Review / Derleme

DOI: 10.4274/cayd.galenos.2023.49002
J Pediatr Emerg Intensive Care Med 2023;10:66-83

Nutrition in Pediatric Intensive Care Units

Çocuk Yoğun Bakım Ünitelerinde Beslenme

Hasan Ağın[1], Ali Ertuğ Arslanköylü[2], Nazik Aşılıoğlu Yener[3], Ayşe Berna Anıl[4], Oğuz Dursun[5], Tanıl Kendirli[6], Dinçer Yıldızdaş[7]

[1]University of Health Sciences Turkey, Dr. Behçet Uz Pediatric Diseases and Surgery Training and Research Hospital, Clinic of Pediatric Intensive Care, İzmir, Turkey
[2]Mersin University Faculty of Medicine, Department of Pediatrics, Division of Pediatric Intensive Care, Mersin, Turkey
[3]Ondokuz Mayıs University Faculty of Medicine, Department of Pediatrics, Division of Pediatric Intensive Care, Samsun, Turkey
[4]İzmir Katip Çelebi University Faculty of Medicine, Department of Pediatrics, Division of Pediatric Intensive Care, İzmir, Turkey
[5]Akdeniz University Faculty of Medicine, Department of Pediatrics, Division of Pediatric Intensive Care, Antalya, Turkey
[6]Ankara University Faculty of Medicine, Department of Pediatric Intensive Care, Ankara, Turkey
[7]Çukurova University Faculty of Medicine, Department of Pediatrics, Division of Pediatric Intensive Care, Adana, Turkey

Abstract

The limited energy stores and fast metabolism of sick children in the intensive care unit, as well as the intense stress caused by the critical illness, reveal the importance of nutrition. Adequate and balanced nutritional care for critically ill children improves the clinical course and prognosis. In order to provide appropriate nutritional support, it is important to evaluate the nutritional status of the critical patient in detail and integrity. In the critically ill child with a functioning gastrointestinal tract, the enteral route is preferable to parenteral nutrition. In cases where the digestive system is not used completely or adequately, parenteral nutrition should be applied.

Keywords: Pediatric intensive care, nutrition, malnutrition

Öz

Çocuk yoğun bakım ünitelerinde izlenen kritik hasta çocukların kısıtlı enerji depoları ve hızlı metabolizmaları yanı sıra kritik hastalığın yarattığı yoğun stres durumu beslenmenin önemini ortaya koymaktadır. Kritik hasta çocuklara yönelik yeterli ve dengeli nutrisyonel bakım hastalık sürecini olumlu yönde etkiler. Uygun beslenme desteğinin sağlanabilmesi için kritik hastanın beslenme durumunun değerlendirilmesinin ayrıntılı ve bütünlük içerisinde yapılması önemlidir. Sindirim sistemi işlev gören kritik hasta bir çocukta enteral yol parenteral beslenmeye tercih edilmelidir. Sindirim sisteminin tümüyle ya da yeterince kullanılmadığı durumlarda ise parenteral beslenmeye başvurulmalıdır.

Anahtar Kelimeler: Çocuk yoğun bakım, beslenme, malnutrisyon

Introduction

It is known that nutrition is among the important factors affecting morbidity and mortality in critically ill patients followed in pediatric intensive care units. Children need adequate and balanced nutrition not only for their basal metabolism, organ functions and daily movements, but also for their growth. For this reason, ensuring optimal nutrition of patients treated in pediatric intensive care units forms the basis of patient care. While malnutrition of the critically ill patient causes an increase in the frequency of infection, prolongation of the wound healing process, deterioration in digestive system functions, secondary immunodeficiency, prolonged stay on mechanical ventilator and hospitalization, thus increased morbidity and mortality, overnutrition will also cause hyperglycemia, hyperlipidemia, fatty liver, congestive heart failure due to volume overload, increase in respiratory

Yazışma Adresi/Address for Correspondence: Hasan Ağın, University of Health Sciences Turkey, Dr. Behçet Uz Pediatric Diseases and Surgery Training and Research Hospital, Clinic of Pediatric Intensive Care, İzmir, Turkey
E-posta: hasanagin@gmail.com **ORCID ID:** orcid.org/0000-0003-3306-8899
Geliş Tarihi/Received: 16.12.2022 **Kabul Tarihi/Accepted:** 05.01.2023

workload due to increased carbon dioxide production, prolongation of mechanical ventilation, and increase in morbidity and mortality. Nutrient requirements should be able to meet the needs of the growing organism and should be meticulously planned individually after evaluating the current nutritional status for each patient.

Evaluation of Nutritional Status

Malnutrition is defined as a nutritional disorder that causes measurable adverse effects on body mass and functions due to a deficiency or excess of protein, energy and other nutrients. Children's macronutrient reserves are lower than adults, while their energy needs are higher. Malnutrition is reported to be as high as 35-72% in critically ill children during hospitalization in the intensive care unit.[1,2] In addition, compared to baseline values, a decrease in nutritional parameters is observed in approximately one third of the patients during intensive care hospitalization.[3] It is known that both the nutritional status at the time of admission and the nutritional support given in the intensive care unit are effective on the prognosis of the patients. Negative nutritional status is associated with increased hospital-associated infection, mortality, prolonged intensive care stay and duration of ventilation.[4,5] While malnutrition is more common in this group, overnutrition is also associated with increased morbidity. Evaluation of nutritional status and providing adequate and appropriate nutrition are very important, especially in the management of critically ill children. In patients hospitalized in the pediatric intensive care unit, the nutritional status should be evaluated in detail as soon as possible (in the first 48 hours at the latest).[6] It is recommended to repeat the nutritional assessments of all patients once a week in terms of nutritional problems that may develop during the intensive care unit stay.

When assessing the need for any nutritional support, both the current nutritional status should be evaluated and the underlying causes of nutritional deficiency should be examined. This process includes a detailed dietary history, physical examination, and anthropometric measurements (weight, height, head circumference in young children). In addition, in some cases, measurement of skinfold thickness and mid-upper arm circumference can be used to determine body composition. Anthropometric measurements should be done carefully and appropriately and the measurements should be evaluated in standard growth charts. It is appropriate to use a corrected age up to 2 years in the evaluation of the measurements of premature babies. In patients with ascites and edema, such as chronic liver disease and nephrotic syndrome, anthropometric measurements that are not affected by these, such as middle-upper arm circumference and triceps skinfold thickness, should be preferred. Head circumference of infants younger than 36 months should also be measured. The patient's nutritional status is evaluated by calculating the body mass index (BMI) Z-score (<2 years, weight for height Z-score) by measuring the body weight and height of the patient during hospitalization in the pediatric intensive care unit. If the patient's height is unknown, the patient's nutritional status is evaluated by calculating the weight Z-score for age.[6,7] There are different classifications for assessing the degree of malnutrition. The GOMEZ classification uses weight for age, the Waterlow classification uses height for age, and the WHO classification uses weight for height (Table 1).

Along with malnutrition, obesity has also become a serious health problem worldwide. The most accepted method in obesity screening is BMI calculation. Abnormal BMI is evaluated in specific percentile curves for age and sex. Children over two years of age are considered overweight if their BMI is above the 85th percentile, obese or overweight if they are above the 95th percentile, and morbidly obese if they are above the 99th percentile.

Critically ill children have a high risk of malnutrition during their hospitalization in the intensive care unit, as well as at admission. Disease-related malnutrition in children is associated with nutrient loss, increased energy consumption, decreased food intake, or altered food use. Early recognition and intervention of malnutrition or preventing its development by foreseeing it will both contribute to the recovery process of the patient's primary disease and reduce morbidity and mortality. For this reason, it is important to evaluate the nutritional status of inpatients at frequent intervals. This evaluation can be made with nutrition-oriented physical examination considering nutritional history, changes in anthropometric measurements, and functional status.

Numerous nutritional screening methods have been developed to predict malnutrition that may develop and to identify malnutrition risk early. Some of them are the pediatric

Table 1. Gomez, Waterlow and WHO classifications

Degree of malnutrition	Weight for age (%) (Gomez)	Height for age (%) (Waterlow)	Weight for height (%) (WHO)
Normal	>90%	>95%	>90%
Mild	75-90%	90-95%	81-90%
Moderate	60-74%	85-89%	70-80%
Severe	<60%	<85%	<70%

Yorkhill malnutrition score (PYMS)[8], screening tool for risk of impaired nutritional status and growth (STRONGkids)[9], pediatric nutrition screening tool (PNST)[10] and screening tool for the assessment of malnutrition in pediatrics (STAMP).[11] Of these methods, PYMS and STRONGkids can be preferred due to ease of application, standardization, high specificity and sensitivity. PYMS is a 4-step screening method, which can be applied between the ages of 1 and 16 years and one of whose criteria is BMI. When the total risk score is calculated as 0, there is no risk and a repeat PYMS is recommended after 1 week. If the score is 1, the test is repeated after 3 days. Cases with a score of >2 are in the risk group for malnutrition and immediate evaluation is required (Table 2). STRONGkids can be applied between the ages of 1 month and 18 years and it consists of 4 separate steps. When the total risk score is calculated as 0, nutritional intervention is not required, weekly evaluation is recommended. For those with a score between 1 and 3, weight control should be done twice a week, taking into account the nutritional intervention. Cases with a score of 4-5 are in the risk group in terms of malnutrition and it is recommended to be evaluated immediately (Tables 2, 3).

