9.4c: Enteral Glutamine vs. Parenteral Dipeptide Supplementation

Question: Does enteral or parenteral glutamine-supplementation result in improved clinical outcomes in critically ill patients?

Summary of evidence: There was one level 1 study that compared the use of IV glutamine dipeptide infusion and polymeric formula (Ensure) to enteral glutamine supplemented formula (Alitraq) x 5 days (Uranjek 2013) in surgical and critically ill trauma patients and one level 2 study that compared the use of IV glutamine dipeptide infusion and polymeric EN (Nutrison Standard) to the same EN plus enteral glutamine supplements (Glutamine Resource) x 5 days (Sungurtekin 2015).

Mortality: When the two studies were meta-analyzed, glutamine supplementation administered enterally vs parenterally had no effect on ICU mortality (RR 0.59, 95% CI 0.10, 3.61. p=0.56, heterogeneity I^2=64%; figure 1). Uranjek et al also reported on 6 month survival and also found no effect (p = 0.51).

Infections: When the two studies were meta-analyzed, glutamine supplementation administered enterally vs parenterally had no effect on overall infectious complications (RR 1.00, 95% CI 0.51 1.97, p=1.00, heterogeneity I^2=44%; figure 2). Uranjek et al also reported on the number of patients with pneumonia and also found no effect (p=0.83).

Length of Stay: Both studies reported on ICU LOS but only Sungurtekin reported it in mean and standard deviation, therefore, the data could not be aggregated. Sungurtekin et al found a significant reduction in ICU LOS in patients receiving IV glutamine vs enteral glutamine (p=0.001), whereas Uranjek et al observed a trend in the reduction of ICU LOS in patients receiving enteral glutamine vs IV glutamine (p=0.10), Uranjek et al also observed a trend towards a reduction in hospital LOS in the enteral glutamine group (p=0.10).

Duration of ventilation: Both studies reported on ICU LOS but only Sungurtekin reported it in mean and standard deviation, therefore, the data could not be aggregated. Sungurtekin et al found a significant reduction in the duration of ventilation in patients receiving IV glutamine vs enteral glutamine (p=0.001), whereas Uranjek found no effect between groups (p =0.29).

Conclusions:
1) Enteral glutamine supplementation versus parenteral dipeptides has no effect on ICU mortality, or 6-month mortality.
2) Enteral glutamine supplementation versus parenteral dipeptides has no consistent effect on ICU and hospital LOS.
3) Enteral glutamine supplementation versus parenteral dipeptides has no consistent effect on infectious outcomes or duration of ventilation.
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 Enteral vs. Parenteral glutamine in critically ill patients

Study	Population	Methods (score)	Intervention	Mortality # (%)*		Infections # (%)†	
				EN GLN	PN GLN	EN GLN	PN GLN
1) Uranjek 2013	Surgical and critically ill trauma patients N=90	C.Random: yes ITT: other Blinding: single (outcomes) (9)	EN formula containing supplemental GLN (Alitraq) x 5 days w dose dependent on EN prescription, supplemental PN as needed vs EN (Ensure) + IV glutamine dipeptide infusion x 5 days, supplemental PN as needed Grams glutamine/kg/d received EN GLN 0.22 (0.12–0.23) IV GLN 0.19 (0.18–0.23)	ICU 1/42 (2) 6-month 6/42 (14)	ICU 5/39 (13) 6-month 8/39 (21)	All 12/42 (29) Pneumonia 11/42 (26)	All 15/39 (38) Pneumonia 11/39 (28)
2) Sungurtekin 2015	Mixed ICU patients requiring EN for ≥ 5 days N=40	C.Random: no ITT: yes Blinding:no (7)	EN + enteral L-Gln powder (Glutamine Resource) at 0.5 g/kg/d vs EN + IV 20% L-Ala-L-Gln dipeptide (Dipeptiven) at 0.5 g/kg/d	ICU 8/20	ICU 7/20	All 9/20	All 6/20

Table 1. Randomized studies evaluating Enteral vs. Parenteral glutamine in critically ill patients (continued)

Study	LOS days		Ventilator days		Other Outcomes	
	EN GLN	PN GLN	EN GLN	PN GLN	EN GLN	PN GLN
1) Uranjek 2013	ICU 11.5 (8.0–21.25) Hospital 29.5 (16.0–50.0)	ICU 17.0 (10.0–25.0) Hospital 30.0 (21.0–40.0)	6.0 (4.75-13.25)	9.0 (4.0–20.4)	Kcal/kg/d 17.32 (15.22–22.08) Grams nitrogen/kg/d 0.15 (0.11–0.17) EN start (h) 10.5 (6–15)	17.81 (14.72–20.66) 0.13 (0.12–0.14) 12.00 (6–20)
2) Sungurtekin 2015	ICU 18 ± 9.9 (20)	ICU 9.8 ± 4.3 (20)	16.2 ± 8.2 (20)	8.3 ± 4.1 (20)	NR	

* presumed hospital mortality unless otherwise specified † refers to the # of patients with infections unless specified

Figure 1. ICU Mortality

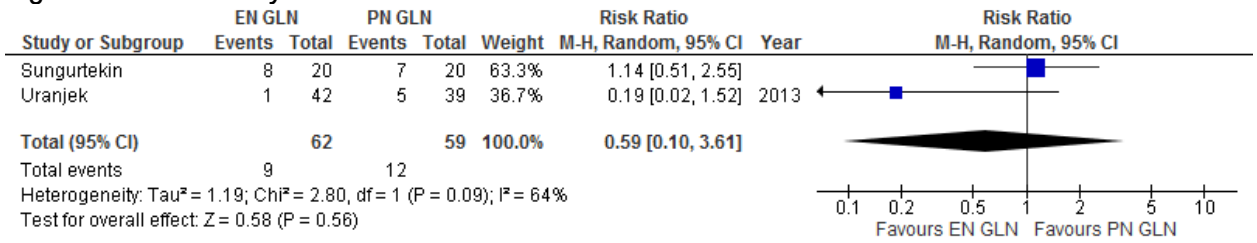

Figure 2. Infectious Complications