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Review Article

GLUTAMINE: PRESENT AND FUTURE

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ABSTRACT
Glutamine is the most abundant free amino acids in humans, contributing more than 50% of the body's free amino acid pool. Traditionally regarded as nonessential Amino acid but recently it has been found that during catabolic states resulting from major surgery, severe trauma or sepsis, glutamine consumption may exceed its endogenous production. Glutamine supplementation is critically ill patient's augments immune function, reduces intestinal permeability, improves organ function and reduces oxidative stress. Administration of glutamine can also prevent oxidative stress damage and lower rate of infectious complications and pneumonia. In critically ill patients Glutamine administration for 9 days was found to have improved survival than in patients receiving Glutamine for 5 days. The effects of glutamine are better if it is administered as more stable dipeptides (i.e, Alanyl glutamine or Glycyl-glutamine) intravenously. Intravenous administration of 20-40 g/24 hr of Glycyl-glutamine improves short term outcome in patients. In burn patients addition of glutamine to standard enteral formula has been shown to improve intestinal permeability, wound healing and reduced plasma endotoxin level and duration of hospital stay and mortality. In trauma patients it has shown to lower the prevalence of bacteraemia, pneumonia and sepsis. Glutamine has also shown to have improved glycaemic control when administered at a dose of 0.2 – 0.4 g /kg /day.

Keywords: *Glutamine, Amino Acid*

INTRODUCTION
Glutamine is a non essential amino acid which is synthesized and released from the skeletal muscle. It is conditionally essential during stress (trauma, burn, sepsis). It contributes too many functions including immune function, gluconeogenesis, cellular energy supply, maintenance of organ integrity and function, wound healing, acid base homeostasis and nitrogen transport.
Rationale of use of glutamine is an area of interest in evidence based medicines especially in an era where antibiotic resistance is on a gradual rise.

Evidence Based Clinical Situations where Glutamine Usage is recommended

A. Oncology (Indispensable Nutrient)

1. Diminishes risks of high dose chemotherapy and radiation.
2. Beneficially affects outcome in patients undergoing bone marrow transplantation.
3. Reduces incidence of stomatitis.
4. Weakens the immunosuppressive effect of chemotherapeutic L-asparaginase.
5. Improves immune function and nitrogen balance in patients with colorectal cancer postoperatively.

B. Systemic Inflammatory Response Syndrome (SIRS)

1. Decreases Simplified Acute Physiology (SAPS II) Scores. Leukocytes and natural killer (NK) cell count, which might be associated with suppressing inflammation and improving clinical recovery.
2. B and T lymphocytes increased which in turn improves immune system.
3. Decreases infection related complications and length of hospital stay.

C. Stress Handler

Glutamine is an essential precursor of glutamate for the synthesis of glutathione (GSH) which is a tripeptide protecting cells from oxidative stress.

D. Critical Illness Myopathy

The addition of enteral glutamine to parenteral regimen (not already containing supplemental glutamine) should be consideration in burn, trauma and mixed ICU patients (Grade: B) . It reduces ICU stay and mortality, when given in 0.3-0.5g/ Kg/day dose. It has also trophic influence on intestinal epithelium and maintenance of intestinal integrity.

E. As an Immunonutrient and Immunomodulator

Glutamine is essential for immune nutrition in the critically ill. Impairment of immune system functioning contributes to the development of sepsis. Monocytes show reduced expression of human leukocyte antigens (HLA-DR) . Glutamine is required by the cells of the immune system both as a primary fuel and as a carbon and nitrogen donor for nucleotide precursor synthesis. Glutamine is essential for optimal immune cell functioning for monocytes, lymphocytes and neutrophils. It helps in nitrogen transport maintaining cellular redox state.

F. Total Parenteral Nutrition with or without I.V Glutamine in Severe Acute Pancreatitis

The main reasons for the high mortality and incidence of acute respiratory distress syndrome (ARDS) and multiple organ dysfunction syndromes (MODS) in pneumonia are enterogenous bacteraemia and endotoxaemia. It mainly results from endotoxins and translocation of bacteria to extraintestinal organs, which is closely related to an imbalance of the enteral flora and because of the damage of the peristalsis and barrier function of the gut.

Glutamine is not only an essential fuel for the rapidly growing and differentiating epithelial cells of enteric mucosa but also an important regulatory factor in maintaining the balance of the enteric micro-ecological environment, mucosal structure, barrier and immunological function. Thus glutamine reduces endotoxaemia and infections complications.

G. Glutamine during Continuous Renal Replacement Therapy (CRRT)

Glutamine requirement increases in patients on CRRT.

H. In Major Surgeries including Trauma

Routine use of I.V. glutamine in patients with mild preoperative weight loss or surgical stress or in elective Surgery is not suggested. Glutamine improves 6 months outcome in critically ill patients. Glutamine is indicated in pre- and postoperative catabolic states, trauma and sepsis.

Route and Form of Administration

Both oral and I.V. formulations are available with more evidence in favour of I.V. glutamine. Based on 4 levels I studies and 13 level II studies when parental nutrition is prescribed to critically ill patients, parental supplementation with glutamine is strongly recommended.

Free Glutamine is unstable in aqueous solution and cannot be heat sterilized. Hence it is provided as a dipeptide Glycyl-glutamine or Alanyl-glutamine. 0.3 unit dipeptide is equivalent to 0.2 unit glutamine. Simultaneous administration along with TPN is recommended to favour the process of assimilation. It can be administered orally and also through central or peripheral line.

Future Perspectives

1. Attenuates expansion of extracellular and total body water
2. Decreases glucose intolerance, insulin resistance.
3. Secretagogue effect on eneteroendocrine L-cells producing glucagon like peptide- 1 and 2.These two controls satiety, GI motility, islet hormone secretion and regulation of β cell proliferation and survival.
4. Indirect precursor of glutathione.
5. Cardioprotective action of glutamine needs further evidence.
6. Further studies are required to look into the exact difference between Glycyl-glutamine and Alanyl-glutamine though it is suggested that glycine might enhance the uptake of glutamine into human monocytes leading to enhanced expression of Tumor necrosis factor (TNF-α).

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