Update on Enteral Nutrition in Trauma Patients

A symposium organized by Nestlé Nutrition Institute was held in conjunction with the European Society of Intensive Care Medicine Summer Conference – Trauma Update in May 2012. The meeting was chaired by Dr Jacque Duranteau and Dr Martin Dünser, and leading experts discussed the important aspect of enteral nutrition in trauma. Dr Annika Reintam Blaser reviewed evidence suggesting a beneficial effect for the implementation of early enteral nutrition. Dr Richard Beale discussed evidence and practical aspects of glutamine supplementation in clinical practice.

Early enteral nutrition: Practical aspects

Dr Annika Reintam Blaser
Bern, Switzerland
Tartu, Estonia

When is early?

The benefits of early enteral nutrition (EN) were first reported by Moore et al. Their study showed that early EN (initiated within 18 hours and advanced to 3,000 mL/day within 72 hours) maybe associated with better outcomes, such as significantly fewer septic complications (p<0.025).

There has been debate regarding the definition of early EN. In various guidelines, it has been defined as nutritional support provided within a period of up to 72 hours. Recent meta-analysis has shown that early EN, defined as within 24 hours, was associated with a significant reduction in pneumonia and mortality outcomes compared with standard care. Therefore, early EN can be defined as the provision of a standard EN formula via any feeding tube route within 24 hours of the initial injury or intensive care unit (ICU) admission.

“Today the cut-off point should be set at 24 h following the injury or ICU admission

When we give EN there are a number of physiological changes: cardiac output increases, blood flow to the gastrointestinal (GI) tract increases proportionally, and optimization of the local and systemic immune response takes place (e.g. splanchic hyperemia, increase in immunoglobulin A, secretion of trophic and vasoactive hormones and maintenance of intestinal microflora).

Without feeding, critically ill patients lose on average 5–10% of their skeletal muscle mass per week during their ICU stay. There is a correlation between malnutrition and poor outcomes, including length of hospital stay and the incidence of complications. So called ‘bowel rest’, associated with total parenteral nutrition (TPN) or delayed EN, results in atrophy of the gastrointestinal mucosa, which in turn compromises the integrity of the mucosal barrier and increases exposure to bacteria and/or endotoxins.

Which route should be used?

The early initiation of post-pyloric feeding instead of gastric feeding does not appear to confer any clinically significant advantages in critically ill patients. A systematic review of the literature revealed that gastric feeding was initiated significantly earlier than post-pyloric feeding. Routine use of post-pyloric feeding is not recommended but post-pyloric feeding should be promptly considered if gastroparesis is not resolved with prokinetics.

“Start early EN via gastric tube

EN nutritional targets remain to be determined

The current data on the amount of support required for starting EN or early EN is inconclusive. A randomized study in mechanically ventilated patients (n=200) has not shown a difference in clinical outcomes for initial trophic EN (10mL/h for 6 days) versus full-energy EN (initiated at 25 mL/h, increased every 6 hours). The European Society for Parenteral and Enteral Nutrition guidelines (ESPEN) recommend that during the acute and initial phases of critical illness (even up to 96 hrs) an exogenous energy supply in excess of 20-25 kcal/kg BW/day should be avoided, whereas, during recovery, the aim should be to provide a supply of 25-30 total kcal/kg BW/day. The American Society of Parenteral and Enteral Nutrition (ASPEN)/Society for Critical Care Medicine (SCCM) guidelines recommend to advance patients towards goal within 48-72 hours. Prospective cohort data in patients with an ICU stay of >96 hours suggest that moderate caloric intake (33 to 65% of American College of Chest Physicians targets; approximately 9-18 kcal/kg/day) is associated with better outcomes than higher levels of caloric intake. However, recent data indicate that increased energy and protein intake up to 2000 kcal/day may have a linear correlation with improved clinical outcomes [adjusted OR for reduced 60-day mortality for every 1000 kcal/day, p<0.014] in critically ill ICU patients.

Early additional PN is not recommended

The impact of early parenteral nutrition (PN) in critically ill adult patients completing EN was evaluated in the EPaNIC trial. Late initiation of PN was associated with faster recovery and fewer complications, as compared with early initiation. Optimal timing and amount of parenteral support remains to be clarified, but initiation of PN within the first 24 hours of acute injury is not supported by any evidence.

Overfeeding is detrimental

The administration of more aggressive early EN (reaching 100% on day 1) to mechanically ventilated patients is associated with an increased incidence of pneumonia and a prolonged hospital stay. Energy intake as glucose in excess of the body’s needs results in increased carbon dioxide production and a fatty liver: intake of more than 27 kcal/kg/day may lead to liver dysfunction. Hyperglycemia increases the risk of infective complications. Even slight overfeeding (110-120% of targets) might be harmful. Overfeeding with EN is less likely to occur compared to PN. It is also important to take into consideration non-nutritional calories such as those delivered with propofol.
Early EN improves clinical outcomes
An increasing body of evidence indicates that early EN is associated with a significant reduction in the incidence of infections, a reduced length of hospital stay and reduced mortality.25,26 The recent meta-analysis by Doig et al. included 6 randomized controlled trials with 234 patients, where early EN was defined as EN within 24 hours. This meta-analysis showed significant reductions in mortality and pneumonia associated with early EN (OR 0.34 (95% CI 0.18-0.85) and 0.31 (95% CI 0.12-0.78), respectively).9

Early PN is not recommended
In a new meta-analysis of 4 randomized controlled trials in 126 trauma patients, with ISS >20, the provision of early EN was associated with a significant reduction in mortality (OR = 0.20, 95% CI 0.04–0.91, I2 = 0).10 These results are limited by the small number and limited scale of studies available for the meta-analysis and the findings still need to be confirmed in larger studies.

