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Chronic Toxic Hepatitis and Features of Structural Changes in the Small Intestinal Mucosa

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Abstract: The article presents literature data on the study of the effect of chronic toxic hepatitis on the structural and functional features of the small intestine of rats, and considers the prospects for further research in this direction.
Key words: small intestine, chronic hepatitis, enterocytes, enzymes.

Relevance: As a result of the improvement of diagnostic methods, it was revealed that liver damage constitutes a significant proportion among other diseases of internal organs. At the same time, a significant part of all liver diseases is accounted for by toxic lesions [1, 2, 3, 8]. They are caused by chemicals widely used in industry and agriculture [4, 7, 19]. There are also substances of plant origin with a pronounced hepatotoxic effect, which include heliothrin, synthesized at the Institute of Chemistry of Plant Substances of the Academy of Sciences of the Republic of Uzbekistan and widely used in experimental studies in order to reproduce an adequate model of toxic hepatitis [4, 18 , 32, 33, 34]. The relevance of the problem of hepatitis in our region is due to the fact that despite the ongoing medical and preventive measures, the pathology of the hepatobiliary system still reaches high values [4, 44]. This situation is aggravated by the fact that chronic hepatitis reaches high numbers among women of childbearing age, and this, in turn, negatively affects the development of offspring, namely, the development of their immune, digestive systems and, in general, the development of offspring [5, 6, 22, 23, 24, 25, 26, 27, 30, 31, 39, 42, 45].

A number of researchers [4, 16, 18] identify structural changes in the liver that occur with heliothrine hepatitis with changes observed in the liver with viral hepatitis B. Morphologically, heliothrine hepatitis, in contrast to hepatitis caused by CC14, is characterized by more severe changes that progress despite the abolition of hepatotropic poison. With the progression of the process, the authors note the loss of the lobular structure, the appearance of foci of hyperplasia, as well as giant hepatocytes with large nuclei. Subsequently, with the formed cirrhosis, they noted the development of various calibers of false lobules surrounded by fibrous tissue.

With a long-term effect of heliothrin on the structure of the liver, it has been established [4, 7, 8, 16, 18]. showed that 40-day seeding leads to pronounced disorders of the inflammatory-dystrophic nature. Morphological changes in the liver in heliothrine hepatitis of 60- and 90-day duration were more severe and manifested by a complex of structural disorders characteristic of cirrhosis (presence of bridging necrosis, proliferation of connective tissue, formation of false lobules).

To date, a significant number of works have accumulated that testify to violations of cellular and humoral immunity in diseases of the digestive system [42, 46, 48]. At the same time,

a number of researchers assign a large role in the immune reactivity of the digestive system to the liver, where a number of immunoregulatory factors are synthesized, mainly immunosuppressive, acting not only in the liver itself, but also in the blood, causing the development of immunological reactions of the whole organism. On the other hand, bile, participating in the transport of secretory IgA, provides local immunoreactivity in the mucosa of the gastrointestinal tract. In the local immunoreactivity of the digestive organs, the most effective even is secretory IgA, the fraction of which is closely associated with nonspecific defense mechanisms.

In liver diseases, there is a violation of IgA clearance, which leads to a breakdown in the defense mechanisms of the mucous membranes of the digestive tract. Antigens that have overcome protective barriers and penetrate into the bloodstream are included in the composition of immune complexes that enter the intestine through the biliary tract, simultaneously being inactivated by bile. This mechanism makes it possible to remove antigens from the circulation with the least possible development of a systemic immune response [4, 13, 16].

Even in the "Canon" of medical science, Abu Ali Ibn Sina, describing diseases of the liver, noted that when liver tissue is damaged, blockage of blood vessels and a violation of the secretion of its juices cause a change in the digestive process in the intestine due to its secondary involvement in the disease. In the chapter on liver diseases, he gave a detailed, at that time, differentiated picture of enterocolitis of hepatic origin due to various causes. Clinical and experimental observations in various types of pathology of the hepatobiliary system confirmed the fact of the conjugated reaction of the liver and intestines. In diseases of the hepatobiliary system, disturbances in the structure and function of the intestine are clearly manifested due to the syndrome of bile acid deficiency [46, 48].

Morphological changes in the mucosa of various parts of the small intestine are of the same type and were found even in cases where a favorable course of pathological processes in the hepatobiliary system was clinically noted and patients did not show characteristic complaints from the intestines [13, 19, 20, 21].

In chronic hepatitis and cirrhosis of the liver, the most significant morphological changes are atrophic changes in the intestinal mucosa of varying severity, accompanied by an increase in the number of goblet cells, increased mucin formation of the epithelial lining, up to the formation of cysts. In the connective tissue of the submucosa, along with fibrous changes, there is a dense infiltration of lymphoplasmacytic elements.

Studying the kinetics of cell populations of the epithelium of the small intestine in chronic hepatitis and cirrhosis of the liver, a number of authors explain the atrophy of the intestinal mucosa by a violation of the dynamic balance between the production of cells in the crypts and their extrusion on the villi. The decrease in the proliferative pool of the crypt epithelium is due both to a decrease in DNA-synthesizing cells and cells entering the mitosis phase. The deceleration of proliferative potencies is accompanied by impaired differentiation and increased extrusion of dystrophically altered epithelium, which leads to shortening of the villi and a decrease in the thickness of the mucous membrane [10, 11, 12].

