Use of 'High' Protein Feeds in Refeeding Syndrome

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Refeeding syndrome is defined as the potentially fatal shifts in fluids and electrolytes that may occur in malnourished patients on refeeding following a period of starvation.[1] The phenomenon is principally driven by too rapid introduction of carbohydrate to starving cells, which precipitates a number of metabolic and pathophysiological complications. Refeeding syndrome can be more common in patients receiving artificial nutrition but can also occur in those on an oral diet. Each case of refeeding syndrome will present differently but early detection is advised to prevent complications.[2]

Dietitians, doctors and nutrition teams are integral to the effective management of refeeding syndrome, as long as they have the appropriate skills and training.[1] A true multidisciplinary team (MDT) approach is often required with stringent monitoring.[3] The most prominent advice concerning refeeding prevention and management can be found in the NICE Clinical Guideline (2006) Nutrition Support for Adults: *Oral Nutrition Support, Enteral Tube Feeding and Parenteral Nutrition*.[1] This guideline provides a general overview, but there is a limited body of supporting studies, so conducting research in a specific area may be more useful to clinicians.[4]

Patients are deemed at high risk of refeeding syndrome if they meet the following criteria:[1]

The patient has one or more of the following:

- Body mass index <16 kg/m^2.
- Unintentional weight loss >15% in the past three to six months.
- Little or no nutritional intake for >10 days.
- Low levels of potassium, phosphate, or magnesium before feeding.

Or the patient has two or more of the following:

- Body mass index <18.5 kg/m^2.
- Unintentional weight loss >10% in the past three to six months.
- Little or no nutritional intake for >5 days.
- History of alcohol misuse or drugs, including insulin, chemotherapy, antacids, or diuretics.

If the patient is considered to be at high risk of refeeding syndrome, the following steps are advised by NICE:[1]

- Start nutrition support at a maximum of 10 kcal/kg/day, increasing levels slowly to meet or exceed full needs by four to seven days.
- Restore circulatory volume and monitor fluid balance and overall clinical status closely.
- Provide immediately before, and during the first ten days of feeding: oral thiamine 200–300 mg daily, vitamin B compound strong tablets one or two, three times a day (or full dose daily intravenous vitamin B preparation, if necessary) and a balanced multivitamin and trace element supplement once daily.
- Provide oral, enteral or intravenous supplements of potassium (likely requirement 2–4 mmol/kg/day), phosphate (likely requirement 0.3-0.6 mmol/kg/day) and magnesium (likely requirement 0.2 mmol/kg/day intravenously, 0.4 mmol/kg/day oral) unless pre-feeding plasma levels are high. Pre-feeding correction of low plasma levels is unnecessary.

In circumstances such as extremes of body mass index, BMI (less than 14 kg/m^2) or negligible nutrient intake for more than 15 days then 5 kcal/kg/day is recommended.[1] This nutrition target, however, should only be used in extreme circumstances and rarely happens in general clinical practice (but may be, for example required in specialist eating disorder centers). This level of nutrient restriction exacerbates the problem of inability to provide adequate nutrition to patients that are already at concerning level of malnutrition.[5] Further research is required in this area of practice.[1]

The level of energy (calorie) restriction required in order to control the amount of carbohydrate provided in the early phases of feeding often confers difficulty in providing a sufficient intake of protein. Ensuring that an adequate amount of protein is delivered during the early stages of feeding is challenging, even today. Historically this has also been problematic, in part due to the nutritional profiles of the enteral and parenteral feeds that were available five to ten years ago. In recent years, somewhat driven by the shift towards prescriptions for 'higher' protein, especially in critical care, nutrition companies have developed products with a 'lower energy, higher protein' content. Such products have applications in the early stages of feeding, as they enable relatively greater amounts of protein to be supplied per calorie, compared to products often known as 'standard feeds.'

At Rotherham General District Hospital, we stock a variety of enteral feeds. The 'high protein' enteral feed provides 8.2 g of protein per 100 kcal; in contrast our 'standard' feeds have a protein content of 3.8 g per 100 kcal.

