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BILIRUBIN METABOLISM AND PATHOMORPHOLOGICAL CHANGES IN THE HEPATOBILIARY SYSTEM IN ITS DISORDERS

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Abstract: bilirubin metabolism is one of the important stages of heme metabolism in the human body. Bilirubin is mainly formed as e result of the breakdown of erythrocytes, and it's subsequent biochemical transformations are closely related to liver function. Under normal conditions, bilirubin is processed in the liver and excreted from the body through bile. Any disturbance occurring at any stage of this complex process leads to an increase in bilirubin levels in the body, that is, hyperbilirubinemia. Disorders of bilirubin metabolism have a direct impact on the structural and functional state of the hepatobiliary system – the liver and bile ducts. As a result, various pathomorphological changes are observed in this system, including damage to hepatocytes, bile stasis (cholestasis), and occumulation of pigments in tissues. These changes lead not only to impairment of liver function but also to disruption of metabolic processes throughout the body.

The aim of this article is to study and analyze the pathomorphological changes occurring in the hepatobiliary system as aresult of disorders in bilirubin metabolism

Keywords: bilirubin, hyperbilirubinemia, hepatobiliary system, cholestasis, jaundice, liver diseases.

Introduction

Bilirubin metabolism is an important final stage of heme metabolism in the body, and includes complex biochemical processes associated with the processing of heme, which is mainly formed as a result of the physiological breakdown of erythrocytes. This process consists of several stages, which end with the conversion of heme to biliverdin, and then to free bilirubin, its uptake by the liver, conjugation and excretion through the bile. Violations occurring at any stage of the bilirubin metabolism process lead to the development of pathological conditions in the body.

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The hepatobiliary system is considered the central link in bilirubin metabolism, and its main function is to neutralize bilirubin and remove it from the body. Liver cells play an important role in the uptake of bilirubin, its conjugation with glucuronic acid into a water-soluble form, and its excretion through the bile ducts. Therefore, any functional or structural changes in the hepatobiliary system lead to disruption of bilirubin metabolism.

Bilirubin metabolism disorders are often manifested in clinical practice by jaundice syndrome, which is divided into hemolytic, hepatocellular and obstructive types according to its origin. Each type has its own pathogenesis and is accompanied by different pathomorphological changes in the hepatobiliary system. For example, in hemolytic jaundice, increased erythrocyte destruction is observed, in hepatocellular jaundice, damage to liver cells predominates, and in obstructive jaundice, obstruction of the bile ducts is the main factor.

Relevance of the problem. Bilirubin metabolism disorders today occupy an important place among hepatobiliary system diseases and are one of the most urgent problems in clinical and pathomorphological terms. Jaundice syndrome, which occurs as a result of impaired bilirubin metabolism, reflects not only the degree of liver dysfunction, but also manifests itself as an important diagnostic sign of many systemic changes in the body. These processes require special attention, especially in modern medicine, due to the increasing incidence of liver diseases, hemolytic conditions, and hereditary enzyme pathologies.

In recent years, the global health system has been witnessing a widespread occurrence of hepatobiliary pathologies, including viral hepatitis, alcohol- and drug-induced liver damage, as well as liver diseases associated with metabolic syndrome. This leads to an increase in the number of disorders associated with bilirubin metabolism. The problem of distinguishing physiological and pathological jaundice in the neonatal period, as well as early detection of subclinical hepatobiliary diseases in adults, remains relevant.

In the pathogenesis of bilirubin metabolism disorders, functional insufficiency of liver cells (hepatocytes), obstruction of the bile ducts, and increased erythrocyte breakdown play a key role. As a result of these processes, various pathomorphological changes develop in the hepatobiliary system, including hepatocyte dystrophy, necrosis, intrahepatic cholestasis, fibrosis, and cirrhosis, which can lead to serious complications. A thorough study of these changes is important not only for understanding the nature of the disease, but also for making the correct diagnosis and developing effective treatment measures.

Despite the development of diagnostic methods, a comprehensive assessment of the pathomorphological basis of bilirubin metabolism disorders, especially the differential analysis of changes occurring under the influence of various etiological factors, has not been sufficiently studied. Therefore, there is an increasing need for a systematic study of morphological changes in the hepatobiliary system, their correlation with clinical manifestations, and their integration with modern diagnostic criteria.

In this regard, the study of pathomorphological changes occurring in the hepatobiliary system in bilirubin metabolism disorders, the identification of their mechanisms, and their application in clinical practice are among the urgent tasks of modern medicine.

Bilirubin metabolism. Bilirubin is a product of heme catabolism, formed mainly from the breakdown of erythrocytes, partly from cytochromes and myoglobin. The main part of bilirubin is formed in the cells of the spleen and bone reticuloendothelial system. In these organs, bilirubin is bound to albumin and transported to the liver with the blood. In the liver, hepatocytes accept unconjugated bilirubin and bind it with glucuronic acid using the enzyme UDFGK-bilirubin transferase. Glucuronic acid binds to the carboxyl groups of propionol residues, forming bilirubin glucuronides. Conjugation with glucuronic acid changes the properties of bilirubin.