Ultrastructural studies of intestinal epithelial cells in hepatitis and cirrhosis of the liver revealed dystrophic disorders of intracellular structures. At the same time, the main changes were a decrease in the number of ribosomes, a decrease in the shape and height of microvilli, a weak development of the glycocalyx on the apical parts of the cells, as well as a decrease in the diameter and swelling of mitochondria with a violation of their structure. At the same time, the development of the Goldki complex with the presence of a large number of vacuoles was

observed in differentiated cells of the villi. A decrease in the height of microvilli and their reduction are regarded as a morphological equivalent of impaired membrane digestion [13, 14].

Experimental studies of the state of the duodenum and small intestine in hepatitis reproduced by CC14 and heliothrin revealed, along with atrophy of the mucous membrane, changes in the morphometric parameters of the crypt-villus, accompanied by inhibition of the secretory, absorption and enzyme excretory functions of the intestine [4, 18].

In patients with viral and alcoholic hepatitis complicated by posthepatitis hyperbilirubinemia and liver cirrhosis, along with subtotal intestinal atrophy, an increase in the number of goblet cells was revealed [46, 48]. The absorptive epithelium covering the deformed villi of the small intestine in the zone of round cell infiltration showed a pronounced activity of acid phosphatase. The authors associate such a reaction of the mucous membrane of the small intestine with the toxic effects of products formed against the background of liver failure, but excluding the effects of the virus itself. In the pathology of the hepatobiliary system, not only structural changes in the intestinal mucosa were revealed, but also deep dysbacteriosis, manifested both in the qualitative and quantitative composition of the microbial flora of the studied departments [12, 13, 21, 46, 48].

The intestinal microflora under physiological conditions is involved not only in the formation of the immunobiological activity of the body, the synthesis of vitamins C, K and B, enzymes and the transformation of bilirubin and cholesterol, but also affects the structure of the mucous membrane [21]. Despite the exogenous and endogenous factors affecting the body, the composition of the intestinal microflora is relatively constant.

Bile and its acids, having a bactericidal and bacteriostatic effect, to a certain extent form the microecology in the digestive tract, as evidenced by studies by a number of authors [46] linking dysbacteriosis in the intestine with a weakening of the bactericidal properties of bile in various pathological conditions in the hepatobiliary system.

Long-term changes in the quantitative and qualitative composition of the microflora cause the development of dysbacteriosis, which creates a background for the penetration of pathogenic foreign microorganisms into the corresponding biotope and aggravates the course of the underlying disease. At the same time, the severity of dysbacteriosis correlates with the severity of the pathological process in the intestinal mucosa [20, 35].

An essential feature of the structure of the mucous membranes of the small intestine is the presence of close contact of lymphocytes with the epithelium. Using electron microscopy, it has been established [10, 11, 28, 29] that cells of the immune system (lymphocytes, eosinophils, macrophages) penetrate the basement membrane and penetrate into the epithelium, through which absorbable macromolecules or immune signals of immune system cells can also pass.

Strengthening of lymphoplasmacytic infiltration is regarded by a number of authors as a reaction of the intestinal mucosa in response to changes in automicroflora and the accumulation of toxic metabolic products in the lumen of the small intestine. Lymphoplasmacytic infiltration is considered as an activation factor of the immune process. Antibodies as inducers of cell cytolysis, having a direct damaging effect, are involved in the destruction of the epithelium. Primarily disturbed mechanisms of immunoregulation and proliferation in nonspecific inflammatory bowel diseases lead to disruption of regeneration processes with subsequent atrophy and autoaggression [16].

These data are also confirmed by other researchers [10, 16, 28, 29], who found a violation of the immunoregulatory function of lymphocytes of the lamina propria of the intestinal mucosa in its nonspecific inflammatory diseases.

Immunoregulation of morphodynamic processes reflects the regulatory effect of immune factors on cell renewal (cell differentiation and growth), as well as intercellular communications. At the same time, the pathologically altered structure of the small intestine can cause secondary immunodeficiency with a decrease in immunoglobulins associated with an increased loss of proteins due to exudative enteropathy [13, 18].

From the literature data it follows that the pathology of the hepatobiliary system changes the state of the intestine (duodenal, jejunum and ileum). However, the nature of structural disorders in various parts of the small intestine under chronic toxic effects has not been studied enough. The existing studies of the intestine [10, 11, 13] without the use of a complex of modern research methods cannot sufficiently deeply assess the essence of pathomorphological changes. At the same time, they do not make it possible to make a comparative analysis of morphofunctional changes in the proximal and distal parts of the small intestine, as well as to reveal the dynamics of their recovery during treatment.

Thus, on the basis of the foregoing, it can be concluded that a targeted and integrated approach is needed to study the mechanisms of structural and functional rearrangements in the duodenum, jejunum and ileum in chronic toxic heliotrine hepatitis, in addition, an increase in chronic toxic hepatitis among extragenital pathologies in women of childbearing age [35 , 40, 41, 48, 49, 50], which, in turn, can contribute to disruption of the development of the immune [5, 6, 37, 38] and digestive systems [9, 40, 43, 45] of the offspring for the purpose of subsequent study of intersystem and interorgan relationships and development of pathogenetically substantiated corrective therapy.

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