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Immuno-nutrients for ARDS: An Update Essay

Essay

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Ahmed Abd El-basset Ahmed Mustafa

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LIST OF ABBREVIATIONS

ADH	Antidiuretic hormone
ALI	Acute lung injury
ACE	Angiotensin-converting enzyme
AP-1	Activator protein-1
APACHE	Acute Physiology and Chronic Health Evaluation
ARDS	Acute respiratory distress syndrome
ASPEN	American Society for Parenteral and Enteral Nutrition
ATP	Adenosine triphosphate
AVP	Arginine vasopressin
BCAA	Branched-chain amino acids
BEE	Basal Energy Expenditure
BMR	Basal metabolic rate
CD	Cluster of differentiation
CHO	Carbohydrates
CO2	Carbon dioxide
DHA	Docosahexaenoic acid
DNA	Deoxyribonucleic acid
EDEN	Early Versus Delayed Enteral Feeding
EN	Enteral nutrition
ENaC	Epithelial sodium channel
EPA	Eicosapentaenoic acid
FAs	Fatty acids
FiO2	Fraction of inspired oxygen
GLA	Gamma-linolenic acid (γ-Linolenic acid)

IC	Indirect calorimetry
ICAM	Intercellular adhesion molecule
ICU	Intensive care unit
IL	Interleukin
JAM-C	Junctional adhesion molecule C
LIS	Lung injury score
LT	Leukotriene
MV	Mechanical ventilation
NADP	Nicotinamide adenine dinucleotide phosphate
NHLBI	National Heart, Lung and Blood Institute
NO	Nitric oxide
NF	Nuclear factor
PAF	Platelet-activating factor
PaO2	Partial pressure of arterial oxygen
PEEP	Positive end-expiratory pressure
PG	Prostaglandin
PUFA	Poly unsaturated fatty acids
RAGE	Receptor for Advanced Glycation End Products
RCT	Randomized controlled trial
REE	Resting energy expenditure
RNA	Ribonucleic acid
RQ	Respiratory quotient
SCCM	Society of Critical Care Medicine
SP-D	Surfactant protein D
TNF	Tumor necrosis factor
USA	United States of America
VAP	Ventilator-associated pneumonia
VCO2	Rate of Elimination of Carbon Dioxide

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INTRODUCTION

The stress response to injury involves hypermetabolism, impaired protein synthesis, and a catabolic state. This leads to a metabolic derangement that requires appropriate nutritional support to counteract loss of body protein, improve the metabolic and immunologic responses, and improve overall morbidity and mortality. Optimizing nutritional therapy is based on fully understanding the premorbid nutritional status of the patient and the pathophysiology of the underlying critical illness. ***(Codner, 2012)***

Over last two decades the role of certain nutrients has been found to have pharmacologic effect on immune and inflammatory parameters. The modulation of the activities of the immune activation by nutrients or specific food is defined as Immunonutriention. Few examples are omega-3 polyunsaturated fatty acid, Glutamine, Arginine, Nucleotides and many more. ***(Dullo and Vedi, 2010)***

The importance of nutrition support in critically ill patients with acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) cannot be overstated. ALI and ARDS are characterized by a proinflammatory response associated with hypercatabolism that could lead to significant nutrition deficits. Nutrition support is necessary to prevent cumulative caloric deficits, malnutrition, loss of lean body mass, and deterioration of respiratory muscle strength. Furthermore, early delivery of enteral nutrition has been associated with the modulation of stress and the systemic immune response as well as the attenuation of disease severity. ***(Krzak et al, 2011)***

During the last decade, the seemingly simple task of feeding critically ill patients has become exceedingly complex with much controversy. While many consider nutrition support “an afterthought” current evidence suggests that in critically ill patients the approach to nutritional support directly impacts patient outcome. (**Marik, 2015)**

Aim Of The Essay

The aim of this essay was to understand the role of optimizing special nutritional therapy in improving the outcome of critically ill cases with ARDS

Chapter (1)

Pathophysiology of Acute Lung Injury and Acute Respiratory Distress Syndrome

The first report of acute respiratory distress syndrome (ARDS) was published in 1967, and even now acute lung injury (ALI) and ARDS are severe forms of diffuse lung disease that impose a substantial health burden all over the world. Recent estimates indicate approximately 190,000 cases per year of ALI in the United States each year, with an associated 74,500 deaths per year. Common causes of ALI/ARDS are sepsis, pneumonia, trauma, aspiration pneumonia, pancreatitis, and so on. ***(Tsushima et al, 2009)***