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Bilirubin is insoluble in water, therefore it is transported in the blood bound to albumin. Bilirubin glucuronide is soluble in water and is easily excreted in the bile. Bilirubin is toxic to the brain, while bilirubin glucuronate is not toxic. In the intestine, glucuronic acid is hydrolytically cleaved from bilirubin glucuronides by bacterial enzymes. The newly formed bilirubin is sometimes re-conjugated with double bonds, forming two groups of products: urobilinogens and stercobilinogens. The main part (95%) of these substances is excreted with feces. The rest is reabsorbed from the intestine into the blood and enters the liver through the portal vein, where it is broken down into di- and tripyroles. A very small amount of stercobilinogen is absorbed through the hemorrhoidal veins, enters the general bloodstream and is excreted through the kidneys. Urobilinogen and stercobilinogen are colorless substances. After being excreted from the body with feces and urine, they are oxidized by atmospheric oxygen and turn into yellow urobilin and stercobilin.

Hyperbilirubinemia. Hyperbilirubinemia is a pathological increase in the amount of bilirubin in the blood, which is externally manifested by a change in skin color (jaundice). Normally, the level of this pigment should not exceed 20.5 μmol / l, and higher indicators indicate the presence of liver dysfunction.

The causes of hyperbilirubinemia can be physiological and pathological. Physiological causes include uncontrolled intake of certain drugs, prolonged starvation, and immaturity of metabolic processes in newborns. In newborns, increased bilirubin in the first days of life is usually harmless and often passes without treatment within the first week. If a resource conflict occurs between mother and child, the baby may develop hemolytic jaundice. In this case, jaundice lasts longer and, unlike physiological jaundice, is more dangerous and requires treatment.

Pathological causes include liver diseases (cirrhosis, which develops due to hepatitis viruses or chronic alcoholism), biliary tract diseases (due to gallstone disease), oncological diseases (tumors of internal organs that provide bile flow), genetic diseases (for example, Gilbert's syndrome), chronic diseases of the abdominal cavity, and injuries (accompanied by numerous hematomas).

Hemolytic (suprahepatic) jaundice. When erythrocytes are broken down too quickly, bilirubin is produced in large quantities, and its rate of conversion to glucuronides in the liver and its excretion into the intestine increases. However, the rate of bilirubin formation may exceed the rate at which the liver removes it from the blood. As a result, the concentration of bilirubin in the blood increases, and the excretion of stercobilinogen in the urine increases. The spleen enlarges. In this case, the color of the urine does not change, the color of the feces becomes dark brown. The skin color becomes bluish-yellow.

Jaundice associated with liver cells. This type of jaundice occurs in infectious diseases such as viral hepatitis, yellow fever, malaria, Weil's disease. In this case, liver cells are damaged, and as a result, bile production decreases. In addition, as a result of damage to the liver parenchyma, bile is released not only into the bile ducts, but also into the blood. Urobilinogen increases in the urine and becomes orange in color. The color of the feces becomes brown. The skin becomes yellow.

Obstructive (subhepatic) jaundice. When the bile ducts are blocked (tuberculosis of the bile ducts, tumor of the head of the pancreas, blockage of the bile ducts by stones), bile does not pass into the intestine. Hepatocytes continue to produce bile. As a result, bile begins to pass into the blood. The concentration of direct and indirect bilirubin in the blood increases. Direct bilirubin,

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being a water-soluble and low-molecular substance, is filtered into Bowman's capsule and excreted with urine. Since bilirubin does not pass into the intestine, there are no urobilinogen and stercobilinogen in the urine. The color of the urine becomes dark brown (beer color). The feces become discolored ("dog feces color"). The skin becomes saffron-yellow.

The purpose of the study: to determine the direct impact of disorders occurring at different stages of bilirubin metabolism on the liver parenchyma and biliary tract system. In this case, the degree of damage to hepatocytes, their morphological reconstruction, as well as changes in intracellular structures are systematically assessed. In particular, the dynamics of the development of dystrophic processes, foci of necrosis and signs of regeneration are considered an important direction. Also, the degree of accumulation of bile pigments in hepatocytes and bile capillaries, their effect on cell activity, and the mechanisms by which these processes lead to subsequent fibrotic changes are analyzed. The correlations between clinical and laboratory indicators of the pathomorphological changes that occur are determined. In this case, the correlation between the level of bilirubin fractions and structural changes in liver tissue is analyzed. This approach creates an important scientific basis for assessing the severity of the disease and prognosis.

Pathomorphological changes that occur as a result of bilirubin metabolism in the hepatobiliary system include the following.