A multicentre, cluster-randomized clinical trial of Algorithms for Critical-Care Enteral and Parenteral Therapy (ACCEPT) demonstrated that the use of evidence-based recommendations (Figure 1), including initiation of EN within 24 hours, improved the implementation of nutritional support as well as clinical outcomes. Length of hospital stay was reduced (p=0.003) and there was a trend towards reduced mortality (p=0.058) in the ICUs where the protocol was implemented.25

Overfeeding should be avoided
Who should not receive early EN?
Studies in haemodynamically compromised patients undergoing cardiac surgery26 and those with severe sepsis27 reported a beneficial effect of EN even in patients receiving vasopressors. In cardiac patients, postoperative EN increased the cardiac index and splanchnic blood flow. Furthermore, this produced an adequate metabolic response indicating that the nutrients had been utilised.26 Hepato-splanchnic energy metabolism was similarly increased following initiation of low-dose post-pyloric EN in patients with severe sepsis who were receiving noradrenaline.27

ASPSN guidelines recommend that early EN should be withheld in patients requiring significant haemodynamic support including high-dose catechol-

amine agents until the patient is fully resuscitated and/or stable (Grade E). The ESPEN 2006 guidelines indicate that early EN should not be given to patients who are expected to be on a full oral diet within 3 days. The Austrian guidelines state that EN is not recommended for patients with the following: intestinal ischemia, intestinal obstruction or perforation, acute abdomen, acute GI bleeding, and abdominal compartment syndrome. For both EN and PN, the Austrian guidelines state the following contraindications: acute phase immediately after surgery or trauma, any state of shock, serum lactate >3-4 mmol/L, hypoxaemia with pO2 <50 mmHg, severe acidosis (pH <7.2), and hypercapnia (PCO2 >75 mm Hg). In the ACCEPT trial, early EN feeding was not provided in patients with: acute pancreatitis, enteric anastomosis or fistula, bowel obstruction, ischemic bowel, high nasogastric losses, imminent endoscopy or imminent bowel resection.25

The contraindications for EN are poorly studied and recommendations given in guidelines are not supported by evidence, but based on expert opinion. Statements regarding systemic contraindications are therefore often indefinite.

Barriers to early EN
There are a number of barriers to the implementation of early EN. An evaluation of 40 ICUs involving 377 patients who were mechanically ventilated for at least 6 hours reported a number of reasons why patients do not receive nutritional support (Figure 2).28 Specific reasons were not reported in as many as 58% of patients not receiving their target calories, while several reasons were documented in 16% of patients. GI symptoms, including absent bowel sounds, vomiting, high gastric residuals, diarrhoea, bowel distension, GI bleeding and constipation, were the most commonly cited reasons. In addition to these reasons for reducing/withholding EN, procedures and shock were important barriers to EN implementation.

Early EN within 24 h may result in a significant reduction in mortality and infectious complications
Recently a Working Group of the European Society of Intensive Care Medicine published new definitions of GI dysfunction in ICU patients.29 Definitions for acute GI injury with its four grades of severity, as well as for feeding intolerance syndrome and GI symptoms have been proposed. These definitions should assist in clinical assessment of GI problems and help to unify future studies.
Feeding intolerance should be considered as a general term indicating intolerance of enteral feeding for whatever clinical reasons (e.g. vomiting, high gastric residual volumes, diarrhoea, GI bleeding, presence of enterocutaneous fistulas). A patient should be considered to have feeding intolerance if at least 20 kcal/kg/day via the enteral route cannot be reached within 72 hours of a feeding attempt. There is no feeding intolerance if enteral feeding is electively not prescribed or is withheld/interrupted due to procedures.15

Conclusion
In summary, current evidence suggests a beneficial effect of implementation of early EN in ICU patients and there is no convincing evidence regarding any harmful effect. According to the latest data, early EN is defined as the provision of a standard EN formula via any feeding tube route within 24 hours of initial injury or ICU admission. The systemic contraindications for EN remain to be clarified. Early PN is not recommended. There are issues to be addressed with respect to patients who do not tolerate EN. A large well-designed multicentre trial is needed to clarify issues surrounding the optimal use of EN.

Immunonutrition: Glutamine – what is the evidence?