Timing in Enteral and Parenteral Nutrition

The delivery of nutrients to the digestive organs through the oral route or gastric tubes is called enteral nutrition. Enteral nutrition (EN) should be preferred for the delivery of nutrients in pediatric intensive care units (PICU). EN meets the energy and protein needs of the patient, and it also provides additional contributions such as protecting the integrity of the intestine, preventing bacterial translocation and creating a trophic effect in the intestinal villi. It is also more economical than parenteral nutrition (PN) and is better tolerated by patients.[12] If the patient is hemodynamically and respiratoryly stable, enteral feeding can be started within the first 24-48 hours after admission to the PICU, if there are no contraindications for enteral nutrition. The amount of nutrition should be increased in a way that takes into account food intolerance with a stepwise feeding algorithm.[6,7]

EN contraindications:

- Increased vasoactive/inotropic support
- Hemodynamic instability with ongoing fluid resuscitation
- Suspicion or diagnosis of necrotizing enterocolitis

Table 2. Pediatric Yorkhill malnutrition score (PYMS)*

Is BMI below the lower limit value?	No Yes	0 2
Is there a loss in body weight recently?	No Yes	0 2
Has there been a decrease in food intake in the last one week?	No Yes, food intake decreased in the last 1 week Yes, no food intake in the last 1 week	0 1 2
Will next week's nutrition be affected by current hospitalization/ health condition?	No Yes, decreased food intake and/or increased nutrient requirements and/or increased losses Yes, no food intake	0 1 2

*When the total risk score is calculated as 0, there is no risk and a repeated PYMS is recommended after 1 week. If the score is 1, the test is repeated after 3 days. Cases with a score of >2 are in the risk group in terms of malnutrition and should be evaluated immediately, BMI: Body mass index

Table 3. *Screening tool for risk of impaired nutritional status and growth

1-Subjective clinical assessment (1 point) Is the patient in a poor nutritional status (diminished subcutaneous fat and/or muscle mass and/or hollow face)?	No Yes	0 1
2-High-risk disease (2 points) Is there an underlying illness with a risk of malnutrition or expected major surgery?	No Yes	0 2
3-Nutritional intake and losses (1 point) Is one of the following items present? Excessive diarrhea (>5 times/day) and/or vomiting (>3 times/day) in the last few days Reduced food intake in the last few days Previously advised nutritional intervention Inability to consume adequate food because of pain	No Yes	0 1
4-Is there weight loss or no weight gain during the last few weeks/months (for infants aged <1 year)?	No Yes	0 1

*When the total risk score is calculated as 0, nutritional intervention is not required, weekly evaluation is recommended. For those with a score between 1-3, weight control should be done twice a week, taking into account the nutritional intervention. Cases with a score of 4-5 are in the risk group in terms of malnutrition and it is recommended to be evaluated immediately

- Mechanical intestinal obstruction
- Significant gastrointestinal bleeding
- Ischemic intestine

EN can be applied in pediatric intensive care patients if no fluid loading has been performed in the last two hours and the general condition of the patient is stable despite receiving inotropic therapy. If active fluid replacement or general resuscitation is performed, and the general condition of the patient is not stable despite the use of more than one vasoactive agent, EN is not continued.[6,7] It is not recommended to start PN within the first 24 hours in the PICU. PN should be given to patients for whom enteral feeding is contraindicated or inadequate. The initiation time of PN should be individualized according to the patient, and PD can be delayed for up to one week after admission to the PICU for patients who are in a normal nutritional state at the time of hospitalization.[6,7] However, if patients with malnutrition or a high risk of nutritional deficiency cannot be fed enterally during hospitalization in the PICU, it is recommended that PN can be started within the first week.[6]

EN

a- Energy requirement

Indirect calorimetry is the first choice for determining energy needs. If indirect calorimetry cannot be measured, the Schofield and WHO equations can be used. Stress factors should not be added when using these equations. During EN, the aim should be to provide at least 2/3 of the energy requirement calculated at the end of a week.[6]

Schofield equation (Kcal/day):

<3 years	Men: 60.9 x weight (kg) - 54
	Women: 61.0 x weight (kg) - 51
3-10 years	Men: 22.7 x weight (kg) + 495
	Women: 22.5 x weight (kg) + 499
10-18 years	Men: 17.5 x weight (kg) +651
	Women: 12.2 x weight (kg) + 746

When calculating the energy need of the patients, factors that decrease or increase the energy need should be taken into consideration. In case of obesity in the patient, energy and protein requirements should be calculated according to the ideal weight for the patient's age.

Factors that increase energy need

- Fever
- Sepsis
- Burn
- Trauma
- Cardiac/pulmonary disease
- Major surgery

Factors that reduce energy need

- Sedation
- Mechanical ventilation
- Paralysis
- Pentobarbital coma

b- Protein need

0-2 years: 3 g/kg/day protein intake provides positive nitrogen balance

2-13 years: 2 gr/kg/day protein intake provides positive nitrogen balance.

At least 1.5 g/kg/day of protein should be given to patients to ensure positive nitrogen balance in patients followed up in the pediatric intensive care unit.[6]

c- Selection of enteral feeding method and route

A stepwise algorithmic approach should be applied in the selection of enteral feeding method and route. The application of algorithms that start with a small amount and gradually increase the EN will ensure that the feeding is done safely and that the goals are achieved. A multidisciplinary nutrition support team should be established for nutritional practices in the PICU. A dietitian responsible for the intensive care unit together with the pediatric intensive care team must be in this team. After deciding to start EN, the route in which the nutrients will be given should be determined. EN can be performed by the gastric or postpyloric route. The first choice for EN in patients followed up in the PICU is gastric feeding.[6]

Gastric route

- Orogastric/nasogastric tube
- Gastrostomy

Postpyloric route

- Nasojejunal/basoduodenal tube
- Jejunostomy

Advantages of gastric feeding

- Physiological
- Anti-microbial effect
- Trophic effect (hormonal)
- Being a reservoir
- Ability to provide hyperosmolar feeding due to osmotic tolerence
- Being suitable for bolus feeding and not requiring the use of a pump.
- Easy to place and allowing free activity

Risks of gastric feeding

- Gastroesophageal reflux and aspiration

Postpyloric feeding using a nasoduodenal or nasojejunal tube should be preferred in cases in which gastric feeding cannot be tolerated and in cases with very high aspiration risk.

Indications for postpyloric nutrition

- Aspiration history
- Gastroparesis
- Gastric outlet obstruction
- Previous gastric surgery

Disadvantages of postpyloric nutrition

- Difficulty in placement
- Able to gradually increase nutrition with continuous infusion
- Inability to apply high-energy-hyperosmolar nutrition
- Lack of taste/oral motor function development

Nasoduodenal/nasojejunal tube

The most common indications are aspiration risk and gastroparesis. Only continuous feeding can be done with the postpyloric route. Bolus feeding cannot be performed. The most important disadvantage of postpyloric feeding is the difficulty of placing the nasoduodenal and nasojejunal tube, which also causes a delay in the initiation of feeding. The following methods can be used for the placement of postpyloric feeding tubes. It is aimed to place the transpyloric feeding tube on the distal to the ligament of Treitz.

Nasoduodenal/nasojejunal tube placement methods

- Blind method using peristaltism or tube weight
- Fluoroscopic
- Endoscopic
- With medication (metaclopromide, erythromycin)

Gastrostomy/Jejunostomy

While it is appropriate for short-term EN to be made by tube, enterostomy tubes placed by endoscopic or surgical method are used in patients who need long-term nutrition. Considering the patient's underlying disease, gastrostomy/jejunostomy is indicated in cases for which EN is required for more than 6-12 weeks.[13] Gastrostomy can be opened through percutaneous endoscopic, radiological (fluoroscopic), surgical or laparoscopic surgical methods. The algorithm for deciding the EN location and method is given in Figure 1.

