Parenteral Nutrition in Hospitalized Children

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Results: 303 children (67 newborns) were enrolled. Patients were referred from different departments across the hospital. The median duration of PN was 18 days (1-160). PN was mainly prescribed to critically ill children on intensive care (66/303), those undergo surgery (63/303) and bone marrow transplantation (28/303). The ESPGHAN recommendations were followed in 91.7% (278/303) of cases (newborns 64/67, 95.5%; children 214/236, 90.8%). The use of PN was considered inappropriate in 12/303 patients and in 13/303 it was not possible to reach a conclusion.

Conclusion: Although the indications for inpatient PN in children is mostly justified, there is still a proportion of patients receiving intravenous nutrition unnecessarily highlighting the need for more PN training and better access to nutritional support teams.

Keywords: Pediatric parenteral nutrition; ESPGHAN guidelines; Indications; Appropriateness

Abbreviations

PN: Parenteral Nutrition; EN: Enteral Nutrition; ESPGHAN: European Society of Paediatric Gastroenterology, Hepatology and Nutrition; GI: Gastrointestinal; NEC: Necrotising Enterocolitis; IC: Intensive Care; NST: Nutritional Support Team; IF: Intestinal Failure

Introduction

Parenteral Nutrition (PN) is an invasive therapy used when the oral or enteral application of nutrition is not possible [1]. The European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society for Clinical Nutrition and Metabolism, supported by the European Society of Paediatric Research have published guidelines in 2005 to aid medical teams caring for such patients in prescribing PN appropriately [2].

Malnutrition is a common problem amongst hospitalised children and has a negative impact on recovery and length of hospital stay [3,4]. Newborns in particular are affected by suboptimal nutrient intake making them more prone to infections and prolonged ventilatory support [5].

Specialised nutritional support therapy is aimed at those who cannot meet their nutritional requirements orally and consists of both enteral and parenteral nutrition [6]. The enteral route is generally preferred due to its major role in the maintenance of mucosal structure and function of the intestine [7] as well as for the known cost and complications associated with PN [8]. However, in well selected patients, PN is undoubtedly a potential lifesaver and has become a well established practice in children and newborns with intestinal failure.

In most European countries PN is prescribed in line with the 2005 ESPGHAN guidelines [2]. The purpose of these guidelines was to identify the most common and reasonable indications for the use of PN in newborns, infants and children in order to reduce the inappropriate use of PN.

Sepsis, electrolyte disturbances, metabolic bone disease, micronutrient deficiencies, liver disease, pulmonary embolism and loss of central venous access are well known complications of PN [9,10].

Moreover inappropriate prescribing does not only increase the burden of disease to the patient but also has a substantial economic impact on the health care system [11].
The aim of this observational study was to get a better understanding as to why hospitalised children are started on PN and if the indications, based on the 2005 ESPGHAN guidelines, were appropriate. We wanted to use this knowledge to develop strategies to avoid inappropriate PN prescribing in the future.

Methods

All patients admitted to a large national referral centre for children who were started on PN between October 2013 and March 2014 were identified from the pharmacy database and entered into the study prospectively. Children who were already established on home PN were excluded.

Information was obtained from the PN prescription, medical, nursing and dietetic records. Patient demographics, underlying diagnosis, referring department, feeding regimen prior to and on PN documented, and the current pathology, indication for PN and its duration recorded.

Clinical scenarios justifying the use of PN were divided into medical and surgical, due to primary intestinal failure (IF), defined as directly related to underlying anatomical or structural gut pathology, or secondary IF as a consequence of other conditions leading to enteral feed intolerance.

PN indications were classified as appropriate, inappropriate or indeterminate based on the ESPGHAN 2005 guidelines [2].

In infants and children PN was classified as appropriate if the energy and nutrient demands of the patient were not met through the enteral route; in particular following the ESPGHAN guidelines on pediatric enteral nutrition (EN), enteral support was considered to have failed if 60-80% of calorie requirements were not met for more than 5 days in children older than one year of age and more than 3 days in infants [11].

