

UPDATES IN PARENTERAL NUTRITION

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Abstract

Parenteral nutrition (PN) represents an alternative or additional approach when other nutrition routes are not succeeding or when using other routes is not possible or would be unsafe. The main goal of PN is to deliver a nutrient mixture closely related to requirements in a safe manner and without complications. The concentration of parenteral solutions (PS) determines their osmolarity, according to which, the solutions will be infused by peripheral or central venous access. The solutions used in central PN contain more glucose, which, together with amino acids and electrolytes, determines a hyperosmolar solution, which has to be administered in a large caliber vein. Central venous access may be maintained over long periods of time. In peripheral PN there are used solutions with a lower concentration of dextrose in order to obtain (solutions with the) an osmolarity lower than 900 mOsm/L, which can be administered in a peripheral vein. Peripheral PN is used over short periods of time because of the limited tolerance for a long term of peripheral veins. PN is an efficient method to ensure the nutritional support which can be associated with numerous complications, some of them severe, with lethal potential. Patients with PN need a daily physical examination and laboratory tests.

key words: *parenteral nutrition, nutritional requirement*

Introduction

PN refers to the intravenous infusion (perfusion) of specialized nutrition solution. This method of feeding may be required when the gastrointestinal tract is not functional or leaking, cannot be accessed, or the patient cannot be adequately nourished by oral or enteral means. Commercially premixed solutions can provide adequate nutrition over short periods, but for more complex patients, it is important to have a flexible system for personalizing PN [1].

PN is complex, expensive and should therefore be used with good clinical guidance.

The purpose of this review is to present the indications for PN, the nutritional assessment of eligible patients, determination of PN requirements, initiation and monitoring of its complications, etc. [1].

Indications of total PN

Total PN is indicated in patients with AIDS (Acquired Immuno-Deficiency Syndrome), in which other methods of nutritional support have failed; patients with anorexia and severe malnourishment (body weight less than 65% the ideal or weight deficit higher than 30% of the

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ideal body weight) and intolerance to enteral nutrition; liver diseases (hepatic failure); acute pancreatitis; renal failure [2]. In chronic inflammatory bowel diseases (Crohn's disease or ulcerative colitis) PN can be used to maintain normoponderal status or in the case of a surgical intervention [2].

PN is required for an indefinite period in patients with bowel shorter than 60 cm (short bowel syndrome); patients with malignant tumors in which phenomena of gastrointestinal toxicity occur as side effects of chemotherapy. PN is indicated also if a hypercatabolic state is longer than 4-5 days and enteral nutrition is not possible [2].

In surgical patients, PN is indicated: preoperatively for 7-10 days before surgical intervention in those with severe malnourishment, and postoperatively for approximately 3 days in patients with mild or moderate forms of malnourishment, if enteral nutrition cannot be used.

Also PN can be used in children with growth retardation caused by systemic diseases or chronic idiopathic diarrhea; newborns with tracheoesophageal fistula, gastroschisis, omphalocel, intestinal atresia [3].

Contraindications for PN

PN is contraindicated in the presence of a functioning gastrointestinal tract (in this case enteral nutrition is the preferred route); inability to obtain venous access; a prognosis that does not warrant aggressive nutrition support; when the risks of PN are judged to exceed the potential benefits [4].

Nutritional requirements in PN

Energy requirements

Energy requirements are usually determined using a range of standard predictive equations. These take into consideration the patient's age,

sex, height and weight and may make adjustments for the patient's degree of stress. For the majority of patients stress can be resolved over a few days. Calorie requirements are expressed in terms of kcal/kg and refer to total calories. Patient's requirements should be reviewed on a regular basis, taking into account their clinical condition [1].

A safe starting point is 25 kcal/kg/day (total calories) as an initial goal rate. Once reached, this should be reviewed to assess the patient's tolerance, progress and nutritional needs.

In the case of severe stress or significant protein energy malnutrition, requirements may be higher. Ongoing monitoring is particularly important in these patients to prevent over- or underfeeding and to assess the patient's tolerance, progress and nutritional needs. An upper limit of 35 kcal/kg/day should not be exceeded [1].

