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Glutamine Peptides

DESCRIPTION

Glutamine peptides refer to certain dipeptides used in total parenteral nutrition (TPN) as delivery forms of L-glutamine. The term also refers to peptides containing L-glutamine, which are found in some nutritional supplements, particularly those marketed as sports and fitness products.

L-glutamine depletion is a typical feature of such metabolic stress conditions as trauma (including surgical trauma), infection, sepsis, cancer and severe burns. The metabolic response to these conditions is characterized by catabolism and negative nitrogen balance. Under these conditions, L-glutamine, which is normally manufactured by the body (mainly in skeletal muscles) in sufficient quantities to satisfy physiological demands, is required exogenously. Under these conditions, L-glutamine becomes an essential amino acid and must be supplied to the body in order to prevent breakdown of muscle tissue, immune dysfunction and compromise of the gut mucosal barrier function with consequent bacterial translocation into the body. L-glutamine is arguably the most needed amino acid and, indeed, one of the most needed nutrients under these circumstances.

Until recently, L-glutamine was lacking from TPN. The reason for this is because L-glutamine is not very soluble in water—one gram dissolves in 20.8 ml of water at 30 degrees Celsius—and L-glutamine is unstable in solution. The problem has been solved by the synthesis of glutamine-containing dipeptides, which are very soluble in water and stable in solution.

Two synthetic glutamine-containing dipeptides that may be used in TPN are L-alanyl-L-glutamine (Ala-Gln) and glycyl-L-glutamine (Gly-Gln). The molecular weight of Ala-Gln is 217.24 daltons, and L-glutamine comprises 67% of the dipeptide. L-glutamine comprises 72% of Gly-Gln, and its molecular weight is 203.22 daltons.

ACTIONS AND PHARMACOLOGY

ACTIONS

Glutamine peptides may have immunomodulatory, anticatabolic/anabolic, gut mucosal barrier-protective and antioxidant actions.

MECHANISM OF ACTION

The glutamine dipeptides, Ala-Gln and Gly-Gln, have demonstrated immunomodulatory, anticatabolic/anabolic, gastrointestinal mucosal protective and antioxidant activities when used in TPN. These activities have not yet been demonstrated with glutamine peptides marketed as nutritional supplements for fitness purposes. The mechanism of the immunomodulatory action of the glutamine dipeptides is unclear. The mechanism may in part be due to the ability of L-glutamine to ameliorate the negative effects of TPN on the immune system. Also, L-glutamine is the preferred respiratory fuel for lymphocytes and appears to be required to support the proliferation of mitogen-stimulated lymphocytes, as well as the production of interleukin-2 (IL-2) and interferon-gamma (IFN-gamma). It also appears to be required for the maintenance of lymphokine-activated killer cells (LAK). It can also enhance phagocytosis by neutrophils and monocytes.

The anticatabolic/anabolic action of the glutamine dipeptides can be explained by their effect in sparing skeletal muscle L-glutamine stores. Most of the L-glutamine in the body is synthesized in skeletal muscle, where it is also stored. Under conditions of metabolic stress, skeletal muscle can be depleted of its L-glutamine, which is used for metabolic activities of other tissue/cells, such as enterocytes and lymphocytes.

The gastrointestinal mucosal-protective effect of the glutamine dipeptides can be explained in a few ways. L-glutamine is the preferred respiratory fuel for enterocytes and colonocytes. Maintaining the bioenergetics of these cells is fundamental to maintaining the integrity of the intestine. In addition, L-glutamine helps maintain secretory IgA, which functions primarily by preventing the attachment of bacteria to mucosal cells. L-glutamine may inhibit translocation of Gram-negative bacteria from the intestine into the body.

Metabolic stress goes hand in hand with oxidative stress. L-glutamine can help in ameliorating oxidative stress by serving as precursor to glutathione.

PHARMACOKINETICS

Glutamine dipeptides in TPN are transported via the circulation to the various tissues of the body, where they are taken up by cells and metabolized. Ala-Gln is first metabolized to L-alanine and L-glutamine, while Gly-Gln is metabolized to glycine and L-glutamine. L-glutamine participates in various metabolic activities, including the production of L-glutamate and other amino acids, glutathione, energy, proteins, pyrimidine and purine nucleotides and amino sugars. L-glutamine is eliminated by glomerular filtration and is almost completely reabsorbed by the renal tubules.

Most of the glutamine dipeptides administered orally or enterally are absorbed intact from the lumen of the small intestine into the enterocytes. A portion of the glutamine dipeptides gets metabolized within the enterocytes. That which is not metabolized enters the portal circulation from whence it is transported to the liver. Again, some metabolism takes place in the liver, and that portion not metabolized enters the systemic circulation and is distributed to various tissues of the body.

INDICATIONS AND USAGE

Like glutamine itself (see Glutamine), the dipeptide forms added to TPN are credited with helping in the recovery of trauma, surgical and other critically ill patients. There is as yet no credible evidence that oral use of glutamine peptide supplements has anabolic or ergogenic effects in those who are not metabolically compromised.

RESEARCH SUMMARY

Studies have shown that glutamine and glutamine dipeptides exert similar metabolic effects. The dipeptides themselves are now being used in clinical nutrition.

In one recent, double-blind, randomized, controlled study, duration of hospital stay was significantly reduced in patients who had undergone major abdominal surgery and who had received glutamine dipeptides via TPN over a five-day period. Mean cumulative nitrogen balance was significantly better in these patients, as was immune function, as measured by lymphocyte counts and generation of cysteinyl leukotrienes by polymorphonuclear neutrophils, a measure of neutrophil function.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

CONTRAINDICATIONS

Glutamine peptides are contraindicated in those hypersensitive to any component of a glutamine peptide-containing product.

PRECAUTIONS

The use of glutamine dipeptides in TPN must be done under medical supervision.

Those with renal and liver failure should exercise caution in the use of glutamine peptide supplements.

Pregnant women and nursing mothers should avoid the use of oral glutamine peptide supplements unless prescribed by their physicians.

ADVERSE REACTIONS

There are rare reports of constipation and bloating with high dose glutamine peptides in TPN.

INTERACTIONS

DRUGS

See L-Glutamine.

OVERDOSAGE

No reports of overdosage.

DOSAGE AND ADMINISTRATION

The use of glutamine dipeptides in TPN is relatively recent. The two synthetic dipeptides used are L-alanyl -L-glutamine and glycyl-L-glutamine. Doses suggested (given as L-glutamine) are 12 grams daily for surgical trauma and about 25 grams daily for severe trauma and infections.

Those who use oral glutamine peptide supplements for fitness or sports purposes use 1.5 to 4.5 grams (as L-glutamine) daily.

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Glutathione

DESCRIPTION

The term glutathione is typically used as a collective term to refer to the tripeptide L-gamma-glutamyl-L-cysteinylglycine in both its reduced and dimeric forms. Monomeric glutathione is also known as reduced glutathione and its dimer is also known as oxidized glutathione, glutathione disulfide and diglutathione. In this monograph, reduced glutathione will be called glutathione— this is its common usage by biochemists—and the glutathione dimer will be referred to as glutathione disulfide.