Moreover PN was considered appropriate if the child/infant was expected not to meet 60-80% of the expected calorie requirements for more than 7 days in all those situations where EN was contraindicated such as paralytic or mechanical ileus, anatomical disruption of the gastrointestinal (GI) tract, intestinal obstruction, necrotising enterocolitis (NEC), GI ischemia, diffuse peritonitis, perforation or a state of severe shock [11-13].

In the neonatal group PN was considered appropriate in all premature infants <32 week of gestation and <1500 g and all seriously ill infants with more than 32 weeks of gestation, in particular surgical neonates, with acquired or congenital disease causing GI failure [2,14].

PN was considered inappropriate in infants and children in the absence of evidence of a non-functioning gut when EN could have been easily established or supplementation with intravenous calories was nutritionally not indicated. In patients older than 1 year of age a duration of PN therapy for <5 days was also considered inappropriate, unless the child was undernourished [13,15,16]. Under-nutrition was defined according to the WHO criteria [17].

In newborns the start of PN was considered inappropriate in all neonates >32 week of gestation and a birth weight of more >1500 g without primary gut pathology, who were clinically well and could hence be expected to establish full enteral.

The use of PN was considered indeterminate if a judgement could not be made due to scanty information, if EN was achievable but not used because of concerns over potential complications associated with feeding or a delay in passsing a suitable enteral feeding tube, eg if the child rejected or if jejunal feeding was required but jejunal access was unsuccessful.

The study was approved by the Ethical Committee of Great Ormond Street Hospital and informed consent was obtained from parents or legal guardians of the patients.

All data collected were analysed using Microsoft Access and Excel.

Results

In the study period PN was prescribed to 318 patients; 15 children were home PN dependent. The total number of patients enrolled was hence 303 (165 (54.5%) females) of which 67 (22.1%) were newborns, 98 (32.3%) were infants and 138 (45.5%) were children and adolescents. Median age was 38 months, ranging from 0 to 223 months. Median duration of PN was 18 days (1-160 days). At the end of the study period 15 patients were still on PN, 233 (76.9%) children had received PN <28 days.

All but 17 of the enrolled patients had an underlying diagnosis at the start of PN. Congenital heart disease, malignancies and GI disorders were the most common (Table 1).

Table 1: Pre-existing diagnosis.

| Pre-existing diagnosis                                      | No  | Percentage |
|------------------------------------------------------------|-----|------------|
| Cardiopathy                                                | 90  | 29.7       |
| Tumour                                                     | 68  | 22.4       |
| GI pathology                                               | 41  | 13.5       |
| congenital pathologies of the immune system                | 20  | 6.6        |
Among the children with a malignancy 37 (54.4%) had leukemia, and 31 (45.6%) a solid tumour. In the group of patients with pathologies of the GI tract 26 (66.6%) were born with a congenital malformation, 5 (12.8%) had short bowel syndrome, 3 were diagnosed with inflammatory bowel disease, 6 suffered from a GI motility disorder and 1 a congenital enteropathy.

Patients were referred from medical specialities (34%—majority oncology 64/103), surgery (35%—majority cardiothoracic 81/106) and intensive care (IC) units (31%, majority pediatric IC 57/94) (Table 2).

| Referring department               | No  | Percentage |
|------------------------------------|-----|------------|
| Medical                            | 103 | 34.0       |
| Dermatology                        | 2   | 0.6        |
| Endocrine                          | 5   | 1.6        |
| Gastroenterology                   | 15  | 4.9        |
| haematology/oncology               | 64  | 21.1       |
| Immunology                         | 6   | 2.0        |
| Metabolic                          | 11  | 3.6        |
| Surgical                           | 106 | 35.0       |
| Cardiothoracic surgery             | 81  | 26.8       |
| GI surgery                         | 19  | 6.3        |
| Other surgery                      | 4   | 1.3        |
| Orthopedic                         | 1   | 0.3        |
| Urology                            | 1   | 0.3        |
| IC                                 | 94  | 31.0       |
| Pediatric IC unit                  | 57  | 18.8       |
| Neonatal IC unit                   | 37  | 12.2       |

The remaining patients (42.6%) were admitted for surgery of which most was not related to the GI tract (61.7%). Only 38.3% of children had primary intestinal failure as a consequence of GI surgery.

