DIAGNOSIS OF DYSFUNCTIONAL LIVER CONDITION IN NEWBORNS AND THEIR CORRECTION

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Liver dysfunctional state in newborns with prolonged physiological jaundice manifested only by disturbance of liver excretory functions and is a compensatory stage of liver syndromes. Usage of Hofitol in infants with prolonged jaundice showed a significant trend of faster dynamics of reducing in bilirubin and cholesterol levels, alkaline phosphatase activity, and earlier clinical resolution of conjugation jaundice.

Keywords: newborns, jaundice, liver dysfunction, Hofitol

Currently, there are serious problems with the quality of health of fetus and newborn. Compared to developed countries, Volodin (2004) noted that infant mortality rates remain high [2]. In-depth study of the biological processes that ensure normal functioning of fetus and adaptation of newborn to external environment, as well as identifying risk factors for health in this important period of life are the real basis of prevention of various pathological conditions in children. Reducing the frequency of dysfunctional states of newborn, we can create conditions for a better prediction of health and development in the future. According to Wolyniec (2005) and Dementyev (2001), one of the organs, which are very often involved in the pathological process in various diseases in newborns, is the liver [3, 5].

Liver dysfunction in infants may be a consequence of the impact of various factors, both infectious and non-infectious, during fetal life and after birth. Intrauterine infection and sepsis can cause liver damage with the development of hepatitis and liver failure [2]. In the occurrence of dysfunctional liver condition in newborns may play the role such various pathogens as: Listeria monocytogenes, Candida fungi, paroviruses, enteroviruses, cytomegalovirus (CMV), rubella virus, etc. [1].

The following non-infectious diseases may induce liver failure: antenatal hypoxia, congenital heart disease with decreased cardiac output syndrome, carotid apnoea. According to some reports, a cause of liver dysfunction in neonates may be inborn metabolic disorders [11], in particular oxidative phosphorylation [8]. In newborns, there are no clear standards for determining liver dysfunction, no information on the epidemiology of this complication, no studies on clinical features of liver dysfunctional state have been conducted, and there is no standard therapy.

Objective: differential analysis of clinical and diagnostic signs in detecting hepatic dysfunction in infants with prolonged physiological jaundice and, based on these studies, to standardize therapy.

Materials and methods of research

We examined 44 children at neonatal age of gestation from 32 to 40 weeks with hyperbilirubinemia of conjugation genesis, who had received treatment in the Department of Neonatal Pathology of the 1st clinic of TMA. Selection of patients for the study was carried out on the basis of clinical and biochemical parameters, indicating impaired liver function. The starting point of a sick newborn screening for the study was the high level of conjugated bilirubin in blood serum, which is regarded as a sign of liver damage at any age [4].

Further, we conducted a longitudinal (prospective) study, i.e. dynamic monitoring of sick children during the entire period of the disease, with daily clinical evaluation, laboratory parameters, instrumental methods. There were determined the following biochemical indexes in the biochemical analyzer: blood bilirubin, total protein, albumin, prothrombin index, the activity of transaminases and alkaline phosphatase. In order to elucidate an etiology of liver dysfunctional state, by immunoenzymatic method there were examined such infections as: CMV, HSV, mycoplasmosis, chlamydia, Candida fungi, toxoplasmosis, adenovirus, etc.

Results of research and their discussion

Signs of liver damage were: early appearance of jaundice syndrome (up to 24 hours of life), later growth of jaundice (after 3-4 days), long duration of hyperbilirubinemia (>3 weeks), increased concentration of bilirubin in blood (more than 256 mcmol/L), relative increase in direct fraction of bilirubin levels (15%), increased alkaline phosphatase activity. Liver ultrasound study showed in patients changes in the biliary system in form of thickening of gallbladder wall and heterogeneity of its contents.

The high level of indirect bilirubin in newborns as a result of increased erythrocyte hemolysis, or violation of its conjugation, causes toxic effects on many organs and tissues. Traditionally, neonatologists consider that indirect bilirubin is neurotoxic. However, there are other toxic effects of the biochemical substrate. Indirect bilirubin, as a hypolipidemic agent, in high concentrations has a toxic effect on kidney tissue, pancreas, heart, alters blood rheology. In particular, there is evidence that its concentration in blood serum

of more than 255 mcmol/L has a depressing effect on the immune system [6]. High concentrations of indirect bilirubin cause the violation of functional state of the left ventricular myocardium, which requires appropriate therapy [6]. Some researchers point to the possible impact of indirect bilirubin on the membrane of hepatocytes [7, 9]. From this standpoint, we can assume that changes in liver of neonates were due to toxic effects of indirect bilirubin in the physical and chemical properties of bile. One of the main reasons that causes a disturbance of bile formation is the change of cholesterol metabolism in hepatocytes or biliary excretion slowdown. Some researchers called this condition «the accumulation of bile syndrome» with some modifications in clinical terms – with the presence of hepatomegaly, hypocholic stool in a majority of newborns. In our interpretation, this phenomenon can be interpreted as a violation of excretory liver function (table).