Several pathologic stages of ALI/ARDS have been described: acute inflammation with neutrophil infiltration, fibroproliferative phase with hyaline membranes, with varying degrees of interstitial fibrosis, and resolution phase. There has been intense investigation into the pathophysiologic events relevant to each stage of ALI/ARDS, and much has been learned in the alveolar epithelial, endobronchial homeostasis, and alveolar cell immune responses, especially neutrophils and alveolar macrophages in an animal model. However, these effective results in the animal models are not equally adoptive to those in randomized, controlled trials. The clinical course of ALI/ARDS is variable with the likely pathophysiologic complexity of human ALI/ARDS ***(Tsushima et al, 2009)***

Definition:

The first description of acute respiratory distress syndrome (ARDS) was in 1967 by ***Ashbaugh et al, 1967*** who described 12 patients with acute respiratory distress, cyanosis refractory to oxygen therapy, decrease lung compliance, and diffuse infiltrates on chest radiography.

In 1988, an expanded definition was proposed based on the level of positive end-expiratory pressure (PEEP), the ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen, the static lung compliance, and the degree of infiltration evident on chest radiography. Another measurement, the lung injury score (LIS), has

been widely used to quantify the disease severity in clinical trials, although it has not been shown to accurately predict outcome during the first 24 to 72 hours after the onset of ARDS. ***(Tsushima et al, 2009)***

In 1994, a new definition was recommended by the American-European Consensus Conference Committee **(Table 1)**, which recognized the variability in severity of lung injury, and separated patients into two groups: those with less severe hypoxemia were categorized as having acute lung injury (ALI), and those with more severe hypoxemia were defined as having ARDS. However, factors such as the underlying cause and involvement of other organ systems are not a part of the existing definition. ***(Tsushima et al, 2009)***

Table (1): Definitions of the Acute Respiratory Distress Syndrome

(Tsushima et al, 2009)

Reference	year	Definition of criteria	Advantages	Disadvantages
Petty and Ashbaugh (1)	1971	Severe dyspnea, tachypnea Cyanosis refractory to oxygen therapy Decreased pulmonary compliance Diffuse alveolar infiltrates on chest radiography Atelectasis, vascular congestion, hemorrhage, pulmonary edema, and hyaline membranes at autopsy	First description Summarizes clinical features well	Lacks specific criteria to identify patients systematically
Murray et al. (2)	1988	Preexisting direct or indirect lung injury Mild-to-moderate or severe lung injury Nonpulmonary organ dysfunction	Includes 4-point lung injury scoring system Specifies clinical cause of lung injury Includes consideration of the presence or absence of systemic disease	Lung-injury score not predictive of outcome Lacks specific criteria to exclude a diagnosis of cardiogenic pulmonary edema
Bernard et al. (3)	1994	Acute onset Bilateral infiltrates on chest radiography Pulmonary-artery wedge pressure <18mmHg or the absence of clinical evidence of left atrial hypertension Acute lung injury considered to be present if PaO_2:FiO_2 <300 Acute respiratory distress syndrome considered to be present if PaO_2:FiO_2 <200	Simple, easy to use, especially in clinical trials Recognizes the spectrum of the clinical disorder	Does not specify cause Does not consider the presence or absence of multiorgan dysfunction Radiographic findings not specific

PaO_2 denotes partial pressure of arterial oxygen, and FiO_2 fraction of inspired oxygen.

Recently, a new consensus definition of ARDS, the Berlin definition, has been published. The new definition of ARDS maintains a link to the 1994 definition with diagnostic criteria of timing, chest imaging, origin of edema, and hypoxemia According to the revised definition of ARDS, a minimum level of positive end-expiratory pressure (PEEP) and mutually exclusive PaO2/FiO2 thresholds was chosen to differentiate between three levels of severity (mild, moderate, and severe) of ARDS. The revised definition appears to have improved predictive validity for mortality of its spectrum of severity. The revised definition presents a severity oriented method for respiratory management of ARDS. ***(Koh, 2014)***

In a large, multi-ICU cohort of patients with ARDS *by* ***Kangelaris et al, 2014*** both LIS and the Berlin definition severity stages were associated with increased in-hospital morbidity and mortality. However, predictive validity of both scores was marginal, and there was no additive value of LIS over Berlin. Although neither LIS nor the Berlin definitions were designed to prognosticate outcomes, these findings suggest that the role of LIS in characterizing lung injury severity in the era of the Berlin definition ARDS may be limited.

Epidemiology, incidence and mortality:

Epidemiology:

Bacterial or viral pneumonia is the most common cause of ALI and ARDS. Sepsis due to nonpulmonary infections, aspiration of gastric contents, and major trauma with shock also commonly precipitate the injury. Less commonly, acute pancreatitis, transfusions, drug reactions, fungal and parasitic lung infections are linked to ALI and ARDS. The coexistence of two or more of these risk factors can enhance the likelihood of developing ALI or ARDS. ***(Matthay et al, 2012)***