Nutritional method

Feeding can be performed as intermittent bolus or continuous infusion. Bolus feeding is a feeding made in specific amounts at specific intervals. Continuous nutrition, on the other hand, is the delivery of nutrients 24 hours a day as a continuous infusion of nutrients at a constant rate via a pump. There is no recommended method in the first place, as there is insufficient evidence that one of the two feeding methods is superior to the other.[6,14]

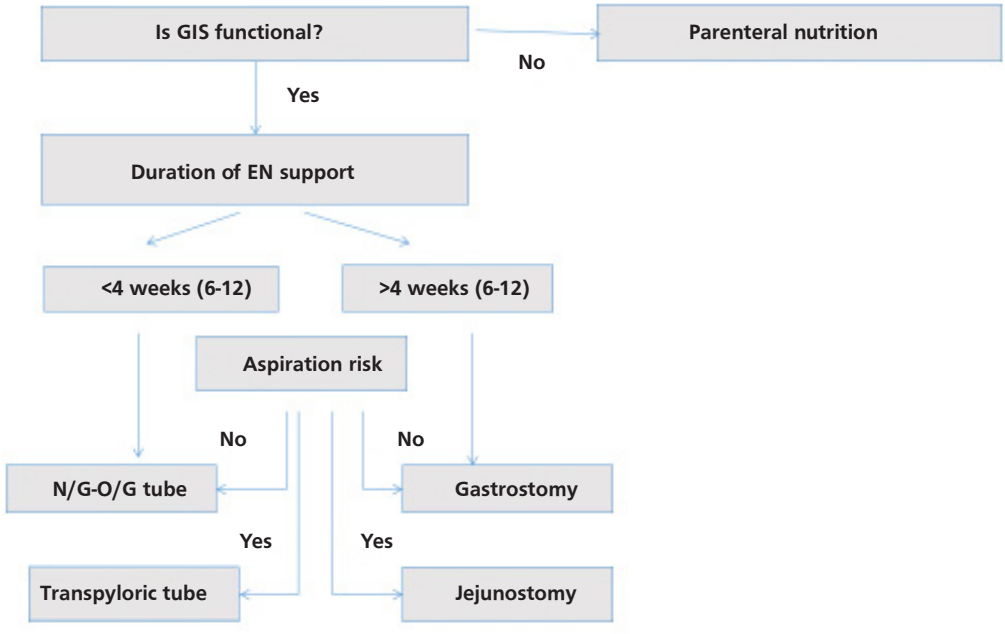

Figure 1. Algorithm for deciding the place and method of enteral nutrition

Features of bolus feeding:

- It can imitate meals, be supplement
- It is more physiological
- It may not require a pump
- It provides freedom between meals
- It may predispose to osmotic diarrhea
- It is not suitable for jejunal feeding

Features of continuous feeding:

- Slow infusion may increase tolerance and absorption.
- It can be given during the night not to prevent daytime activity.
- It promotes intestinal adaptation with mucosal stimulation.

When bolus or continuous feeding is applied, it will be appropriate to use feeding algorithms, such as starting the feeding with a small amount and increasing it gradually.

d- Nutritional intolerance

One of the main reasons for termination or interruption of EN in the pediatric intensive care unit is nutritional intolerance, which is generally assessed by gastrointestinal symptoms and/or gastric residual volume (GRV).

GIS findings of nutritional intolerance

- Vomiting/nausea
- Diarrhea (>2 mL/kg)
- Abdominal distention
- Abdominal discomfort
- Constipation
- Aspiration
- Gastrointestinal bleeding

Gastric residual volume

Measurement of the amount of residue cannot be a clinical indicator of gastric emptying or an accurate indicator of nutritional intolerance. The correlation between the clinical findings of nutritional intolerance, such as abdominal distention and decreased bowel sounds, and the amount of residue is weak. The correlation between radiological findings such as air-fluid levels and the amount of residue is also not significant. A low GRV will not guarantee tolerance, nor can a normal GRV rule out intolerance. For these reasons, routine GRV testing is not recommended to show nutritional intolerance.[15-17] However, it is still widely used in practice in many PICUs. Although there is no broad agreement on how much GRV means a nutritional intolerance, a GRV of ≥150 mL or >3-5 mL/kg is considered significant.

There are also centers that consider GRV more than half of the previous feeding amount in bolus feeding and more than 2-hour total feeding rate in continuous feeding as significant.[18]

Situations for which feeding should be interrupted with gastrostomy or jejunostomy include the presence of pain during feeding, fresh bleeding, leakage of gastric contents, prolonged or severe pain after the procedure, and physiological instability.[19]

e- Pediatric enteral nutrition products and selection of product

Human breast milk, age-appropriate formulas and age-appropriate enteral products can be used for enteral nutrition. For enteral nutrition, polymeric products are most often used. Unless there is a contraindicated situation, polymeric products should be the first choice in the nutrition of critically ill patients.[7] In the following special cases, oligomeric and monomeric products can be used.[19] In order to reach nutritional goals in children with fluid restriction, products with high protein and energy concentrations can be preferred (Table 4).

The following factors should be considered in the selection of enteral products.

- Age
- Degree of nutrient requirement
- Intestine, liver and pancreas functions
- Presence of food intolerance or allergies
- Enteral product delivery route and method
- Enteral product features
- Taste, cost, osmolarity, renal solute load

Standard polymeric products contain complete protein, complex carbohydrates and long chain fatty acids. They are isoosmolar solutions containing 1 kcal energy in one milliliter and they meet all needs because their nutritional content is balanced. Polymeric products can be classified as follows.

Classification of Polymeric Products

According to energy content

- Standard polymeric products
- High energy polymeric products

According to age group

- Infantile period
- 1-12 years
- ≥12 years

According to fiber content

- Fibre containing products
- Fibre-free products

Oligomeric Products

Oligomeric products are the products that have been hydrolyzed to varying degrees. It is recommended in cases

Table 4. Nutritional product recommendations according to age and bowel functions of patients*	
First 1 year of age	
Normal bowel function	**Bowel dysfunction**
Human breast milk	Human breast milk
Standard infant formula at >6 month	Lactose-free formula Semi-elemental formula Highly hydrolyzed formula Elemental formula Modular products if no formula can be tolerated
1-6 years of age	
Normal bowel function	**Bowel dysfunction**
Standard pediatric formula +/- fiber 1-1.5 kcal/mL	Semi-elemental/elemental pediatric formula 1 kcal/mL, can be increased to 1.5 kcal/mL if necessary
>10 years of age	
Normal bowel function	**Bowel dysfunction**
Standard pediatric formula/product may continue to be used. Adult products can be used.	Semi-elemental pediatric formula Elemental pediatric formula Adult semi-elemental/elemental products
*Adapted from the references of[20,21]	

where complete protein cannot be tolerated. There is no need for pancreatic and bile secretion.

Content;

- Protein; dipeptide or tripeptide
- Carbohydrate; glucose polymers-maltodextrin, disaccharides
- Fat; MCT (30-50%) - LCT
- They are expensive and taste bad.

Monomeric Products

They are fully hydrolyzed products (aa based). They are recommended in cases where complete protein cannot be tolerated. There is no need for pancreatic and bile secretion.

Content;

- Protein; free amino acids
- Carbohydrate; glucose polymers-maltodextrin, disaccharides
- Fat; MCT (30%)-LCT
- They have high osmolarity
- They are expensive and taste bad.

Indications for Using Oligomeric and Monomeric Product

- Malabsorption Syndromes
- Short bowel syndrome

- Intestinal insufficiency
- Chronic congenital diarrhea

- Pancreatic Diseases

- Cystic fibrosis
- Acute-chronic pancreatitis

- Chronic liver diseases
- Crohn's disease complicated by fistula
- Cow's milk protein allergy

Immune nutrition is defined as practices for reducing inflammation by using various dietary components (Arginine, glutamine, etc.) to correct the immune response in patients followed in the pediatric intensive care unit and replacing the nutrients that have been reduced due to stress. However, since the benefit of immune nutrition has not been proven yet, immune nutrition is not recommended in intensive care patients.[6,7] There is also insufficient evidence for the use of prokinetics to facilitate gastric emptying and prevent nutritional intolerance.[7]

EN monitoring is given in Table 5, and possible complications and precautions are listed in Table 6.

Parenteral Nutrition

In cases in which the digestive system cannot be used completely or adequately, the delivery of nutrients necessary for life via the intravenous (IV) route is called PN. PN is not physiological in nature, as nutrients are delivered directly into the systemic circulation, bypassing the digestive tract and portal circulation. Parenteral nutrients given IV in this way do not have the "first pass" effect in the liver. In addition, malnutrition is known to cause thinning of the digestive system mucosa, blunting of the villi and an increase in bacterial translocation.[22]

Total PN should be the last choice when the combination of oral intake, EN and PN is not possible. Indications for PN or total PN are given in Table 7.