Ideally, the Basal Energy Expenditure (BEE) is measured using indirect calorimetry. If this method is not available, than BEE can be estimated using the Harris-Benedict equations:

$$\text{Men: BEE (kcal/day)} = 66 + 13.7 \times \text{Wt (kg)} + 5 \times \text{Ht (cm)} - 6.8 \times \text{Age (years)}$$

$$\text{Women: BEE (kcal/day)} = 655 + 9.6 \times \text{Wt (kg)} + 1.7 \times \text{Ht (cm)} - 4.7 \times \text{Age (years)}$$

Ht= height; Wt = body weight

Total energy requirement is calculated by multiplication of BEE with a correction factor, which depends on clinical status and physical activity of the patient. Most patients have a caloric requirement of 1.3-1.7 x BEE or 25-30 kcal/kg/day.

Fluid requirements

Fluid requirements will depend on the following considerations: clinical condition; fluid status/balance (dehydration or fluid overload); other sources of fluid input (IV/intravenous, oral, enteral); fluid losses (drains, urine, vomiting, diarrhea, fistula) [1].

Fluid requirement is 20-40 mL/kg/day or 1 mL fluids/kcal plus pathological fluids loss (polyuria, vomiting, diarrhea, excessive perspiration). In febrile patients, for each Celsius grade of body temperature over 37⁰, 250 ml are added to the daily need of fluids [5,6].

Carbohydrates requirement

Carbohydrates should represent 50-65% of the daily caloric intake (2-5 mg/kg/min). Studies have shown that the rate of glucose oxidation in the body is limited. The excess of glucose which is not oxidized is converted to lipids. Glucose is the preferred carbohydrate energy source. The maximal capacity to oxidize glucose is 6 mg/kg/min (35 kcal/kg/day from glucose). Infusion of carbohydrates above this rate may induce complications such as hyperglycemia and fatty liver [1].

Protein requirement

In order to ensure the patient is receiving adequate levels of proteins, patients need to be assessed on an individual basis, taking into consideration prior nutritional status, disease status/severity of illness, projected length of time on PN; patients need to be monitored regularly for tolerance (intolerance is indicated by a rising blood urea concentration) and adequacy, and protein input adjusted accordingly [1].

Proteins should represent 15-20% of the daily caloric intake (0.8-2 g/kg/day). To conserve the body weight, protein intake should be 0.8-1 g/kg/day, in patients with physiologic metabolism, and 1.2-2 g/kg/day in patients with hypercatabolic states. Essential amino acids should represent 40-50% of daily protein intake [2,5,6].

Lipids requirement

It is generally recommended that PN be started slowly at 1 g lipid/kg/day and blood monitored for lipemia. After the first day, the

infusion rate can be increased depending on the patient's requirements. The lipid infusion rate should not exceed a maximum of 2 g/kg/day. Patients with severe liver and renal dysfunction should not exceed 1 g/kg/day. Lipid should ideally be given as a continuous infusion over 24 hours, which is better tolerated, metabolized more effectively, and allows for the clearance of the lipid as a chylomicron. Higher infusion rates are associated with complications such as fat overload syndrome and lipemia which may damage the liver.

For central PN, the average is 30% of total calories from lipid. However, this can be up to 50% in some cases. The greater amount of lipid reduces glucose intolerance. Lipid tolerance is reduced in some conditions such as pancreatitis, unstable diabetes, hypertriglyceridemia and severe liver disease.

For peripheral PN, solutions may contain lipid up to 40-60% total (66% non-protein) calories to reduce the osmolarity of their PN solution and minimize the risk of thrombosis or damage to the vein epithelium [7,8].

In patients with hyperglycemia and with respiratory insufficiency, the daily lipid intake should be greater than 30% of the daily caloric intake, while the carbohydrate intake should be lowered.

To prevent the deficit of essential fatty acids, a daily minimal intake of linoleic acid (representing 2-4% of the daily caloric intake) is necessary. To prevent the lipidic overload, the maximal lipid intake should be less than 2 g/kg/day (maximum 60% of the daily caloric intake) [2,6,7].

Electrolytes requirement

Sodium (1-2 mmol/kg/day); potassium (1-2 mmol/kg/day); calcium (10-15 mmol/day); magnesium (8-20 mmol/day); phosphorus (20-40 mmol/day) [1].

Microelements requirement

Zn (3.3- 6.6 mg/day); Cu (0.3-0.5 mg/day); Cr (10-20 µg/day); Mn (275 µg/day). Also supplements of Se (31.6- 118 µg/day), I (130 µg/day), Mo (38 µg/day), Cu (0.3- 1.2 mg/day) and Fe (1 mg/day) [1].

