ongoing effort to find out and try strategies which would improve outcome of this population. 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 ***(Annane et al., 2003).***

The risk factors of sepsis are advanced age, compromised immune status, increased use of cytotoxic, immunosuppressant agents, malignancy, diabetes mellitus, chronic renal failure, hepatitis, malnutrition, chronic illness and surgical/invasive procedures***(Daniel and RemicK, 2007).***

Treating sepsis is expensive resulting in consumption of major health care resources. With the development of newer and potent anti microbial agents, mortality due to sepsis had been markedly reduced, but remains un-acceptably high, recently various strategies like fluid therapy, low dose corticosteroids, tight glycemic control, recombinant human activated protein c (rhapc) and lung protective ventilation have shown favorable results. Furthermore it is though that combination of these strategies in the form of “bundles” can improve the outcome***(Khilnani and Hadda, 2009).***

Any identified patient within the first six hours of presenting symptoms, who has identified source of infection and hypotension or a presenting lactate

≥4mmol/L is a candidate for EGDT(Early Goal Directed Therapy). However, many cases are not so obvious, as initial presentation of septic shock may be different than later presentation of the disease process. The use of lactate as a biomarker for tissue oxygenation and perfusion has enhanced the early identification of patients with severe sepsis. Early identification allows for rapid treatment initiation with significant lower mortality benefit. Lactate ≥4mmol/L, independent of blood pressure was used as major entry criteria for the EGDT study which demonstrated a 16% mortality benefit***(Levy et al., 2003).***

Hydroxyethyl starches (HESs) are artificial colloid solutions that are modified natural polysaccharides with volume-expansion properties, composed of amylopectin obtained from maize or potato starch and vary in their molecular weight, hydroxyethyl moieties and the ratio of c2 to c6 substitutions. Natural starches cannot be used as plasma substitutes because circulating amylase hydrolyzes these unstable organic compounds rapidly. HESs are increasingly being used for the prevention and treatment of hypovolemia in numerous clinical situations, such as surgical, trauma, burn and intensive-care patients***(Westphal et al., 2009).***

For fluid therapy to be effective, it is imperative that it reaches the microcirculation to promote tissue perfusion. For this purpose, Hydroxyethyl starch (HES) solutions have been the most commonly used plasma substitutes among colloid solutions***(Boldt et al., 2005).***

Colloids are more effective in resuscitation than crystalloids with lower volume and rarely cause peripheral edema. Several studies have shown that colloids are more efficient regimen to ensure adequate microcirculatory flow than crystalloids***(Lang et al., 2001).***

Aim Of The Essay

The aim of this essay was to highlight the effects of hydroxyethyl starch (HES) in patients with severe sepsis and its effect on mortality rate and end-stage kidney failure in these patients.

Chapter (1)

Incidence, Terminology and Pathophysiology of Sepsis Syndrome.