Glutamine Supplementation for Common Side Effects of Chemo and Radiation Therapies in Oncology Patients

Sarah Bushbaum, ASU-VA Dietetic Intern, BS, DTR

Katherine Petersen, MS, RD, CSO

Patients undergoing chemo and radiation therapies are at risk of a variety of physical complications that have the potential to negatively impact their nutrition, quality of life, and may even interfere with scheduled therapies. Mucositis, neuropathy, and GI upset are seen amongst a large portion of the oncology population and have a significant impact on these patients. Radiation has been shown to cause oral mucositis in approximately 80% of patients with head and neck cancer who undergo this treatment method, with 56% experiencing severity grades of 3 and 4[1]. Chemotherapy-induced peripheral neuropathy (CIPN), commonly interferes with dosing and affects around 30-40% of patients treated with this therapy to varying severities[2]. GI toxicities of all types are seen in patients undergoing all types of cancer treatments, estimated at about 25% of the population. Chemotherapy-induced diarrhea being a major contributor at about 50-80% of patients developing this side effect, with 30% of those patients struggling at a severity grade of 3[3]. Oral glutamine is an ideal treatment option for this population as it is a simple self-administration with little to no adverse side effects. Dependent upon the specific therapy complication, glutamine is provided for consumption or a swish and swallow method.

Research into the use of oral glutamine to alleviate such symptoms has provided us with both statistically and clinically significant results. Thirteen articles have reported on the role of glutamine for mucositis among oncology patients. Nine of these articles, including RCTs, systematic reviews, and meta-analyses showed positive results, while 4 showing no difference when compared to best

supportive care. As part of a double-blind, randomized, placebo-controlled study, previously untreated patients with primary squamous cell carcinoma of the nasopharynx, oropharynx, hypopharynx, or larynx were found to have a significant decrease in mucositis severity induced by CRT (Chemo-XRT) through the use of 10 g of glutamine 3 times per day[4]. This was seen to make the biggest impact through weeks 4-6 when the adverse side effects of CRT were the most severe. Positive results were also seen in a prospective cohort study of 262 HNC patients, in which oral glutamine at the same dose of 10 g 3 times per day resulted in prevention of oral mucositis and odynophagia, as well as decreased treatment interruptions and the need for use of analgesics or a nasogastric tube[5].

Peripheral neuropathy is also commonly seen in the oncology population; which can have a considerable impact on patients' quality of life as they undergo the before mentioned cancer therapies making sensations difficult and even putting the patient at higher risk for burns, infection, and falls[6]. 8 articles investigating the impact of oral glutamine on peripheral neuropathy were identified upon review of the recent literature. 4 articles, including both reviews and RCTs, demonstrated positive results and 4 concluded either a potential for use after further research conduction for validation or no difference as compared to best supportive care. Wang et al. found that a dosage of 15 g of oral glutamine 2x/day was effective in significantly reducing the incidence and severity of peripheral neuropathy of MCRC patients undergoing treatment with oxaliplatin, without interfering with the patient's response to chemotherapy and survival[7]. Similarly, a recent investigation of the recent advances in the treatment of drug-induced neuropathies concluded that the use of glutamine reduced the clinical development of neuropathy in patients receiving paclitaxel[8].

Many patients undergoing chemo and/or radiation therapies report experiencing a variety of GI symptoms including some persistent cases of diarrhea. 5 articles specific to GI toxicity were found to show positive results with supplementation of oral glutamine. All literature reviewed found that glutamine had at least a minor positive impact on patient GI toxicity and/or quality of life. In a

meta-analysis focused on the use of glutamine supplementation for relief of chemotherapy induced diarrhea found that oral glutamine was effective in significantly reducing the duration[9]. GI toxicity in chemo and radiation treated patients carry a strong risk for malnutrition, as conditions such as stomatitis and esophagitis can make it extremely difficult to consume adequate nutrients. A state of malnutrition puts them at an even higher risk of interruptions in treatment. Administration of oral glutamine in the face of these conditions has shown to provide a protective effect to GI tract tissues.

Just as with any type of supplement or medication, there are instances in which it is not ideal to prescribe oral glutamine to patients. Several studies have shown that the supplementation of glutamine has the potential to have a significant impact on the liver, with evidence that it can transiently raise AST/ALT levels[10]. This influence on liver function applies contraindications of use for patients with hyperammonemia or hepatic encephalopathy. Additionally, critically ill patients with multiple organ failure and those with sepsis are contraindicated for use of oral glutamine supplementation.

Condition	Recommended Administration	Recommended Dose*	Special Considerations for ALL Conditions
Mucositis/Stomatitis	Oral Swish & Swallow (for topical needs)	10 grams - TID	Patient tolerance/adherence may require adjustments to dosage and/or division of doses. Recent research demonstrates positive impact of divided doses of 20-30 grams per day. *While research suggests the before mentioned recommended doses, dividing the doses appears to be most significant factor as it allows for increased enterocyte contact.
Peripheral Neuropathy	Oral	15 grams - BID	
GI Toxicity	Oral	10 grams - TID	

Table 1: Recommendations for Glutamine supplementation in Oncology patients, based upon lit review.

As research into the use of oral glutamine grows, results continue to favor the use of oral glutamine for a wider variety of conditions. It is not only easy to use, cost effective, and well tolerated, but is also easily absorbable especially when given in divided doses. While there is still some debate that exists around its use in certain circumstances, studies have shown time and time again that oral glutamine is a safe and effective treatment option to alleviate specific patient discomforts during cancer therapies.

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