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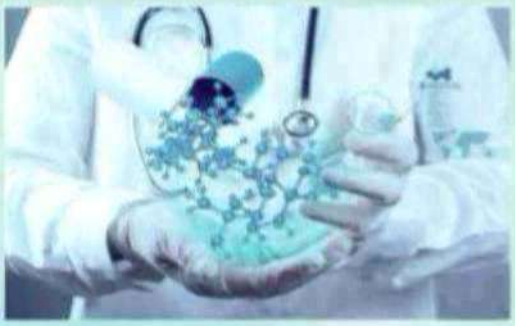

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THE ROLE OF GAMMA-GLUTAMYLTRANSPEPTIDASE IN THE DIAGNOSIS OF CHOLESTATIC SYNDROME IN CHILDREN

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✓ ***Resume***

In today's world, the search for and study of new biological markers that facilitate the early diagnosis of cholestatic syndrome in children remains relevant. These markers can serve as a laboratory tool for assessing the effectiveness of therapy, a prognostic marker of possible adverse clinical outcomes, and a significant criterion for risk stratification. This review presents the results of scientific research on gamma-glutamyltranspeptidase in cholestasis in children.

A threshold concentration of GGT >148.7 U/L has been established, indicating a high risk of developing CH in children.

Keywords: gamma-glutamyltranspeptidase, cholestasis, children.

BOLALARDA XOLESTATIK SINDROM TASHXISINI QO'YISHDA GAMMA-GLUTAMILTRANSPEPTIDAZANING ROLI

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✓ ***Rezyume***

Bugungi dunyoda bolalarda xolestatik sindromni erta tashxislashni osonlashtiradigan yangi biologik markerlarni izlash va o'rganish dolzarbligicha qolmoqda. Ushbu markerlar terapiya samaradorligini baholash uchun laboratoriya vositasi, mumkin bo'lgan salbiy klinik natijalarning prognostik marker va xavfni stratifikatsiya qilishning muhim mezoni bo'lib xizmat qilishi mumkin. Ushbu sharh bolalarda xolestazda gamma-glutamiltranspeptidaza bo'yicha ilmiy tadqiqotlar natijalarini taqdim etadi.

GGT ning chegaraviy konsentratsiyasi >148,7 U/L aniqlangan, bu bolalarda CH rivojlanish xavfi yuqori ekanligini ko'rsatadi.

Kalit so'zlar: gamma-glutamiltranspeptidaza, xolestaz, bolalar.

РОЛЬ ГАММА-ГЛУТАМИЛТРАНСПЕПТИДАЗЫ В ДИАГНОСТИКЕ ХОЛЕСТАТИЧЕСКОГО СИНДРОМА У ДЕТЕЙ

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✓ ***Резюме***

В современном мире поиск и изучение новых биологических маркеров, облегчающих раннюю диагностику холестатического синдрома у детей, остается актуальной задачей. Эти маркеры могут служить лабораторным инструментом для оценки эффективности терапии, прогностическим маркером возможных неблагоприятных клинических исходов и важным критерием стратификации риска. В данном обзоре представлены результаты научных исследований гамма-глутамилтранспептидазы при холестазе у детей.

Установлена пороговая концентрация ГГТ >148,7 Ед/л, указывающая на высокий риск развития холестаза у детей.

Ключевые слова: гамма-глутамилтранспептидаза, холестаз, дети.

Relevance

Recently, researchers have been attracted to the enzyme gamma - glutamyltranspeptidase (GGT), which has long been known in clinical medicine and whose elevation in the blood is associated with inflammatory liver diseases. Along with alanine aminotransferase and aspartate aminotransferase, GGT is recognized as an indisputable marker of hepatobiliary disorders [2,5]. The active center of gamma-glutamyl transpeptidase [6] participates in the regulation of the extracellular signal-regulated kinase (ERK) pathway and the p38 protein kinase (MAPK) pathway of the mitogen-activated protein kinase (MAPK) pathway.

GGTP participates in the regulation of the extracellular signal-regulated kinase (ERK) pathway and the p38 protein of the mitogen-activated protein kinase (MAPK) pathway, and is also involved in the regulation of cytokine synthesis, alphaTNF, alpha and beta interferons [4,8].

It is known that cholestatic syndrome characterizes gamma glutamyltranspeptidase enzymes located in the hepatocyte membrane, mainly near the biliary pole, as well as in the cells of the bile ducts. GGT is the earliest and most sensitive test marker for cholestasis syndrome. It is contained in hepatocytes in the cytoplasm and is associated with microsomal membranes, therefore, an increase in GGT in blood serum indicates cytolysis. Consequently, the development of jaundice in the neonatal period can be predicted based on GGT activity in umbilical cord blood [1,7].

Congenital cholestatic diseases in young children, especially in the first three months of life, are phenotypically similar to each other and to secondary manifestations of liver dysfunction due to prematurity, asphyxia, or sepsis: clinical signs of neonatal cholestasis may be identical (hypocholic stool, dark urine, jaundice, hypoglycemia). Some forms of neonatal cholestasis can be identified biochemically and genetically, or using imaging techniques [8].

