

Parenteral nutrition in intensive care



**Will
Ne-Hooi Loh**
MBBS, FRCA



Gregory Barton
BSc (Hons)
MRPharmS



**Professor
Richard D
Griffiths**
BSc, MD
FRCP, FHEA

Nutritional support in the intensive care unit (ICU) is a challenge due to the difficulties predicting nutritional requirements in a variety of pathologies. Parenteral nutrition in the ICU is instituted when there is a failure to deliver adequate nutrition. The pharmacist has to monitor this complex therapy.

prescribed due to gut intolerance and interruptions. A large multinational study [5] showed that only about half of the nutritional target was achieved. There is also an increased risk of aspiration associated with EN as critically ill patients are prone to increased gastrointestinal intolerance. A perceived benefit of EN over PN is that a failure to maintain EN is associated with immunological changes and impairment of the gut-associated immune system; this in turn leads to the intestine becoming a source of pro-inflammatory stimulants. However, a significant reversal of these defects has been shown in animal models with modern PN containing glutamine [4].

When is the best time to start PN?

There is no clear cut answer to this question, but it is generally accepted that starvation or underfeeding is detrimental to the patient and may increase morbidity and mortality [3]. The European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines suggest that all patients in whom EN is not tolerated or is contraindicated and where the patient is not expected to be on normal diet within three days, should have PN started within 24–48 hours [3].

Route of PN

PN with a low osmolarity (< 850 mOsmol/L) has been designed to be administered peripherally but is unlikely to meet the macro- or micro-nutritional needs of the critically ill patient therefore a higher osmolarity, centrally administered PN is often the most appropriate choice. With regard to the central access, there is evidence to suggest that administration via a dedicated lumen in a central venous catheter has a lower rate of incidence of complications, such as thrombotic episodes, than that with

peripherally inserted central catheters [3].

Calorie requirements

Energy requirements in the critically ill patient can vary massively depending on activity levels, the underlying condition and how long the patient has been unwell on intensive care. Uehara et al [6] showed that in the first week on intensive care, the ratio of total energy expenditure to resting energy expenditure was 1.0 in septic patients and 1.1 in trauma patients but rose to 1.7 and 1.8, respectively in the second week. This equates to an average of 25 and 31 kcal/kg of ideal body weight (IBW)/day in the first week, increasing to 47 and 59 kcal/kg IBW/day in the second week.

A target of 25 kcal/kg IBW/day is recommended as a starting point in the ESPEN guidelines [3] and this should then be titrated up to the individual patients needs. In patients with extremes of body mass index (less than 25 or greater than 35), there is some evidence that increased intake of energy and protein relative to their ideal body weight will reduce mortality [7]. The energy deficit accumulated as early as 2–3 days in ICU from inadequate nutrition has been shown to have detrimental outcomes [8]. In healthy subjects on bed rest hypocaloric feeding led to greater protein and muscle loss impairing the postprandial anabolic effects of amino acids [9]. What substrates, e.g. lipid, carbohydrate, etc., should provide these calories and in what proportions is discussed later.

Overfeeding versus underfeeding

The concept that ‘more is always better’ may add to the metabolic challenges of the stress response. Avoiding caloric overfeeding can lead to benefits such as

More than a decade ago there was a shift away from parenteral nutrition (PN) towards enteral nutrition (EN) as it was suggested that PN may be harmful and that its use increased mortality [1]. Overfeeding and an increase in infection rates are the main complications described as being associated with PN.

Overfeeding, which can be due to the easy delivery of PN and not taking into account calories from other sources such as drugs, for example, propofol contains 1 kcal/mL, can exacerbate the problem of impaired glucose storage associated with insulin resistance, which is common in the critically ill. This in turn, along with the highly nutritious bacterial growth promoting nature of PN, increases the risks of central venous catheter infections, and may lead to an increased length of stay [2–4].

Conversely, EN is also not without its problems. There is a major risk of underfeeding as we rarely deliver the dose

improved glycaemic control, decreased ventilator days, length of ICU stay and infection rates [2]. Giving the right amount is important and in part this can be helped by having a clear feeding protocol on the unit or perhaps via indirect calorimetry [8].

Tight glycaemic control and nutrition

Hyperglycaemia is a common response in critically ill patients as a result of the normal response to illness, drug therapy and overfeeding. Hyperglycaemia (glucose > 10 mmol/L) has been shown to contribute to serious complications such as infections, organ dysfunction and patient mortality [10]. Hypoglycaemia has also been reported to increase patient mortality. Therefore, the physiological benefits of tightly controlling blood glucose levels are obvious. However, there is current debate surrounding the optimal glucose range to be used in ICU. Reductions in mortality rates have been reported in ICU patients when blood glucose is maintained between 4.5–6.1 mmol/L [10], but not in another study, in which mortality increased with this strategy [11]. No unequivocal recommendations have been made by ESPEN, therefore it is important for the hospital pharmacist to be aware if their institution has a protocol in place targeting glucose levels, to avoid morbidity from poor glycaemic control.

