Use of Peptide Feeds in Children with Disease-Related Malnutrition

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Paediatric patients represent a particularly vulnerable group with specific nutritional requirements, but feeding difficulties are unfortunately a common occurrence. Up to 75% of critically ill children and 90% of chronically ill children may be malnourished or have suboptimal nutrition, which in turn can lead to impaired growth and development. There is increasing evidence to show that inadequate nutrition can prolong the length of hospital stay and worsen overall clinical outcome in various paediatric patient groups.[1,2]

Nutritional needs in children with complex conditions

Causes of faltering growth in children with complex medical conditions are normally multifactorial. An inability to take in sufficient nutrition is often a significant factor, but children with multiple, complex diseases may also have increased requirements for energy, protein and micronutrients.[3] Basal metabolic rate may also be increased in acute presentations, such as trauma, burns, inflammation, fever, as well as chronic disease states (e.g. cardiac or pulmonary). Children presenting with pre-existing malnutrition will also need additional energy to correct growth deficits.[4] Malabsorption or maldigestion of nutrients are other key players. Patients often have reduced gastric tolerance with impaired motility and compromised digestive-absorption functions that may be related to their underlying condition and/or arise because of treatments they are receiving. As adequate nutrition is required for preserving gastrointestinal (GI) function, malnutrition related GI alterations together with GI dysfunction associated with the clinical condition are becoming increasingly recognised as exacerbating the malnourished state, with the cumulative effects on energy imbalance further impacting patient outcome.[5] This simultaneous interplay between malnutrition and compromised GI function emphasises the importance of appropriate nutritional support in malnourished children, and it is well recognised that appropriate nutrition support with optimal energy delivery is vital when treating the unwell child.[6]

Choosing an appropriate formula

Several different types of formula are available when nutrition support is indicated, which are normally described in accordance with their protein and/or lipid source. Polymeric formulas contain whole/intact proteins, carbohydrates and predominantly long-chain triglycerides as the fat source and are usually adequate for the majority of patients.[5]

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However, manifestations of feeding intolerance to these formulas, such as abdominal distension, vomiting, aspirations and diarrhoea, are recognised complications that can occur in numerous patient groups.[7] Reduced tolerance to enteral feeds not only increases intestinal losses but can also decrease the ability to achieve target enteral intake with feed withdrawal for gut rest often occurring, likely to fuel an increase in nutrient reserve catabolism.[8] Therefore, a method of providing nutrition support that addresses the overlapping and interacting effects of diarrhoea, enteropathy, and malnutrition is needed. Peptide feeds can therefore be a suitable alternative for these patients displaying signs of intolerance and where absorption and digestion of nutrients is likely to be impaired.

Why might a peptide formula be beneficial?

Peptide formulas contain proteins that have been hydrolysed into chains of varying length (peptides), carbohydrates and fat (usually including medium-chain triglycerides [MCT]). Peptides, in theory, require less digestion than whole proteins within the GI tract. They are actively absorbed by the enterocytes (intestinal absorptive cells) where they are metabolised into free amino acids. This is considered advantageous with absorption of peptides occurring more quickly and efficiently, enabling better utilisation within the body, especially in those with intestinal disease and mucosal damage.[9]

The development of peptide-based enteral formulas is considered a significant milestone in the advancement of clinical nutrition, and there is a growing body of evidence showing improved clinical outcomes from its use compared with elemental or whole protein formulas for certain groups of patients. Studies have demonstrated overall improved GI tolerance, better nitrogen retention, lower risk of diarrhoea and bacteria translocation and improvements in gut integrity.[10] Protein hydrolysates are also considered to improve sodium and jejunal water absorption alongside nutrient absorption, which is likely to be beneficial with intolerance of feed frequently manifesting as diarrhoea.[11] It is with this in mind that peptide feeds could, in certain circumstances, actually be superior to elemental formulas. Elemental formulas contain free amino acids as the protein source, but several studies have suggested that the majority of nitrogen is absorbed as peptides and amino acids may be absorbed more efficiently in the form of peptides.[12, 13] The combined characteristics of more efficient uptake of di- and tripeptides and a lower osmolality compared to amino acid feeds may be advantageous for enteral nutrition management of various disease states.[14]

The evidence?

Unfortunately, controlled trials examining specific use of peptide feeds in paediatric patients remains limited. However, while there is a lack of clear evidence supporting their general use, it is recognised that some specific patients may benefit from changing to a peptide formula. In clinical practice, peptide feeds are increasingly being used as an enteral feed of choice to support nutrition when managing children with acute and chronic disease and illness.[15] The use of peptide formulas is reported where polymeric formulas have failed, or it is expected/predicted that polymeric formulas will fail due to the specific anatomical or pathophysiological condition of the child. For example, patients with conditions such as liver disease, protein losing enteropathies, cystic fibrosis, short gut that have known malabsorption issues or those undergoing chemotherapy or bone marrow transplant therapy where treatment can significantly impact gut function.[16]

Making comparisons between effectiveness of different feeds and drawing conclusions from the available research is complicated, in part due to there being no universally agreed definition of 'intolerance'. Although, overall, peptide feeds appear to be well tolerated in paediatric patients with a variety of medical conditions that have complex pathologies,[17] with markers of improved tolerance typically being cited as decrease in gastric aspirates, upper GI symptoms, such as vomiting, frequency of bowel movements, and abdominal pain and/or distention. It is also becoming increasingly recognised that peptide feeds can be beneficial in groups of patients not typically predicted to have tolerance issues (as listed above) or pathologies predominantly related to the GI tract. This includes patients with neuro-developmental delay, cardiac patients and critical care patients, with studies suggesting improved growth and long-term development, fewer GI complications, improved nutritional status and decreased rates of mortality.[18, 19, 20] Further research is needed to define the clinical situations more precisely in which peptide-based formulas should be prescribed over polymeric or amino acid-based formula.

