Sobolewska-Samorek Agnieszka, Zarzycka Danuta, Trojanowska Alina, Brodowicz-Król Magdalena, Dońka Katarzyna, Szewczyk Monika, Hordyjewska Anna, Warowna Marlena, Sikora Kamil, Łuczyk Robert, Łuczyk Marta. New insight of parenteral nutrition in children – short review. Journal of Education, Health and Sport. 2020;10(6):56-67. eISSN 2391-8306. DOI http://dx.doi.org/10.12775/JEHS.2020.10.06.006
https://apcz.umk.pl/czasopisma/index.php/JEHS/article/view/JEHS.2020.10.06.006
https://zenodo.org/record/3884500

The journal has had 5 points in Ministry of Science and Higher Education parametric evaluation. § 8. 2) and § 12. 1. 2) 22.02.2019.

Received: 25.05.2020. Revised: 30.05.2020. Accepted: 08.06.2020.

New insight of parenteral nutrition in children – short review

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Abstract

Admission. Parenteral nutrition (parenteral) is the supply of all essential nutrients - proteins, carbohydrates, fats, electrolytes, vitamins, trace elements and water intravenously. Parenteral nutrition is a generally available method of nutritional treatment used when the supply of food through the gastrointestinal tract is impossible, insufficient or contraindicated. Complete parenteral nutrition should be replaced as soon as possible with feeding to the gastrointestinal tract. Chronic diseases in children are often complicated by serious nutritional deficiencies.

Key words: parenteral nutrition, newborns, children, carbohydrates, lipids, amino acids

Parenteral nutrition

The need for parenteral nutrition in children usually occurs for reasons primarily associated with intestinal insufficiency. The most common cause of chronic parenteral nutrition is short bowel syndrome [1, 2]. The short bowel syndrome in children may occur as a result of resection, among others in the course of necrotic enteritis, tumors or gastrointestinal malformations or small intestinal atresia. This disease is characterized by anatomical or functional loss of more than 50% of the small intestine. It is a congenital defect of the gastrointestinal tract, which is one of the more common causes of gastrointestinal obstruction [2, 3, 4, 5].

Other illnesses that induce parenteral nutrition include diseases that occur with intestinal motility disorders, such as Hirschprung's disease or pseudointic obstructive syndrome. As a result of these diseases, malabsorption occurs due to diarrheas which cannot be treated [3, 6,].

A much smaller group of patients requiring chronic parenteral nutrition are children burdened with diseases resulting from parenteral causes such as metabolic or cystic fibrosis [4, 7, 8]. Other causes of chronic parenteral nutrition include complications of chemotherapy, acute pancreatitis, catabolism associated with trauma, surgery or burns, and prematurity. In preterm infants, the indication for feeding are: parenteral immaturity of the digestive tract and necrotizing enterocolitis [3, 7] (Fig. 1).

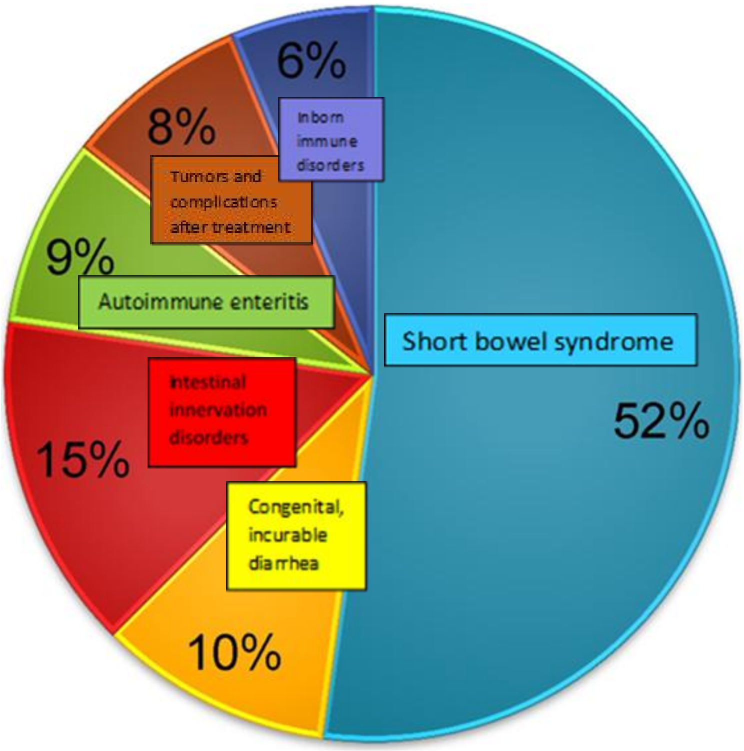

Figure 1. Indications for chronic parenteral nutrition in children [2,3,4,6,7,8].

