

## Issue 77

### In a nutshell

Glutamine is a fuel for gut and immune cells and seems to lessen cellular injury from stresses such as chemotherapy.

Some early trials show that it can lessen the clinical side-effects of chemotherapy, such as mouth ulcers and 'leaky gut'.

## Glutamine in chemotherapy

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## NUTRITION RESEARCH REVIEW

### Study one: Parenteral supplementation

Parenteral glutamine can significantly reduce the adverse effects of chemotherapy on the gastrointestinal mucosa, according to a recently published study from Germany.

**Subjects:** 24 patients with metastatic colorectal carcinoma receiving chemotherapy (5-fluorouracil and calcium folinate).

**Method:** A prospective intervention trial in which patients were randomised to have or not have parenteral glycyl-L-glutamine with their chemotherapy. Mucosal side-effects were assessed by endoscopy and histomorphometric measurements.

**Results:** When judged by endoscopy, there was a significantly lower level of mucositis and ulcerations of the gastric and duodenal mucosa after the third course of chemotherapy in the glutamine supplemented group ( $p < 0.01$  for gastric and  $p < 0.05$  for duodenal).

This group also had a significantly higher villus height/crypt depth ratio after therapy. (1st course  $p < 0.01$ ; 3rd course  $p < 0.05$ )

However, there was no significant difference in the level of clinical side-effects reported.

Ref: Decker-Baumann C et al. Reduction of chemotherapy-induced side-effects by parenteral glutamine supplementation in patients with metastatic colorectal cancer. *Eur J Cancer* 1999;35:202-7

### Study two: Oral glutamine and gut permeability

A Japanese study used objective measures of lymphocyte health and gut permeability to demonstrate a positive protective effect of oral glutamine supplementation in chemotherapy/radiotherapy patients.

**Subjects:** 13 patients with esophageal cancer about to receive combination of mediastinal radiotherapy and 5-fluorouracil/cisplatin chemotherapy.

**Method:** Randomised, controlled intervention study in which active treatment was oral glutamine (30 g/day for 28 days from start of radiochemotherapy). Lymphocyte count and phytohemagglutinin-stimulated blast formation were measured. Gut permeability was assessed using a phenolsulfonphthalein (PSP) urine excretion test.

**Table: Glutamine vs placebo supplementation in patients on chemo- and radiotherapy**

	Glutamine	Placebo	Signif.
Lymphocyte count	1,007	567	$p < 0.05$
Blast formation	33,860	19,478	$p < 0.01$
PSP excretion *	7.4	15.4	$p < 0.05$

\* lower value means less permeability

**Results:** There were significant benefits in relation to all three parameters in the active vs placebo treated group.

Ref: Yoshida S et al. Effects of glutamine supplements...on systemic immune & gut barrier function in patients with advanced esophageal cancer. *Ann Surg* 1998;227:485-91

### Study three: oral glutamine and mucositis

No positive effect on mucositis was found from giving oral glutamine to chemotherapy patients by an American study just published.

**Subjects:** 66 patients receiving their first 5-fluorouracil-based chemotherapy.

**Method:** Double-blind, randomised trial in which patients were given either oral glutamine supplementation or placebo along with their chemotherapy. Mucositis was assessed both by a standard physicians' evaluation and patient self-report.

**Results:** No significant differences were seen between active and placebo groups in regard to mucositis.

Ref: Okuno SH et al. Phase III controlled evaluation of glutamine for decreasing stomatitis in patients receiving fluorouracil (5-FU)-based chemotherapy. *Am J Clin Oncol* 1999;22:258-61

### Study four: Oral glutamine and mouth pain

Another American trial of oral glutamine which included paediatric as well as adult chemotherapy patients did find positive results, specifically in relation to mouth pain.

**Subjects:** 16 children and 8 adults having chemotherapy for cancer.

**Method:** Randomized, double-blind, placebo-controlled intervention trial in which patients were given oral glutamine (4.0 g amino acid/sq m in two divided doses). The solution was swished and then swallowed. Assessment of mouth pain and its impact on eating was self-reported by patients.

**Results:** Patients given glutamine had 4.5 days less mouth pain compared with placebo treated patients ( $p=0.0005$ ), and had 4 days less of having to eat soft food because of mouth pain ( $p=0.002$ ).

Ref: Anderson PM et al. Oral glutamine reduces the duration and severity of stomatitis after cytotoxic cancer chemotherapy. *Cancer* 1998 Oct 1;83:1433-9

## Comments

Glutamine, which is not regarded as an essential nutrient in health, seems to be more important in illness and acute stress. Some have referred to it as 'conditionally essential' for this reason. It acts as a fuel for gut and immune cells.

There is already quite a considerable body of laboratory and animal evidence that it can lessen cell damage in acute cellular stress, such as chemotherapy or inflammatory insult. This may be at least in part because glutamine can act as a 'nitrogen shuttle' and enhances protein metabolism in various ways, including preserving or enhancing levels of glutathione.

One particular area of interest has been in the use of glutamine to protect patients against the adverse side-effects of chemotherapy and radiotherapy on immune and gut cells. The studies summarised here are part of a slowly increasing trickle of research looking at this particular potential clinical application.

Whilst the results are encouraging, some caution is still in order. Most trials published so far have involved only small numbers of subjects and not all have had a positive result. But it is interesting to see positive outcomes when objective measurements are made, such as assessment of crypt depth, gut permeability etc.

But we are still not at the point where we have a practical picture of how glutamine might best be used, if at all, as an adjunct to chemotherapy. This includes knowing what dose and what route will have the best effect, and whether parenteral administration has any special advantages over oral.

This series on glutamine supplementation is continued in issue #78, which considers its application in severe illness.

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