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Turkish Neonatal Society guideline on parenteral nutrition in preterm infants

Türk Neonatoloji Derneği prematüre bebeklerin parenteral beslenmesi rehberi

Canan Türkyılmaz[1], Hülya Bilgen[2], Nilgün Kültürsay[3]

[1]Division of Neonatology, Department of Pediatrics, Gazi University, Faculty of Medicine, Ankara, Turkey
[2]Division of Neonatology, Department of Pediatrics, Marmara University, Faculty of Medicine, İstanbul, Turkey
[3]Division of Neonatology, Department of Pediatrics, Ege University Faculty of Medicine, İzmir, Turkey

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Abstract

Postnatal growth failure due to inappropriate and insufficient nutrition is a risk for preterm infants, especially for very-low-birth-weight or extremely-low-birth-weight infants. This extrauterine growth failure causes negative effects on long-term neurodevelopment. Early initiation of intensive parenteral nutrition with appropriate protein and energy supply is a nutritional emergency when enteral feeding cannot be achieved. This approach prevents protein catabolism and helps achievement of positive protein balance and postnatal growth. Protein, lipid, and glucose initiation with appropriate doses that reach timely goals constitute the major elements of parenteral nutrition. The transition to enteral nutrition with the mother's milk at the earliest convenience must be targeted in parenteral nutrition.

Keywords: Feeding, parenteral nutrition, preterm

Öz

Prematürelerin özellikle çok düşük doğum ağırlıklı ve aşırı düşük doğum ağırlıklı bebeklerin uygun ve yeterli beslenememelerine bağlı postnatal dönemde büyüme geriliği riskleri vardır. Bu ekstrauterin büyüme geriliğinin prematürede uzun dönem nörogelişimsel olumsuz etkileri gösterilmiştir. Enteral beslenmenin başarılamadığı durumlarda, erken ve yoğun parenteral beslenmenin uygun protein ve enerji sağlayarak başlanması, bu riskli prematüreler için yaşamsal bir acil durum kabul edilmektedir. Bu sayede protein katabolizması önlenmekte, pozitif protein dengesine erişmelerine ve büyümelerine olumlu katkı sağlanmaktadır. Parenteral beslenmede protein, lipid ve glukozun uygun dozda başlanarak belli hedeflere erişmesi prematüre bakımının ana elemanlarından biridir. Parenteral beslenen bebeklerin en kısa zamanda anne sütü ile enteral beslenmeye geçişleri de hedeflenmelidir.

Anahtar sözcükler: Beslenme, parenteral beslenme, prematüre

Parenteral nutrition of preterm infants

As in healthy term infants, the ideal food for preterm and sick term infants is breast milk. Breastfeeding should be initiated as soon as possible after delivery, but for babies who cannot be fed fully enterally, total parenteral nutrition (TPN) must be started immediately to meet the energy and protein requirement (1-6). Intensive early parenteral nutrition together with early enteral nutrition has been shown to decrease extrauterine growth retardation in very-low- birth-weight (VLBW) infants and to improve mental developmental scores (7-13). In particular, TPN should be started within the first 24 hours (preferably from the first hour) at the hospital for all preterms less than 32 weeks or infants with limited enteral intake (1, 2). As the baby tolerates feeding over time, parenteral nutritional support should be reduced while enteral feeding is increased. TPN should be continued until 75% of the total protein and energy requirement of the baby is met with enteral nutrition. Whenever enteral feeding is interrrupted, TPN should be started again (1).

Because of medical problems such as prematurity, lung problems requiring endotracheal intubation-mechanical ventilation, hypothermia, infections and hypotension,

Corresponding Author / Sorumlu Yazar: Canan Türkyılmaz E-mail / E-posta: drcananturkyilmaz@gmail.com

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enteral nutrition of preterm infants cannot be initiated early, mostly delayed. Moreover, early enteral nutrition and gradual introduction of feeding is more often delayed because of feeding intolerance and the fear of necrotizing enterocolitis (NEC). Early and aggressive TPN in the first weeks is very important to reduce intrauterine growth retardation, to maintain positive nitrogen balance, to reduce postnatal weight loss, to prevent postnatal growth retardation, to reduce mortality, and even to improve neurodevelopmental outcomes and prevent morbidity such as bronchopulmonary dysplasia (BPD) and NEC (7, 14-16).