Table 5. Enteral nutrition monitoring

		At admission	At hospital	Outside hospital
Anthropometric measurements	Weight Height	Daily Initially	Daily Weekly	Weekly/monthly Monthly
Intake	Calories, protein, fluid	Daily	Weekly	Monthly
Tolerance	Abdominal circumference, vomiting, residue	In the presence of intolerance findings		
Stool/ostomy	Volume, frequency, consistency	Daily	Daily	In the occurrence of changes in stool
Tube placement		Before each nutrition		
Tube field		Daily	Daily	Daily

Table 6. Enteral nutrition complications and precautions

Complication	Prevention/intervention
Diarrhea/abdominal cramp	Decrease delivery rate Review and discontinue medications that may cause diarrhea Choose products containing fibre Review osmolarity, add modular additives Semi-elemental or elemental formulas if necessary
Nausea/vomiting	Make sure that the product is brought to room temperature before tube feeding. Raise the head of the bed (30-45 °C) Post-pyloric or continuous feeding
Hyperglycemia	Decrease delivery rate Prefer formulas containing minimal simple sugar. Insulin if clinically indicated
Blockage in nutrition tube	Check tube diameter Make sure to wash the tube every 4-8 hours for residue control, boluses or continuous feeding. Post-pyloric or continuous feeding
Gastric retention	Check tube location If the amount of residue is high, stop feeding 1 hour later, see the residue again. Post-pyloric or continuous feeding Lay the patient on his/her right side
Constipation	Make sure the patient is getting optimal fluids Increase the amount of free water Products containing fibre

Table 7. Indications for parenteral nutrition in children

Congenital anomalies of the gastrointestinal system that can be corrected surgically	
- Gastrointestinal atresia - Tracheo-esophageal fistula - Malrotation and volvulus - Omphalocele	- Gastroschisis - Diaphragmatic hernia - Meconium ileus and peritonitis - Hirschsprung's disease
Intestinal diseases	
- Necrotizing enterocolitis - Chronic resistant diarrhea - Pancreatitis	- Inflammatory bowel diseases - Short bowel syndrome - Pseudomembranous enterocolitis
Situations in which nutritional needs cannot be met with maximum enteral nutrition	
Severe burns	
Multiple organ failure	
Bone marrow and organ transplantation	
Malignant diseases	
- Radiation enteritis - Effects of chemotherapy on the digestive mucosa	- Cancer cachexia

If it is anticipated that infants and children who cannot be fed enterally will need nutritional support for 7 days or more, it means that there is an indication for PN. PN should not be used for short periods of time, as the risks may outweigh the benefits.[23] Unless the patient has severe malnutrition, there is no need to initiate PN to prepare for surgery.[24]

Whether administered peripherally or centrally, PN should be administered only in patients who are hemodynamically stable and can tolerate the required fluid. Particular attention should be paid to children with electrolyte imbalance, kidney or liver failure, metabolic acidosis or alkalosis, and it should not be administered to correct metabolic imbalances. Acid-base and electrolyte abnormalities must be corrected before starting PN. PN is not more effective than EN in children and adolescents receiving cancer treatment, whether or not they have malnutrition.[25]

a. Route of Delivery

Ensuring reliable venous access is extremely important for PN. PN can be administered through a peripheral or central vein. In general, the choice of peripheral or central venous access depends on the anticipated duration of nutritional therapy. Although the main advantages of peripheral catheters are ease of insertion, low infection and complication rates, the maximum osmolarity that can be delivered through a peripheral vein is 900 mOsm/L, which limits the amount of nutrients that can be delivered through the peripheral vein. The osmolarity of a PN solution can be determined with the following equation.[6]

mOsm/L = (gram amino acid/L × 10) + (gram dextro/L × 5) + [(mEq Na + mEq K) × 2] / L + (mEq Ca × 1.4)/L

Considering this osmolarity restriction, it is often impossible to provide all essential nutrients with peripheral PN and central venous access will be required to fully meet the nutritional needs of the child. Therefore, if PN support is anticipated for more than two weeks, a central venous catheter (CVC) should be placed to meet the patient's nutritional needs.

In addition, it should be noted that the presence of a CVC is the main risk factor for major, potentially fatal complications such as nosocomial bloodstream infection and venous thrombosis. Moreover, the most important risks associated with complications arising from the use of CVC are PBN administration, young age, and long-term use.[26,27] CVC-related complications, patient morbidity and mortality, and health care costs increase significantly in children receiving long-term PN treatment.

A catheter with a minimum number of ports or lumens for PN should be used for only PN administration if possible. If a multi-lumen CVC is present, it is necessary to reserve a lumen for PN and avoid blood sampling, transfusion, and central venous pressure monitoring from that lumen. In order to improve the quality of life of patients with long-term PN, blood sampling from CVC for routine follow-up can only be recommended if a full aseptic protocol is followed.[28]

Use of routine heparin has not been shown to be superior to saline flushing for the prevention of thrombotic occlusions in CVC in children. Moreover, there is insufficient evidence to justify the use of prophylactic anticoagulants to prevent catheter-related thrombosis, occlusion, and infection in children undergoing PN at home.[28] Recombinant tissue plasminogen activator or urokinase can be used to open a blocked catheter.[29]

Before and after vascular intervention, skin cleaning should be done with 2% chlorhexidine solution in 70% isopropyl alcohol. After applying the antiseptic (before catheter placement or dressing), it should be allowed to air dry.[30]

Sterile gauze or transparent semi-permeable polyurethane dressing can be used to cover the catheter application site. If there is bleeding or leakage at the catheter site, sterile gauze should be preferred. For short-term CVCs, sterile gauze should be replaced every 2 days and a transparent dressing every seven days. If it becomes damp, loose or soiled, it should be replaced sooner.[31] Routine topical antimicrobial therapy is not applied to the catheter insertion site, as it may increase the risk of Candida infection and antimicrobial resistance, and damage the catheter surface.[28]

b. PN Preparation

The energy provided to the patient by nutrition should meet the patient's nutritional needs, including basal metabolic rate, physical activity, growth, diet-induced thermogenesis, and correction of pre-existing malnutrition. Generally, for pediatric critically ill patients, PN is arranged considering the needs of the patient.

Energy

A practical approach to the determination of energy needs in PN is to identify the approximate range of energy needs based on the patient's age, body weight, and stage of the disease. Table 8 shows the predicted values, in accordance with the recently published ESPGHAN guideline, for energy needs of acute, clinically stable patients and those at the recovery phase for different age groups.[32]

Fluid-electrolyte

Total fluid requirement in infants apart from those in the neonatal period and children: Maintenance fluid is based on the replacement of ongoing losses (drain, urine and stool losses) and existing losses. During maintenance fluid therapy, the target should be to prevent dehydration, electrolyte disturbances, ketoacidosis, and protein breakdown. Loss

from urine and stool and insensible losses from the skin and lungs should be replaced, the volume of maintenance fluid administered should put minimal burden on the kidney and ensure that the urine is isotonic.[33]

Although the Holliday-Segar method is most commonly used to calculate the maintenance fluid, many individual factors such as age, disease status, fluid balance, latent water losses, and changes in metabolic rate and respiratory rate affect fluid requirement. Infants and children generally need at least 115 mL of fluid for the 100 kcal of energy provided. Appropriate fluid management requires constant monitoring and regulation according to the patient's fluid losses and hydration level. The hydration and electrolyte status of the patient should be evaluated clinically, considering body weight, serum electrolyte and acid-base balance, hematocrit and blood urea nitrogen (BUN) values, urine output and density, osmolarity and ions, and if possible, with ultrasonography (vena cava inferior collapsibility index, etc.). Fluid losses should be measured frequently and replaced exactly. For a critically ill child, applied medical treatments and blood and blood products must be taken into account and deducted from the total fluid to be given to the patient. Digestive system losses due to stoma, fistula or short bowel syndrome can reach 1-3 liters per day. In this case, the measured net loss amount should be replaced separately from the PN solution. The fluid and electrolyte content of the PN solution should be calculated individually, and should not be used as the sole fluid source in metabolically variable patients or to correct electrolyte abnormalities.

Sodium-potassium-chlorine

Conventional parenteral fluids have been administered as hypotonic saline (Na 35-77 mmol/L in 5% dextrose), but a potential risk for hospital-acquired hyponatremia has been observed.[34-36] However, there is some concern that normal saline solution is not physiological as it contains equal concentrations of Na and Cl. It is on the agenda that it would be more appropriate to use IV solutions containing less Cl than Na, as increased Cl load may cause hyperchloremia and acidosis.[37] To avoid a sodium concentration in the PN solution, which could cause hyponatremia, the use of balanced solutions has recently been recommended.

In critically ill children fed parenterally, serum electrolyte concentrations are monitored daily during the first days of treatment and subsequent monitoring intervals are adapted to the clinical condition of the patient.