The frequency of clinical-laboratory and instrumental parameters for liver function abnormalities in infants with prolonged physiological jaundice

Symptoms	Abs.	%
Jaundice (direct hyperbilirubinemia)	44	100
Indirect hyperbilirubinemia	26	59
Hepatomegaly	7	15,9
Ultrasound visualization of gallbladder and its contents	19	43,2
Ultrasound visualization of liver vascular system	3	6,8

Clinical-laboratory and instrumental data obtained in infants with prolonged physiological jaundice showed only a change of viscous-flow properties of bile: enhancement of its viscosity, sludge and reactive changes of the gallbladder.

One of the characteristics of children in newborn period is the relative immaturity of liver enzyme systems that ensure the capture of bile components of blood, their intracellular transport and excretion in the intrahepatic biliary system. Directly, in the biliary tract play a role the permeability of intercellular compounds, low cholekinetic activity of biliary system, and increase of reabsorption of bile components in intestine. Violations of the adaptation period of newborns, acute and chronic hypoxia, and associated perinatal pathology significantly lengthen the time of formation of these functional systems and can lead to an increase in the content of bile components in blood, increasing the size of liver. Underlying these changes may be transient and destructive changes in the bile ducts, increased permeability of the membranes of liver cells.

A variety of causes, influencing on liver, during prolonged course of physiological jaundice in newborns create tension in the functioning of the hepatobiliary system. In turn, this naturally leads to disturbances of synthesis, conjugation, enterohepatic circulation, and excretion of bile acids. Any of these violations are conditioned in infants with abnormal liver function modified viscous-flow properties of bile and reactive changes of the gallbladder.

Classically, cholestasis is considered to be a stagnation of bile in liver, but in newborns with prolonged physiological jaundice, apparently, dominated bile sludge, not its expressed stagnation. This assumption is indirectly confirmed by the absence of hepatomegaly and short duration of liver dysfunction in most patients.

Thus, we can conclude that the morphological substrate for liver dysfunction in the examined infants with prolonged physiological jaundice is the only violations of the viscous-flow properties of bile and reactive changes of the gallbladder. Changes in hepatocytes, if they present, had not structural, but functional character with benign course.

Some drugs used in neonates with icteric syndrome, contribute to passage disorder of bile. Using many of choleretic agents in neonates is limited. One of the restrictive aspects is that many cholagogue preparations contain dried bovine bile and, hence, the primary bile acids, whose formation at this age are so great.

To evaluate the effectiveness of pharmacotherapy for jaundice, patients were divided into two groups: 20 children of 1st group (control) received traditional treatment with phototherapy, infusion of 5% glucose solution, sorbents, Phenobarbital; 24 children of 2nd group (basic) additionally received Hofitol per os for 10 days, 3 times a day for 20 minutes before feeding of child in dosa of 0,3-0,5 ml. Hofitol increases bile flow, reduces intrahepatic cholestasis, enhances liver antitoxic function, influences on the liver enzyme system [10, 12].

In 72,7% of newborns of control group was marked a tendency to a longer course of jaundice syndrome (more than 3 weeks). Duration of jaundice frequently crossed the border of the first month of life (in 17,3%). Decrease of bilirubin in this group was slow, and by the 20th day of life this index remained high (187,3 ± 4,5 mcmol/L). In basic group, where children additionally received Hofitol, there was a significant trend of faster dynamics in reducing of bilirubin levels in serum (up to 112,4 ± 4,1 mcmol/L by the 10th day of life), and earlier clinical resolution of jaundice con-

jugation (by the 14-16th day). Along with the normalization of the levels of indirect and direct fraction of bilirubin in newborns in studied group, there was observed a positive dynamics of indicators of cholestasis syndrome: reduced activity of alkaline phosphatase, and cholesterol content in blood serum.

Conclusions.

1. Liver dysfunctional state in newborns with prolonged physiological jaundice manifested only by disturbance of liver excretory functions and is a compensatory stage of liver syndromes.

2. In order to correct violations of the viscous-flow properties of bile and reactive changes of the gallbladder in infants, it is recommended to use Hofitol per os for 10 days, 3 times a day for 20 minutes before feeding of child in dosa of 0,3-0,5 ml.

3. Usage of Hofitol in infants with prolonged jaundice showed a significant trend of faster dynamics of reducing in bilirubin and cholesterol levels, alkaline phosphatase activity, and earlier clinical resolution of conjugation jaundice.

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