International Journal of Pediatrics and Genetics
Vol. 2 No. 11 (2024)
ISSN: 2995-5483

OPTIMIZATION OF EARLY DIAGNOSIS OF INTRAHEPATIC CHOLESTASIS OF PREGNANT WOMEN

Khusanova Durdona Tog'oymurodovna
Assistant, Samarkand State Medical University
Faculty General Medicine -1
Department of Obstetrics and Gynecology No. 3

Abstract: Cholestatic liver disease in newborns and young children is a common cause of malnutrition. Many diseases have a chronic progressive course with the formation of biliary cirrhosis, liver failure and require early liver transplantation. Nutritional status is an important prognostic indicator of morbidity and mortality in patients both during the waiting period and after transplantation, and determines the importance of correcting the lack of basic macro and micronutrients in time. Available literature data and our experience show the need to use a high-calorie diet high in medium-chain triglycerides, polyunsaturated fatty acids, proteins, fat-soluble vitamins and minerals in this category of children.

Key words: cholestasis syndrome; cholestatic liver diseases; medium chain triglycerides; poor nutrition; nutritional support

Intensive care unit

Cholestatic liver diseases (CLD) in children lead to the development of malnutrition, including protein-energy malnutrition and specific nutritional deficiencies (lack of fat-soluble vitamins, micro- and macronutrients) [1, 2] . Severe malnutrition occurs in 40–70% of children with CKD [3].

In the neonatal period, CKD occurs in approximately 1 in 2500 full-term live births [2]. The etiopathogenesis of CKD has a diverse spectrum. The most common causes of extrahepatic cholestasis in children in the first months of life are biliary atresia (BA) (25-40%) and other malformations of the biliary tract. The etiology of intrahepatic cholestasis is more diverse and includes a large group of genetically determined diseases, congenital disorders of protein and carbohydrate metabolism, endocrine and infectious diseases, as well as temporary cholestasis caused by parenteral nutrition and other reasons. takes [4-6].

Many diseases in newborns and young children have a chronic progressive course, requiring biliary cirrhosis, liver failure and early liver transplantation (LT). Nutritional status is an important prognostic indicator of morbidity and mortality in patients before and after LT. Thus, malnutrition syndrome and negative nitrogen balance have been shown to be negative prognostic indicators of overall survival in CKD patients [7 , 8]. In addition, long-term malnutrition in young children with cholestasis syndrome leads to slow brain growth, impaired psychomotor development, and decreased resistance to infections. In children with biliary atresia before transplantation, the level of malnutrition was found to be a predictor of cognitive performance in the years after transplantation [9].

Timely and adequate nutrition is an important component of complex therapy for cholestasis syndrome in children.

Pathogenetic mechanisms of malnutrition formation

In liver diseases with cholestasis syndrome, bile flow is impaired and the concentration of bile salts necessary for fat absorption decreases. Monoglycerides and free fatty acids formed as a result of the hydrolysis of dietary lipids in the intestinal lumen are added to mixed micelles with bile acids and thus transferred to the intestinal epithelium (Fig. 1). During cholestasis, the decrease in the flow of bile acids

into the duodenum leads to a sufficient intraluminal concentration of bile acids for the formation of micelles, which impairs the absorption of dietary lipids. Due to impaired digestion and absorption of fats, the absorption of fat-soluble vitamins, micro- and macroelements is impaired. Lack of fats as one of the main sources of energy first leads to the formation of a deficit in the body weight of the child, and then slows down growth with long-term cholestasis and insufficient food supply. Low growth rates in children with CKD may also be due to a lack of insulin-like growth factor-1 synthesis by liver cells [2].

FFA - free fatty acids; FA - bile acids; TG - triglycerides; CS - cholesterol; ApoB - apolipoprotein B; HM - chylomicrons.

Basic principles of assessment of nutritional status in children with cholestatic liver diseases

Assessment of the nutritional status of a child with cholestasis syndrome is based on anthropometric indicators, but it should be taken into account that these indicators are invalid when ascites or peripheral edema occurs. Correspondence between body weight, height, circumference and body mass index is based on centile curves developed by the World Health Organization (WHO) [10]. For very low and very low birth weight infants, the Intergrows scale should be used until 62 weeks post-conception, and then adjusted for age when switching to the WHO scale [11, 12].

Biochemical markers of nutritional status include serum total protein, albumin, glucose, cholesterol, triglycerides, urea, fat-soluble vitamins (A, D, E, K) and minerals (calcium, zinc, magnesium, etc.) [13] . Blood lipid levels should be taken into account when interpreting serum vitamin E test results. In hyperlipidemia, the level of vitamin E (mg/dL) in the blood may be elevated, so its ratio to total lipids (g/dL) should be evaluated. Deficiency of this vitamin is indicated by <0.6 mg/dL in children under 12 years of age and <0.8 mg/dL in older children and adults [14]. The main clinical manifestations of fat-soluble vitamin deficiency are presented in the table. 1.

Nutritional support

Children with cholestasis syndrome should increase their daily caloric intake, which is provided by increasing the amount of high-calorie foods with the addition of glucose polymers and partially degraded lipids. Growth spurts often require more protein in the diet. Supplementation of fat-soluble vitamins in these patients deserves special attention due to the development of their deficiency. Oral feeding is the priority. However, the frequent anorexia in children with CKD due to the presence of hepato- and splenomegaly, ascites, and portal hypertension may require nasogastric and parenteral nutrition [2].

Energy

Children with CKD exhibit a hypermetabolic state with increased energy expenditure, possibly due to intracellular activation of thyroid hormones by bile acids [15]. To correct the nutritional status, it is necessary to increase the daily calorie intake by 30-40%. In young children with CKD, the estimated energy requirement is 125-140% of the age norm, or 120-150 kcal/kg per day at baseline; for older children, it can vary up to 170%. A study by Maria Tessitore calculated a 29% higher energy requirement in AD patients than in healthy children [15]. In children with end-stage liver disease, energy requirements may increase to 150% of normal, especially with sepsis, cholangitis, or bleeding from esophageal varices [15].

Carbohydrates

For patients with CKD, carbohydrates are the main source of energy (about 60% of non-protein energy) because they are better absorbed than lipids or proteins. Short-chain glucose polymers (maltodextrin) are commonly used due to their low osmotic load, which prevents diarrhea. Starch supplementation is a possible alternative, but there is a risk of side effects such as bloating and diarrhea due to the enzymatic maturation of amylases in young children [15].

Squirrels

Currently, there are no specific recommendations for protein requirements in cholestasis, but in young children with CKD (under 2 years of age), the daily protein requirement is approximately 2-3 g/kg per day to maintain a positive nitrogen balance. . It is also known that increased oxidation of both exogenous

and endogenous proteins, which leads to muscle proteolysis, is found in patients with biliary atresia in the presence of repeated infectious processes, usually associated with cholangitis. Such children require more protein and energy to restore nitrogen balance, while the development of hyperammonemia up to 120 mmol does not require protein restriction [15]. A decrease in protein supplementation should be considered if blood ammonia levels >120 mmol/l and/or clinical signs of encephalopathy associated with liver failure and development of portal hypertension develop, bypass shunts occur.

Plasma aminograms of children with cholestasis syndrome may reveal low levels of branched-chain amino acids (BCAAs) and increased aromatic amino acids. This is due to the increased use of APCs in muscles, where they are an alternative substrate for gluconeogenesis under the influence of hyperinsulinemia, as well as impaired metabolism of aromatic amino acids in hepatocytes. There is evidence to suggest that diets rich in APCs may provide significant nutritional benefits in children with CKD [15]. In an animal model of cholestasis, oral administration of APC significantly improved nutritional status and growth. However, formulations containing APC and medium-chain triglycerides (MCT) are very expensive and not always available [2].

Formulas containing casein are acceptable for use in children with CKD. Hydrolyzed whey protein formulas can only be used temporarily in severe malnutrition in this group of patients. The palatability of food is important when feeding patients with cholestasis, otherwise children refuse to eat, which leads to a lack of nutrients and energy; Thus, mixtures based on protein hydrolyzate can be used only in selected clinical cases [1].

Children with normal parameters of body weight and length (height) should receive the same amount of protein as healthy children [1].

Oils

Lipids are the main source of energy required for growth, psychomotor development, and serve as a source of essential polyunsaturated fatty acids (PUFA) and fat-soluble vitamins. Absorption of long-chain triglycerides (LCTs) is significantly impaired in CKD due to impaired micelle formation [15]. Unlike DCTs, which require the dissolution of bile acid micelles, MCTs, which are highly water-soluble, are absorbed in the stomach and small intestine without the presence of bile acids. In addition, bypassing any changes in the intestinal wall, they enter the portal vascular system, from there to the liver and, without requiring carnitine as a transport system, enter the mitochondria in the metabolism of fatty acids (β-oxidation with subsequent energy). production) [18].

