

# Research Background: Glutamine



## Oral glutamine supplementation can reduce the severity and duration of oral mucositis in cancer patients.

A randomized, double-blind, crossover trial in cancer patients (adults and children) receiving chemotherapy found a low dose oral glutamine supplementation during and after chemotherapy significantly reduced both the duration and severity of chemotherapy associated stomatitis.

**Research Paper:** Anderson et al, Cancer, 1998; 83:1433-9.

A randomized, double-blind, placebo-controlled study in patients undergoing bone marrow transplant showed a low dose oral glutamine supplementation reduced the duration and severity of mouth sores.

**Research Paper:** Anderson et al, Bone Marrow Transplantation, 1998; 22:339-344.

An early pilot study (non-randomized, adult cancer patients) demonstrated oral supplementation with glutamine significantly decreased the severity of chemotherapy-induced stomatitis, an important cause of morbidity in the treatment of patients with cancer.

**Research Paper:** Skubitz et al, J Lab Clin Med, 1996; 127[2]:223-8.

A systematic review of clinical trials found glutamine reduced the severity and duration of oral mucositis by (i) inhibiting the production of pro-inflammatory cytokines, and (ii) meeting the demands of mucosal tissue during wound healing. However, because glutamine is only moderately soluble in water, and undergoes nonenzymatic degradation in the stomach, its bioavailability is limited, when administered orally or parenterally.

**Review Paper:** Sayles et al, Nutrition in Clinical Practice, 2016; 31[2]:171.

A randomized, prospective case-control study (adult head and neck cancer patients undergoing radiation therapy) demonstrated grades 3 and 4 mucositis were observed significantly less in patients receiving glutamine than in the control group.

**Research Paper:** Chattopadhyay et al, South Asian Journal of Cancer, 2014; [3]1:8-12.

A double-blind, randomized, placebo-controlled study (pediatric patients undergoing hematopoietic stem cell transplantation) showed oral supplementation with glutamine significantly decreased the severity of oral mucositis.

**Research Paper:** Aquino et al, Bone Marrow Transplantation, 2005; [36]:611-16.



## Glutamine powder, when combined with mono- or di-saccharides then mixed with liquid to form a suspension, significantly increases glutamine absorption in the tissues that line the mouth, throat and esophagus, among cancer patients receiving chemotherapy.

A clinical study found when glutamine is complexed with a mono- or di-saccharide, the mucosal absorption of glutamine was shown to increase by more than 1,000 times. The authors conclude the efficacy and safety of a glutamine powder in an oral suspension was shown for the prevention and treatment of oral mucositis in patients receiving cancer chemotherapy.

**Clinical Study:** Peterson et al, Cancer, 2007; 109:322-31.



## Preliminary research suggests trehalose, a non-cariogenic disaccharide, does not affect plasma insulin levels, and may have anti-inflammatory and antioxidant benefits.

In vitro and vivo studies showed when cells were induced by a particular stressor, trehalose suppressed vasospasm, inflammatory response and lipid peroxidation.

**Research Paper:** Echigo et al, Journal of Translational Medicine, 2012; 10:80.

In a crossover study of healthy adults, blood glucose and insulin levels were found to be lower after consuming trehalose, compared with glucose.

**Research Paper:** Yoshizane et al, Nutrition Journal, 2017; 16:9.



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# Research Background: Oral Mucositis



## **Oral mucositis can lead to negative clinical outcomes resulting in reduced quality of life for patients.**

The pathogenesis of oral mucositis is multifactorial and complex and can negatively affect nutrition and quality of life of patients undergoing cancer treatment, sometimes leading to a dose-limiting complication of therapy.

**Review Paper:** Lalla et al, Dent Clin North Am., 2008; 52(1):61-75.

A multinational, prospective study of patient-reported outcomes, showed virtually all head and neck patients undergoing radiation treatment, with or without chemotherapy, developed mouth and throat sores of a sufficient severity that reduced quality of life (QOL) and required analgesics, which provided inadequate relief.

**Research Paper:** Elting et al, Cancer, 2008; 113[10]:2704-13.



## **Oral mucositis increases costs of care among cancer patients undergoing treatment.**

A review paper showed the side effects of cancer treatments, particularly those affecting the gastrointestinal tract (oral mucositis, diarrhea, nausea and vomiting) had significant clinical and economic costs associated with primary cancer therapy, largely attributable to increased hospitalization rates and lengths of hospital stay.

**Review Paper:** Carlotto et al, PharmacoEconomics, 2013; 31:753-766.

A retrospective study among patients with head and neck cancer and non-small lung cancer who received radio-chemotherapy found medical costs were greater for those who developed severe mucositis/pharyngitis, than for those who did not.

**Research Paper:** Nonzee et al, Cancer, 2008; 113[6]:1446-52.

Chemotherapy- and radiation-induced oral mucositis has been shown to have a significant economic impact due to costs associated with pain management, liquid diet supplements, gastrostomy tube placement or total parenteral nutrition and management of secondary infections and hospitalizations.

**Review Paper:** Lalla et al, Dent Clin North Am., 2008; 52(1):61-75.

A retrospective study found oral mucositis was associated with an incremental cost of \$1,700-\$6,000 per patient, depending on the grade, among patients with head and neck malignancies.

**Research Paper:** Elting et al, Int'l. J. Radiation Oncology Biology Phys., 2007; 68[4]:1110-1120.



## **Management of oral mucositis has primarily focused on palliative care, although new therapeutic solutions are being studied in context of current evidence-based clinical management guidelines.**

Current clinical management of oral mucositis is largely focused on palliative measures such as pain management, nutritional support and maintenance of good oral hygiene. However, this paper reviewed several promising therapeutic agents in various stages of clinical development for the management of oral mucositis, in the context of recently updated evidence-based clinical management guidelines.

**Review Paper:** Lalla et al, Dent Clin North Am., 2008; 52(1):61-75.



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