Dr Richard Beale
Kings’ Health Partners
London, UK

Glutamine supplementation in critically ill patients: guidelines and studies
Plasma concentrations of glutamine are relatively low in many critically ill patients.29 Glutamine is largely synthesized in the skeletal muscle but during critical illness the body is unable to produce sufficient amounts of glutamine causing profound depletion in tissue and plasma glutamine levels.30 Low plasma glutamine concentrations are an independent risk factor for unfavourable outcomes in the ICU.29 Therefore, in critically ill patients receiving PN, intravenous glutamine supplementation is reported to improve outcomes and is the standard of care.29

Parenteral glutamine supplementation
The 2009 Canadian guidelines recommend parenteral supplementation with glutamine when PN is prescribed to critically ill patients.30 These recommendations are based on evidence which indicates that the use of parenteral glutamine is associated with a marked reduction in mortality, length of hospital stay, and a moderate reduction in infectious complications.29,30 There was not enough evidence to support PN glutamine supplementation in patients on EN.

Appropriate administration is important
The more recent randomized, blinded, controlled Scottish Intensive care Glutamine or selenium Evaluative Trial (SIGNET) is the largest (n=502) study of glutamine supplementation in critically ill patients to date.35 Glutamine supplementation of 20g was administered in conjunction with PN, and EN was initiated in parallel. No beneficial effects on new infections or 6-month mortality rates were reported following glutamine supplementation in patients requiring parenteral feeding.35 However, it should be noted that patients only received a mean of 5 days of glutamine supplementation (up to a maximum of 10 days), and a low, poorly defined dose of glutamine was administered.29

“Guidelines recommend enteral glutamine supplementation in burn and trauma patients
A Scandinavian glutamine study has also been published recently. In this study, intravenous glutamine supplementation was administered separately from the nutritional support, and supplementation continued for the duration of the ICU stay.34 Patients received nutritional support via PN and/or EN. This study reported lower ICU mortality rates in patients receiving glutamine supplementation compared with the control group, although this reduction was not maintained, as there was no reduction in 6-month all-cause mortality rates.34 If there would be signal to harm this type of study would show it. These results suggest the potential for further benefits if glutamine supplementation had been continued post-ICU.

Enteral glutamine supplementation
Enteral glutamine is good for gut cells but a lot of glutamine is absorbed by entrocytes. While standard EN formulations contain some glutamine (2-4 g/L), the dose is not sufficient to normalize glutamine plasma concentrations and supplementation may be required.29 The Canadian guidelines state that enteral glutamine should be considered in burns and trauma patients but there are insufficient data to support its routine use in other critically ill patients.34 A meta-analysis of enteral glutamine supplementation reported a reduction in infectious complications and length of stay (Table 1).34

“Glutamine supplementation has no suggestion of harm with overall signal to benefit – if the dose is adequate
A randomized controlled double-blind trial in 55 critically ill septic patients requiring enteral feeding compared an immunonitrition formula plus an enteral supplement containing conditionally essential nutrients (glutamine) and a standard formula plus a control solution, both administered within 48 hours of study enrolment.36 Enteral glutamine supplementation with an antioxidant was associated with more rapid resolution of sequential organ function assessment (SOFA). The results of this small study were repeated and confirmed. Enteral glutamine supplementation resulted in significantly faster recovery of organ function, as assessed by the normalized delta daily SOFA, compared with a control solution (Figure 3).

A meta-analysis of studies evaluating enteral and parenteral supplementation demonstrated that the evidence favours a beneficial effect of glutamine supplementation on mortality outcomes (p=0.008).32

Glutamine supplementation in clinical practice
Glutamine supplementation at 0.3 g/kg/day resolves the glutamine deficiency typically observed in critically ill patients, if administered for a...
sufficient duration. It is important to remember that in this context, glutamine is not being administered as a drug. Therefore, intravenous glutamine supplementation is sensible. Currently, there is increasing recognition of protein/calorie malnutrition in critically ill patients, and the potential of mixed EN/PN feeding for nutritional support. Supplemental PN, in combination with EN, may provide an effective alternative to achieve 100% of energy and protein targets, although this remains to be determined in further studies.36

Large studies indicate that there is no harm associated with glutamine supplementation.33,34 It is likely to be beneficial in subgroups of patients, particularly if administered appropriately. Therefore, it is reasonable to give glutamine if also administering PN. It is more difficult to perform EN studies hence the evidence on enteral glutamine is less clear. Direct delivery to the gut lumen remains attractive. However, EN may not provide effective supplementation overall, although glutamine will reach the gastrointestinal and portal system. Therefore, a combined approach may be more beneficial.

There is an ongoing debate on glutamine supplementation because glutamine was not initially included in currently available nutritional supplements, and as a result it has now become a premium product. Glutamine supplementation should be administered provided it is cost effective.

Conclusion
In conclusion, the context of the glutamine debate is changing along with the context of the feeding debate. In critical care, the concept of deficiency versus supplementation versus therapy should be considered separately. However, questions remain as to whether intravenous or EN supplementation or a combination of the two would be most beneficial in critically ill patients. There is no suggestion of a harmful effect and overall, EN glutamine supplementation appears to be of benefit, provided the dose is adequate.

References: