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Glutamine as an Alternative Nutrition in Clinical Practices

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Abstract
Glutamine appears as an essential amino acid in patients with catabolic disease. Glutamine is the most abundant amino acid in the blood and free amino acid pool in the body that has a five-carbon Glutamine supplementation has been associated with reduced mortality, infections and hospital length of stay in critically ill patients and patients undergoing major surgery. Parenteral nutrition (PN) glutamine supplementation may be advantageous in certain other adult surgical patients or critically ill non-ventilated patients requiring PN. A positive impact of PN glutamine supplementation in hematopoietic stem cell transplant recipients, burn patients, and patients with severe acute pancreatitis remains unclear and warrants large, well designed, randomized control trial

I. INTRODUCTION

Glutamine is one of the most abundant non-essential amino acids in the human body and plays a significant role in different biochemical process.[1,2] It has numerous functional in normal physiology, for example it acts as a precursor for protein synthesis; and it transport amino-nitrogen to intestine, liver and kidney. It also plays key role in acid-base homeostasis. [3,4,5] Glutamine may affect stress-induced accumulation of extracellular fluid by changing the cellular hydration state. [6] Glutamine drop may be due to glutamine's central role in nitrogen transport within he body, whith contributing to both precursors for nucleic acid synthesis, as well as antioxidant defenses through the production of glutathione. In addition, glutamine is the preferred fuel for rapidly dividing cells, such as enterocytes in the small intestine and immune cells, such as lumphocytes, monocytes and macrophages. For some patients, the shynthesis and release of glutamine from skeletal muscle is insufficient to meet demands, and a deficiency in glutamine may lead to permeability and bacterial translocation. These negative effects, along with immunosuppression, may all contribute to an increase probability of secondary infection risk, which may impede the recovery time of the patient, or worse, increase in-patient mortality rates. [7] During certain pathological conditions, such as critical illness, the body is unable to produce sufficient amounts of glutamine causing profound depletion in plasma and tissue glutamine levels making it a conditionally essential amino acid. [4,8,9,10] Low plasma and tissue levels of glutamine have been associated with poor clinical outcome. [11] More than a dozen clinical studies have suggested that provision of parenteral or enteral glutamine supplementation in both critically ill and surgical patients. Some studies also have demonstrated beneficial effects of glutamine supplementation while significant reports of negative of adverse effects have not been published. A systematic review of glutamine supplementation demonstrated that parenteral glutamine supplementation was more beneficial than enteral suplemetation in term of reduced mortality and hospital length of stay. High dose supplementation (i.e., > 0.2 g/kg/day) lowered infectious complications in surgical patients compared to low dose (i.e., < 0.2 g/kg/day).[10,12] Current best evidence which includes four RCTs involving a total 190 participant demonstrated that glutamine is effective for severe acute pancreatitis. [13] Twelve RCT that enrolled 505 patients with acute pancreatitis also demonstrated that glutamine supplementation significantly reduced risk of mortality (RR 0.58; 95% CI, 0.39 to 0.87; $P = 0.009$) but not length of stay (MD -135; 95% CI, -3.25 to 0.56, P = 0.17). [14]

II. PROBLEM DEFINITION

A. Limitations to use of free glutamine

In theory, the intracellular glutamine depletion caused by hypercatabolic states which can be caused by several factors such as in critically ill patients and patients undergoing major surgery. It should be treatable by glutamine replacement, so maintaining muscle protein. However the limit solubility (3 g/dL at 20 °C) and instability of free glutamine hamper its use for this purpose. [15] The rate of breakdown depends on temperature, pH and anion concentration. Free glutamine can be provided by

adding the crystalline aminoacid to a commercially available aminoacid solution before administration, but this is time consuming. [15]