On the surgical wards PN was mostly used as nutritional support in the pre and perioperative period (20.8%) and mainly given to children who underwent surgery for congenital
heart defects (61/63), followed by NEC (7.3%) and intestinal resection for congenital malformations of the GI tract (6.9%) (Table 3).

Table 3: Pathologies with an indication for PN.

| Pathologies with an indication for PN                                      | No | Percentage |
|---------------------------------------------------------------------------|----|------------|
| Pre-peri surgery nutritional support                                      | 63 | 20.8       |
| Post operative nutritional support                                       | 3  | 1.0        |
| Post surgical ileus                                                      | 4  | 1.3        |
| Intestinal resection in congenital malformation of the GI tract          | 21 | 6.9        |
| Other intestinal resections                                              | 10 | 3.3        |
| NEC                                                                       | 22 | 7.3        |
| Organ transplant                                                         | 6  | 2.0        |
| Autoimmune disorder associated with intestinal failure                   | 4  | 1.3        |
| Feed intolerance                                                         | 25 | 8.2        |
| GI dysmotility                                                           | 4  | 1.3        |
| Meconium aspiration                                                      | 2  | 0.7        |
| Malnourishment                                                           | 3  | 1.0        |
| Condition associated with malabsorption                                  | 9  | 3.0        |
| BMT                                                                       | 28 | 9.2        |
| Mucositis due to chemo                                                   | 19 | 6.3        |
| Critical illness                                                         | 66 | 21.8       |
| Decompensation in patients with metabolic condition                      | 7  | 2.3        |
| Acute pancreatitis                                                       | 2  | 0.7        |
| Heart cachexia                                                           | 1  | 0.3        |
| Miscellaneous                                                            | 4  | 1.3        |

The use of PN was considered appropriate in 278/303 (91.7%), inappropriate in 12 (4.0%) and indeterminate in 13 (4.3%) patients.

In the group of children older than 12 months 16 (11.6%) had less than 5 days of PN. Five of them did not meet the ESPGHAN criteria as their nutritional status was good. In seven patients the use of PN was felt to be appropriate irrespective of the short duration as two children were malnourished (2/7) and in five the assumption that PN would be required longer was justifiable. Four cases were considered indeterminate as it was not possible to establish if the use of PN was truly indicated or not.

Four infants were given PN despite a functional GI tract and one was kept nil by mouth and given PN for one day for query NEC. Two term newborns were prescribed PN unnecessarily as they were able to tolerate >80% of their requirements enterally when PN was started and PN was only given for one day. Table 4 summarizes patients who received PN inappropriately.

Table 4: Inappropriate use of PN: Patients.

| Number | Inappropriate PN use                                                                 |
|--------|-------------------------------------------------------------------------------------|
| 5      | PN <5 days in child >12 months of age with a proper nutritional status according to WHO criteria |
| 4      | Infant with functional GI tract. Enteral route not attempted as first line therapy  |
| 2      | Term infant with >80% feed tolerance enterally                                       |
| 1      | Infant >32 weeks GA PN for 1 day only (suspected NEC, not confirmed)                  |

According to age PN was defined as appropriate in 95.5% of newborns and in 90.8% of infants and children (Table 5).

Table 5: Appropriateness of PN divided by age.

| Current Audit | Newborns No, Percentage | Infants/children No, Percentage |
|---------------|-------------------------|--------------------------------|
Discussion

The administration of PN is well a established practice in Paediatrics providing nutritional support to infants and children with a non functioning gut or to those who cannot meet their nutritional requirements enterally. However, PN is by far no panacea and complications can be serious with significant consequences to the patient and financial burden to the health care system [8-10]. The joint ESPGHAN/ESPEN guidelines published in 2005 make recommendations when PN should be prescribed to children [2].

However, suboptimal care in the administration of PN in newborns and children remains a concern [18]. In our cohort we considered the use of PN appropriate in 95.5% of newborns and 90.5% of children (age 1 month-18 years). PN is still prescribed inappropriately in a number of patients despite the 2005 ESPGHAN guidelines: enteral feeds in children with a functional gut were not tried vigourously enough and conditions associated with a predictable short term feed intolerance such as post-operative ileus were too agressively treated with PN. In children older than 12 months with a good nutritional status, post operative PN is only considered beneficial if the child is expected to remain nil by mouth for more than 7 days and when PN is administered for at least 5 days, otherwise the risk associated with the administration outweighs the benefits [16,17,19,20]. Although poor peri operative nutritional status has been linked to an increase in postoperative complications and less favourable outcome too little emphasis is placed on improving the preoperative nutritional status of children undergoing planned or semi elective surgery [21].