Research objective: to study GGT activity in newborns and infants with jaundice syndrome.

Materials and methods

In order to predict the outcome of prolonged jaundice in newborns, we conducted a follow-up observation of children in the study group during the first 3 years of life. Thirty-five young children (2-comparative group) hospitalized for cholestasis syndrome at the BODMPMTS were examined. For comparative analysis, 30 healthy young children (2-control group) who visited the BODMPMC outpatient clinic were selected. Viral and autoimmune hepatitis (AMA antibody titer <1:40, ANA antibodies – negative) were excluded in the children selected for the study. A comparative assessment of the studied biochemical blood parameters in young children with a history of "prolonged jaundice" was performed. The study of GGT in the blood was carried out in the laboratory of Standard Diagnostics LLC in Bukhara. Blood samples were taken on the 14th day of life of newborns with prolonged jaundice and at the time of examination of young children. All children underwent biochemical blood analysis to determine the levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), bilirubin, and its fractions. Statistical analysis of the results was performed using methods of variational statistics.

Research results and discussion

The results of studying biochemical and immunological indicators in newborns and in the dynamics of young children who had prolonged jaundice showed a 1.5-fold decrease in AST in newborns with prolonged jaundice compared to the control group (27.8± 7.7 units/L and 42.1±5.7 units/L, respectively), an increase in total bilirubin levels by 2.37 times compared to the control group (28.1± 5.81 mmol/L), and an increase in ALP in newborns in the main group by 1.7 times compared to the control group ($p<0.005$) Fig. 1.

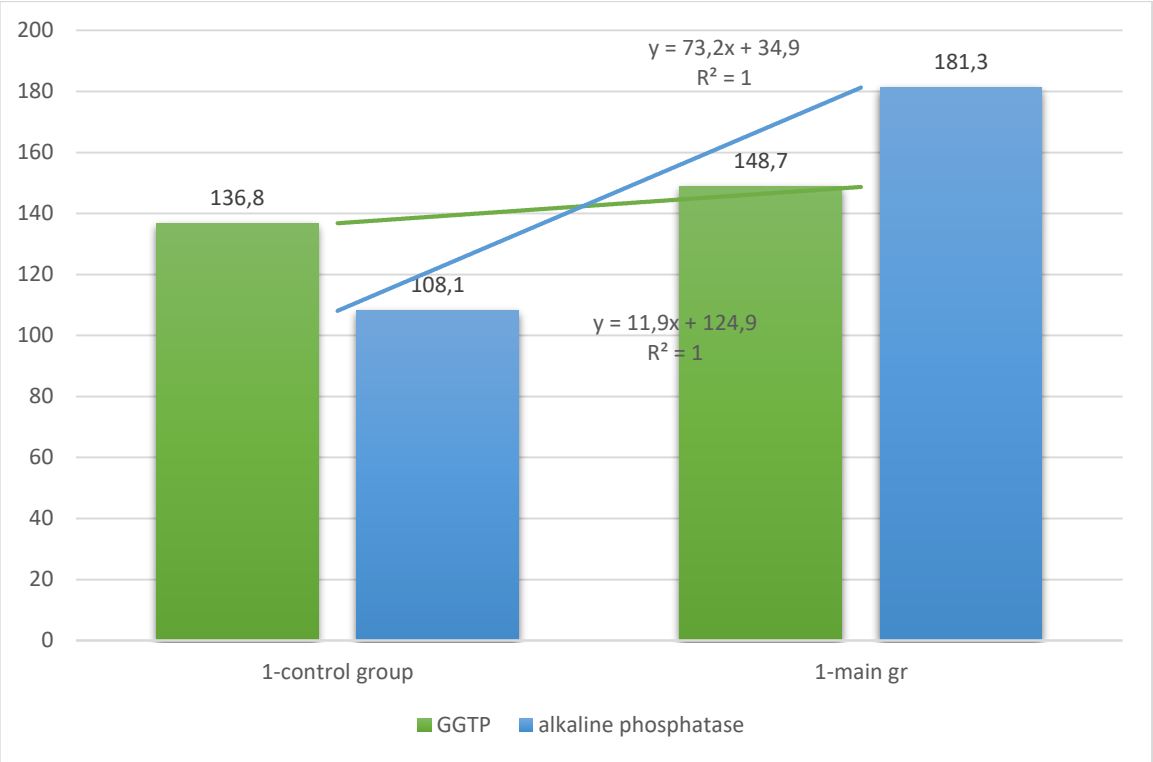

Figure 1. Biochemical indicators in newborns with prolonged jaundice

Although in newborns with prolonged jaundice, GGT and ALP levels were within the reference values, a significant increase in ALP to 181.3 ± 22.8 units/L was detected compared to the control group (108.1 ± 6.8 units/L, p<0.005). Newborns with prolonged jaundice have hyperbilirubinemia against a background of a 1.5-fold decrease in AST and a 1.7-fold increase in ALP, which predicts the risk of developing CH in children. A statistically significant increase in the levels of liver aminotransferases and total bilirubin was found compared to the control group: ALT—6.0 times, AST—7.6 times, total bilirubin—11.0 times, p<0.005.