Therefore, diets containing MCTs have been successfully used to reduce steatorrhea, improve energy balance, and promote growth in children with chronic cholestasis [2]. An MCT content of 30 to 50% of total fat is recommended as optimal nutritional support for cholestasis [2 , 3 , 15], while high MCT content (>80%) may lead to essential fatty acid deficiencies [15]. Mixtures high in MCT and fat emulsions (FA) can be used as substrates. It should be noted that VEs are less palatable than other nutrients, but they are an important supplement due to their high energy value, low osmolarity and PUFA content.

Polyunsaturated fatty acids

Long-chain polyunsaturated fatty acids (LCPUFAs), including arachidonic acid and docosahexaenoic acid, play an important role in the growth and development of the brain and retina [19]. DPFAs are also precursors of eicosanoids - mediators of the immune system and platelet aggregation. Classical essential fatty acids, including linoleic and linolenic acids, are usually supplied through the diet and subsequently undergo further transformation in the liver and brain [2]. Breastfed babies get arachidonic and docosahexaenoic acids from breast milk lipids. Infants bottle-fed with standard milk formulas based on vegetable oils do not receive significant amounts of DPFA and depend on the use of their body stores or the endogenous synthesis of essential fatty acid precursors.

Absorption and metabolism of long-chain fatty acids are impaired in CKD. A combination of malabsorption of long-chain triglycerides and insufficient energy intake can lead to PUFA deficiency.

Because newborns have small reserves of linoleic acid, fat malabsorption in cholestasis increases the risk of developing PUFA deficiency. In addition, linoleic and linolenic acids that enter the body can be oxidized to produce energy. To date, there are no specific recommendations for the use of PUFAs in children with cholestasis. In children with CKD, supplemental PUFA (eg, soybean or canola oil) should exceed 10% of total energy. It is generally accepted that the minimum amount of linoleic acid needed to prevent PUFA deficiency is 3-4% of caloric intake. In clinical practice, it is desirable to use vegetable oils rich in PUFA and/or egg yolk as food supplements [2, 21].

Fat soluble vitamins and minerals

Malabsorption of fat-soluble vitamins is one of the main nutritional problems in CKD. It is known that the intestinal absorption of vitamins A, D, E and K depends on the adequate secretion of bile acids into the intestinal lumen (see Figure 1). When the intraluminal concentration of bile acids falls below the critical micellar concentration of 1.5-2.0 mmol / L, malabsorption of fat-soluble vitamins is often observed. The use of sorbents that bind bile acids (for example, cholestyramine) for the treatment of itching can worsen their absorption. In addition, esters of vitamins A and E require hydrolysis by bile acid-dependent intestinal esterase before absorption in the intestine. With cholestasis in newborns, rapid depletion of already low reserves occurs, which leads to biochemical and clinical signs of fat-soluble vitamin deficiency.

In addition, there are other factors that cause an increase in the amount of certain fat-soluble vitamins, for example, vitamin E. Among these factors is the increased lipid peroxidation observed in children with CKD, which leads to its deficiency. components of the antioxidant system [1]. Additional use of some fat-soluble vitamins (A, D, K) is effective in the formation of their deficiency, the use of vitamin E is not always effective [1]. The water-soluble form of fat-soluble vitamins is preferable, since absorption occurs directly in the enterocyte, without the formation of micelles. It is also worth noting that the absorption of other fat-soluble vitamins is improved when administered simultaneously with a water-soluble form of vitamin E (polyethylene glycol 1000-succinate) [18]. When severe deficiency of fat-soluble vitamins occurs, they are administered parenterally [22].

Recommendations for the use of fat-soluble vitamins in CKD are presented above (see Table 1) [1, 18, 21, 22].

Children with CKD may also have decreased levels of minerals, including selenium, zinc, magnesium, and calcium. Zinc and selenium are important components of the antioxidant system. The use of these minerals is carried out under the control of their serum composition [2, 23]. Iron should not be given routinely to children with CKD because iron deficiency is uncommon in them. On the other hand, when iron supplements are used off-label, oxidative stress and fibrogenesis are increased [24].

