Glutamine Supplementation for Critically Ill Adults

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**Review Question**

This review sought to determine the effects of glutamine supplementation in critically ill adults and after major surgery on infection rate, mortality, and other clinical outcomes, as well as to investigate potential heterogeneity across different patient groups and different routes of nutrition.1

**Relevance to Critical Care Nursing**

Plasma levels of glutamine, a nonessential amino acid, are lower in patients who are critically ill or undergoing major surgery. Numerous clinical trials and a systematic review have provided evidence to suggest that glutamine supplementation may reduce infection and mortality rates in these patients. However, 2 recently published, large randomized clinical trials (RCTs) did not find any benefit of glutamine supplementation in critically ill patients.2,3 This review sought to include the most recent RCTs and evaluate all of the evidence in order to determine what impact glutamine supplementation may have on outcomes for critical care and major surgery patients.

**Study Description and Results**

Studies selected for this review included randomized or quasi-randomized controlled trials, excluding cross-over trials. Participants were adults with a critical illness or those undergoing elective major surgery. Any participants receiving prophylactic glutamine supplementation before surgery were excluded. The intervention of interest was glutamine supplementation via the parenteral or enteral route, whereas control groups received placebo or no intervention. Primary outcome measures included the number of infectious complications as well as 1- and 6-month mortality rates. Secondary outcomes included length of intensive care unit (ICU) and hospital stay, days of mechanical ventilation, side effects, and quality of life.

Two review authors independently screened abstracts, assessed full texts using a standardized data extraction form, assessed for risk of bias, and resolved any disagreements by discussion. Of the 89 full-text studies retrieved, 57 articles from 53 studies met inclusion criteria and were analyzed in the review (n = 4671 participants). The trials were grouped as follows: 19 studies on ICU patients with various diagnoses, 18 studies on patients undergoing abdominal, thoracic or laryngectomy surgery, 8 studies on burn patients, 7 studies on patients with acute pancreatitis, and 1 study on patients from ICU and other departments.
Dichotomous data were analyzed by calculating the risk ratio, along with number needed to treat when appropriate. Continuous data were analyzed as the difference between means. Heterogeneity was assessed by visual inspection of forest plots and with $\chi^2$ and $I^2$ statistics. If tests indicated no heterogeneity, a fixed-effect model meta-analysis was performed. If substantial heterogeneity existed, a random-effects model was used with cautious interpretation. Publication bias was assessed qualitatively using a funnel plot. All statistical tests were performed using RevMan software (version 5.2) and reported with 95% confidence intervals (CIs).

Summary of Main Results

- Pooled data on nosocomial infection rates showed that glutamine supplementation statistically significantly reduced infectious complications in critically ill or major surgery patients (33 studies: relative risk (RR) 0.79, 95% CI 0.71-0.87, $P < .001$) and that 12 patients needed to be supplemented to prevent 1 infection.
- Analysis showed no statistically significant difference between glutamine supplement groups and controls in short-term mortality (36 studies: RR 0.89, 95% CI 0.78-1.02, $P = .10$) or long-term mortality (11 studies: RR 1, 95% CI 0.89-1.12, $P = .94$).
- Subgroup analysis of infectious complications and mortality outcomes did not find any statistically significant differences between elective surgical patients and critically ill patients, in patients with malignant versus nonmalignant disease, or in patients receiving enteral versus parenteral supplementation.
- Hospital length of stay was statistically significantly shorter in the supplementation group than in controls (36 studies: mean difference [MD] -3.46 days, 95% CI -4.61 to -2.32, $P < .001$). ICU stay was slightly longer in the glutamine-supplemented group (22 studies: MD 0.18 days, 95% CI 0.07-0.29, $P = .002$).
- Days of mechanical ventilation were found to be slightly shorter in the intervention group than in the control group (14 studies: MD -0.69 days, 95% CI -1.37 to -0.02, $P = .04$)
- There was no clear evidence indicating a difference between the groups for side effects and quality of life, as evidence on side effects was mixed and different measures of quality of life were used.
- Sensitivity analysis of only studies that had low risk of bias found that glutamine supplementation had beneficial effects in reducing the length of hospital stay (8 studies: MD -2.9 days, 95% CI -5.3 to -0.5), with no statistically significant difference between the groups for all of the other outcomes.

Nursing Implications

The available evidence on glutamine supplementation in critically ill or major surgery patients should be interpreted with caution as many of the included studies were at high risk of bias and had moderate heterogeneity. Nonetheless, the review found moderate evidence that glutamine supplementation can reduce infection rates and days of mechanical ventilation, and lower quality evidence that supplementation with glutamine can reduce hospital length of stay. There is no evidence that mortality, length of ICU stay, and incidence of side effects are affected by glutamine supplementation in these patient populations.

Financial Disclosures

None reported.

References

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