B. Glutamine-supplemented enteral feeding

All enteral nutrition (EN) formulations contain some glutamine with several commercially available formulas containing additional supplemental glutamine. Oral glutamine products aew available for oral supplementation of use with EN formulations. In the critically patient on the intensive-care unit, parenteral nutrition is used only when enteral feeding is unsuccessful or impractical. Conventional enteral feeds provide some glutamine (protein-based enteral products 6-8 g/day, and peptide-based products 1-5 g/day), but this is insufficient for the critically ill patient and some workers argue for supplement of 10-20 g/day. [16] 50-80% of free glutamine is absorbed by the gut during routine enteral feeding and plasma glutamine can be seen ti rise with supplementation. Supplemented enteral feeds can reverse the changes in intestinal permeability associated with parenteral feeds, possibly by yielding a high glutamine concentration (> 2.5 mmol/L) in the gut lumen. [17,18] Some researchers find that addition of glutamine to enteral nutrition formulas in critically ill patients reduces rates of pneumonia, sepsis and bacteremia, with shortened hospital stay and lower hospital cost, [17-20] but others report no benefit. [21]

C. Glutamine-supplemented parenteral feeding.

Parenteral free L-glutamine has limited stability in aqueous solutions compared to the currently manufactured crystalline amino acid solutions therefore it is not included in thw standard amino acid solutions used to compound PN. Appropriate compounding of free L-glutamine for administration alone or admixed in PN requires a strict aseptic environment and storage at 4 °C when cold membrane sterilization is performed. Because the risk of precipitation, final concentratios of free L-glutamine should not exceed 1.5%. [8,9,22] Two preparations available for addition to parenteral nutrition are L-alanyl-L-glutamine (Ala-Gln) and glycyl-L-glutamine. [23,24] In contrast to free L-glutamine, dipeptide formulations with glutamine residues at the C-terminal position confer high water solubility, stability during heat sterilization and capability for prolonged self-life (e.g., 2 years). When given intravenously, the dipeptide is hydrolyzed by peptidase on the surface of the endothelium releasing free L-glutamine within 3 to 10 minutes of administration. [10]

D. Clinical studies

Some studies also have demonstrated beneficial effects of glutamine supplementation while significant reports of negative of adverse effects have not been published. [10] The results of 19 meta analyses indicate that parenteral and/or enteral intakes of 0.3 to 0.45 g/kg/day can provide statistically significantly reductions in the incidence of infectious complications for 15 of the 19 meta analyses with relative risks of all 19 ranging between 0.42-0.93.[7] The results of 18 meta analyses demonstrate that parenteral and/or enteral intakes of 0.3 to 0.45 g/kg/day can provide statistically significantly reduction in length of stay in hospital for 12 of the 18 meta-analysis.[7] The results of 15 meta analyses indicate that parenteral and/or enteral intakes of 0.3 to 0.45 g/kg/day provided statistically significant reduction in mortality for only four of the 15 meta-analysis with relative risk for all 15 meta-analyses ranging between 0.64 to 1.28. [7] Three meta-analyses have been published about PN glutamine supplementation use in critically ill patients. The first was published in 2006[12] and was combination of surgical patients (8 studies) and critically ill patients (6 studies). The meta-analysis showed trends toward improved mortality and incidence of infections in the glutamine supplementation patients but these differences were not statistically significant. Glutamine supplementation patients had a significantly shorter hospital LOS. In sub group analysis, the critically ill study patients still had trends toward reduced mortality (RR 0.77; 95% CI 0.57 to 1.03) and reduced infections (RR 0.86; 95% CI 0.68 to 1.08) but no significant difference in hospital LOS (Mean Weighted Difference (MWD) 0.9 days; 95% CI -4.9 to 6.8). The second meta-analysis was published in 2006[25] and divided the studies into those involving critically ill patients alone, those involving surgical patients alone, and those with combination of critically ill patients and surgical patients. The meta-analysis on the studies involving critically ill patients alone showed no differences in mortality or incidence of infections. The third meta-analysis was presented as a part of Canadian critical care guidelines released in 2009[26]. This

meta-analysis demonstrated a significant decrease in hospital mortality, infectious compliactions and hospital LOS

III. CONCLUSION

Parenteral glutamine supplementation most likely to benefit in critically ill patients and patients with high risk of gut dysfunction such as patients undergoing major abdominal surgery. PN glutamine supplementation should probably be given early and in dose > 0.2 g/kg/day to be effective

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