PARENTERAL NUTRITION ON THE INTENSIVE CARE UNIT (ICU)

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Parenteral Nutrition (PN) has had a bad reputation on the intensive care unit with its use often being reserved for patients with complete gut failure. Enteral nutrition is seen as the gold standard for nutritional support and lack of success in establishing it is often seen as a failure by the ICU team.

Recent studies have, however, suggested that this should not be the case and when given in appropriate amounts, at the right time, through the right access device, it is as safe and beneficial as enteral nutrition. Indeed, withholding it during prolonged failed attempts to establish enteral nutrition may result in increased mortality in malnourished patents.

In 1998, Heyland published a meta-analysis of studies of PN in ICU and surgical patients.[1] This compared standard therapy-iv dextrose and oral diet vs PN and reached the conclusion that PN should not be used on the ICU as it was associated with increased septic morbidity. Subsequent papers suggested that enteral nutrition (EN) was safer than PN[2] and guidelines promoted the use of EN[3] leading to a negative attitude towards PN.

It is possible to explain the negative findings of the Heyland meta-analysis, as many of the studies included were carried out in the 1980s and 1990s when hyperalimentation was common and huge energy and nitrogen loads were given to metabolically stressed patients, possibly without the stringent line care that is often employed today. It is well accepted that most of the complications of PN, including hyperglycaemia, hyperlipidaemia, azotaemia and liver dysfunction, are due to overfeeding.[4] In particular, hyperglycaemia in the days before intensive insulin therapy[5] could be responsible for the poor outcomes and increased sepsis.[6] Furthermore, the first generation lipids used in many of the studies were high in pro-inflammatory omega-6 fatty acids.

More recent studies have shown that PN may actually be safer than EN in patients with questionable gut function[7,8] and a 2005 meta-analysis found improved survival with PN in patients who could not be successfully fed enterally within 24 hours of ICU admission.[9] In fact, this EN has almost certainly been dispelled by the CALORIES trial published last year.[10] In this large scale trial carried out in 33 ICUs across the UK, 2388 patients were randomised to early EN or PN. There were no differences in outcomes, including infection rates and 30-day mortality between the two modes of feeding. Another particularly interesting finding was that around 50% of patients in both groups failed to meet their estimated energy target of 25kcal/kg, with the mean energy intake for each being around 20kcal/kg. This can lead us to the conclusion that if you avoid overfeeding, especially in the early stages of critical illness, the outcomes are the same for EN and PN.

WHEN TO USE PN

Although modern PN is safe, the general consensus from expert groups is that enteral nutrition should be used as the first line of feeding because of its protective effect on the gut barrier and its favourable influence on the gut associated lymphoid tissue (GALT) and immune function.[11] It is an often overlooked fact that around 70-80% of an adult's immunological tissue is situated in the gut[12] and the theoretical benefits of keeping it healthy should not be ignored. EN should, therefore, be used where possible and PN employed

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quickly in patients with gut failure, including bowel obstruction, ischaemic bowel, short bowel syndrome and certain types of gastrointestinal leaks and fistulae. However, many patients on the ICU do not fit clearly into these categories and how quickly to start PN in patients with questionable gut function or poor tolerance of EN is a subject for debate.

WHEN TO START PN

How early to start PN became particularly controversial when a study by Casaer[13] recommended withholding PN for up to eight days in critically ill adults. In the 'Early Parenteral Nutrition to supplement insufficient enteral nutrition in Intensive Care Patients' (EPaNIC) study, 4640 ICU patients were fed as much enterally as possible and then randomised to early initiation of parenteral nutrition (day 2) or late (day 8) to meet a calculated energy target. The late initiation group showed improved outcomes with less infections, less cholestasis, fewer days of mechanical ventilation and renal replacement therapy, as well as a relative increase of 6.3% in the likelihood of being discharged from ICU alive. However, in this study, patients who were largely not malnourished were fed to a very high energy intake of up to 36kcal/kg/day in the early stages of their critical illness.

Furthermore, patients who were most likely to benefit from PN, such as those with BMI <17kg/m2 or those with short bowel syndrome, were actually excluded from the study. Many patients had diagnoses such as cardiac surgery suggesting that they could have been enterally fed if a more aggressive approach to their EN had been used. Indeed, the study protocol reveals that a very low gastric residual volume (GRV) threshold of 250mls was used to define tolerance to enteral feed, which is contrary to the recommendations of ASPEN[11] who suggest EN should not be withheld for anything less than a GRV of 500mls. The EPaNIC study simply serves to reinforce our conclusions from previous studies: that feeding excessive amounts of PN to patients with a functioning gut who are not malnourished in the early stages of critical illness is associated with poor outcomes.

In contrast, a Swiss study[14], that carefully introduced PN at day 4 where EN was clearly not tolerated due to gut dysfunction, showed improved outcomes. In a randomised study of 305 patients, indirect calorimetry was used to determine an energy target and PN initiated to supplement EN in achieving energy balance, alongside the maintenance of tight glycaemic control. Careful use of combined EN and PN without excessive energy provision to patients with gut dysfunction resulted in fewer infections, more antibiotic free days and shorter duration of mechanical ventilation.