Amino acids in parenteral nutrition

Amino acid preparations used in parenteral nutrition of children, especially newborns, are most often modeled on the amino acid composition of human milk, umbilical cord blood or derived from pharmacokinetic studies in newborns [1, 9]. Nine amino acids have been recognized as essential in newborns. They are valine, isoleucine, leucine, threonine, methionine, tryptophan, phenylalanine, lysine, histidine [5, 10]. In the case of neonates with a low birth weight, essential amino acids include both arginine, which has a positive effect on reducing the risk of necrotic enteritis, and cysteine and taurine, which are important for the proper development of the central nervous system [11, 12].

Amino acids are recommended to be included in parenteral nutrition, in the first 2 hours of life in a dose dependent on the birth weight of the child [6, 9, 13]. The starting dose of amino acids for newborns with a birth weight higher than 1500 g should start from 2.0 g/kg of body weight per day [2, 12]. The dose should be increased in the following days by 0.5 g/kg of body weight per day until 3.5 g/kg of body weight per day. On the other hand, neonates with a birth weight of less than 1500 g should start with a dose of 2.5 g/kg of body weight per day, gradually increasing the supply to 4.0-4.1 g/kg of body weight per day, until reaching a weight of 1500 g (Tab.1). This is to ensure not only proper growth after birth, but also to supplement residual energy reserves [13, 14]. In the case of newborns additionally burdened with diseases of particular organs or systems, amino acid preparations adapted to individual clinical situations are also available. Preparations containing less phenylalanine, methionine and tryptophan, and more branched chain amino acids are recommended for patients with hepatic insufficiency [3, 8]. Amino acid solutions containing glycine-L-tyrosine should be selected in patients with renal insufficiency [15, 16].

Table 1. Supplying of amino acids in parenteral nutrition [2,12,13,14].

Amino acid dose	**Newborn with birth weight above 1500g**	**Newborn with birth weight under 1500g**
Output/Initial dose	2 g/*kg of body weight*/24h	2,5 g/ *kg of body weight*/24h
Final dose	3,5 g/*kg of body weight*/24h	4,0 – 4,1 g/*kg of body weight*/24h

Fats in parenteral nutrition

Fats are a high energy substrates. The supply of lipids in parenteral nutrition should cover from 25 to 40% of the extra-cerebral energy needs [17, 18]. Newborns born prematurely, especially those with very low birth weight less than 1500 g, are particularly sensitive to deficiency in nutrition, because they have less fat in the body compared to the newborns [18, 19, 20]. In premature babies, the 2 or 3-day limitation of fat supplying causes the emergence of a clinical condition known as a deficiency of essential fatty acids. To avoid this disorder, premature babies should receive fat from the first day of life [7]. The total fat supplying should be about 3-4 g/kg of body weight per day (Tab. 2) [17, 20, 21]. Preparations containing a higher dose of phospholipids may increase the risk of hyperlipidemia [5, 20, 22]. In European Union, three types of lipid emulsions are registered for children [6, 23]. The first type is based solely on soybean oil. It is characterized by a high content of polyunsaturated omega-6 fatty acids and a relatively low omega -3 fatty acids content. Such composition may involve the risk of overproduction of pro-inflammatory cytokines and may increase oxidative stress [3, 8, 24]. Soybean oil can suppress the cells of the immune system, and the phytosterols present in it can contribute to the occurrence of cholestasis - one of the complications of parenteral nutrition [8, 11, 25, 26]. The second type of lipid emulsion consists the soybean oil and the olive oil. The olive oil contains two times more of α-tocopherol and much less of polyunsaturated fatty acids as compared to soybean oil [20].

The third emulsion is a combination of soybean oil with MCTs oil (medium-chain triglyceride fatty acids derived from coconut oil). MCTs, as a result of better solubility and more efficient intravascular metabolism, are faster purified from plasma [17, 21, 27].

Pediatric patients receiving fat emulsions should periodically monitor the serum triglyceride levels [6, 23, 26, 28]. It is also recommended to avoid excessive supplying of lipids in children diagnosed with acute respiratory failure, because the supply of emulsion may deteriorate the child's respiratory efficiency [4, 29]. However, lipids should not be avoided in parenteral nutrition because complete cessation of their supplying may carry a risk of a deficiency of free fatty acids [1, 6, 30]. The use of lipid preparations containing omega-3 fatty acids from fish oil significantly reduces the incidence of cholestasis and hepatic complications in children, dependent on parenteral nutrition [17, 20, 21].

Table 2. Lipids dose in parenteral nutrition [18, 19, 20].

Lipids dose	**Newborn with birth weight above 1500g**	**Newborn with birth weight under 1500g**
Output/Initial dose	0,5 g/ *kg of body weight*/24h	
Final dose	3 - 4 g/*kg of body weight*/24h	2,5 - 3 g/*kg of body weight*/24h

Carbohydrates in parenteral nutrition

Carbohydrates are the main source of energy and should cover 40-60% of the child's energy needs [31]. Carbohydrate administration provides the energy, reduces gluconeogenesis, ensures optimal consumption of amino acids needed for protein synthesis and regulation of fat metabolism [32]. The basic carbohydrate used in parenteral nutrition is glucose. It is a source of energy for all tissues of the body, especially for the brain, spinal cord, kidneys and erythrocytes [8, 33, 34]. In parenteral nutrition, it should provide 60-75% of non-protein calories. The supplying of glucose in parenteral nutrition should ensure normoglycemia [35, 36].

Excessive supplying of glucose inhibits fat oxidation, stimulates lipogenesis, increases fat deposition in tissues, leading to fatty hepatic steatosis and hyperglycaemia. Excessive glucose also increases production of CO_2 and directly effects on the acceleration of lung ventilation [1, 31, 34]. Newborns with very small and extremely low body weight are at risk for hypoglycaemia [2, 5]. Therefore, it is necessary to start the infusion of glucose as soon as possible and ensure its serum concentration above 40-50 mg/dl. European recommendations for parenteral nutrition for children advise the inclusion of glucose in parenteral nutrition during the first 2 hours of life. The purpose of this procedure is to prevent hypoglycaemia, i.e. blood glucose levels below 40 mg%. The risk of such low glycemia in small premature babies is high due to insufficient glycogen reserves [31, 36, 37]. The initial dose of glucose should be 8-10 g/kg of body weight per day and should be increased in subsequent days (Tab. 3) [35, 38]. In the first days of life, it is necessary to monitor blood glucose every 3-4 hours [31, 39]. In children with very low birth weight, glucose intolerance may occur, which is an indication for the use of a constant infusion of insulin in order to maintain normoglycemia [6, 31]. Hyperglycaemia, should be prevented because it causes the increase of serum osmolality, osmotic diuresis and water-electrolyte disturbances [37, 40]. Hyperglycemia is associated with increased mortality, as well as an increased incidence of peri-ventricular and intraventricular bleeding, retinopathy of pre-term infants and sepsis [34]. Glucose concentrations during to parenteral nutrition with dose over of 150-180 mg/dl are considered to cause the hyperglycemia [8, 31].

Table 3. Glucose dose in parenteral nutrition [7, 35, 38].

Glucose dose	**Output/Initial dose**	**Final dose**
Newborn	8 – 10 g/*kg of body weight*/24h	17 g/*kg of body weight*/24h

Vitamins in parenteral nutrition

Newborns with very low birth weight have low endogenous systemic resources of microelements and vitamins [8]. Vitamin A is one of the great importance in the development of connective and cartilage tissues. Its presence affects the rate of formation of mucopolysaccharides, which are the basic component of connective tissue [5, 8, 41].

Vitamin A plays an important role in the development of the lungs, in the functioning of the immune system and in the visual processes. It takes part in the regeneration of the epithelium in the process of convalescing of premature's with bronchopulmonary dysplasia (BPD - brocho pulmonary dysplasia) [2, 42]. Newborn babies born prematurely have low levels of vitamin A in the blood serum and small amounts of it in the liver compared to newborns born at the time [8, 43]. During parenteral nutrition, the supplying of vitamin A is about 40%, as a result of its disintegration under the influence of light and the drainage of walls. The recommended dose of vitamin A ranges from 500-1500 IU/kg of body weight per day. The supply of this vitamin should be started from the second day of life. (80 ml/kg of body weight per day) (Tab.4) [7, 44]. Usually, the supply of that vitamin at its upper limits is insufficient to compensate for its deficiencies, especially in premature infants with low birth weight <1000g [8, 42, 44].