Vitamins requirement

Vitamin (Vit.) A (3300 UI/day); Vit. B1 (6 mg/day); Vit. B2 (3.6 mg/day); Vit. B6 (6 mg/day); Vit. B12 (5 µg/day); Vit.C (200 mg/day); Vit. D (200 UI/day); Vit. E (10 UI/day); Niacine (40 mg/day); Pantotenic acid (15 mg/day); Biotine (60 µg/day); Folic acid (600 µg/day); Vit K (15 µg/day) [1].

Venous access for PN administration

The type of catheter and choice of vein depends on several factors including: risks associated with the placement method; potential complications (thrombotic, infectious and mechanical); ease of site care; number of infusions; anticipated duration of therapy.

There are a number of considerations that need to be made when choosing the route of venous access. These include: history of patient (history of thrombosis, multiple previous intravenous lines resulting in damaged veins and limiting the choice of either peripheral or central venous access, lymphedema); individual circumstances (haematological stability, allergies); resources available (access to skilled professionals, nutrition support teams, vascular access teams); osmolarity and pH of the solution; risk of infection; duration of PN; type of line access available; other IV therapies required by the patient, as a multilumen catheter may be needed [1].

The concentration of parenteral solutions (PS) determines their osmolarity, according to which, the solutions will be infused by peripheral or central venous access.

The solutions used in PN are hypertonic and, when administered incorrectly, they can cause complications (venous thrombosis, thrombophlebitis) [2,6]. The PS osmolarity depends first of all of their content of dextrose (5 mOsm/g dextrose), amino acids (10 mOsm/g amino acids) and electrolytes (1 mOsm/mmoL electrolyte) [2,6].

The maximal osmolarity tolerated by a peripheral vein is 900 mOsm/L [2,6,8].

The solutions which are administered by peripheral venous access contain more fats as an energetic source than those administered by central venous access [2,6].

The central venous catheter is a catheter the tip of which reaches the vena cava or the right atrium. Generally central venous access is preferred in PN because the rapid blood flow dilutes hypertonic parenteral solutions. Insertion of a central venous catheter is indicated if it is anticipated that the patient will need nutritional support for at least 7 days or needs PN and does not tolerate the increased fluid load which is necessary in peripheral PN in order to ensure the energy requirements [2,6].

The solutions used in central PN contain more glucose (15-20%) which together with amino acids and electrolytes determine a hyperosmolar solution (1300-1800 mOsm/L), which have to be administered in a large caliber vein, usually the superior vena cava. Central venous access may be maintained over long periods of time (weeks, years) [2,6].

In peripheral PN are used solutions similar to those used in central PN, but with a lower concentration of dextrose (5-10% of final concentration) in order to obtain solutions with the osmolarity lower than 900 mOsm/L, which can be administered in a peripheral vein. The solutions used in peripheral PN have a bigger content of fluids and fats [2,6].

Peripheral PN may be used for patients with suspected or moderate malnutrition who cannot be nourished orally or enterally, in order to ensure a total or partial nutritional support. Usually, peripheral PN is used over short periods of time because of peripheral veins limited tolerance for long term perfusion. PN is accompanied by a high risk of phlebitis [9]. Adding heparin (1U/ml) and hydrocortisone (10 mg/L) in parenteral solutions might prevent thrombophlebitis.

Perfusion solutions used in PN

Dextrose (glucose) is the main energetic source in parenteral solutions [2]. It is available in concentrations of 5%, 10%, 20%, 25%, 35%, 50% and 70% [3]. It provides 4.1 kcal/g glucose [5]. Dextrose solution 70% is the dextrose solution with the highest concentration which ensures the biggest energetic content, being used as an energy source for patients with hydric restrictions, or with high energetic requirement (traumas, burns). The maximal administration rate of dextrose will not overpass 5 mg/kg/min [2,6].

Lipid emulsions represent an alternative energetic source for patients with glucose intolerance or low clearance of CO₂ (the CO₂ production by the oxidation of lipids represents 70% of the production resulting from the oxidation of glucose) [7]. Lipid emulsions contain soybean oil, sunflower oil and water [2]. They are available in concentrations of 10% (1.1 kcal/ml), 20% (2 kcal/ml) and 30% (2.9 kcal/ml) [6,10]. They can ensure up to 60% of the energetic requirement and can be mixed with glucose and amino acids in order to obtain 3-in-1 solutions. The optimum administration rate of lipid emulsions is 1 g/kg/day, and the maximal administration rate is 2 g/kg/day [2,6].