Calcium-phosphorus-magnesium

Sufficient amounts of Ca, P and Mg should be provided to ensure optimal growth and bone mineralization in children and adolescents fed parenterally. The recommended amounts according to age groups are given in Table 9. Due to the risk of metabolic bone disease in children who have been treated with PN for a long time, Ca, P, ALP and vitamin D levels and bone mineral contents should be monitored as well as routine serum and urinary electrolytes.[38]

The targeted Ca/P ratio (in mg) in PN is 1.7/1. The solubility of calcium and phosphorus varies with temperature, type and concentration of amino acid solution, glucose concentration,

Table 8. Energy needs for different age groups in parenteral nutrition according to the stages of the disease (kcal/kg/day)*

	Acute phase[a]	Stable phase[b]	Recovery phase
0-1 year	45-50	60-65	75-85
1-7 years	40-45	55-60	65-75
7-12 years	30-40	40-55	55-65
12-18 years	20-30	25-40	30-55

[a]The patient needs vital support (sedation, mechanical ventilation, fluid resuscitation, vasopressor). [b]The patient is stable but unable to wean from vital support. *Taken from reference[32]

Table 9. Recommended daily amounts of calcium, phosphorus and magnesium for children on parenteral nutrition mmol (mg)/kg/day*

	Ca	P	Mg
0-6 months	0.8-1.5 (30-60)	0.7-1.3 (20-40)	0.1-0.2 (2.4-5)
7-12 months	0.5 (20)	0.5 (15)	0.15 (4)
1-18 years	0.25-0.4 (10-16)	0.2-0.7 (6-22)	0.1 (2.4)
Preparate contents			
1 mL 10% Ca gluconate	9.8 mg (0.45 mEq) elemental calcium		
1 mL 10% Ca chloride	27 mg (1.4 mEq) elemental calcium		
1 mL 15% $MgSO_4$	150 mg elemental magnesium		
1 mL potassium phosphate	0.6 mmol phosphorus and 1 mmol potassium		

*Adapted from reference[38]

pH, type of calcium salt, order of addition of calcium and phosphorus, calcium/phosphorus ratio, and presence of lipids. Since amino acid solutions increase the acidity of the fluid, higher calcium and phosphorus can be given with high amino acid solutions. In modern mix preparation devices in total PN preparation units, the system can calculate the precipitation itself and give a warning.

The precipitation factor is calculated as follows:

If the amount of amino acids in the liquid is ≤2.5%, the precipitation factor should be adjusted as ≤26 and if >2.5% then the factor should be kept ≤35.

Carbohydrate

Carbohydrates are the only energy source for the brain, renal medulla and erythrocytes. Adequate carbohydrate supply should be provided in critical illness. While determining the amount of glucose to be given in PN, the balance between meeting energy needs and the risks of overfeeding/excessive glucose load, the stage of the critical illness (acute, stable, recovery), growth, and the amount of glucose administered with treatments other than nutrition should be considered.[39]

In parenteral nutrition, the dextrose monohydrate form, which contains slightly less energy (3.4 kcal/g) than the carbohydrate concentration in foods (4 kcal/g), is used. The recommended parenteral glucose amount according to body weight and disease stage in infants and children is given in Table 10.

Recurrent and/or prolonged hypoglycemia (<60 mg/dL) should be avoided in all critically ill patients. Excess glucose and hyperglycemia should be avoided as well as. Hyperglycemia causes increased lipogenesis and hepatic steatosis with adipose tissue deposition and increased production of VLDL triglycerides in the liver. In critically ill children, these adverse effects appear in the form of increased CO_2 production and minute ventilation. Since it may cause an increase in morbidity and mortality in critically ill children, blood glucose values above 145 mg/dL should be avoided, and insulin therapy should be initiated when recurrent hyperglycemic values above 180 mg/dL are detected.[39]

Since glucose concentrations above 12.5% and high osmolarity in PN may damage the vessels, it should not be given peripherally. The upper limit of glucose concentration to be administered via the central vein is 30%. Starting glucose infusion and concentration at low dose and gradually increasing it prevents the development of hyperosmolarity, hyperglycemia and osmotic diuresis, and gives time for hormonal adaptation.[39]

Protein

Proteins are essential structural and functional components of all cells in the body. Protein needs may vary depending on the severity of the disease. Stress factors such as sepsis, burns, surgery, trauma and stomal losses increase the protein need. Urinary nitrogen excretion due to primary kidney disease with the use of steroids or diuretics may also increase protein requirement. In kidney diseases, liver failure and congenital metabolic diseases, it may be necessary to reduce the amount of protein given.[40] It is necessary to give 0.3-0.6 g/kg amino acids per day in chronic kidney patients who need protein restriction. On the other hand, in patients who receive continuous renal support treatments, amino acid should be given as 2-3 gr/kg/day for 0-2 years of age, 1.5-2 gr/kg/day for 2-13 years of age, and 1.5 gr/kg/day for 13-18 years of age.[41] Although protein solutions rich in branched-chain amino acids are recommended as 0.8-1.2 g/kg per day in liver failure, it would be more rational to determine the amount of amino acids to be given according to ammonia levels.[42]

In order to avoid negative protein balance, it is recommended to give at least 1.0 g/kg of protein daily in infants aged 1 month to 3 years with stable general condition, and at least 1.0 g/kg and at most 2.0 g/kg of protein in older children and adolescents. It has been shown that at least 57 kcal/kg of energy and 1.5 g/kg of protein should be given daily to ensure positive protein balance in critically ill children on mechanical ventilators.[43] In children with normal organ functions, daily protein targets per weight should be 2.5 g/kg till 3 years of age and 2 g/kg between 3 and 18 years of age.

Table 10. Recommended glucose amounts according to body weight and disease stage in children fed parenterally (mg/kg/min-g/kg/day)*

	Acute phase[a]	Stable phase[b]	Recovery phase
28 days-10 kg	2-4 (2.9-5.8)	4-6 (5.8-8.6)	6-10 (8.6-14)
11-30 kg	1.5-2.5 (2.2-3.6)	2-4 (2.8-5.8)	3-6 (4.3-8.6)
31-45 kg	1-1.5 (1.4-2.2)	1.5-3 (2.2-4.3)	3-4 (4.3-5.8)
>45 kg	0.5-1 (0.7-1.4)	1-2 (1.4-2.9)	2-3 (2.9-4.3)

[a]Life-threatening condition or organ failure and need for vital support (sedation, mechanical ventilation, fluid resuscitation, vasopressor, etc.). [b]The patient is clinically stable but still needs vital support. *Taken from reference [39]

Lipid

Intravenous lipid emulsions (ILEs) are an indispensable part of pediatric PN due to their high caloric content and low osmolality. For most patients, it is initially started at 1 g/kg/day. If necessary, the dose of fat can be increased up to 3 g/kg/day (2 g/kg/day in children over 10 years of age) to ensure adequate energy intake.[44]

Carnitine facilitates the transport of long-chain fatty acids across the mitochondrial membrane, making them suitable for β-oxidation. Carnitine is found in human breast milk and cow's milk formulas, but PN solutions usually do not contain carnitine. Carnitine is synthesized in the liver and kidney from lysine and methionine. Therefore, patients with renal or hepatic failure may be at risk of carnitine deficiency. Carnitine supplementation may be considered in pediatric patients expected to receive PN for more than 4 weeks.[44]

In critically ill children fed parenterally, the amount of ILE should be reduced if serum triglyceride concentrations exceed 265 mg/dL in infants and 400 mg/dL in older children.[44]

Malnourished children have low lipoprotein lipase levels, which reduces the clearance of intravenously administered lipid. In patients with metabolic stress such as sepsis and trauma, or organ dysfunction such as liver and kidney, the production of cortisol, catecholamines and cytokines that cause lipolysis is increased, and the risk of hypertriglyceridemia increases during IV lipid administration.[45]

In patients with severe unexplained thrombocytopenia, serum triglyceride concentrations should be monitored and parenteral lipid dose reduction should be considered. Although lipid emulsions do not appear to affect platelet count and function, some concerns have been expressed regarding their effect on platelet aggregation. Long-term administration of PN with pure soy-based lipid emulsions may stimulate hemophagocytosis in the bone marrow by inducing recurrent thrombocytopenia due to shortened platelet lifespan and the activation of the monocyte-macrophage system.[45]

Fat overload syndrome is a well-known complication of IV administration of lipid emulsions at high dosages or at excessive infusion rates. It is characterized by headache, fever, jaundice, enlarged liver-spleen, respiratory distress and bleeding tendency. Other symptoms include anemia, leukopenia, thrombocytopenia, low fibrinogen levels, and coagulopathy. Although mostly associated with the use of soy-based lipid emulsions, it has recently been shown to be related to the rate of infusion and not the type of lipid emulsion.[46]

It has been reported that administration of IV lipid emulsions mixed with other nutrients in total PN bags does not cause an increase in the risk of bloodstream infection rates.[47] In pediatric patients, heparin should not be routinely given with lipid infusion.

The amino acid and lipid solutions available in our country and their properties are listed in Table 11.