Objectives in parenteral nutrition

The goal of TPN in the newborns is to provide the optimal growth and development, until full enteral feeding is achieved. TPN is also started to babies with major congenital anomalies who don not tolerate enteral feeding or to support the nutritional and metabolic needs of babies, before and after surgery (17-20).

Indications of total parenteral nutrition in newborns

Total parenteral nutrition is started to preterm infants below 32 weeks who cannot achieve full enteral feeding, severely ill term/preterm babies who cannot be fed enterally, babies with NEC, preterm infants who need surgery for gastrointestinal anomalies, and babies with heart disease requiring fluid restriction, sepsis, short bowel, and ileus (1, 2, 7, 16).

Parenteral and enteral fluid, electrolyte, and nutrient requirements for term and preterm infants

Fluid, electrolyte, energy, protein, and carbohydrate requirements of the newborn, especially preterm infants, vary depending on the gestational week, birth weight, postnatal age, presence of intrauterine growth retardation, and clinical factors. The fluid, protein, and energy requirements of preterm infants are shown in Tables 1 and 2 (1, 21).

Knowing that nutrition is an urgency for preterm infants, early and intensive parenteral nutrition should be initiated in neonatal intensive care units. Today, there is no universally accepted consensus on nutrition of preterm babies (22-29). In order to create evidence-based data and recommendations in the nutrition of preterm infants, many studies are being conducted with the contribution of neonatal associations around the world (30, 31).

The guideline of the Turkish Neonatal Society (TND) about parenteral fluid, electrolytes, energy, and nutritional requirements are prepared in accordance with expert recommendations and are shown in Table 3 (1, 2).

Table 1. Fluid requirements according to birth weights and postnatal age

Birth weight (g)	Days 1-2 (mL/kg)	Days 3-7 (mL/kg)	Days 8-30 (mL/kg)
<750	100-200	120-200	120-180
750-1000	80-150	100-150	120-180
1001-1500	60-100	80-150	120-180
>1500	60-80	100-150	120-180

Table 2. Protein and energy requirements in preterm infants according to body weight

Body weight (g)	Protein (g/kg/day)	Energy (Kcal/kg/day)	Protein/energy (g/100 Kcal)
500-700	4.0	105	3.8
700-900	4.0	108	3.7
900-1200	4.0	119	3.4
1200-1500	3.9	125	3.1
1500-1800	3.6	128	2.8
1800-2200	3.4	131	2.6

Preparation of total parenteral nutrition solutions, vascular access preferences, and infusion characteristics

Total parenteral nutrition solutions should be prepared in a special center or department with special mixing systems under laminar flow and aseptic conditions. Special sets and filters should be used for newborns. Total parenteral nutrition bags and sets should be changed daily (29, 32).

Central catheters in newborns are umbilical artery/vein or peripherally inserted central venous catheters. After insertion of the catheter, the location of the catheter should be checked using direct radiography before starting the fluid infusion. The tip of the central catheter should be located in larger veins, preferably the superior or inferior vena cava, provided that it is outside the heart. Single lumen catheters should be preferred over multi-lumen catheters due to the lower risk of infection and sepsis. Catheters should be inserted under full aseptic conditions, kept as long as necessary with proper care, and should be removed as soon as the requirement is completed, again in accordance with aseptic conditions. Arterial and venous catheters should not be kept in place longer than 7, 14 days, respectively. If total parenteral nutrition is to be continued, a peripherally inserted central catheter (PICC)

Table 3. Recommendations for parenteral nutrition in preterm infants (Turkish Neonatal Society Nutrition Group)

