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ESPEN Endorsed Recommendation

Avoiding the use of long-term parenteral support in patients without intestinal failure: A position paper from the European Society of Clinical Nutrition & Metabolism, the European Society of Neurogastroenterology and Motility and the Rome Foundation for Disorders of Gut–Brain Interaction

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SUMMARY

The role of long-term parenteral support in patients with underlying benign conditions who do not have intestinal failure (IF) is contentious, not least since there are clear benefits in utilising the oral or enteral route for nutritional support. Furthermore, the risks of long-term home parenteral nutrition (HPN) are significant, with significant impacts on morbidity and mortality. There has, however, been a recent upsurge of the use of HPN in patients with conditions such as gastro-intestinal neuromuscular disorders, opioid bowel dysfunction, disorders of gut–brain interaction and possibly eating disorders, who do not have IF. As a result, the European Society of Clinical Nutrition and Metabolism (ESPEN), the European Society of Neuro-gastroenterology and Motility (ESNM) and the Rome Foundation for Disorders of Gut Brain Interaction felt that a position statement is required to clarify - and hopefully reduce the potential for harm associated with – the use of long-term parenteral support in patients without IF.

Consensus opinion is that HPN should not be prescribed for patients without IF, where the oral and/or enteral route can be utilised. On the rare occasions that PN commencement is required to treat life-threatening malnutrition in conditions such as those listed above, it should only be prescribed for a time-limited period to achieve nutritional safety, while the wider multi-disciplinary team focus on more

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appropriate biopsychosocial holistic and rehabilitative approaches to manage the patient's primary underlying condition.

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1. Introduction

In 2015, the European Society of Clinical Nutrition and Metabolism (ESPEN) recommended that intestinal failure (IF) should be defined as 'reduced gut function below the minimum necessary for the absorption of macronutrients and/or water and electrolytes, such that intravenous supplementation is required to maintain health and/or growth' [1]. Thus, the consensus recommendations stipulated that two simultaneous criteria were needed for the diagnosis of IF: 'reduced absorption of macronutrients and/or water and electrolytes' and, in tandem, the associated 'need for intravenous supplementation'. The principal pathophysiological mechanisms that lead to reduced absorption of macronutrients and/or water and electrolytes include short bowel, intestinal fistula, intestinal dysmotility, mechanical obstruction and extensive small intestinal mucosal disease, all of which can occur in benign and malignant underlying conditions [1]. The authors of the recommendations were clear that other clinical scenarios where clinicians may have prescribed intravenous supplementation – for example, patients declining effective oral and/or enteral nutrition – should not be considered as IF [1].

While the indications for long-term parenteral support – including home parenteral nutrition (HPN) - for patients with IF are clear, the appropriateness of offering HPN or home intravenous fluids to patients without IF needs careful consideration. The recently published ESPEN practical guideline on this subject state that 'HPN can be considered for patients without IF who do not want to meet their nutritional requirements via the oral/enteral route' [2]. The example cited within these practical guidelines is of patients with cancer suffering from dysphagia who have an indwelling central venous access device for chemotherapy, noting that the patient may have chosen to decline 'otherwise effective and clinically-recommended enteral nutrition'. The guidelines do stress that it is important to fully inform such patients about the risks of PN. A recent international survey of IF teams revealed that around one-quarter of respondents reported using HPN in patients with advanced malignancy without IF, although this practice differed between countries [3], with some national guidelines recommending that palliative HPN for patients with cancer should only be offered to those with IF, with the enteral route being preferred for patients with a functional gut [4].

While the reasons for this variation in practice between countries in patients with cancer warrants further evaluation, particularly as to whether oncologists rather than IF physicians are the principal proponents of using HPN in patients without IF, there has also been a recent upsurge in commencing long-term parenteral support in patients with underlying benign conditions who do not have IF [5]. Given this recent trend and the inherent risks of parenteral support, the Home Artificial Nutrition and Chronic Intestinal Failure Specialist Interest Group of ESPEN, together with the European Society of Neurogastroenterology and Motility (ESNM) and the Rome Foundation for Disorders of Gut–Brain Interaction, felt that a position statement is required to clarify - and hopefully reduce the potential for harm associated with – the use of long-term parenteral support in patients without IF.