A comparative assessment of blood biochemical parameters in young children with a history of prolonged jaundice showed an increase in liver transaminases and total bilirubin compared to the control group.

In young children with prolonged jaundice, a 10-fold increase in AST was found compared to the control group: 208.0± 52.3 U/L and 27.5± 8.9 U/L, respectively. The result confirms the phenomenon of cholestasis in young children. Analysis of liver damage markers for the differential diagnosis of the genesis of CH showed an increase in GGT levels to 154.7± 18.9 in young children with CH compared to the control group - 13.9± 2.4 units/L, (P<0.01).

In the study in favor of CH, a 10-fold increase in GGT levels was found in young children compared to the control group of the same age, an increase in ALP levels compared to control values to 352.6± 53 units/L compared to the control group of 185.1±5.8 units/L, Fig. 2. Consequently, the data obtained show an active release of GGT in the blood serum in CH in young children, which indicates a risk of developing cholangitis and chronic hepatitis at an early age.

Thus, CH in children occurs against a background of hyperbilirubinemia with an imbalance in the synthesis of bilirubin metabolism indicators, an increase in ALP levels by 1.9 times, and GGT by 11.2 times, which predicts the risk of CH progressing to chronic hepatitis. At the same time, studying the level of GGT also makes it possible to conduct a differential diagnosis of extrahepatic jaundice from intrahepatic jaundice, which is important for accurate diagnosis and determining further management tactics for patients in this category.

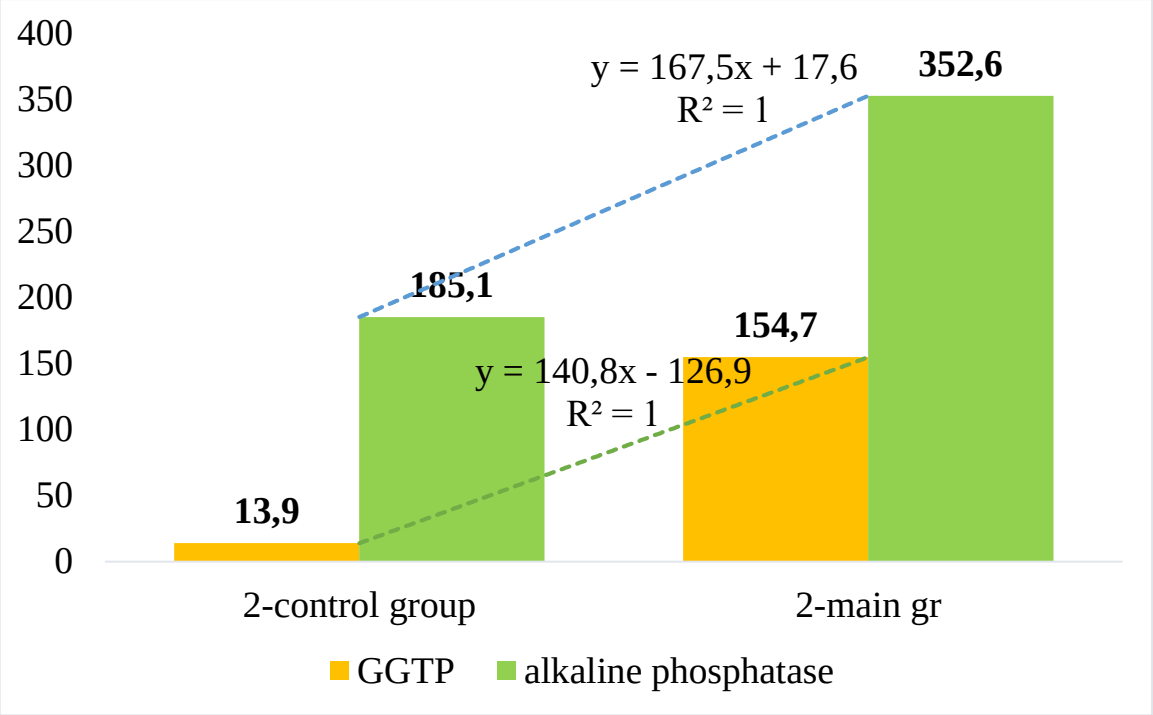

Figure 2. Biochemical indicators in young children with cholestasis syndrome

Conclusion

Based on the results of the study, it was established that effective indicators for predicting CH in children with prolonged jaundice are GGT and ALP. Their threshold concentrations are: GGT >148.7 U/L and ALP >181.3 U/L, which indicate a high risk of developing CH in children.

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