Component Kg/day	ELBW (<1000 g) infants			VLBW (<1500 g) infants		
	First day	2-7 day	Growth	First day	2-7 day	Growth
Energy (Kcal)	40-50	70-80	90-100	40-50	60-70	90-100
Protein (g)	2-3	3.5	3.5-4.0	2-3	3-3.5	3-3.5
Glucose (g)	7-10	8-15	13-17	7-10	8-15	13-17
Fat (g)	2	2-3	3-4	2	2-3	3
Na (mEq)	0	2-4	3-7	0	0-4	3-5
K (meq)	0	0-2	2-3	0	0-2	2-3
Ca (mg)	20-60	60	60-80	20-60	60	60-80
P (mg)	0	45-60	45-60	0	45-60	45-60
Mg (mg)	0	3-7.2	3-7.2	0	3-7.2	3-7.2

ELBW: extremely-low-birth-weight; VLBW: very-low-birth-weight

must be replaced with the umbilical catheter before its withdrawal (29, 32, 33).

The venous route for parenteral nutrition should not be used for antibiotics or other drugs, they should rather be administered via another route. When necessary, TPN may be given through the umbilical artery (provided that it does not contain calcium) (32-34).

The osmolarity tolerance of peripheral veins varies between 700-900 mOsm / L (1, 29, 32). Low concentrations of glucose (<12.5%) can be given via peripheral vessels, unless there is an additional content that increases osmolarity. Aminoacid solutions should not be given at a concentration of >2% from peripheral vessels. At most, 30% concentration dextrose may be given from the central veins. Because the intravenous lipid solutions's osmolarities are the same as serum, they can be given by a peripheral vein. They can also be given by the central route, but lipid solutions are not recommended to be given via peripheral central catheters because of the risk of occlusion (29, 32, 33).

The timing of initiation and duration of the total parenteral nutrition

Aggressive TPN is initiated immediately after birth within the first few hours in order not to interfere with the growth and development of the baby, and not to provoke catabolism and energy deficiency in the transition period from intrauterine to extrauterine life. Enteral nutrition should be started from the first days together with TPN. Total parenteral nutrition is gradually decreased until full enteral feeding is achieved. Parenteral nutrition can be discontinued when 75 % of the total protein and energy requirements are met enterally. It is recommended to discontinue TPN when enteral nutrition reaches 100 mL/kg/day. However, nowadays, there is a tendency to prolonge the duration of TPN to increase the caloric and protein intake of extremely low birth weight (ELBW) infants. Practically, when the amount of enteral nutrition reaches 80 mL/kg/day, the lipids are stopped first and the amino acids are stopped when 100 mL/kg/day is reached (1, 7, 16, 19).

Energy requirements

The energy requirements of parenteral-fed infants are lower than that of enteral-fed infants and it is 75-85 Kcal/kg/day until the end of the first week. The caloric intake of 50-60 Kcal/kg/day is sufficient to prevent catabolism at the beginning, but higher calories are needed to ensure growth. Neutral energy balance is around 70 Kcal/kg/day (1, 2).

For healthy preterm infants, the average daily energy requirement for metabolic processes and to maintain a growth rate close to the intrauterine growth rate is 90-120 kcal/kg, whereas the parenteral requirement is 80-90 Kcal/kg/day (1). The daily energy requirement of babies born at term is 100-120 kcal/kg. The parenteral energy requirement is calculated as 85% of the energy delivered by the enteral route (24). Carbohydrates and fats are the main source of energy in parenteral nutrition. The optimal caloric distribution of the macronutrients should be as follows: 50% from carbohydrates, 30% from proteins, and 20% from fats (1, 6, 7, 16, 19).

Amino acids

In preterm infants, initiation of amino acids starting from

the first day of life provides positive nitrogen balance, inhibits protein catabolism, increases protein, albumin, and glutathione, which is a main intracellular antioxidant, provides appropriate weight,gain (22-24). Nevertheless, there are conflicting results about the beneficial effects of early (within the first 24 hours) amino acids supplementation on mortality, early and late growth, and neurodevelopmental outcome (4).