The optimal range of vitamin D concentration is 30-50 ng/ml. Values below 20 ng/ml indicate a deficiency of cholecalciferol. In children remaining on total parenteral nutrition, the supply of vitamin D is 160 IU/kg of body weight per day. Newborn babies born prematurely with cholestasis, due to the reduced amount of bile in the small intestine have impaired synthesis and absorption of vitamin D in the liver, should receive vitamin at a minimum dose of 2-5 µg/kg of body weight per day [7, 41,45, 46].

Tocopherol (vitamin E) is considered the most important natural antioxidant that protects cell membranes against destabilization and breakdown in the process associated with lipid peroxidation. It also protects the membranes of erythrocytes from damage associated with the oxidation of unsaturated fatty acids, which are the part of the membrane. Supplementation with vitamin E in preterm infants reduces the frequency of intraventricular hemorrhage and the number of severe cases of retinopathy of prematurity (ROP) and increases level of hemoglobin [7, 44]. In parenteral nutrition, doses 2.8-3.5 mg/kg of body weight per day of vitamin E are used (Tab.4). Higher tocopherol concentrations may increase the risk of sepsis and necrotizing enterocolitis [7, 8, 44].

Vitamin K plays an important role in the synthesis of coagulation factors (like: factors II, VII, IX, X), anti-thrombotic proteins (like: protein C, S and Z) and osteocalcin. In some cases, usually in the first week of life, a deficiency of vitamin K can lead to serious bleeding disorders in the newborn, and to the so-called newborn hemorrhagic disease (VKDB - Vitamin K Deficiency Bleeding) [1, 47,48]. Demand for vitamin K in premature infants was set at 10 µg/kg of body weight per day. In the prophylaxis of vitamin K deficiency in premature infants with birth weight less than 1500 g, vitamin K is used intramuscularly or intravenously at 0.3 mg. In contrast, for children with a birth weight above 1500 g only intramuscularly administration of vitamin K at dose of 0.5 mg is recommended. Vitamin K is administered intramuscularly every 6 weeks because after this administration the proper vitamin K concentration is maintained for 4 - 6 weeks (Tab. 4). The healing intravenous dose of vitamin K is reserved for the treatment of coagulation disorders in newborns and infants who have prolonged prothrombin time (increased INR). After intravenous administration, the half-life of the vitamin is very short and lasts only 24 hours [8, 49]. Parenteral nutrition accounts for as much as 80% of the total supplying of vitamin K in premature infants born below the 28th week of pregnancy in the first two weeks of life. In premature newborns, it is recommended to administer vitamin K at a dose of 10 µg/kg/day. Vitamin K contains preparations of fat-soluble vitamins and fat emulsions based on soybean oil [6, 49, 50].

Table 4. Vitamins dose in parenteral nutrition [7, 41,45, 46].

Vitamins	**A**	**D**	**E**	**K**
Newborn	500-1500 IU/*kg of body weight*/24h	160 IU/*kg of body weight*/24h	2,8-3,5 mg/*kg of body weight*/24h	for newborn with birth weight under 1500g - 0,3 mg/*kg of body weight*/every 6 week
				for newborn with birth weight above 1500g – 0,5mg/*kg of body weight*/every 6 week

Mineral ingredients in parenteral nutrition

Minerals are essential for the proper functioning of the human body. They play many important functions mainly in metabolic processes. In the disturbance of their homeostasis, the changes and abnormal cell's functioning occur. Due to the need for individual mineral components, we divide them into microelements and macroelements [8, 51, 52, 53].

Macroelements

In the last trimester of pregnancy, very intensive growth and mineralization of the fetal skeletal occurs. During this period the fetus accumulates minerals in the amount of approx. 90-150 mg/kg/day of calcium (Ca) and 50-85 mg/kg/day of phosphorus (P). This is related to the child's weight gain [1, 6, 51, 54, 55]. The dietary requirement of calcium is as follows: in infants 400-600 mg/day, in children about 800 mg/day, in young people 1200 mg/day and over 25 years of age - about 800 mg/day. In women during pregnancy and lactation it is about 1200 mg/day (Tab.5). As a reference point in parenteral nutrition, the fetal development period and the supply of calcium and phosphorus at a similar level are taken into account [2, 53]. The higher supplying of amino acids and, therefore, expected increasing of body mass, the higher calcium and phosphates should be supplying. The supply of calcium should be started from the age of 1 year to prevent early hypocalcemia while the supply of phosphates should start from 2-3 days of age. The best absorption of calcium and phosphate is when their ratio in food is - Ca**:**P = *1.3-1.7***:***1*. The presence of lactose and some amino acids improve the absorption of calcium, while excess of fats, phytates, and oxalates inhibit this process [2, 51, 54].

