Updates in Immunonutrition in Sepsis

Essay

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Abstract

Introduction: Sepsis is recently defined as a life-threatening organ dysfunction due to a dysregulated host response to infection. Organ dysfunction is defined as an increase of 2 points or more in the quick Sequential Organ Failure Assessment (SOFA) score, with one point each for hypotension, altered mental status or tachypnea.

Nutritional support products is designed to enhance the host immune response and suppress inflammations, importantly the use of immune modulating diets (IMD) in critically ill patients needs to be translated into improvements in clinically relevant outcomes such as infection, morbidity and mortality and length of stay.

Aim of work: The aim of the work is to study new immune modulating diets called immunonutrients that improve immunity and suppress inflammation and its role in management of sepsis.

Summary: Sepsis cause disruption of hemostasis through a currently cascade of excessive inflammation and coagulation.

Plasma antioxidant micronutrient concentrations are decreased during critical illness and specially sepsis, as a result of losses, low intakes, dilution by resuscitation fluids and the SIRS-mediated redistribution to tissue creating a circulating antioxidant defense deficit. The evidence revealed an increasing antioxidants supplementation contributes in limiting tissue and organ damage caused by sepsis mediators. antioxidants already have undergone successful clinical testing reaching a top level of evidence, selenium improves clinical outcome (infection and organ failure). Other antioxidants as N-acetylcysteine, vitamin E, vitamin c and zink have had clinical benefits in different conditions as antioxidants and diet enhancing immunity.

Keywords: Immunonutrition in Sepsis**,** Immune modulating diets, Management of sepsis.

My thanks are submitted first and foremost to **ALLAH** *Who gave me the strength and ability to complete this work.*

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Mostafa Mahmoud Khaled

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List of Abbreviations

Abbr.	Title
ABW	Actual Body Weight
ACTH	Adrenocoticotrophic Hormone
ALA	Alpha Linolenic Acid
AP-1	Activator Protein-1
APACHE	Acute Physiology And Chronic Health Evaluation
ARDS	Adult Respiratory Distress Syndrome
BMI	Body Mass Index
CD14	Cluster of Differentiation Antigen 14
CNS	Central Nervous System
CRH	Corticotropin Releasing Hormone
CRRT	Continuous Renal Replacement Therapy
DHA	Docosahexaenoic Acid
DTH	Delayed Type Hypersensitivity
EN	Enteral Nutrition
eNos	endothelial nitric oxide synthases
EPA	Eicosapentaenoic Acid
FMLP	FormylMethionine-Leucine-Phenylalanine
GI	Gastrointestinal
GLA	Gamma-Linolenic Acid
Gln	Glutamine
GRV	Gastric Residual Volume

GSH	Glutathione
IBW	Ideal Body Weight
ICAM-1	Intercellular Adhesion Molecule 1
ICU	Intensive Care Unit
IFALD	intestinal failure-associated liver disease
IL-1	Interleukin 1
iNoS	Inducible nitric oxide synthases
IVLE	Intravenous Lipid Emulsions
LCTs	long chain triglycerides
LOS	Length of Stay
LPS	lipopolysaccharide
MCTs	Medium Chain Triglycerides
MD2	muramyl dipeptide 2
MDL-1	Myeloid DAP 12 associating Lectin
NAC	N- Acetyl Cystiene
NF-κB	Nuclear Factor- κB
NK	Natural Killer
nNoS	neuronal nitric oxide synthases
NO	nitric oxide
NOD	Nucleotides Oligomerization domain
NOSs	nitric oxide synthases
NTS	Nucleotides
OKG	Ornithine ketoglutarate
PAMPs	Pathogen Associated Molecular Patterns
PEG	Percutaneous Endoscopic Gastrostomy