For appropriate protein accretion, approximately 30 nonprotein calories are required per gram of amino acid. When calculating amino acid supplementation, the nonprotein calorie/nitrogen ratio should also be calculated. This ratio should be between 150-250. To calculate the amount of nitrogen, the protein as gram is usually multiplied by 0.16 (16, 24).

Amino acid solutions should contain essential amino acids for the newborn. Cysteine and glutamine are not present in amino acid solutions due to a stabilization problem (1, 2). The addition of cysteine hydrochloride to aminoacid solutions improves protein gain, increases calcium-phosphorus (Ca-P) solubility and the level of glutathione, but it may cause metabolic acidosis (1, 2, 35). Although it is recommended to add cysteine just before the TPN solution is ready to use, the intravenous cysteine form is not available in our country. It has been reported that the addition of glutamine does not reduce the mortality rates and the frequency of late sepsis, and has no effect on dietary tolerance, NEC or growth (36).

There are two types of amino acids in our country: primene (10%) and trophamine (%6). Primene is usually preferred in preterm infants because it is prepared according to fetal or neonatal cord blood amino acids levels. It contains essential and semi-essential amino acids. Trophamine (6%) is prepared according to plasma aminoacid concentrations of healthy, term, and breastmilk-fed 30-day-old infants (1).

Turkish Neonatal Society Nutrition Group recommendations for the administration of intravenous amino acids:
It is recommended to start amino acids 2-3 g/kg/day within the first day (first hours) of life and increase up 3.5-4 g/kg/day in ELBW infants and 3.0-3.5 g/kg/day in VLBW infants in a few days (20-25, 28). Although a positive protein balance is provided by early/high-dose amino acid administration, the frequency of hyperammonemia, hyperuremia, and metabolic acidosis does not increase. If the blood urea nitrogen (BUN) level is >10 mg/dl, it can be assumend as acceptable. High BUN values can be tolerated unless there is an inborn error of metabolism or renal failure. In the early postnatal period the high BUN levels are mostly related to dehydration (or negative fluid balance). Therefore, unless increased creatinine levels and oliguria are observed, it is not necessary to reduce amino acid supplementation due to high BUN/urea levels (1, 2).

Due to the risk of Ca-P precipitation, amino acid solutions at a concentration of <1% should not be used. The protein/energy ratio should be targeted at 3-4 g/100 Kcal to promote growth, being at the upper suggested level for smaller infants (1, 2, 24).

The ideal amino acid composition for newborns and especially for VLBW infants is unknown. The existing amino acid solutions have not been shown to be superior each other and cannot meet all the requirements of preterm infants (1, 2, 5, 7, 37).

Glucose

Although there is no consensus on the lower and upper limits of the safe plasma glucose concentration, it is intended to be kept between 60-150 mg/dL. Glucose infusion can be started at 4-6 mg/kg/min, can be increased with 2 mg/kg/min increments as needed, up to 10-12 mg/kg/min by monitoring blood glucose levels. Excessive glucose infusion has many negative effects such as increased energy and oxygen consumption, increased serum osmolality, osmotic diuresis, fatty infiltration of the liver, and accumulation of excessive fat. Applying appropriate concentrations of amino acids reduces the incidence of hyperglycemia by increasing the endogenous secretion of insulin (1, 7, 16, 19).

Although improvement in hyperglycemia was reported to be achieved with routine insulin use, the frequency and severity of hypoglycemia and the mortality rate increased (38). Therefore, routine insulin administration is not recommended in preterm infants. Insulin is only used if hyperglycemia does not improve despite a glucose infusion rate of 4 mg/kg/min. It can be used for a very short period of time with a dosage of 0.05 units/kg/hour if hyperglycemia persists (1, 19, 38).

Lipid

In preterm infants who could not be fed by enteral route, essential fatty acid (EFA) deficiency develops in 3-7 days if the parenteral lipid is not administered. In VLBW in-

fants, starting 2 g/kg of lipid within the first day was well tolerated and did not cause major complications such as death, BPD and sepsis. It is reported that it is safe to reach lipid infusion up to 3-4 g/kg/ day in ELBW and 3 g/kg/day in VLBW infants, with daily increments of 0.5-1g / kg, after starting with ≥2 g/kg/day immediately after birth l (28, 39, 40).