For hospitals where the parenteral nutrition (PN) service is reliant on industry supplied multi-chamber bags (which is common for the majority of UK hospitals due to the lack of compounding capacity), having sufficient product options is essential. The availability of PN products considered to be 'high nitrogen' has increased the ability to meet a patient's specific protein needs, but prescribers can often still find themselves in a situation where a 'best-fit' model is in place. A hospital with greater aseptic services capacity and the facilities to make bespoke 'scratch' bags will be able to supply a PN formulation tailored precisely to a patient's individual requirements.

The 'high nitrogen' PN formulations stocked at Rotherham General District Hospital provide 1.22 g of nitrogen per 100 kcal whereas the 'standard' preparations have a lower relative protein content of 0.75 g of nitrogen per 100 kcal.

Case Study – Parenteral Nutrition

A 51-year-old male presented at Accident and Emergency with acute abdominal pain, and a past medical history of type II diabetes, hypertension and osteoarthritis. The patient had not opened his bowels for a number of days and was passing no flatus. A computed tomography (CT) scan was completed and showed an intra-abdominal mass with likely bowel perforation.

The patient was taken to theatre for laparotomy, with subsequent findings of significant bowel ischemia, and a caecal mass with perforation. A bowel resection was performed with removal of 1.2 m of small bowel, and formation of an end ileostomy (predicted high risk of ileus). On return to the ward, the patient was referred to the nutrition team for initiation of PN.

Anthropometry: Weight 78 kg, Height 1.78 m, BMI 24.6 kg/m^2. Usual weight 82-84 kg.

The patient was considered to be at risk of refeeding syndrome based on NICE criteria – little or no nutritional intake for >5 days and hypokalaemia.[1]

As per NICE guidance the feeding target was initially set at 10 kcal/kg/day = 780 kcal/day.[1]

Protein requirement calculated as 101.6 g protein (equating approximately to 16.2 gN).

Biochemistry: Hypokalaemia with mildly elevated urea and creatinine (**Table 1**).

Table 1: Blood biochemistry levels at initial assessment

Na (133-146 mmol/l)	142
K (3.5-5.3 mmol/l)	3.2
Cr (44-71 mmol/l)	78
Urea (2.5-7.8 mmol/l)	9.3
PO_4 (0.8-1.5 mmol/l)	1.2
Mg (0.7-1.0 mmol/l)	1.0

Clinical presentation: Non-functioning gastrointestinal tract; decision made to start nutrition parenterally as only viable route of feeding. Peripherally inserted central venous catheter *in situ*. Potassium also administered via parenteral route – 40 mmol potassium chloride in 1,000 ml 0.9% sodium chloride solution to correct hypokalaemia.

Diet: Nil oral intake, nasogastric tube on free drainage. Progressively poor oral intake (<50% nutritional requirements) for three to four days followed by two days nil oral intake, vomiting for the last 24 hours.

The nutrition team prescribed a parenteral nutrition regimen consisting of 10.6 g nitrogen and 900 kcal total calories. Multi-chamber PN bags do not contain vitamins and trace elements, so these were added to the multi-chamber bag in the hospital pharmacy prior to patient administration. Given the risk of refeeding syndrome and the patient's history of diabetes, the PN was introduced cautiously, and the patient was closely monitored.

Discussion

The use of 'high nitrogen' PN enabled a greater amount of nitrogen to be administered compared to what would have been achievable prior to the availability of such a product. Previously, when faced with a patient in a similar situation, a 'standard' PN feed containing 4 g nitrogen and 550 kcal would have been prescribed, which, while meeting the requirement to limit calories would have compromised protein intake. Having a 'high nitrogen' option thus effectively translated as an increase in nitrogen provision by almost 7 g on the first day of feeding. The availability of PN with different nutritional profiles means feeds can be advanced to meet changing nitrogen and calorie requirements as the clinical and biochemical pictures allow.

Case Study – Enteral Nutrition

A 42-year-old lady presented with background alcoholic liver disease (~24 units of alcohol daily), and was admitted to hospital with acute abdominal swelling, jaundice, poor appetite and poor food intake. Ascites and a subsequent diagnosis of spontaneous bacterial peritonitis were confirmed. The lady was commenced on intravenous antibiotics. See **Table 2**.

