

9.4b Combined Parenteral and Enteral Glutamine Supplementation

There were no new randomized controlled trials since the 2015 update and hence there are no changes to the following summary of evidence.

Question: Compared to placebo, does combined enteral and parenteral glutamine-supplementation result in improved clinical outcomes in critically ill patients?

Summary of evidence: There was one level 1 study and 1 level 2 study on glutamine supplementation administered via both PN and EN that were included.

Mortality: Based on the single study that reported on this outcome, glutamine supplementation administered via both PN and EN was associated with a significant increase in hospital (RR 1.20, 95% CI 1.02, 1.40, $p=0.02$), 28-day (RR 1.19, 95% CI 1.00, 1.42, $p=0.05$), 3-month (RR 1.20, 95% CI 1.04, 1.38, $p=0.01$), and 6-month mortality (RR 1.19, 95% CI 1.03, 1.36, $p=0.02$); and was associated with a trend towards a increase in 14-day mortality (RR 1.21, 95% CI 0.99, 1.48, $p=0.07$).

Infections: Based on the single study that reported on this outcome, glutamine supplementation administered via both PN and EN had no effect on overall infectious complications (RR 1.10, 95% CI 0.92, 1.31, $p=0.32$) or ventilator associated pneumonia (RR 1.08, 95% CI 0.82, 1.43, $p=0.59$).

Length of Stay: Based on the single study that reported on this outcome, glutamine supplementation administered via both PN and EN was associated with a trend towards an increase in ICU length of stay (WMD 1.80, 95% CI -0.76, 4.36, $p=0.17$), but had no effect on hospital length of stay (WMD 1.30, 95% CI -4.05, 6.65, $p=0.63$).

Duration of ventilation: Based on the 2 studies, no effect in duration of ventilation was seen with (WMD 0.28, 95% CI -2.85, 3.41, $p=0.86$; figure 1).

Conclusions:

- 1) Combined parenteral and enteral glutamine supplementation is associated with an increase in hospital, 28-day, 3-month, and 6-month mortality, and may be associated with an increase in 14-day mortality.
- 2) Combined parenteral and enteral glutamine supplementation has no effect on overall infectious complications, ventilator associated pneumonia or duration of mechanical ventilation.

3) Combined parenteral and enteral glutamine supplementation may be associated with an increase in ICU length of stay but has no effect on hospital length of stay.

Level 1 study: if all of the following are fulfilled: concealed randomization, blinded outcome adjudication and an intention to treat analysis.

Level 2 study: If any one of the above characteristics are unfulfilled.

Table 1. Randomized studies evaluating glutamine (PN + EN) in critically ill patients

Study	Population	Methods (score)	Intervention	Mortality # (%)*		Infections # (%)†	
				GLN PN+EN	Placebo	GLN PN+EN	Placebo
1) Heyland 2013	Multicentre mixed ICUs N=1218	C.Random: yes ITT: yes Blinding: double (12)	GLN supplementation (0.35 g/kg/day) parenterally vs placebo; additional GLN supplementation (30 g/day) enterally vs placebo	Hospital 227/611 (37) RR 1.20, 95% CI 1.02, 1.40, p=0.02 14-day 157/611 (26) RR 1.21, 95% CI 0.99, 1.48, p=0.07 28-day 198/611 (32) RR 1.19, 95% CI 1.00, 1.42, p=0.05 3-month 252/611 (39) RR 1.20, 95% CI 1.04, 1.38, p=0.01 6-month 264/611 (44) RR 1.19, 95% CI 1.03, 1.36, p=0.02	Hospital 188/607 (31) 14-day 129/607 (21) 28-day 165/607 (27) 3-month 209/607 (32) 6-month 221/607 (37)	All 183/611 (30) RR 1.10, 95% CI 0.92, 1.31, p=0.32 VAP 88/611 (14) RR 1.08, 95% CI 0.82, 1.43, p=0.59 All 166/607 (27) VAP 78/607 (13)	
2) Koksai 2014	Septic, malnourished ICU patients N=120	C.Random: yes ITT: other Blinding: single (outcomes) (9)	15 g/day parenteral glutamine + 15 g/day enteral glutamine + EN vs EN, no placebo, no supplemental glutamine	NR	NR	NR	NR

Table 1. Randomized studies evaluating glutamine (PN + EN) in critically ill patients (continued)

Study	LOS days‡		Ventilator days‡	
	GLN PN+EN	Placebo	GLN PN+EN	Placebo
1) Heyland 2013	ICU 14.9 ± 29.1 (611) WMD 1.80, 95% CI -0.76, 4.36, p=0.17 Hospital 31.0 ± 52.6 (611) WMD 1.30, 95% CI -4.05, 6.65, p=0.63	ICU 13.1 ± 14.0 (607) Hospital 29.7 ± 42.1 (607)	11.6 ± 26.3 (611)	9.8 ± 12.3 (607)
2) Koksai 2014	NR	NR	12.9±5.3	14.3±5.4

NR: not reported

VAP: ventilator associated pneumonia

GLN: glutamine

* presumed hospital mortality unless otherwise specified

† refers to the # of patients with infections unless specified

‡ LOS and ventilation statistics calculated using all patients who were discharged; for patients who died, death date was substituted for discharge date.

ITT: intent to treat

ICU: intensive care unit

PN: parenteral nutrition

C. Random: concealed randomization

WMD: weighted mean difference; CI: confidence interval

EN: enteral nutrition

Figure 1: Duration of Mechanical Ventilation