Amino acid solutions contain 40% essential amino acids and 60% nonessential amino acids. They are available in concentrations of 5.5%,

8.5%, 10%, 15% and 20% [11]. Solutions with a higher concentration may be used for fluid-restricted patients. The energetic content of amino acids is 4 kcal/g [11]. Routine usage of solutions which contain only branched-chain amino acids and essential amino acids is not recommended because their efficiency has not been proved and they are very expensive [2,6].

Daily electrolytic requirements may be ensured for the majority of patients by adding 1-3 *standard electrolytic packages*. A standard electrolytic package contains: Na-25 mmol; K-40.6 mmol; Ca-5 mmol; Mg-8 mmol; acetate-33.5 mmol; gluconate-5 mmol; Cl-40.6 mmol. The standard electrolytic package does not contain phosphate, which has to be added separately [2,6]. The content of a multivitamin *standard package* is recommended daily for all patients with PN, except for those with renal failure. The parenteral standard multivitamin package contains: Vit. A (3300 UI); Vit. D (200 UI); Vit. E (10 UI); Vit. C (100 mg); Vit. B1 (3 mg); Vit. B2 (3.6 mg); Vit. B3 (40 mg); Vit. B6 (4 mg); pantothenic acid (15 mg), folic acid (400 µg); biotin (60 µg); Vit. B12 (5 µg). Vit. K in a 10 mg/week dose will be administered in order to maintain the prothrombin time within the normal limits. Vit. K will not be administered to patients receiving warfarin treatment [2,6].

All patients with PN need a daily administration of a *standard microelements parenteral package*: Zn (5 mg); Cu (1 mg); Mn (0.5 mg); Cr (10 µg); Se (60 µg); I (70 µg). Iron is not included in the standard parenteral package because it may influence other PS component's stability. Iron deposits are usually sufficient for avoiding the need of supplementation during PN of short term [2,6].

PN monitoring parameters

Monitoring during PN is particularly important because the patient is at greater risk of toxicity, deficiency and other complications.

Key aspects of monitoring include: risk of refeeding syndrome; indicators of overfeeding; hyperglycaemia and hypoglycaemia; micronutrient deficiency and toxicity; complications of line access including line infection; other long term complications.

Patients with malnutrition need a daily physical examination [11]. The body weight is to be controlled daily, being a simple method for monitoring the hydric status and it offers a good energetic balance prediction [2,6]. Laboratory tests are used in order to monitor the protein-caloric balance, the hydric balance, the electrolytic balance, the acid-alkaline balance, the organs functions and the response to infection [2,6].

PN complications

PN is an efficient method to ensure the required nutritional support but can be associated with numerous complications, some of them severe, with lethal potential [11]. These include:

Liver Dysfunction

It is acceptable for markers of liver function to rise slightly after the commencement of PN, but these biochemical markers should return to normal once PN ceases [12].

Hepatic Steatosis

This is the most common liver dysfunction in adults receiving PN, defined as an accumulation of fat in the hepatocytes and characterized by a non-specific rise in liver function tests. The main cause for hepatic steatosis is represented by an excess of calories, specifically an excess of carbohydrate calories (a

fat-free bag). Although more rare, it can occur when fat is included.

Gall Bladder and Biliary Complications (Cholestasis and Cholethiasis)

These are more common in pediatric PN patients, but are also likely in adults on long-term PN nutrition who have a complete lack of enteral/oral nutrition (for example patients with short bowel syndrome) or are overfed in total calories. The impaired release of, or a complete obstruction of, bile is characterised by a rise in bilirubin, ALP and GGT (although these can be elevated due to other reasons).

Management of Liver Dysfunction

Management of liver dysfunction includes the following measures: 1) Ensure a balance of carbohydrate, lipid and amino acid in the parenteral formula; 2) Do not exceed overall calories. For patients with liver dysfunction, the maximum amount of fat is 1g/kg/day and the maximum of carbohydrate is 4g/kg/day; 3) Initiate oral or enteral nutrition as soon as possible, even if it is in very small amounts, since this stimulates gall bladder emptying; 4) Some research into the role of the amino acid carnitine indicates it may prevent hepatic steatosis but there is no clear evidence on adults at this point [1].

Conclusions

PN is a valuable and necessary medical treatment for many patients, providing both nutritional sustenance and life extension at a time when it is not possible to sustain them in any other way.

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