

Supplementary Table S6. Pharmaconutrition

Study, year (country)	Study design	n	Population	Age mean/median, years	Group 1 control (n)	Group 2 (n)	Group 3 (n)	Main Findings (Group 1 versus 2 vs 3)
Cai et al. ³⁶ 2006 (China)	RCT	90	APACHE II score 16–28 and HLA-DR <30%	79.5±6.8	Standard nutrition support (30)	Standard nutrition support + IV Gln (10% Gln 100ml/day) for 2 weeks (30)	Standard nutrition support + IV Gln (10% Gln 100ml/day) + IM recombinant human growth hormone (10U/day) for 2 weeks (30)	<ul style="list-style-type: none"> • Isocaloric and isonitrogenous treatments • APACHE II at day 14: 17.45±4.57 vs 15.33±4.25 vs 11.58±2.95 (Group 2 and 3 vs Group 1: $P<0.01$; Group 3 vs Group 2: $P<0.01$) • MODS score at day 14: 8.35±2.76 vs 7.26±2.12 vs 5.12±1.82 Group 2 and 3 vs Group 1: $P<0.01$; Group 3 vs Group 2: $P<0.05$) • Duration of MV: 17.2±5.9 vs 15.6±5.7 vs 14.9±5.2 (not significant) • ICU LOS: 23.8±5.1 vs 22.1±4.9 vs 20.5±4.6 (not significant) • 28-day survival rate: 66.7% vs 70.0% vs 76.7% (not significant)
Cai et al. ³⁷ 2008 (China)	RCT	110	Age ≥65 years, severe sepsis in medical ICU with APACHE II score 16–28 and HLA-DR score ≤50%	Group 1: 81.3±6.8 Group 2: 79.8±7.2	Standard nutritional support (55)	Standard nutrition support + IV Gln (10g/day) for 2 weeks (55)	-	<ul style="list-style-type: none"> • Isocaloric and isonitrogenous treatments • APACHE II at day 14: 17.75±4.46 vs 10.35±4.35 ($P=0.001$) • MODS score at day 14: 8.55±2.76 vs 5.46±2.17 ($P=0.03$) • ICU LOS: 23.8±5.1days vs 22.1±4.9days ($P=0.4$) • Duration of MV: 17.2±5.9days vs 15.6±5.7days ($P=0.4$) • 28-day survival rate: 63.6% vs 69.1% ($P=0.2$)
Barros et al. ³⁸ 2013 (Brazil)	Non-randomised interventional clinical trial	49	Age 60–80 years, enterally fed ICU patients	Group 1: 71.9±2.6 Group 2: 71.8±1.7	Standard EN: polymeric formula without fish oil (34)	EN + IV FLE (0.2g lipid/kg body weight) over 6 hours for 3 consecutive days (15)	-	<ul style="list-style-type: none"> • Isocaloric and isonitrogenous intake throughout 3 days • ICU LOS: 12.4±1.6days vs 10.0±1.6days ($P=0.356$) • Duration of MV: 9.54±1.15days vs 6.85±1.15days ($P=0.15$) • ICU mortality: 44.1% vs 40.0% (not significant)
Han et al. ³⁹ 2014 (China)	RCT	90	Age ≥60 years, unable to initiate oral feeding, APACHE II score 10–30,	Group 1: 77.8±10.3 Group 2: 75.2±12.0 Group 3: 76.6±9.3	Initiate with TPN and gradually transition to full EN; no	EN + lower Gln dose (0.3g/kg/day) via nasogastric tube, SPN as needed. Once achieve full	EN + higher Gln dose (0.6g/kg/day) via NG tube, SPN as needed. Once	<ul style="list-style-type: none"> • Isocaloric and isonitrogenous intakes • Albumin and nitrogen balance; no difference between groups at day 7 and 14 • Transferrin (mg/L) at day 7: 1.69±0.46 vs 2.03±0.39 vs 1.93±0.55 ($P=0.023$)

			NRS-2002 score >3		supplemental Gln (30)	EN, stop Gln (30).	achieve full EN, stop Gln (30).	<ul style="list-style-type: none"> • Prealbumin (mg/L) at day 7: 172.6±47.5 vs 196.5±53.9 vs 184.2±56.2 (<i>P</i>=0.047) • Haemoglobin (g/L) at day 14: 102.7±13.9 vs 113.6±13.6 vs 112.0±11.1 (<i>P</i>=0.003) • Incidence of delayed gastric emptying at day 14: 23.3% vs 3.3% vs 0% (<i>P</i>=0.003) • Diarrhoea and bloating: no difference between groups at day 7 and 14
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APACHE II: Acute Physiology and Chronic Health Evaluation II; EN: enteral nutrition; FLE: Fish oil lipid emulsion; Gln: glutamine, HLA-DR: D-related human leukocyte antigen; ICU: intensive care unit; IM: intramuscular; IV: intravenous; LOS: length of stay; MODS: multiple organ dysfunction syndrome; MV: mechanical ventilation; RCT: randomised controlled trial; SPN: supplemental parenteral nutrition; TPN: total parenteral nutrition
Superscript numbers: Refer to REFERENCES