2. Risks of long-term parenteral support

The complications associated with HPN are well documented within the international literature and associated guidelines, such that an extensive review of the risks of HPN is not required for this Position Statement [2,6]. Briefly, these include central venous catheter-related complications such as catheter related bloodstream infections (CRBSIs), thrombosis, occlusion and other mechanical complications, as well as metabolic complications due to factors related also to the underlying disease and mechanism of IF, such as hepatic, renal and bone complications. Such complications often require recurrent hospitalisations and will lead to significant morbidity and sometimes mortality. A recent very large single-centre study of more than 1000 patients over a four-decade period from a national reference centre in the U.K. demonstrated that the average life years lost for an HPN-dependent patient was greater than 17 years compared to the general population [7]. While the causes of death comprised HPN-related complications, underlying IF disease and non-IF related reasons, it is of course vital that all patients are fully informed of the potential for life-threatening complications associated with the use of long-term parenteral support, with a carefully considered multi-disciplinary assessment of the risks and benefits of this therapy for each individual patient.

Beyond the life-limiting risk of HPN-related complications, it is unequivocal that the restrictive nature of HPN impacts adversely on multiple aspects of a patient's quality of life, such as ability to work, travel and socialise [6]. While it is clear that the need for HPN can often adversely affect a patient's mental health [8], its associated impact on family members should also not be underestimated, with recent data demonstrating that a concerning proportion struggle to work [9] and that the health and wellbeing of people living with HPN-dependent patients can be adversely affected [10].

It is undoubtedly easier to weigh the risks of HPN against the benefits for patients with IF, where – without it - the underlying condition will pose a clear threat to life. However, the same does not, of course, necessarily hold true for those without IF, where the lower risk and more physiological oral and/or enteral route can be utilised, such that it is incumbent on clinicians not to commence long-term parenteral support in patients without IF, apart from in exceptional circumstances, where there may be a clear risk to life without it and where the patient has been fully informed of the life-threatening risks and burden associated with parenteral therapy. It may be useful to consider the commonest clinical conditions where HPN has been used in recent times for patients without IF; patients with gastrointestinal neuromuscular disorders, disorders of gut–-brain interaction (DGBI; previously labelled as functional gastrointestinal disorders) and patients with eating disorders such as avoidant and restrictive food intake disorder (ARFID) and anorexia nervosa.

3. Gastro-intestinal neuromuscular disorders (GINMD)

Gastro-intestinal Neuromuscular Disorders of the small bowel broadly comprise Chronic intestinal pseudo-obstruction (CIPO) and Enteric Dysmotility [6,11]. CIPO is readily diagnosed on cross-sectional imaging, with a chronically dilated small bowel in the

absence of mechanical obstruction. This can be due to myopathies or neuropathies and is more likely to result in true IF due to absent or disordered peristalsis. Patients with CIPO are also less likely to wean off HPN, with worse survival likely in those with underlying systemic causes such as systemic sclerosis [11,12]. Enteric dysmotility, on the other hand, is a much less well-defined GINMD than CIPO and is distinguished from it by abnormal small bowel manometry with a non-dilated small intestine [6]. It has also been associated with neuropathies and myopathies [11]. Access to, and patient tolerance of, small bowel manometry is however limited and its correlation with both patient symptoms and with GINMD histopathology is also limited [5,12,13]. Whether patient intolerance of small intestinal feeding can occur primarily through a pain sensory nervous system disorder (i.e. visceral hypersensitivity) is almost completely unexplored to date. For pragmatic reasons, therefore, sometimes the group of patients with a non-dilated small bowel and small intestinal feeding intolerance is termed "severe dysmotility" [14] or "non-CIPO" [12]. Furthermore, in clinical practice, where patients may feel intolerant of small bowel feeding or even undergoing small bowel manometry, a simple contrast study via the oral route or via any established enteral tube can be useful to demonstrate normal passage of luminal contents. Notably, the non-CIPO group of patients are more likely to be able to wean off PN than the CIPO group [12]. This can be achieved through a multi-disciplinary biopsychosocial holistic and rehabilitative approach including psychology input and optimised symptom management, as well as close nutrition supervision and monitoring. In the absence of severe progressive life-threatening malnutrition, particularly given the risks of long-term parenteral support as outlined above, we would therefore recommend avoiding the commencement of PN in patients with non-CIPO and pain-related small intestinal feeding intolerance, whilst comprehensive multi-disciplinary team (MDT) biopsychosocial holistic and rehabilitative approaches are engaged with persistence of dietitian-overviewed effortful oral feeding and/or enteral nutrition to maintain nutritional status.