1. Hepatocyte damage.

Degeneration is a reversible change that occurs as a result of a violation of the metabolic processes of hepatocytes. In these processes, water accumulation inside the cell, swelling of the cytoplasm, and the formation of vacuoles are observed. There is also granular degeneration, in which small granules appear in the cytoplasm, which is associated with mitochondrial dysfunction. Pigmentary degeneration is characterized by the accumulation of bilirubin and other pigments and is important in cases of jaundice.

Necrosis is the irreversible death of hepatocytes, which occurs as a result of severe damage.

Fatty dystrophies are characterized by the pathological accumulation of triglycerides in hepatocytes.

2. Cholestasis.

Bile stagnation is the accumulation of bile in the bile ducts inside hepatocytes. This process is usually associated with functional disorders in hepatocytes, and even if bile synthesis is normal, its ability to secrete it decreases.

Expansion of bile capillaries - as a result of increased pressure in the bile capillaries and sinusoids, their expansion occurs. This expansion increases the decrease in bile flow along the liver lobules and negatively affects the metabolic activity of hepatocytes

Accumulation of bile pigments - mainly bilirubin accumulates in hepatocytes and bile ducts. This accumulation is manifested by the formation of pigment vacuoles in the cells and is clinically expressed by jaundice.

3. Fibrosis and cirrhosis.

Connective tissue hyperplasia – as a result of prolonged hepatocyte damage and cholestasis, collagen and extracellular matrix elements increase in the liver parenchyma.

Liver architectural dysfunction – as a result of connective tissue hyperplasia, the liver architecture is disrupted. The normal structure between the lobules is lost.

4. Pigmentation

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Bilirubin accumulation in tissues – bilirubin diffuses through the blood to the tissues. As a result, bilirubin accumulates in the cells and extracellular matrix. Pigment vacuoles are formed in the tissues.

Yellowing of the skin and mucous membranes – manifested by the accumulation of bilirubin in peripheral tissues. The skin, conjunctiva, lips and mucous membranes turn yellow. The degree and extent of jaundice are important clinical signs in assessing the severity of the disease and determining the treatment strategy

In recent years, advances in molecular biology, genetics, and clinical biochemistry have allowed us to consider bilirubin metabolism not only as a simple pigment metabolism, but as a complex regulatory system. Separate determination of direct and indirect bilirubin fractions is important in differential diagnosis. For example, an increase in indirect bilirubin is more likely to indicate hemolytic processes, while an increase in direct bilirubin is associated with liver cell damage or cholestasis. Today, several highly accurate methods are used to assess the hepatobiliary system.

Biochemical blood test is the most basic and widely used method, allowing to determine several parameters. For example, total bilirubin and its fractions, alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyltransferase (GGT). These parameters are used to assess the degree of liver cell damage, the presence of cholestasis and metabolic disorders.

Ultrasonography (USG) is a non-invasive and safe method that allows to determine the size of the liver, liver structure, condition of the bile ducts and gallstones. With the help of modern USG devices, even minimal structural changes can be detected.

Computed tomography (CT) and magnetic resonance imaging (MRI) provide high-resolution images and are important in the detection of tumors, fibrosis, cirrhosis, and biliary obstruction. In particular, MRI-based MR cholangiopancreatography (MRCP) allows for non-invasive evaluation of the biliary tract.

Liver biopsy is one of the "gold standard" diagnostic methods, allowing for the detection of morphological changes at the hepatocyte level. Biopsy accurately assesses the degree of inflammation, fibrosis, cirrhosis, and pigment accumulation.

According to molecular genetic studies, genetic tests have been widely used in recent years to detect hereditary hyperbilirubinemias such as Gilbert's syndrome and Crigler-Najjar syndrome. This contributes to the development of individual (personalized) treatment approaches.

Due to its clinical significance, assessment of bilirubin metabolism is important not only in diagnosis, but also in determining the prognosis of the disease. For example:

1. A sharp increase in bilirubin levels may indicate the development of liver failure.
2. Dynamic monitoring allows you to assess the effectiveness of treatment.
3. Monitoring bilirubin levels in the neonatal period is important for preventing encephalopathy.

Also, bilirubin levels are one of the main criteria for determining the severity of liver diseases in many clinical scoring systems (for example, Child-Pugh classification).

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Modern studies show that bilirubin also has antioxidant properties, and its low physiological increase may protect against some cardiovascular diseases. This indicates the need to consider bilirubin not only as a pathological marker, but also as a biologically active substance.

Conclusion. Bilirubin metabolism is a process that is being studied very deeply in modern science. Since this process is inextricably linked with all organ systems, its disruption causes changes in the body. A comprehensive study of bilirubin metabolism allows for early diagnosis of hepatobiliary diseases. A deep study of the process is important not only for theoretical but also for practical medicine.

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