PEP	Phosphoenolpyruvate
PGE	Prostaglandin E
PICC	peripherally inserted central catheter
PMNs	Polymorphonuclear leucocytes
PN	Parenteral Nutrition
PPN	Peripheral Parenteral Nutrition
PRRs	Pattern Recognition Receptors
REE	Resting Energy Expenditure
RIG-I	Retinoic Acid Inducible Gene I
ROI	Reactive Oxygen Intermediates
ROS	Reactive Oxygen Species
SIRS	Systemic Inflammatory Response Syndrome
SNP	single nucleotide polymorphism
TLRs	Troll Like Receptors
TNFα	Tumor Necrosis Factor Alpha
TREM	Triggering Receptor expressed on Myeloid cell
TxA	Thromboxane A
VCAM-1	Vascular Cell Adhesion Molecule 1
ω-3PUFA	Omega 3 Polyunsaturated Fatty Acid

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Introduction

Sepsis is recently defined as a life-threatening organ dysfunction due to a dysregulated host response to infection. Organ dysfunction is defined as an increase of 2 points or more in the quick Sequential Organ Failure Assessment (SOFA) score, with one point each for hypotension, altered mental status or tachypnea **(Singer et al., 2016).**

The incidence of sepsis is expected to rise owing to the aging population, a growing immunosuppressed population, the increased use of invasive catheters and prosthetic materials and the growing resistance of antibiotics **(Angus et al., 2001).**

The immune system acts to protect the host from the infectious agents that exist in the environment (bacteria, viruses, fungi, parasites) and from other harmful insults. To this end, it depends on two functional branches: the innate and the acquired, both involving the diversity of blood-borne factors (complement, antibodies and cytokines) and cells (lymphocytes, macrophages, polymorphonuclear cells). Early hemodynamic optimization, administration of appropriate antimicrobial therapy and effective source control of infection are the cornerstones in defending

sepsis. The adequate functioning of this defensive system is critically determined by nutrition. The immune system could be impaired by under nutrition due to inadequate intake of energy and macronutrients and also due to deficiencies in specific micronutrients. These changes suppress the immune functions that's necessary to host protection leading to increased risk of infection, which in turn produce some catabolic changes worsening the nutritional status **(Chandra et al., 2006).**

The nutrients most often studied for immunonutrion are arginine, glutamine, omega-3- fatty acids and antioxidants **(Anetta et al., 2015).**

Arginine may be considered as essential amino acid in sepsis by improving microcirculation and protein anabolism as arginine catabolism is markedly increased by enhanced use of arginine via arginase and nitric oxide pathways **(Luiking et al., 2005).**

The administration of exogenous glutamine in conjunction with anabolic agents that promote nutrient uptake may be beneficial. The cells of the immune system (lymphocytes and macrophages) are major glutamine consumers during inflammatory state in which cell proliferation is increased. So, Glutamine availability can

become a rate limiting key for phagocytosis and antibody production **(Karinch et al., 2001).**

The use of short term high dose omega-3 fatty acids plus antioxidant therapy in patients with early sepsis seems to be safe and associated with promising effects on the inflammatory cascade by decreasing production of inflammatory eicosanoids, cytokines, reactive oxygen species and the expression of adhesion molecules **(Hosny et al., 2013).**

Nutritional support products is designed to enhance the host immune response and suppress inflammations, importantly the use of immune modulating diets (IMD) in critically ill patients needs to be translated into improvements in clinically relevant outcomes such as infection, morbidity and mortality and length of stay **(Peterik et al., 2009).**

Aim of the Work

The aim of the work is to study new immune modulating diets called immunonutrients that improve immunity and suppress inflammation and its role in management of sepsis.

Chapter (1)

Pathophysiology and the Principles of Nutritional Support of Sepsis

The normal host response to infection is a complex process that localizes and controls bacterial invasion, while initiating the repair of injured tissue. It involves the activation of circulating and fixed phagocytic cells, as well as the generation of proinflammatory and antiinflammatory mediators. Sepsis results when the response to infection becomes generalized and involves normal tissues remote from the site of injury or infection **(Remi et al., 2013)**.

NORMAL RESPONSE TO INFECTION:

The host response to an infection is initiated when innate immune cells, particularly macrophages, recognize and bind to microbial components. This may occur by several pathways; Pattern recognition receptors (PRRs) on the surface of host immune cells may recognize and bind to the pathogen-associated molecular patterns (PAMPs) of microorganisms. There are three families of PRRs: toll-like receptors (TLRs), nucleotide-oligomerization domain (NOD) leucine-rich repeat proteins, and retinoic-acid-