Magnesium (Mg) is the second most abundant intracellular cation. In human organism it plays numerous roles of essentials importance. Due to its physicochemical properties, intracellular magnesium can bind to the nucleus, ribosomes, cell membranes or macromolecules occurring in the cell's cytosol. Being an activator of about 300 enzymes, magnesium takes part in plenty of metabolic pathways, such as: glycolysis, β-oxidation, Krebs cycle or ions' transport across cell membranes, which are very important, especially for a newly developing organism such as a newborn baby [53,54]. Because magnesium plays a key role in the regulation of functions of mitochondria and ATP production, the symptoms of its deficiency in newborns can lead to disturbances of muscles, lungs functions as well as to disturbances of cardiovascular and gastrointestinal systems. The dietary requirement for magnesium in infants is 40-60 mg/day whereas in children 80-170 mg/day (Tab.5) [52,54].

Potassium (K), sodium (Na) and chlorine (Cl) are electrolytes responsible for water, electrolyte and acid-base management in the body. They are an essential component of parenteral nutrition. They should be used in accordance with daily requirements and current serum concentration. Their concentration in the blood serum of newborn babies born prematurely, should be controlled daily for the first 3-7 days of life or more frequently [8, 51, 54, 56, 57]. Sodium is the main electrolyte of extracellular fluids, whereas potassium is primarily found inside the cells. These elements are responsible for the exchange of substances through the cell membrane and the spread of electrical stimuli in the nerve fibers [7, 51, 56, 57].

The potassium is the main cation of the intracellular space, being a sodium antagonist and its opposite action is based on the reducing the volume of extracellular fluids, which helps to control the amount of water in the body. Potassium, being also a calcium antagonist, is responsible for proper muscle tone (tonus), by regulating the potential of cell membranes and the excitability of nerve and muscle cells. The dietary potassium requirement increases in age-dependent way and is equal: in infants 400-1200 mg/day, in children below 7 years of age 550-2500 mg/day, in older children 1000-4500 mg/day (Tab.5) [52, 57].

Sodium is the most important extracellular cation. It is responsible for maintaining the osmotic pressure and regulating the acid-base economy. Sodium is involved in regulating the permeability of cell membranes and affects the maintenance of normal neuromuscular excitability. It is mainly excreted in the urine and through the skin. The daily requirement for this element depends on age and is equal to: 120-750 mg/day in infants; 320-1350 mg/day in children under 7 years of age; 600-2700 mg/day in older children (Tab.5) [56, 57].

Chlorine is an anion of extracellular space, in the human body it is in the form of chloride anion (negative ion), mainly in extracellular fluids (including blood plasma), in the stomach as a component of hydrochloric acid, and in saliva. It is also found in the skin, subcutaneous tissue and bones [51, 53]. Chlorine, like sodium and potassium, regulates water-electrolyte and acid-base balance and activates digestive enzymes of saliva (including salivary amylase) and participates in the production of hydrochloric acid in the stomach [52, 54].

Microelements

Trace elements are elements that together account for less than 0.01% of the total body weight. These include: iron, iodine, chromium, zinc, copper, selenium, molybdenum, manganese and fluorine. These are important elements that are involved in many metabolic processes. In children, who are fed parenterally, trace elements should always be added to nutrient mixtures at a daily dose. In the case of detecting deficiencies of specific elements, for example due to severe diarrhea or fistulas of the gastrointestinal tract, the nutrient mixture is enriched with additional amounts of individual elements in the form of separate preparations [8,51, 54].

Chromium (Cr) is an essential element involved in the metabolism of carbohydrates and lipids. This element is a part of the glucose tolerance factor (GFT-Glucose Tolerance Factor), which is needed for the proper metabolism of glucose, and enhances the action of insulin. Its dietary requirement increases in age-dependent way from 10-60 mg/day in infants to 50-200 mg/day in adults (Tab. 5) [51, 54, 58].