Lipid solutions

Intravenous lipid solutions contain soybean, fish oil, olive oil, and medium chain triglycerides (MCT) in different ratios (1, 7, 40, 41). Lipid solutions derived from soybean oil (such as Intralipid®) contain omega-6 PUFA (predominantly linoleic acid). While they do not contain omega-3 PUFA (especially docosahexaenoic acid: DHA). For the prevention of omega-3 deficiency, among the lipid solutions, SMOFlipid®, which contains omega-6 and omega-3, is increasingly being used. It has been reported that it is well tolerated in preterm infants and causes lower bilirubin levels and decreases the frequency of retinopathy of prematurity (ROP) (42). The use of pure soybean oil solutions has been shown to be associated with a mildly increased risk of sepsis, cholestasis, proinflammatory cytokines, and oxidative stress. Preparations containing fish oil have not been shown to prevent cholestasis but they reduce cholestasis once it has occurred (1, 7, 40, 41).

In a Cochrane meta-analysis that compare pure soybean oil with newer alternative fat emulsions (medium chain triglyceride, long chain triglyceride-MCT, fish oil, olive oil, borage oil), all of the examined lipid emulsions were reported to be safe and well tolerated by preterm babies (42). Compared to pure soybean, the mixture of MCT-olive oil-fish oil-soybean oil emulsion was shown to provide a reduction in the frequency of early stage ROP (Stage 1-2) in a study. However, no difference was found between pure soybean-based emulsions and the newer alternative fat emulsions in clinical parameters such as death, growth rate, BPD, sepsis, advanced ROP (stage ≥3), and the frequency of TPN associated liver diseases.

In our country, Intralipid® (100% soybean oil), SMOFlipid® (30% soybean, 25% olive oil, 30% MCT, 15% fish oil) Clineoleic® (20% soybean oil, 80% olive oil) are available and they contain 20% lipid. Omegaven® is a 10% lipid solution including fish oil.

Turkish Neonatal Society Nutrition Group recommendations on intravenous lipid administration:

Lipid solutions are started on the first day at 2 g/kg/day and increased by 0.5-1 g/kg every day to reach 3-4 g/kg/day in ELBW infants and 3 g/kg/day in VLBW infants.

Twenty percent lipid preparations should be preferred because they are more easily metabolized. Although SMOFlipid® emulsions containing omega-3 were shown to reduce early-stage ROP in one study, the clinical results of different lipid solutions were found similar and superiority to each other could not be shown (42). The fatty acid profile of all lipid solutions is completely different from that of breast milk (1, 2, 42).

Lipids should be given by continuous infusion for more than 24 hours (maximum: 0.2 g/kg/h) to enhance its clearance and not to disrupt oxygenation. In order to reduce lipid peroxidation (especially if vitamins are added), the protection of the lipid solutions from light is recommended, although its importance and efficacy have not been fully proven. It is not recommended to routinely add heparin to lipid solutions (29).

There is no need for routine follow-up of serum triglyceride levels in infants who tolerate enteral feeding and those whose parenteral nutritional support is gradually reduced. However, in VLBW and at risk infants, triglyceride levels can be monitored at each dose increase with 24-hour intervals and weekly thereafter. The serum triglyceride level should be kept below 200 mg/dL, although there is no clear evidence (1, 16).

Clinical conditions that lipid infusion should be reduced are severe sepsis, hyperbilirubinemia at the upper limits for exchange transfusion, severe respiratory distress syndrome in which hypoxia cannot be controlled, and/or pulmonary hypertension and cholestasis. In the presence of cholestasis, lipid infusion should be reduced to 1 g/kg/day and 2-3 times per week. Although no definite evidence has been reported, fish oil containing lipid preparations may be preferred in patients with cholestasis (39-45). These problems usually resolve after full enteral feeding.