Table 11. Amino acid and lipid solutions available in our country and can be used in the childhood age group

Amino acid solutions
• PF pediatriamine
• TrophAmine® 6%
• Primene 10%
• PF hiperalamine 8.5% and 10%
• Aminoven® 5%, 10%, 15%
• PF Nephricamine 5.4% (contains high concentration of aromatic amino acids and methionine)
• Nephrotect® 10% (The dipeptide glycyl-tyrosine in its content meets the increased tyrosine requirement in renal failure)
• 6% PF K-Camine 8% (contains high concentration of branched-chain amino acids, low concentration of methionine and aromatic amino acids)
• Aminoplasmal® Hepa 10% (contains high concentration of branched-chain amino acids, low concentration of methionine and aromatic amino acids)
• Aminosteril® N-Hepa 8% (contains high concentration of branched-chain amino acids, low concentration of methionine and aromatic amino acids)
Lipid solutions
• Intralipid® 10%, 20% (contains 100% soya oil) • Lipofundin® 10%, 20% (contains 50% MCT, 50% soya oil) • Lipoplus® 20% (contains 50% MCT, 40% soya oil, 10% fish oil) • SMOFlipid® 20% (contains 30% soya oil, 30% MCT, 25% olive oil, 15% fish oil) • Clinoleic 20% lipid (contains 20% soya oil, 80% olive oil)
• Omegaven (contains long-chain omega-3 fatty acids especially EPA and DHA)
MCT: Medium chain fatty acids (coconut oil is used), EPA: Eicosapentaenoic acid, DHA: Docosahexaenoic acid

Vitamins

Children on PN should be given vitamin preparates daily. Vitamin stability should be ensured by adding both water-soluble and fat-soluble vitamins to lipid emulsions or mixtures containing lipids. Although optimal vitamin doses for children have not been fully determined, daily recommended parenteral vitamin doses based on expert opinion are given in Table 12. Patients on long-term PN should be monitored periodically for vitamin D deficiency and patients with serum 25(OH) vitamin D levels of <50 nmol/L should be provided with vitamin D supplementation.[48]

Trace Elements

Trace elements play a role in wound healing and immune response. Although parenteral doses have not been determined exactly, the recommended daily doses according to expert opinion are given in Table 13. Commercial preparates are in the form of ampoules containing all these trace elements and added to the PN solution.[49]

a. Standard PN Solutions

Standard PN solutions are commercially available as two-in-one (carbohydrate and protein) or three-in-one (carbohydrate, protein and lipid) bag systems. The advantages of these products are lower cost and longer shelf life (up to 28 days). These formulations will generally meet the needs of some pediatric patients and can be safely used for short periods of up to 2-3 weeks in stable pediatric patients. It should be stated that they are also suitable for patients undergoing PN at home. In intensive care patients, they can be used as initial formulas for PN until an individual PN solution is prepared, but individual PN solutions should definitely be preferred for

Table 12. Daily recommended parenteral doses of fat and water soluble vitamins for children and content of parenteral vitamin preparates in our country *

	<12 months	1-18 years	Soluvit ®N (10 mL)	Vitalipid ®N infant (10 mL)	Cernevit® Venavit® Todavit® (5 mL)
Vitamin A	150-300 mcg/kg/day or 2300 IU/day	150 mcg/day	-	690 mcg 2300 IU	3500 IU
Vitamin D	400 IU/ day or 40-150 IU/kg/day	400-600 IU/day	-	400 IU	220 IU
Vitamin E	2.8-3.5 mg/kg/day	11 mg/day	-	6.4 mg	10.2 mg
Vitamin K	10 mcg/kg/day	200 mcg/day	-	200 mcg	-
Vitamin C	15-25 mg/kg/day	80 mg/day	100 mg	-	125 mg
Thiamine	0.35-0.50 mg/kg/day	1.2 mg/day	2.5 mg	-	3.51 mg
Riboflavin	0.15-0.2 mg/kg/day	1.4 mg/day	3.6 mg	-	4.14 mg
Pyridoxine	0.15-0.2 mg/kg/day	1.0 mg/day	4 mg	-	4.53 mg
Niacin	4-6.8 mg/kg/day	17 mg/day	40 mg	-	46 mg
Vitamin B12	0.3 mcg/kg/day	1 mcg/day	5 mcg	-	6 mcg
Pantothenic acid	2.5 mg/kg/day	5 mg/day	15 mg	-	17.25 mg
Biotin	5-8 mcg/kg/day	20 mcg/day	60 mcg	-	69 mcg
Folic acid	56 mcg/kg/day	140 mcg/day	400 mcg	-	414 mcg

*Adapted from reference [48]

Table 13. Daily recommended amounts of trace elements (mcg/kg/day) for children fed parenterally and contents of parenteral trace element preparates in our country*

	0-3 months	3-12 months	1-18 years	Tracutil® (mg/10 mL)
Iron	50-100	50-100	50-100	1.95
Zinc	250	100	50	3.27
Copper	20	20	20	0.76
Iodine	1	1	1	0.13
Selenium	2-3	2-3	2-3	0.02
Manganese	≤1	≤1	≤1	0.55
Molybdenum	0.25	0.25	0.25	0.01
Chromium	0.2	0.2	0.2	0.01

*Adapted from reference [49]

critically ill children who are metabolically unstable and have abnormal fluid-electrolyte losses.[50]

b. Cyclic Parenteral Nutrition

Cyclic feeding means that the PN solution is given in less than 24 hours and then left for several hours without PN for the patient. Cyclical feeding can be initiated after patients have tolerated the full amount of PN and have stabilized both clinically and biochemically for at least one week. In general, while the duration of PN-free time is increased, the infusion rate of the PN solution is increased to compensate, so that the total daily PN volume remains unchanged. Cyclic PN allows the increase and decrease of meal-related hormones, and has a protective effect against intestinal failure-associated liver disease. Thanks to the night infusion, it gives freedom to the patient during the daytime and improves the quality of life. Children can usually tolerate the night infusion for more than 10-14 hours. Cyclical PN should definetly be tried while the patient is in the hospital, its tolerance and safety should be determined before being discharged home.[51]

c. Follow-up of the Parenterally Fed Patient

Follow-up of the parenterally fed patient requires frequent clinical evaluation together with the evaluation of nutritional status and laboratory findings. The biochemical tests requested should be adjusted according to the underlying clinical condition and also to the duration of PN (Table 14).

Before starting parenteral nutrition, basic biochemical values and anthropometric measurements should be recorded. After starting parenteral nutrition, electrolytes, glucose, BUN, creatinine, triglyceride, glucose and ketone presence in the urine, and urine density should be checked every day for the first week, and if C-reactive protein is >1 mg/L, weekly pre-albumin level can be checked. Weight follow-up and intake-output monitoring should be done. Daily biochemistry control is required until the targeted amounts are reached or when changes are made, and weekly biochemistry control is required after the patient is stable. Vitamin and trace element levels should be checked once a week until clinical and metabolic stabilization is achieved, and monthly thereafter,

Table 14. Laboratory monitoring of parenterally fed children

Test	Sample	Before PN	During PN, before clinical and metabolic stabilization			During PN, during clinical and metabolic stabilization		
			Every 1-2 days	At least once a week	As needed	Every 1-2 weeks	Once a month	As needed
Na, K, Ca	S	X	X			X		
P	S	X	X					
Cl	S	X	X					X
Mg	S	X			X	X		
Zinc	S				X			X
Blood gas	CapB	X				X		
Glucose	CB, CapB	X	X			X		
T. protein	S	X		X		X		
Albumin	S	X		X			X	
BUN, creatinine	S	X		X			X	
Triglyceride, cholesterol	S	X			X			X
Bilirubin, AST, ALT	S	X			X		X	
GGT, ALP	S	X			X			X
Complete blood count	CB	X		X		X		
INR	S	X			X		X	
CRP	S	X			X			X
Vitamin B12	S				X			X
Fe, ferritin	S				X			X
PTH	S							X
25 OHD_3	S				X			X
Trace elements	S			X				X
Urine	US	X		X			X	
Urine electrolytes	US				X			X

X: Time of test, S: Serum, plasma, CB: Complete blood, CapB: Capillary blood, US: Urine sample, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, GGT: Gamma-glutamyl transferase, PN: Parenteral nutrition, BUN: Blood urea nitrogen

and anthropometric measurements should be repeated.[51] Sudden changes in biochemical status are rare in stable patients.

a- Transition from PN to Enteral Nutrition

Even if the patient is in the process of PN, minimal EN should be administered whenever possible to preserve the intestinal mucosal structure, promote adaptation, and reduce the risk of PN-related liver disease. The volume should be increased as soon as a small amount of EN is tolerated. The transition to EN should be carefully planned, should be slow and gradual. Since abrupt termination of PN may cause hypoglycemia, the transition period should not be less than one week. The EN product should be given in normal concentrations and should not be diluted, otherwise the child will achieve normal fluid volume intake without adequate nutrition. The decrease in PN solution should be proportional to or slightly greater than the increase in enteral nutrition. If the chosen strategy fails, it is necessary to try again in smaller increases.[51]

b- Complications of PN

Despite very good application and follow-up, PN is a method with many complications. These complications can be examined in three main groups as mechanical, septic and metabolic complications.