Copper (Cu) is an important component of many enzymes. It is a part of superoxide dismutase, an antioxidant enzyme that protects cell membranes against free radicals. Copper is needed for the formation of red blood cells, it participates in the synthesis of connective tissue and plays an important role in the synthesis of prostaglandins, and therefore has an influence on the work of the heart and blood pressure. The deficit of copper can result in impaired energy production, abnormal glucose and cholesterol metabolism, increased oxidative damage and increased tissue iron (Fe) accrual. The dietary requirement increases in age-dependent way and ranges from 0.4-0.7 mg/day in infants to 1.5-3.0 mg/day in adults (Tab. 6) [2, 8, 52, 53, 54].

Iodine (I) is an essential element, which builds the thyroid hormones: thyroxine and triiodothyronine. Both of these hormones are necessary in regulating the metabolism of the body. Its dietary requirement depends on age and intensity of metabolic processes. It is: 40-50 mg/day in infants and about 150 mg/day in adults (Tab. 5) [53, 54, 59].

Manganese (Mn) is part of many enzymes, such as superoxide dismutase, and activates some hydrolases, kinases or transferases. The dietary requirement for this element changes depending on age and state of health. It ranges from 0.3 to 1.0 mg/day in infants (Tab. 5) [6, 51, 52, 54].

Molybdenum (Mo) is a synergy for enzyme function and enzymes involved in DNA metabolism. The dietary requirement increases in age-dependent way and ranges from 15-40 mg/day in infants to 75-250 mg/day in adults (Tab. 5) [53, 54, 59].

Selenium (Se) is an ingredient in many enzymes, such as: glutathione peroxidase, which is an antioxidant that protects cell membranes from the damaging effects of oxygen free radicals. Selenium is essential for the proper synthesis, activation of thyroid hormones and decompression of the immune system. The dietary requirement for this element ranges from 10-15 mg/day in infants to 40-70 mg/day in adults (Tab. 5) [1, 54, 59, 60].

Zinc (Zn) affects all basic life processes, such as the metabolism of proteins, carbohydrates, fats. It participates in energy processes and nucleic acid metabolism, is a part of many enzymes and plays an important role in bone mineralization, wound healing and immune system function. Newborn babies born prematurely have an increased need for this mineral compared to those born at time [53, 54, 58]. The dietary requirement for zinc is as follows: in newborns 5-10 mg/day, in adults12-15 mg/day. In women during lactation is increased up to 19 mg/day (Tab. 5) [53,58].

Newborn babies born prematurely are particularly at risk of deficiency of the above-mentioned microelements, due to the shorter pregnancy period and due to the increased demand of these substances, especially in the final stage of pregnancy. In the case of long-term parenteral nutrition, trace elements should be administered and periodically monitored in the child's body [4, 51, 53].

Table 5. Mineral ingredients dose in parenteral nutrition in newborns [52,53,54].

<table>
<tr><td><i>Macroelements</i></td><td colspan="2">Ca^{2+}</td><td colspan="2">Mg^{2+}</td><td colspan="2">Na^{+}</td><td>K^{+}</td></tr>
<tr><td>Dose</td><td colspan="2">400-600 mg/day</td><td colspan="2">40-60 mg/day</td><td colspan="2">120-750 mg/day</td><td>400-1200 mg/day</td></tr>
<tr><td><i>Microelements</i></td><td>Cr^{2+}</td><td>Cu^{2+}</td><td>I^{+}</td><td>Mn^{2+}</td><td>Mo^{+4}</td><td>Se^{2+}</td><td>Zn^{2+}</td></tr>
<tr><td>Dose</td><td>10 mg/day</td><td>0.4-0.7 mg/day</td><td>40-50 mg/day</td><td>0.3-1.0 mg/day</td><td>15-40 mg/day</td><td>10-15 mg/day</td><td>5-10 mg/day</td></tr>
</table>

Summary

Parenteral nutrition of children must provide the proper nutrition status and allows the correct somatic growth t and the development of the central nervous system. It provides all necessary nutrients: proteins, carbohydrates, fats, electrolytes, vitamins, trace elements and water via the intravenous route and will be effective only when all nutrients are given to the child in appropriate proportions [37, 38, 41]. Lack or deficiency of any of them prevents the effective use of others. The need for individual nutrients in a pediatric patient is individual. It depends on age, sex, comorbidities, and the initial state of nutrition. Proper planning of parenteral nutrition of a child consists not only in the calculation of the need for individual nutrients, but also in the selection of a specific, most suitable for the patient preparation [2, 7, 11, 16, 37].

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