Minerals

Sodium, potassium and chloride are essential minerals for life. Sodium intake of VLBW infants should be restricted to reduce the risk of BPD in the first week of fluid balance. After the onset of diuresis, usually after the third day, 2-4 mEq/kg/day sodium can be added. VLBW infants may require higher amounts due to renal loss, and this is arranged according to blood levels (1, 2, 7).

Potassium should not be added until diüresis has been observed and renal functions are evaluated in the first few days; 2-3 mEq/kg/day potassium is given to keep blood levels in the normal range.

Calcium and phosphate (Ca-P) should be added from the first day; 60-80 mg/kg of elemental Ca, 45-60 mg/kg of phosphate per day should be given (1, 21, 46). The ideal Ca/P ratio for best bone mineralization (in mg) is 1.7/1 (16, 29). The Ca/P solubility in the TPN solutions depends on the temperature, the type and concentration of the aminoacid solution, the glucose concentration, the pH, the Ca/P ratio, form of phosphate and the presence of lipid. To prevent the risk of Ca-P precipitation, phosphate should be added in an organic-bound form. More Ca and P may be given with high-content amino acid solutions because these solutions increase the acidity of the fluid (1, 16, 21, 29).

Vitamins

All babies receiving TPN should be supplemented with lipid and water-soluble vitamins starting from the second day of life. The recommended doses of parenteral vitamins in newborns, the preparations available in our country, and their use are shown in Table 4 (1, 3, 47).

Vitalipid N-infant (10 ml) at a dose of 4 mL/kg/day in infants <2500 g, 10 mL/day in infants >2500 g; Soluvit N diluted with 10 mL at a dose of 1 mL/kg/day; Cernevit (lyophilized vial) diluted with 5 mL distilled water at a dose of 1-2 mL/kg/day should be used. In practice, preferably vitamin K1 is given to babies receiving TPN at a dose of 1 mg >2000 g and 0.5 mg <2000 g once a week.

Trace elements

Trace elements are important for many cellular functions such as enzymes activity, protein and lipid metabolism, endocrine functions, and immune/inflammatory modulation (1, 2, 47).

Studies and evidence on their use, requirements and supplementation doses in newborns are not sufficient. Zinc should be added to TPN from the first day. Other trace elements are recommended for infants on parenteral feeding for more than two weeks. As the dose of zinc in the combined preparations is not sufficient, extra zinc sulphate should be added to solution. In patients with persistant diarrhea and excessive losses due to ileostomy, extra zinc together with electrolytes should be given (1, 47).

Trace element preparations should not be used in kidney failure (due to the accumulation of chromium), in chronic liver diseases and in cholestasis (due to the accumulation of copper and manganese excreted by bile) (47).

Tracutil®, which is commercially available in our country, is used at a dose of 0.25-0.5 mL/day. For trace element re-

Table 4. Recommended vitamin doses in newborns and commercially available preparations

Vitamin	[a]Term recommended daily intake	Preterm recommended (dose/kg/day)	Cernevit™ lyophilized ampule (5 mL)	SoluvitN 1 mL	Vitalipid N-Infant 1 mL
Vitamin A (IU)	2300	700-1500	3500	–	230
Vitamin D (IU)	400	160	220	–	40
Vitamin E (IU)	7	2.8-3.5	11.2	–	0.7
Vitamin K (mcg)	200	10	–	–	20
Vitamin B6 (mcg)	1000	150-200	4530	490	
Vitamin B12 (mcg)	1	0.3	6	0.5	
Vitamin C (mg)	80	25	125	11.3	
Biotin (mcg)	20	5-8	69	6	
Folic acid (mcg)	140	56	414	40	
Niacin (mg)	17	4-6.8	46		
Pantothenic acid (mg)	5	1-2	17.25	1.65	
Riboflavin (mcg)	1400	150-200	4140	490	
Thiamin (mcg)	1200	200-350	3510	310	

[a]Vanek VW, Boren P, Buchman A, et al. A.S.P.E.N. position paper: recommendations for changes in commercially available parenteral multivitamin and multi-trace element products. Nutr Clin Pract 2012; 27:440-91

quirements in term and preterm infants, and its content, please refer to the Turkish Neonatal Society "Guideline on Nutrition of Preterm and Sick Babies" (48).