Consultation of a Nutrition Support Team (NST) has been shown to reduce the number of children receiving short term PN. Enteral feeds are more frequently started early and catheter and metabolic complications reduced. Utilisation of an NST is therefore cost effective [22,23].

Our hospital NST is staffed with a Consultant paediatric Gastroenterologist, a dietician and a PN pharmacist. All children receiving PN are reviewed by the team once a week and advise on the nutritional management given. However, it is currently not routine practice to consult the NST prior to the start of PN as the initial request is made by the individual speciality caring for the patient.

Studies on adults have shown that mandatory involvement of the NST prior to the start of PN reduced the number of inappropriate PN prescriptions [24,25]. In the future we would like to make a discussion with the NST compulsory prior to a child being started on PN as part of a robust referral pathway.

Table 6: Nutrition screening tools for hospitalized children.

| Appropriateness | 64, 95.5 | 214, 90.7 |
|-----------------|----------|----------|
| Indeterminate   | 1, 1.5   | 12, 6.1  |
| Inappropriate   | 2, 3.0   | 10, 4.2  |

PN has been used in children for over forty years and was initially prescribed to patients with primary GI pathology such as congenital or acquired short bowel syndrome [20]. PN management has evolved since and PN is now commonly used as nutritional support in other conditions [12].

This is strongly supported by our data, as the majority of children receiving PN in our cohort had a non primary GI pathology (61.7% non GI vs 38.3% GI). Sepsis, respiratory, cardiac, renal or multi organ failure (21.8%), pre and perioperative nutritional support - particularly for children undergoing cardiac surgery (20.8%) - were by far the most common conditions leading to feed intolerance and hence the start of PN.

Nutritional support is a significant aspect of the management of critically ill children admitted to paediatric intensive care [26]. However, how these patients should be fed (enteral versus parenteral route) and what the optimal timing for the start nutritional support is [27]. Although early initiation of nutritional support appears to be indicated due to a high risk of rapid nutritional depletion which could contribute to the impairment of vital organ function (Briassoulis, trocki, pollack), there is currently no evidence to support that early PN in such patients is beneficial and may indeed be harmful [28].

Overfeeding in particular may have a negative impact on the number of infections, mortality and length of hospital stay [29] Optimising nutritional therapy could hence lead to better outcomes of critically ill paediatric patients [30].

Given that more and more children are admitted to paediatric IC units urgent randomized controlled trials are needed to guide physicians in the decision making process.

Early involvement of the NST is even more crucial in these patients to select potential candidates for PN carefully before the initiation of intravenous feeding. The NST can also help to raise awareness amongst health professionals on the proper use of nutrition support through a structured teaching program which should be accessible to all persons involved in the care of such children [31]. Even if nutrition training is now included in the junior doctor and nurse teaching curriculum to improve knowledge in nutrition, however the enrollment of nutritionists with a strong scientific background is still required to allow health professionals to make a balanced assessment of the nutritional needs of their patients.

Screening tools designed to identify children at risk of developing malnutrition could help physicians to recognise such patients before their nutritional status deteriorates [32] (Table 6) Although the benefit of nutrition assessment is widely recognised there is no standardised approach for children admitted to hospital [33]. Data comparing existing screening tools should however become available in the future allowing to develop a standard in the nutritional assessment of hospitalised children.
There is evidence in the literature showing a link between over aggressive treatment and availability of resources [34]. Patients in countries with a high socioeconomic status and well funded health care systems have treatment escalated to the maximum earlier and more frequently compared to the developing world. The threshold for starting intravenous nutrition is much lower in hospitals where PN is easily accessible as it is the case in a tertiary children’s hospital like ours. Care plans should hence be in place which focus on the use of the oral/enteral feeding route whenever possible prior to the consideration of intravenous feeding in order to avoid over prescribing of potential risky therapies such as PN.

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