For protocols targeting glucose levels to be effective, adequate calories must be delivered to the patient at a consistent rate. An advantage of PN is the exact and constant delivery of calories compared to the variable delivery (due to absorption, interruptions due to procedures, etc.) of EN. However, one of the clinical signs of overfeeding, severe hyperglycaemia should not be ignored and a reduction in PN delivery rates is usually indicated.

Giving EN and PN together

This is one of the most difficult questions as there is no really strong evidence of risk or benefit however there are two suggested approaches. Firstly, EN and PN may be started together and the PN then weaned off as the EN

becomes tolerated or, as recommended in the ESPEN guidelines [3], if after, for example two days there is a failure to tolerate EN then supplemental PN can be added to achieve nutritional targets. The major concern is that many patients maybe started on PN unnecessarily, leading to complications such as overfeeding and line sepsis. The caloric input and lines should be closely monitored to avoid this.

Carbohydrate requirements

Carbohydrates are integral to many key metabolic processes but can also be synthesised from amino acids. It does however remain a major way of delivering energy to the patient, as consuming amino acids synthesised via the breakdown of muscle, leads to muscle loss which is directly related to ICU mortality [2]. By delivering sufficient quantities of carbohydrate (and insulin), muscle catabolism is therefore reduced. The minimum amount of carbohydrate that should be delivered is at least 2 g/kg IBW/day to reduce protein breakdown together with insulin [3].

Protein requirements

Skeletal muscle loss accelerates during critical illness and prolonged immobility. Protein delivered as a balanced amino acid mix is essential to stimulate protein synthesis and protect skeletal muscle. When infused as a dose of 1.3–1.5 g/kg IBW/day, optimal whole body protein sparing effects were achieved in sepsis and trauma [3].

There is little robust evidence for other amino acid supplementation except for glutamine. Glutamine, a conditionally essential amino acid, is required for immune activity and cellular repair and a low plasma level is associated with a poor ICU outcome. PN containing glutamine at 0.2–0.4 g/kg IBW/day has been shown to reduce mortality with reduced infections or improved glycaemic control [3]. Due to poor stability glutamine is usually not included in the standard amino acid mixtures.

Lipids

Lipids provide a useful energy source, avoiding the high doses of glucose required to achieve a target calorie

requirement with carbohydrate alone. It has also been shown that nutritional support using glucose/lipid mixtures is much better in preserving lean body mass [12]. It is recommended that 15–30% of non-protein calories should be provided as lipids. Lipids can be infused safely at rates of 0.7–1.5 g/kg IBW/day [4]. There is increasing evidence of the immunomodulatory effects of fish and olive oil on inflammation in the critically ill [13]. Newer PN lipid solutions incorporating proportions of fish or olive oil have been shown to reduce levels of pro-inflammatory cytokines, reduce infection rates and ICU stay [13].

Micronutrients

ICU patients are in a hypermetabolic state with increased micronutrient requirements such as trace elements and vitamins. Thiamine, vitamin C, selenium and zinc deficiencies are common in the critically ill. Many once daily commercially available trace element preparations were created for stable patients and may not be entirely suitable for ICU. Typically, ICU patients have increased requirements in chromium, selenium and zinc, and reduced requirements of copper (except in burns), iron, iodine and manganese compared to what commercially available trace element preparations deliver [3]. Therefore, determination of plasma concentrations should be done monthly to detect major deficiencies.

Standard multivitamin preparations should be given in patients on ICU, and increased doses (up to two to three times) given to patients with special requirements such as burns or continuous renal replacement therapy due to loss of water soluble micronutrients [3].

Conclusion

It is increasingly recognised that ICU patients are unique with varying nutritional requirements during their stay and understanding the issues involved such as tight glycaemic control, the effects of over- and underfeeding will ultimately lead to a reduction in morbidity and mortality. The pharmacist should be involved throughout the whole process from prescribing the initial regimen to

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monitoring the patient's biochemical profile, fluid status and medication in response to PN therapy to prevent drug interactions and feed related disorders.

Author for correspondence

Professor Richard D Griffiths, BSc, MD
FRCP, FHEA
Professor of Medicine (Intensive Care)
Pathophysiology Research Unit
School of Clinical Sciences
University of Liverpool
Liverpool L69 3GA, UK
rdg@liverpool.ac.uk

Co-authors

Will Ne-Hooi Loh, MBBS, FRCA
Academic Fellow in Intensive Care
Whiston Hospital, Liverpool, UK

Gregory Barton, BSc (Hons)
MRPharmS
Critical Care Pharmacist
Whiston Hospital, Liverpool, UK

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