Braunschweig[2] found that it was the particularly malnourished patients who benefited from use of PN. Even the aforementioned 1998 Heyland[3] study supports its use in malnourished surgical patients. Thus, the evidence clearly supports cautious early introduction of PN on ICU, especially in malnourished patients with an element of gut dysfunction. Indeed, spending an excessive amount of time unsuccessfully trying to establish EN in this group of patients may be associated with increased mortality.[2,8,9] ESPEN[15] certainly supports this view, recommending that PN should be introduced after 48 hours of arrival on ICU if EN cannot be established.

ESTIMATING REQUIREMENTS

Three previously mentioned major studies[10,13,14] have more or less confirmed that excessive energy provision in the early stages of critical illness is harmful. Failure to meet energy targets later has also been associated with poor outcomes.[14,16,17] The ESPEN[18] recommendation of 20-25kcal may give as good a starting point as any initially, although the very metabolically stressed or those at high risk of refeeding syndrome may

need to start lower at around 10kcal/kg on day 1 as per the recommendations of NICE.[19] Using kcal/kg is probably acceptable in many patients; however, it can under- and over-estimate at the extremes of BMI[20] and is theoretically flawed at the extremes of age as you would be giving the same amount of energy to a 70kg 80-year-old female as to a 70kg 21-year-old male athlete, although their body composition is likely to be entirely different. Here, predictive formulae for basal metabolic rate (BMR) plus around 10-20%, have a theoretical advantage, with the Henry equation best representing the UK population. Use of an obesity adjusted weight for those with a BMI >30kg/m2 has been demonstrated to allow estimation of requirements closer to measured energy expenditure.[21]

Some dietitians prefer the use of ICU specific formulae such as the Penn-State equation; however, a recent study of 5672 patients found that there were no differences in mortality or time to ICU discharge alive for use of kcal/kg and complex equations, including Ireton-Jones, Mifflin-St Joel, Schofield and Harris-Bennedict.[22] It is important to realise that all predictive formulae just give an estimation of needs, especially when taking into account the difficulty in obtaining an accurate dry weight to use in them - most ICU patients are considerably oedematous following fluid resuscitation. Whichever method you decide is best for your patient group, regard this as just a starting point and monitor carefully for signs of overfeeding, such as hyperglycaemia and hyperlipidaemia, with appropriate modification of your energy prescription accordingly. Also be aware that patients require more when they are recovering, with ESPEN recommending an increase to 25-30kcal in the anabolic (recovery) phase.[18]

Nitrogen (N) requirements are possibly one of the most controversial aspects of ICU nutritional support, with some authors suggesting that higher intakes are favourable[23], especially in maintaining lean mass. However, a recent secondary finding of a large multicentre study[24] was that the patients who received the most protein in the first week lost the most muscle mass, especially the more metabolically stressed. It would appear that very catabolic or immobile subjects are unable to utilise high protein loads[24,25,26] especially to synthesise skeletal muscle and, therefore, it seems logical that nitrogen provision follows the same pattern as energy, with less being required at first and more in recovery. Consider following the recommendations of NICE[19] and giving <0.16gN/kg in first few days and increasing to > 0.24gN in the anabolic phase. Signs that a patient is entering an anabolic phase include a drop in inflammatory markers such as C-reactive protein, resolving oedema, reduced hyperglycaemia and insulin requirements, plus the return of appetite and mobility. In addition, Bernstein suggested that a 40mg rise in weekly serial prealbumin levels indicates the switch to anabolism[27].

OPTIMUM COMPOSITION OF PN

It is very important to consider the type of lipid used for ICU PN. It is almost certainly not optimal to use first generation lipids composed exclusively of soy bean oil, as these have long been associated with cholestasis, contain hepatotoxic phytosterols[28] and are rich in omega-6 fatty acids which are the precursors of arachidonic acid and pro-inflammatory eicosanoids. Using second generation lipids where some of the soy bean oil is replaced with olive oil or coconut oil which is high medium chain triglycerides may have theoretical advantages; however, the third generation lipids containing anti-inflammatory omega-3 fatty acids from fish oil have been associated with improved outcomes on the ICU.[29]

Glutamine is a conditionally essential amino acid, with increased requirements in the critically ill. Parenteral supplementation of 0.3-0.5 g/kg has been shown to be safe and is associated with reduced septic morbidity, mortality and length of stay.[30,31] Its use became extremely controversial following the REDOX[32] trial and subsequent Canadian guidelines advising against giving it to critically ill adults.[33] However, the REDOX trial has been criticised for giving a median dose of 0.78g/kg which is way in excess of that previously considered safe. In addition, both the enteral and parenteral routes were used in patients with a functioning receiving enteral nutrition. There is very little evidence to support the use of enteral glutamine, possibly because the GALT can synthesise glutamine from amino acids

derived from the gut lumen. However, the use of parenteral glutamine should be considered in long-term ICU patients who are exclusively parenterally fed. Wischmeyer[31] urged caution in septic patients, or those with multiple organ dysfunction syndrome (MODS); however, this recommendation was largely based on the excessive dose used in the REDOX trial. Previously, it was concluded that smaller doses of parenteral glutamine are likely to be beneficial in these conditions.[34]

Modern parenteral nutrition is safe to use on the ICU and may be associated with improved outcomes including survival. It should be considered for all patients who cannot be established on EN within 48 hours of admission to the ICU, especially those who are malnourished. Avoid excess provision of energy and nitrogen in the initial stages and increase in recovery. PN can be used to supplement EN to ensure requirements are met while conferring the benefits of EN the gut. Third generation lipids containing fish oil should be strongly considered and those exclusively on PN for prolonged periods will most likely benefit from glutamine supplementation.

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