Table 2: Blood biochemistry levels at initial assessment

Na (133-146 mmol/l)	133
K (3.5-5.3 mmol/l)	3.8
Cr (44-71 mmol/l)	125
Urea (2.5-7.8 mmol/l)	10.2
PO_4 (0.8-1.5 mmol/l)	0.9
Mg (0.7-1.0 mmol/l)	0.7

A nasogastric tube (NG) was placed by the medical team, and a dietetic referral completed.

Anthropometry: Weight 60.2 kg (Severe ascites: estimated dry weight 46.2 kg), Height 1.59m, BMI (dry) 18.2 kg/m^2. Normal dry weight six weeks prior to admission was 52.5 kg. Equates to 11% weight loss over a six-week period. Significant reduction in muscle mass.

Patient assessed as being at risk of refeeding based on NICE criteria considering her BMI <18.5 kg/m^2,[1] unintentional weight loss >10% in the past three to six months and a history of alcohol abuse.

As per NICE guidance[1] the initial feeding target was set at 10 kcal/kg/day= 460 kcal/day.

Protein requirement calculated as 69.3 g/day.

Biochemistry: At initial assessment, despite normal electrolyte levels (elevated urea and creatinine) it was noted daily monitoring would be required at feed introduction.

Clinical presentation: Patient not opening her bowels regularly, laxatives added into treatment plan. Patient also struggling to mobilise secondary to ascites, with intermittent mild confusion. Mostly confined to bed and often drowsy.

Diet: Poor appetite and intake, no interest in oral intake and often asleep for meals. Progressively poor oral intake over the last six weeks with associated weight loss already noted. Discussed oral nutritional support but unlikely to take in sufficient amounts based on presentation so NG tube was placed.

The patient was started on the hospital's 'out of hours' feeding protocol with a tube feed providing 500 kcal and 19 g protein in 500 ml, at 25 mls/hour over 20 hours. A dietetic assessment was completed shortly after feeding was commenced and the nutrition prescription was changed to a 'high nitrogen' feed containing 498 kcal and 41 g protein in 408 mls administered at a rate of 17 mls/hour over 24 hours.

Discussion

A number of clinical conditions, including liver disease,[4, 6] necessitate increased protein requirements compared to those of healthy adults. It is therefore important to provide sufficient protein early during feeding if possible due to the consequences of malnutrition. Although the switch of feed following dietetic review did not fully meet the patient's protein requirements, it more than doubled the amount of protein that would have been provided had the patient been maintained on the 'out of hours' protocol. Having the option to provide patients with a relatively higher level of protein from the early stages of feeding until nutritional requirements can be fully met after four to seven days is beneficial.

Summary

Although primarily designed for use in critical care, the availability of 'high nitrogen' parenteral and 'high protein' enteral nutrition tube feed products provides excellent options for nutritional professionals who are aiming to introduce more protein into a patient's nutrition regimen. This can be the objective in a variety of situations that are not limited to the critical care setting and include the early stages of feeding where refeeding syndrome is a concern. Having a wide variety of product profiles allows more tailored nutrition to be provided to individual patients with the aim of improving nutrition provision hence ultimately impacting on clinical outcomes.

References: **1.** National Institute for Health and Care Excellence (2006). NICE Guidelines oral nutrition support, enteral tube feeding and parenteral nutrition. Accessed online: www.nice.org.uk/guidance/cg32/resources/cg32-nutrition-support-in-adults-full-guideline (Oct 2021). **2.** Singer P, et al. (2019). ESPEN Guideline on Clinical Nutrition in the Intensive Care Unit. Clin Nutr.; 38(1): 48-79. **3.** National Confidential Enquiry into Patient Outcome and Death (2010). 'A Mixed Bag' PN Rreport. Accessed online: www.ncepod.org.uk/2010pntoolkit.html (Oct 2021). **4.** British Dietetic Association (2018). The Parenteral and Enteral Nutrition Group (PENG). A Pocket Guide to Clinical Nutrition: 5th edition. **5.** Wagstaff G, (2011). Dietetic Practice in Refeeding Syndrome. J Hum Nutr Diet.; 24(5): 505-15. **6.** Plauth M, et al. (2019). ESPEN Guildine on Clinical Nutrition in Liver Disease. Clin Nutr.; 38(2): 485-521.

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