CASE STUDY

The following case study describes the management of a 9½-year-old girl referred for dietetic intervention with a diagnosis of Crohn's disease (diagnosed age 7). She had been in remission for about 1 year with daily maintenance medical treatment, however, she began to experience an exacerbation of symptoms, presumed to be a Crohn's disease flare. Despite maximising medical treatment with biologic therapy, symptoms persisted, so she was admitted to a tertiary care hospital for observation, further investigation, and disease management.

Presenting symptoms: Patient and parents reported a 4-month history of increased stooling with bowels opening 10-15 times per day, including overnight. These were type 7 on the Bristol Stool Chart (BSC) with blood and mucous. More recently, over the past 2 months she had also suffered with nausea and abdominal pain which resulted in a reduction of oral intake. Oral intake was estimated to be around 400-500 kcal per day over the previous week. Significant weight loss of 7 kg (20% body weight) since symptoms started. The patient was suffering with very low energy levels. A trial previously of oral nutritional supplement drinks but these were not tolerated due to nausea and felt to worsen stooling.

Diagnosis: An endoscopy had been performed 1 month prior to admission which had showed active inflammation predominantly in the colon. Blood tests taken on admission were unremarkable with negative inflammatory markers, normal liver and bone profile (although this was not unusual for this child from previous flares). She had a mild iron deficiency anaemia (Hb 107 g/l, normal range 120-160 g/l). Stool samples showed a faecal calprotectin of >600 µg/g (normal <100 µg/g) as an alternative measure of disease activity.[21]

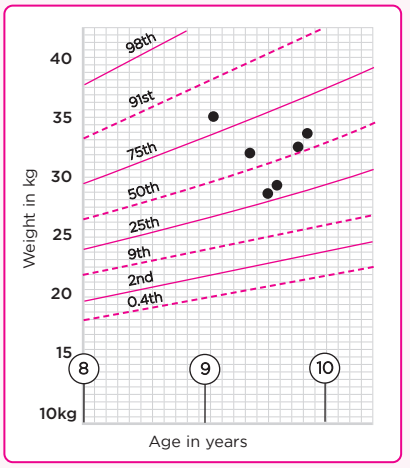
Management pathway: As the child was already on a combination therapy (high dose biologics 10 mg/kg Infliximab weekly and 6-mercaptopurine 25 mg od) and non-responsive to treatment, a decision was made to start exclusive enteral nutrition (EEN) as an additional therapy to pharmaceutical management. Due to a failure to tolerate ONS previously, she commenced on a peptide-based feed via nasogastric tube with a plan to meet her full estimated nutritional requirements of 2000 kcal (59 kcal/kg for target weight) and 28.3 g protein per day. Her weight at point of feeds commencing was 28 kg (25th centile) and height 140 cm (75th centile). The feed was delivered via continuous pump infusion over 16 hours with an 8-hour break overnight. Feed volumes started at 50% on day one (62 ml/hour) and increased gradually over four days to meet full requirements (125 ml/hour). Nil else was allowed orally other than sips of clear fluid.

Within the first 2 days of receiving exclusive nasogastric (NG) feeds with a peptide feed, there was a significant improvement in GI tolerance with no nausea or pain reported. Stool frequency had reduced to 4-5 times per day and was now slightly more formed (type 6 on BSC). After a further 4 days on the peptide feed, stool frequency had improved further; the child was opening her bowels only twice during the day and the stools were formed (type 5).

There was still some blood in the stool, but quantities were reducing. Mother reported that the child was much brighter and feeling more energetic. She had also gained 1 kg since admission. Due to these improvements, the child was discharged home after a week on EEN with a plan to continue with full feeds via nasogastric tube for a further 5 weeks treatment.

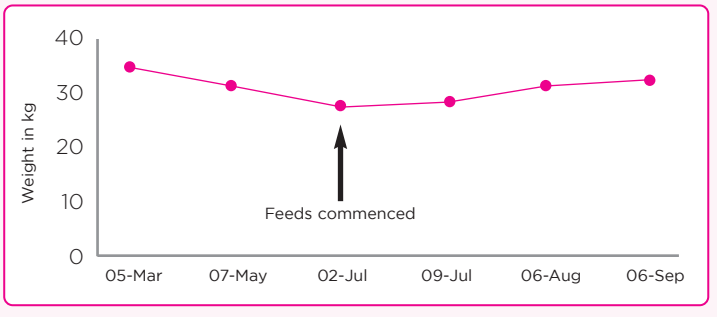
After 6 weeks of additional EEN with a peptide feed, the child's GI symptoms had entirely resolved, and weight was nearly restored with an overall gain of 5 kg. Faecal calprotectin had improved to 200 µg/g (normal <100 µg/g) and iron status normalised. A plan was provided at this point to start a graded reintroduction of solid food alongside reduction in NG feeds over a period of 3 weeks.

Weight-for-age centiles*



*Pre and post EEN with a peptide feed.

Weight pre and post starting EEN with a Peptide Feed



Discussion: EEN is well recognised as an effective treatment for Crohn's disease[22] and has been shown to provide the additional benefits of resolving nutritional deficiencies, improving growth and weight gain.[23] There is no strong evidence to support the use of a peptide feed over polymeric feeds in EEN. However, because there was excess stooling and weight loss and as the trial of whole protein oral supplementation had failed (both in volumes consumed and poor tolerance), it was felt a peptide feed had a greater likelihood of tolerance to give the best possible chance of early feeding success.

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