Standard premixed ready-to-use parenteral nutrition solutions

All over the world there are many problems related with TPN applications in daily practice. These are late initiation of TPN, starting and increasing lower amount of protein and lipid than those recommended in the guidelines, errors in the calculation and application of TPN, the need for continuous education for healthcare personal, requirement for updating the guidelines, the need for central venous access due to high osmolarity, and the increased frequency of catheter-related complications. Recently, pre-mixed, standardized ready-to-use TPN solutions have become available for use. In many studies, it was shown that standardized solutions are more suitable than the individualized solutions (1, 49, 50).

In a study including 14,167 babies from all around France conducted in 2017, the use and reliability of two types of standardized premixed parenteral nutritional solutions were investigated. It was reported that these solutions could be used safely in newborns from birth (50). It was also, reported that these standard solutions with an osmolarity lower than 800 mOsm/L were tolerated without causing any problems such as phlebitis, despite being applied via peripheral veins. It is emphasized that standardized TPN solutions in newborns provide safe administration, improve compliance with the guidelines, can be started from the first hours/day, provide better/appropriate nutrient contents, cause fewer calculation/order and administration mistakes, and reduce the risk of infection and cost (1, 29, 50).

Monitoring of parenteral nutrition in infants

Both the growth indicators and some biochemical values of infants receiving TPN should be monitored at regular intervals; more frequently in the first days of parenteral nutrition, and when a more stable metabolic condition is obtained, once-weekly laboratory examinations should be performed. Blood glucose should be monitored 2-3 times a day when increasing the glucose infusion rate, and after reaching a fixed rate, once-daily monitoring is enough. Serum Na, K, Cl, Ca, P, Mg and BUN values should be monitored 2-3 times in the first week, then once a week. Complete blood counts should be monitored 2-3 times in the first week, then once a week, and liver function tests once a week. The serum triglyceride level can be monitored at each dose increase or when necessary (1).

The aim of nutrition is to achieve a growth level close to intrauterine growth rates in the last trimester of pregnancy. This means that 15-20 g/kg weight gain per day, 0.5-0.8 cm head circumference increase per week, and 0.8-1.1 cm height increase per week. Body weight should be monitored every day, height and head circumferences weekly (1, 7, 16, 19).

Complications of total parenteral nutrition

The most important complications of TPN are parenteral nutrition-associated cholestasis (PNAC) and catheter-related problems. Acute-metabolic complications of TPN include hypoglycemia, hyperglycemia, metabolic acidosis, hypophosphatemia, other electrolyte imbalances, hyperlipidemia, and azotemia. Mechanical complications include leakage into tissues, organs or body cavities, tissue necrosis, infiltration, thrombosis, pleural/pericardial effusion, and cardiac arrhytmias related with catheter malposition. Infectious complications include bacterial and fungal infections (*Candida* species, *Malassezia furfur*) (1, 7, 16, 18, 19).

Cholestasis is defined as a direct bilirubin level over 2 mg/dL in two consecutive measurements, with no other liver disease (7). The frequency is variable, reported up to 50% in patients receiving TPN for two months (16, 19). The etiology is multifactorial. Even small amounts of enteral nutrition reduce the risk in patients on TPN for a long time. Although ursodeoxycholic acid or phenobarbital have been reported to be useful in children and adults in some studies, it is not recommended for the routine use of PNAC in preterm infants (1).

The smaller the baby and the longer the parenteral nutrition, the greater the risk of developing catheter-related sepsis occur. Besides, the rate of sepsis increases in patients with PNAC. The major microorganisms responsible for sepsis are *Staphylococci*, *Candida* species, and *Malassezia furfur*. Coagulase-negative staphylococcal bacteremia and Malassezia furfur fungemia have been associated with intravenous lipid use. To reduce the risk of sepsis, attention should be paid to catheter care, and the catheter should be removed when it is no longer required, and enteral feeding should be started as soon as possible (1, 18).

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