4. Opioid bowel dysfunction

Exogenous opioids can mimic or exacerbate gastrointestinal dysmotility and DGBI, can exacerbate underlying centrally sensitised pain states (opioid induced hyperalgesia or narcotic bowel syndrome) and can invoke opioid-induced nausea and vomiting via multiple peripheral and central mechanisms [15]. At its most extreme, the opioid bowel dysfunction may even mimic features of CIPO [15]. Furthermore, opioids may increase parenteral support-related risks, including CRBSIs. These effects may only be partially or not at all mitigated using opioid antagonists, especially at higher opioid doses. We would therefore recommend that motility testing and diagnoses of GINMD and DGBI be reserved until controlled opioid withdrawal has been achieved and again, in the absence of severe progressive life-threatening malnutrition, PN commencement should be avoided in such patients on opioids. Again, and as outlined with other disorders of gastro-intestinal motility, overview by a MDT including pain specialists is crucial, with the nutrition team at the forefront promoting the oral and/or enteral route.

5. Disorders of gut brain interaction (DGBI)

Functional Dyspepsia (FD) and gastroparesis (GP) likely represent an overlapping spectrum of sensorimotor abnormalities affecting the gastro-duodenum, although nausea and vomiting symptoms are more prominent in patients with a label of gastroparesis [16,17]. Most patients with FD/GP can be managed with optimised oral nutrition, but occasionally patients who develop malnutrition will proceed to small intestinal feeding and a smaller subset develop small intestinal feeding intolerance. In this group of patients, the situation should be considered similarly to the non-CIPO dysmotility group and PN should be avoided in the absence of severe progressive life-threatening malnutrition, with opioid weaning where relevant and focus on MDT biopsychosocial holistic and rehabilitative management. Neuromodulators (e.g. the serotonergic neuromodulator mirtazapine) can be helpful in increasing food tolerance and body weight in patients with DGBI with significant weight loss [18].

Rumination syndrome, cyclical vomiting syndrome, cannabis hyperemesis and chronic unexplained nausea and vomiting are increasingly recognised differential diagnoses of foregut DGBIs with a vomiting-like presentation [17,19]. Once recognised, there are individualised management approaches to these conditions that should not require PN, which again should be avoided, other than in life threatening malnutrition-related extremis and as a temporary bridge to appropriate therapies.

Hypermobility Disorder/hypermobile Ehlers Danlos Syndrome (HD/hEDS) is an emerging condition for which there are increasing referrals for PN [20]. DGBIs, especially functional dyspepsia and irritable bowel syndrome are strongly associated with HD/hEDS [21,22]. There is a large overlap with fibromyalgia and chronic fatigue/myalgic encephalomyelitis (ME) with a core feature of chronic pain due to both peripheral and central sensitisation, overlapping with anxiety and a dysregulated autonomic nervous system including postural orthostatic tachycardia syndrome (POTS). As there is also no established evidence that patients with HD/hEDS have small intestinal malabsorptive failure, PN should be avoided other than again in life threatening extremis as a temporary bridge to pain management and rehabilitative MDT therapies [23]. This may be particularly important since anecdotal clinical experience suggests that HPN-related CRBSI are more frequent in this patient cohort.

6. Eating disorders

Another category of patients suffering from malnutrition in the absence of IF are patients with eating disorders such as ARFID and anorexia nervosa. It is increasingly recognised that there is significant overlap/comorbidity between DGBIs and ARFID. The commonest ARFID presentation in DGBIs associated with malnutrition is fear avoidance of foods due to previous symptom associations. Elimination diets followed by these patients, such as gluten-free or low-FODMAP diet, can increase the risk of developing ARFID [24]. Moreover, the presence of ARFID may perpetuate or exacerbate symptoms related to DGBI [25]. The optimal psychological and nutritional rehabilitation approach in ARFID is graded exposure in a cognitive behavioural therapy (CBT) setting rather than further reinforcing restriction [26]. All patients therefore with a non-CIPO GINMD or DGBI should ideally be screened for ARFID as well as Shape and Weight -motivated eating disorders (SWED) such as anorexia nervosa and bulimia. Parenteral nutrition should be avoided in both ARFID and SWED, other than in life threatening malnutrition extremis as a temporary bridge to optimal eating disorder MDT management [27].

7. Conclusion

Long-term parenteral support carries significant risk and HPN-dependent patients have reduced life-expectancy. In general, HPN should therefore not be prescribed for patients without IF, where the oral and/or enteral route can be utilised. On the rare occasions that PN commencement is required to treat life-threatening

malnutrition in conditions such as GINMD, Opioid Bowel Dysfunction, DGBI or eating disorders, it should only be prescribed for a time-limited period to achieve nutritional safety, while the wider MDT, including pain, psychological and/or eating disorder specialists, where appropriate, focus on more appropriate bio-psychosocial holistic and rehabilitative approaches to manage the patient's primary underlying condition.

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Authors contribution

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Conflict of interest

None declared.

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