Mechanical complications

Among the early complications that may be encountered during the application of the catheter are bleeding, arterial puncture, arrhythmia, air embolism, thoracic duct injury, malposition, hemothorax and pneumothorax. Late mechanical complications include improper functioning of the catheter, venous thrombosis, embolism, cardiac injuries, and nerve damage. About a quarter of catheters become clogged during use. The most common cause of these obstructions is thrombus. Lipid emulsions, calcium-phosphorus precipitates and drug residues are also among the causes. There is insufficient evidence to support the use of heparin instead of saline to keep catheters open. However, it is recommended to wash the catheters 1-2 times a week with 3-5 mL saline containing 5-10 IU/mL heparin. Regular flushing of in-use catheters with heparinized SP is not recommended. Recombinant tissue plasminogen activator is recommended primarily in the presence of thrombus, but urokinase and recombinant urokinase can also be used. 0.1 N hydrochloric acid can be used for drug or calcium precipitation. Clogged catheters should not be attempted to be opened with a guidewire.[52] Drugs that are frequently used in intensive care units but incompatible with PN solution are acetazolamide, amphotericin, acyclovir, ganciclovir, phenytoin, mannitol, metronidazole and sodium bicarbonate.

Infectious complications

Catheter-related bloodstream infections (CR-BSI) are among the most important complications associated with catheters in intensive care units. They are the most serious cause of morbidity and mortality for PN-dependent patients with intestinal failure. The most common infectious agents are *Staphylococcus epidermidis*, as well as *Staphylococcuc aureus* and *Candida* strains, *enterococci* and *enterobacter* strains. The usual approach should be primarily to start treatment with broad-spectrum antibiotics while the catheter is in place. The catheter should be removed if there is clinical worsening despite 72-hour antimicrobial therapy to which the infectious agent is susceptible, or if there is persistent or recurrent bacteremia, severe sepsis, suppurative thrombophlebitis, endocarditis, or bloodstream infection.[52]

In patients with a long-term catheter, who have CR-BSI due to *Staphylococcus aureus, Pseudomonas*, or *Candida* spp., the infected catheter should be removed immediately, except in rare cases where alternative venous access is not available. Treatment of catheter-related fungemia without catheter removal has a low success rate and is associated with higher mortality.

There are no randomized studies on antifungal lock therapy in critically ill pediatric patients with CR-BSI due to *Candida* strains, publications are insufficient, and results are controversial.

Since prevention will be easier than treatment, maximum sterile barrier precautions and aseptic technique should be considered during the intervention.[52] A precautionary package (bundle) including catheter site dressing applications, use of needle-free vascular intervention devices, disposable washing systems and washing technique must be defined.

Metabolic complications

Metabolic complications that may develop in association with PN are as follows:[52]

- Hypo-hyperglycemia
- Thrombocytopenia
- Mineral-vitamin deficiencies
- Coagulopathy
- Electrolyte and acid-base balance disorders
- Essential fatty acid deficiency
- Hepatobiliary dysfunction
- Refeeding syndrome
- Osteopenia
- Hyperlipidemia

Hepatobiliary dysfunction is the most common and serious complication of parenteral nutrition. Early signs of liver injury are elevated ALP and GGT values, bilirubin level rises later; it

can lead to cirrhosis and liver failure. While cholestasis is more common in young children and infants, steatosis is common in adolescents. If there are no contraindications in the treatment approach, EN should be started even if it is little. If long-term PN is to be administered, cyclic feeding can be tried. If the bilirubin is rising and no other cause can be found, the lipid infusion may be discontinued and ursodeoxycholic acid may be started.

Refeeding syndrome, on the other hand, defines metabolic disorders that occur with rapid PN administration, especially to patients with malnutrition. Low serum phosphorus, magnesium and potassium levels and life-threatening results such as disorders of fluid balance and glucose metabolism can be seen. In order to prevent the development of refeeding syndrome, risky patients should be identified beforehand and fluid-electrolyte replacement with PN should be monitored by an experienced, multi-disciplinary team.[52] It should not be rushed to reach the daily calorie target needed; it should be started with low energy and gradually increased over 4-10 days.

c- Home-PN

In particular, pediatric patients who have nutritional problems related to short bowel syndrome, inflammatory bowel disease, AIDS or cancer, who need long-term PN and who do not have any other problems that require hospitalization can continue to be fed at home. A child expected to need PN for more than three months can be discharged as soon as he/she is clinically stable for better quality of life with fewer complications and provided that the following conditions are met:

- The underlying disease taken under control,

- Absence of fluid-electrolyte imbalance, having a reliable vascular access,

- Education of at least one of the parents by a specialist nutrition nurse or team,

- Having been provided appropriate social support,

- Availability of regionally trained health teams that families can reach 7/24 in case of a possible negativity.

Education of families includes the topics of hygiene, catheter care, infusion pumps, PN solutions, and recognition and prevention of potential complications. Physical examinations, biochemical anayses and anthropometric measurements of patients should be performed by home care teams at appropriate intervals (planned as 4 times a year for an uneventful patient) at home or in the hospital when necessary.[53]

Providing PN in this way outside the hospital setting supports a normal lifestyle and reduces complications and medical costs. Moreover, it ensures that nutritional support is continued in a more normal environment, facilitates the development of the child, and allows participation in social activities in the family environment.

Ethics

Peer-review: Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: H.A., A.E.A., A.B.A., O.D., T.K., D.Y., Concept: H.A., A.E.A., O.D., D.Y., Design: H.A., A.E.A., N.A.Y., A.B.A., O.D., T.K., Data Collection or Processing: H.A., A.E.A., D.Y., Analysis or Interpretation: H.A., N.A.Y., A.B.A., Literature Search: H.A., A.E.A., N.A.Y., O.D., D.Y., Writing: H.A., A.E.A., N.A.Y., T.K.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Li J, Li B, Qian J, Zhang J, Ren H, et al. Nutritional survey in critically ill children: a single center study in China. Transl Pediatr. 2020;9:221-30.
2. Delgado AF, Okay TS, Leone C, Nichols B, Del Negro GM, et al. Hospital malnutrition and inflammatory response in critically ill children and adolescents admitted to a tertiary intensive care unit. Clinics (Sao Paulo). 2008;63:357-62.
3. Valla FV, Baudin F, Gaillard Le Roux B, Ford-Chessel C, Gervet E, et al. Nutritional Status Deterioration Occurs Frequently During Children's ICU Stay. Pediatr Crit Care Med. 2019;20:714-21.
4. Jacquot A, Valla FV, Mura T, Tume LN, Bertet H, et al. NUTRI-REAPED study: nutritional assessment of French critically ill children and nutrition practice survey in French-speaking pediatric intensive care units. Ann Intensive Care. 2019;9:15.
5. de Souza Menezes F, Leite HP, Koch Nogueira PC. Malnutrition as an independent predictor of clinical outcome in critically ill children. Nutrition. 2012;28:267-70.
6. Mehta NM, Skillman HE, Irving SY, Coss-Bu JA, Vermilyea S, et al. Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Pediatric Critically Ill Patient: Society of Critical Care Medicine and American Society for Parenteral and Enteral Nutrition. JPEN J Parenter Enteral Nutr. 2017;41:706-42.
7. Tume LN, Valla FV, Joosten K, Jotterand Chaparro C, Latten L, et al. Nutritional support for children during critical illness: European Society of Pediatric and Neonatal Intensive Care (ESPNIC) metabolism, endocrine and nutrition section position statement and clinical recommendations. Intensive Care Med. 2020;46:411-25.
8. Gerasimidis K, Keane O, Macleod I, Flynn DM, Wright CM. A four-stage evaluation of the Paediatric Yorkhill Malnutrition Score in a tertiary paediatric hospital and a district general hospital. Br J Nutr. 2010;104:751-6.

