Role of Glutamic Acid in Immunonutrition of Abdominal Sepsis in Intensive Care Unit Patients

Thesis submitted for M.Sc degree in Anesthesia and Surgical ICU

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Abstract

A lot of data emphasized the immunostimulatory role of supplemental glutamine. Increased counts of circulating total lymphocytes and enhanced T-cell lymphocyte synthesis are consistently found in stressed patients following provision of glutamine.Therefore, if a conditional deficiency occurs in critically ill patients, replacement with glutamine is mandatory. From here, we started the idea of our research which was concerned with studying the effect of parenteral glutamine supplementation in addition to conventional nutritional intake on the clinical outcome of patients suffering from abdominal sepsis. By the time the study was done, there were no adequate studies for the effects of glutamine in patients suffering from abdominal sepsis.

Key word

Immunonutrition

Abdominal Sepsis

Anesthesia

Complement

GSH

Interferon-alpha

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List of Abbreviations

AAs : Amino Acids
ALA : Alpha- Linolenic acid
ALI : Acute lung injury
ALT : Alanine aminotransferase
APACHE II : Acute Physiology and Chronic Health Evaluation II
APC : Activated protein C
ARDS : Acute respiratory distress syndrome
AST : Aspartate aminotransferase
BT : Bacterial Translocation
BUN : Body urea nitrogen
C3 : Complement 3
C5 : Complement 5
CD4 : Cluster of differentiation 4
CD8 : Cluster of differentiation 8
CD17 : Cluster of differentiation 17
CRP : C- reactive protein
CTL : C-type lectins
CVP : Central venous pressure
DHA : Docosahexanoic acid
DIC : Disseminated intravascular coagulopathy
DVT : Deep venous thrombosis
EPA : Eicosapentaenoic acid
GALT : Gut associated lymphoid tissue
Gln : Glutamine
GSH : Glutathione
HDL : High density lipoproteins
ICU : Intensive care unit
IFN-α : Interferon-alpha
IgA : Immunoglobulin-A
IGF-1 : Insulin growth factor- 1
IL-1 : Interleukin- 1
IL-2 : Interleukin- 2
IL-4 : Interleukin- 4
IL-6 : Interleukin- 6
IL-10 : Interleukin- 10
IL-13 : Interleukin- 13

iNOS : inducible Nitric oxide synthase
IV : Intravenous
LDL : Low density lipoproteins
LMWH **:** Low molecular weight heparin
LPS : Lipopolysaccharide
LTC4 : Leukotriene C4
MAP : Mean arterial pressure
MHC : Major histocompatibility
MLNs : Mesentric lymph nodes
MODS : Multiple organ dysfunction syndrome
MOF : Multiorgan faliure
NK : Natural killer
NF-κB : Nuclear factor κB
NO : Nitric oxide
n-3FA : Omega 3 fatty acids
PAMPs : Pathogen associated molecular patterns
PUFA : Polyunsatturated fatty acids
SBP : Systolic blood pressure
SD : Standard deviation
SIRS : Systemic inflammatory response syndrome
SvO_2 : Mixed venous saturation
TCR : T-cell receptor
Th1 : T-helper 1
Th2 : T-helper 2
TLC : Total leukocytic count
TLR : Toll-like receptors
TNF-α : Tumour necrosis factor alpha
TPN : Total parenteral nutrition
UFH : Unfractionated heparin

INTRODUCTION

Glutamine is an amino acid that has received considerable attention during the past 10 years. It has been shown to be beneficial for the metabolically stressed patient, especially the critically ill patients. During acute illnesses patients experience nutritional depletion that is correlated to low plasma and low mucosal glutamine concentrations. Such deficiencies are common among hospitalized patients and are associated with an increased risk of developing infectious complications, organ failure, and death. [1]

Glutamine has many essential metabolic functions in the body. This amino acid is an energy substrate for most cells, especially for enterocytes and lymphocytes; it is also a precursor for nucleotide, glutamate, and, in particular, for glutathione synthesis, an important cellular antioxidant. It plays a central role in nitrogen transport within the body, and is the most important substrate for renal ammoniagenesis. [1]

Thus, its functions within the cell are generally separated into four categories:

1) its role in nitrogen transport;
2) its importance in maintaining the cellular redox state;
3) its position as a metabolic intermediate; and
4) its role as an energy source. [1]

In light of these findings, glutamine has been classified as a 'conditionally essential amino acid', in that it is usually a nonessential amino acid that must be supplemented during situations such as critical illness, when endogenous glutamine production cannot keep up with the increased demand. Several clinical trials of parenteral as well as enteral glutamine supplementation to critically ill patients have shown a beneficial effect both on infectious complications and mortality; however, others were unable to detect improvements in mortality or morbidity with parenteral supplementation. [2]

Depending on the demands, there is increased utilization by the gut, liver, spleen, kidney and immune cells. The process of muscle glutamine release is not fully understood, but it is intimately related to the stress response, particularly cortisol. Recent evidence suggests that just like post-operative insulin resistance, it can be attenuated post-operatively by immediate food intake. [3]

Abdominal sepsis is the most common cause of major morbidity and mortality associated with postoperative abdominal surgeries, with the pathogenesis of such infections remaining unknown. Bacterial translocation (BT) is known as the passage of viable bacteria or endotoxins from the gut to mesenteric lymph nodes (MLNs) and to other organs, which may commence or exacerbate septic states. [3]

Translocation of organisms from the gastrointestinal tract to extraintestinal sites is known to be promoted by factors causing systemic insult or bowel injury. Several studies have demonstrated that intra-abdominal inflammation during acute peritonitis promotes BT in the absence of obvious microscopic injury of the intestine. [4]

Glutamine (Gln) is known as the most significant energy source of enterocytes, and lowers the rate of endotoxemia and translocation by preserving mucosal integrity. [4]

It is known that glutamine is an important fuel for lymphocytes and macrophages. Macrophages and neutrophils are involved in the early, non-specific host defense responses, and play an important role in the pathophysiology and protection against sepsis. In fact, this amino acid is required for the expression of lymphocyte cell surface markers, clusters of differentiation, such as CD8, CD4, and CD17. [1]

AIM OF THE STUDY

The aim of the study is to investigate whether the provision of parenteral glutamine in patients with abdominal sepsis after abdominal surgeries improves infectious morbidity and length of stay in ICU patients or not.

ABDOMINAL SEPSIS

The term systemic inflammatory response syndrome (SIRS) was coined in 1992 by a panel composed of members of the American College of Chest Physicians and Society of Critical Care Medicine. They convened to develop consensus definitions of critical illness for the purposes of clinical trial design. [5]

SIRS describes the host response to a critical illness of infectious or noninfectious cause, such as burns, trauma, and pancreatitis. More specific definitions are as follows:

- Sepsis is SIRS resulting from a presumed or known site of infection.
- Severe sepsis is sepsis with an associated acute organ failure.
- Septic shock, a subset of severe sepsis, is defined as a persistently low mean arterial blood pressure despite adequate fluid resuscitation
- Refractory septic shock is a persistently low mean arterial blood pressure despite vasopressor therapy and adequate fluid resuscitation.

In 2001, the International Sepsis Definitions Conference modified the model of SIRS and developed an expanded view of sepsis after revisiting the literature. This conference developed the concept of a staging system for sepsis based on four separate characteristics designated by the acronym PIRO: