Supplementary Table S6. Pharmaconutrition

<table>
<thead>
<tr>
<th>Study, year (country)</th>
<th>Study design</th>
<th>n</th>
<th>Population</th>
<th>Group 1 control (n)</th>
<th>Group 2 (n)</th>
<th>Group 3 (n)</th>
<th>Main Findings (Group 1 versus 2 vs 3)</th>
</tr>
</thead>
</table>
| Cai et al.36 2006 (China) | RCT          | 90 | APACHE II score 16–28 and HLA-DR <30% | 79.5±6.8 | 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) | • 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% | 81.3±6.8 | Standard nutritional support (55) | Standard nutritional support + IV Gln (10g/d for 2 weeks (55) | - |
| 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) | - |
| Han et al.39 2014 (China) | RCT          | 90 | Age ≥60 years, unable to initiate oral feeding, APACHE II score10–30, | 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 | • 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) |


<table>
<thead>
<tr>
<th>NRS-2002 score &gt;3</th>
<th>supplemental Gln (30)</th>
<th>EN, stop Gln (30)</th>
<th>achieve full EN, stop Gln (30)</th>
</tr>
</thead>
</table>

- Prealbumin (mg/L) at day 7: 172.6±47.5 vs 196.5±53.9 vs 184.2±56.2 ($P=0.047$)
- Haemoglobin (g/L) at day 14: 102.7±13.9 vs 113.6±13.6 vs 112.0±11.1 ($P=0.003$)
- Incidence of delayed gastric emptying at day 14: 23.3% vs 3.3% vs 0% ($P=0.003$)
- Diarrhoea and bloating: no difference between groups at day 7 and 14

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