Methods

The methodology of this study on early diagnosis of intrahepatic cholestasis of pregnancy (ICP) involved a comprehensive approach combining clinical, biochemical, and imaging techniques to enhance diagnostic accuracy. Patients were initially screened based on clinical symptoms such as pruritus and abnormal liver function tests, with a focus on key indicators like elevated bile acid levels and liver enzymes. Biochemical analyses were conducted to measure bile acids and evaluate liver enzyme activity, providing foundational data for early detection of ICP. Imaging techniques, particularly Doppler ultrasound, were employed to assess blood flow in the maternal-fetal circulatory system, helping identify any abnormalities related to ICP. Additionally, fetal monitoring was implemented to observe any signs of distress or growth restriction, both of which are potential ICP complications. A statistical analysis followed to identify correlations between biochemical markers, ultrasound findings, and clinical symptoms, aiming to improve predictive markers for early ICP detection. Through this multi-faceted diagnostic approach, the study aimed to refine ICP diagnostic protocols, allowing for timely intervention and reducing the risk of adverse outcomes.

Thus, the main principles of therapeutic nutrition for children with progressive CKD is a high-calorie diet with the addition of additional sources of lipids, including MCT and PUFA, carbohydrates, proteins, fat-soluble vitamins and minerals. Currently, there are preformulas with a high MCT content (25-30%) on the Russian market, but they are intended for feeding premature babies and cannot be used as the main source of nutrition in full-term babies with cholestasis syndrome (Table 2).). MCTs are also present in formulas based on high protein hydrolysis (38-50%), but in this category of milk formulas, the total amount of protein equivalent and, accordingly, the total calories are reduced, which is important for children with cholestasis syndrome. frequent deficiency of physical development indicators. In mixtures based on highly hydrolyzed protein, the amount of fat-soluble vitamins is also reduced (see Table 2). In addition to the above, the taste qualities of highly hydrolyzed formulas are inferior to whole protein milk formulas, which are of little importance for feeding young children. Available literature data and our experience [25] show that it is necessary not only to increase the level of MCT in the compound formula, but also to increase the amount of total protein, except in cases of protein intolerance.

From the list of used literature:

1. Andryev S. et al. Experience with the use of memantine in the treatment of cognitive disorders //Science and innovation. – 2023. – T. 2. – №. D11. – C. 282-288.
2. Antsiborov S. et al. Association of dopaminergic receptors of peripheral blood lymphocytes with a risk of developing antipsychotic extrapyramidal diseases //Science and innovation. – 2023. – T. 2. – №. D11. – C. 29-35.
3. Asanova R. et al. Features of the treatment of patients with mental disorders and cardiovascular pathology //Science and innovation. – 2023. – T. 2. – №. D12. – C. 545-550.
4. Begbudiyev M. et al. Integration of psychiatric care into primary care //Science and innovation. – 2023. – T. 2. – №. D12. – C. 551-557.
5. Bo'Riyev B. et al. Features of clinical and psychopathological examination of young children //Science and innovation. – 2023. – T. 2. – №. D12. – C. 558-563.
6. Borisova Y. et al. Concomitant mental disorders and social functioning of adults with high-functioning autism/asperger syndrome //Science and innovation. – 2023. – T. 2. – №. D11. – C. 36-41.
7. Ivanovich U. A. et al. Efficacy and tolerance of pharmacotherapy with antidepressants in non-psychotic depressions in combination with chronic brain ischemia //Science and Innovation. – 2023. – T. 2. – №. 12. – C. 409-414.
8. Nikolaevich R. A. et al. Comparative effectiveness of treatment of somatoform diseases in psychotherapeutic practice //Science and Innovation. – 2023. – T. 2. – №. 12. – C. 898-903.
9. Novikov A. et al. Alcohol dependence and manifestation of autoagressive behavior in patients of different types //Science and innovation. – 2023. – T. 2. – №. D11. – C. 413-419.
10. Pachulia Y. et al. Assessment of the effect of psychopathic disorders on the dynamics of withdrawal syndrome in synthetic cannabinoid addiction //Science and innovation. – 2023. – T. 2. – №. D12. – C. 240-244.
11. Pachulia Y. et al. Neurobiological indicators of clinical status and prognosis of therapeutic response in patients with paroxysmal schizophrenia //Science and

innovation. – 2023. – T. 2. – №. D12. – C. 385-391.

12. Pogosov A. et al. Multidisciplinary approach to the rehabilitation of patients with somatized personality development //Science and innovation. – 2023. – T. 2. – №. D12. – C. 245-251.

13. Pogosov A. et al. Rational choice of pharmacotherapy for senile dementia //Science and innovation. – 2023. – T. 2. – №. D12. – C. 230-235.