9. Hulst JM, Zwart H, Hop WC, Joosten KF. Dutch national survey to test the STRONGkids nutritional risk screening tool in hospitalized children. Clin Nutr. 2010;29:106-11.
10. White M, Lawson K, Ramsey R, Dennis N, Hutchinson Z, et al. Simple Nutrition Screening Tool for Pediatric Inpatients. JPEN J Parenter Enteral Nutr. 2016;40:392-8.
11. McCarthy H, McNulty H, Dixon M, Eaton Evans MJ. Screening for nutrition risk in children: the validation of a new tool. Journal of Human Nutrition and Dietetics. 2008;21:395-96.
12. Gramlich L, Kichian K, Pinilla J, Rodych NJ, Dhaliwal R, Heyland DK. Does enteral nutrition compared to parenteral nutrition result in better outcomes in critically ill adult patients? A systematic review of the literature. Nutrition. 2004;20:843-8.
13. Braegger C, Decsi T, Dias JA, Hartman C, Kolacek S, et al. Practical approach to paediatric enteral nutrition: a comment by the ESPGHAN committee on nutrition. J Pediatr Gastroenterol Nutr. 2010;51:110-22.
14. Brown AM, Madsen EC, Leonard CP, Leslie SL, Allen C, et al. Continuous Versus Bolus Gastric Feeding in Children Receiving Mechanical Ventilation: A Systematic Review. Am J Crit Care. 2020;29:33-45.
15. Mehta NM. Approach to enteral feeding in the PICU. Nutr Clin Pract. 2009;24:377-87.
16. Bartlett Ellis RJ, Fuehne J. Examination of accuracy in the assessment of gastric residual volume: a simulated, controlled study. JPEN J Parenter Enteral Nutr. 2015;39:434-40.
17. Martinez EE, Pereira LM, Gura K, Stenquist N, Ariagno K, et al. Gastric Emptying in Critically Ill Children. JPEN J Parenter Enteral Nutr. 2017;41:1100-9.
18. Tume LN, Arch B, Woolfall K, Latten L, Deja E, et al. Gastric Residual Volume Measurement in U.K. PICUs: A Survey of Practice. Pediatr Crit Care Med. 2019;20:707-13.
19. Vermilyea S, Goh VL. Enteral Feedings in Children: Sorting Out Tubes, Buttons, and Formulas. Nutr Clin Pract. 2016;31:59-67.
20. Joeckel RJ, Phillips SK. Overview of infant and pediatric formulas. Nutr Clin Pract. 2009;24:356-62.
21. Kızılkan NU, Yılmaz A, Demir H. Çocuk yoğun bakım ünitesinde beslenme rehberi. Erişim adresi: https://www.pedgastro.org/doc/rehber/Cocuk%20Yogun%20Bakim%20Unitesinde_Beslenme%20Rehberi.pdf
22. Kudsk KA. Effect of route and type of nutrition on intestine-derived inflammatory responses. Am J Surg. 2003;185:16-21.
23. Fivez T, Kerklaan D, Mesotten D, Verbruggen S, Wouters PJ, et al. Early versus Late Parenteral Nutrition in Critically Ill Children. N Engl J Med. 2016;374:1111-22.
24. Braunschweig CL, Levy P, Sheean PM, Wang X. Enteral compared with parenteral nutrition: a meta-analysis. Am J Clin Nutr. 2001;74:534-42.
25. Jones L, Watling RM, Wilkins S, Pizer B. Nutritional support in children and young people with cancer undergoing chemotherapy. Cochrane Database Syst Rev. 2010;CD003298.
26. Advani S, Reich NG, Sengupta A, Gosey L, Milstone AM. Central line-associated bloodstream infection in hospitalized children with peripherally inserted central venous catheters: extending risk analyses outside the intensive care unit. Clin Infect Dis. 2011;52:1108-15.
27. van der Kooi TI, Wille JC, van Benthem BH. Catheter application, insertion vein and length of ICU stay prior to insertion affect the risk of catheter-related bloodstream infection. J Hosp Infect. 2012;80:238-44.
28. Kolaček S, Puntis JWL, Hojsak I; ESPGHAN/ESPEN/ESPR/CSPEN working group on pediatric parenteral nutrition. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Venous access. Clin Nutr. 2018;37:2379-91.
29. Giordano P, Saracco P, Grassi M, Luciani M, Banov L, et al. Recommendations for the use of long-term central venous catheter (CVC) in children with hemato-oncological disorders: management of CVC-related occlusion and CVC-related thrombosis. On behalf of the coagulation defects working group and the supportive therapy working group of the Italian Association of Pediatric Hematology and Oncology (AIEOP). Ann Hematol. 2015;94:1765-76.
30. Darouiche RO, Wall MJ Jr, Itani KM, Otterson MF, Webb AL, et al. Chlorhexidine-Alcohol versus Povidone-Iodine for Surgical-Site Antisepsis. N Engl J Med. 2010;362:18-26.
31. O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, et al. Guidelines for the prevention of intravascular catheter-related infections. Clin Infect Dis. 2011;52:e162-93.
32. Mihatsch WA, Braegger C, Bronsky J, Cai W, Campoy C, et al. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition. Clin Nutr. 2018;37:2303-5.
33. Jochum F, Moltu SJ, Senterre T, Nomayo A, Goulet O, e al. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Fluid and electrolytes. Clin Nutr. 2018;37:2344-53.
34. Moritz ML, Ayus JC. Intravenous fluid management for the acutely ill child. Curr Opin Pediatr. 2011;23:186-93.
35. Foster BA, Tom D, Hill V. Hypotonic versus isotonic fluids in hospitalized children: a systematic review and meta-analysis. J Pediatr. 2014;165:163-9.
36. McNab S, Duke T, South M, Babl FE, Lee KJ, et al. 140 mmol/L of sodium versus 77 mmol/L of sodium in maintenance intravenous fluid therapy for children in hospital (PIMS): a randomised controlled double-blind trial. Lancet. 2015;385:1190-7.
37. Weiss SL, Peters MJ, Alhazzani W, Agus MSD, Flori HR, et al. Surviving sepsis campaign international guidelines for the management of septic shock and sepsis-associated organ dysfunction in children. Intensive Care Med. 2020;46(Suppl 1):10-67.
38. Mihatsch W, Fewtrell M, Goulet O, Molgaard C, Picaud JC, et al. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Calcium, phosphorus and magnesium. Clin Nutr. 2018;37:2360-5.
39. Mesotten D, Joosten K, van Kempen A, Verbruggen S; ESPGHAN/ESPEN/ESPR/CSPEN working group on pediatric parenteral nutrition. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Carbohydrates. Clin Nutr. 2018;37:2337-43.
40. van Goudoever JB, Carnielli V, Darmaun D, Sainz de Pipaon M; ESPGHAN/ESPEN/ESPR/CSPEN working group on pediatric parenteral nutrition. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Amino acids. Clin Nutr. 2018;37:2315-23.
41. Brown RO, Compher C; American Society for Parenteral and Enteral Nutrition Board of Directors. A.S.P.E.N. clinical guidelines: nutrition support in adult acute and chronic renal failure. JPEN J Parenter Enteral Nutr. 2010;34:366-77.
42. Wales PW, Allen N, Worthington P, George D, Compher C, et al. A.S.P.E.N. clinical guidelines: support of pediatric patients with

intestinal failure at risk of parenteral nutrition-associated liver disease. JPEN J Parenter Enteral Nutr. 2014;38:538-57.

43. Bechard LJ, Parrott JS, Mehta NM. Systematic review of the influence of energy and protein intake on protein balance in critically ill children. J Pediatr. 2012;161:333-9.
44. Lapillonne A, Fidler Mis N, Goulet O, van den Akker CHP, Wu J, et al. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Lipids. Clin Nutr. 2018;37:2324-36.
45. Diamond IR, Grant RC, Pencharz PB, de Silva N, Feldman BM, et al. Preventing the Progression of Intestinal Failure-Associated Liver Disease in Infants Using a Composite Lipid Emulsion: A Pilot Randomized Controlled Trial of SMOFlipid. JPEN J Parenter Enteral Nutr. 2017;41:866-77.
46. Hojsak I, Kolaček S. Fat overload syndrome after the rapid infusion of SMOFlipid emulsion. JPEN J Parenter Enteral Nutr. 2014;38:119-21.
47. Pontes-Arruda A, Liu FX, Turpin RS, Mercaldi CJ, Hise M, et al. Bloodstream infections in patients receiving manufactured parenteral nutrition with vs without lipids: is the use of lipids really deleterious? JPEN J Parenter Enteral Nutr. 2012;36:421-30.
48. Bronsky J, Campoy C, Braegger C; ESPGHAN/ESPEN/ESPR/CSPEN working group on pediatric parenteral nutrition. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Vitamins. Clin Nutr. 2018;37:2366-78.
49. Domellöf M, Szitanyi P, Simchowitz V, Franz A, Mimouni F, et al. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Iron and trace minerals. Clin Nutr. 2018;37:2354-9.
50. Riskin A, Picaud JC, Shamir R; ESPGHAN/ESPEN/ESPR/CSPEN working group on pediatric parenteral nutrition. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Standard versus individualized parenteral nutrition. Clin Nutr. 2018;37:2409-17.
51. Puntis J, Hojsak I, Ksiazyk J; ESPGHAN/ESPEN/ESPR/CSPEN working group on pediatric parenteral nutrition. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Organisational aspects. Clin Nutr. 2018;37:2392-400.
52. Hartman C, Shamir R, Simchowitz V, Lohner S, Cai W, et al. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Complications. Clin Nutr. 2018;37:2418-29.
53. Hill S, Ksiazyk J, Prell C, Tabbers M; ESPGHAN/ESPEN/ESPR/CSPEN working group on pediatric parenteral nutrition. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Home parenteral nutrition. Clin Nutr. 2018;37:2401-8.