Glutamine in Oncology – Friend or Foe

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Michalak KP, et.al. Key Roles of Glutamine Pathways in Reprogramming the Cancer Metabolism. Oxidative Medicine and Cellular Longevity. Volume 2015, Article ID 964321, 14 pages. http://dx.doi.org/10.1155/2015/964321

Clinical Discussion:

l-Glutamine the amino acid is one of the most widely used therapeutic substances in natural and integrative clinics as well as some allopathic practices. It has benefit in gastrointestinal illnesses and repair, post-surgical care, renal support, muscle mass maintenance, cachexia and a number of other conditions. Given its wide use in the integrative medical community the concern regarding potential for any adverse or untoward event associated with its use is significant. The primary potential issue is the "feeding" of cancer cells and another related issue is increasing glutathione stores and thereby inactivating standard therapies.

Likely the most concerning of all potential adverse events is potentiation of cancer in a person using therapeutic l-Glutamine (GLN). As with many considerations in medicine it is not a simple answer. The authors state "In analyzing GLN intake as a possible positive or negative factor supporting the cancer growth and/or cancer treatment, one must take into consideration the differences between the metabolism of healthy and cancer cells. The main problem of this analysis is the variety of metabolic changes characterizing different cancer types. Individual types of cancer metabolism should be analyzed with regard to the possible positive or negative effect of glutamine supplementation. Some methods of metabolic analysis of cancer cells are available." They then proceed to elaborate on many of the variations in cancer cells that may cause a difference in metabolism in the presence of GLN.

The authors take an exhaustive look at GLN metabolism in normal and cancerous cells, outlining and elucidating differences in GLN metabolism. What they clearly show is that a simplistic view of the role of GLN in oncology just cannot do justice to the topic. Factors which may alter considerations in the patient with cancer include dose, timing, tumor type and patient depletion.

Potential GLN benefits include but are not limited to:

- Post-surgical healing
- GI repair and maintenance

- Immune system recovery and maintenance
- Muscle cell maintenance and recovery
- Glutathione pool restoration
- HIF-1 alpha inhibition
- And others

In cancer metabolism there is a deterioration of Pyruvate dehydrogenase complex (PDHC) and oxidative phosphorylation (OXPHOS) leading to safety when GLN is in the system. Broadly speaking there are few tumor types that oppose this metabolic change. The availability of GLN even in a supplemented person is often too low to do much more than feed the deficient GI cells, so peripheral use is limited with oral doses.

The one commonly mentioned exception is glioblastoma multiforme (GM). In the case of GM it is theoretically possible that amounts of GLN that were able to cross the GI barrier could be metabolized in a manner promoting of GM energy and health. In the case of GM the authors point out that restricting carbohydrates would likely make the GLN effective in an anti-GM biology. They state: "Thus, the supplementation of GLN as the source of NADH2/FADH2 for the impaired OXPH chain producing many ROS can be potentially beneficial in this case. It should be, however, accompanied with the strong carbohydrate reduction in the diet and/or with the glycolysis inhibition therapy and/or with the increase in amino- and fatty acids in the diet that supports TCA cycle and in this way the oxidative stress in the cell."

Take home points for practice:

1. GLN oral supplementation is likely safe across most tumor types in patients with cancer.
2. In cases of GI damage (during or after chemotherapy and radiation) GLN is indicated.
3. In patients with post oncology therapy depletion or cachexia restoration of the GLN pool is critical to survival.
4. In active cancers, especially those with active PDHC and OXPHOS, carbohydrate restriction improves the safety of GLN supplementation.
5. Once therapeutic repletion or outcome is achieved consider either decreasing the dose of or discontinuing the GLN.
6. In our clinics the standard uses of GLN in the oncology patient are as follows:

a. During and after chemotherapy and radiation GLN powder in liquid or a soft food 1-3 grams BID-TID and HS
b. In cases of post GI surgery recovery 4-6 grams PO TID
c. In active cancer therapy where GLN supplementation is indicated recommend:
    i. Dietary carbohydrate restriction
    ii. In cachexia we replete patients using oral and IV protocols.
    iii. Other metabolic therapies (DCA, LAMC, HBOT etc.) as they are important in many cancers, especially GM.

The authors quote ***"Based on the analysis of GLN metabolism, it can be concluded that if the OXPH chain is deteriorated, GLN cannot be an effective source of ATP for the cancer cell regardless of the metabolic pathway."***

This data, as well as my clinical experience, indicates that l-Glutamine used appropriately is an excellent adjunctive therapy in the oncology setting and with precautions outlined above should not be considered dangerous.