https://doi.org/10.48047/AFJBS.6.7.2024.2800-2815

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

INFLUENCE OF CHRONIC TOXIC HEPATITIS IN THE MATERNAL ON POSTNATAL MORPHOGENESIS OF THE GASTROINTESTINAL TRACT AND LIVER OF THE OFFSPRING

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Article History
Volume 6, Issue 7, 2024
Received: 25 Mar 2024
Accepted: 25 Apr 2024
doi:10.48047/AFJBS.6.7.2024.2800-2815

Abstract

The experiments were conducted on sexually mature female white mongrel rats weighing 170-190 g. The model of toxic hepatitis in the experimental animals was obtained by weekly administration of heliotrin at a rate of 0.5 mg/100 g of animal weight for 6 weeks. Ten days after the last injection, males were added to the females. The experimental animals were rat pups aged 3, 7, 14, 21 days, born and nursed by female mothers with chronic toxic hepatitis. These study periods are consistent with the generally accepted division of age periods in rats: neonatal period (1-5 days), suckling period (6-21 days). The work was carried out in accordance with the "Rules for Carrying Out Work Using Laboratory Animals". Animals were decapitated under ether anesthesia. The control group consisted of rat pups born and nursed by healthy intact females, which were given the corresponding amount of isotonic solution instead of heliotrin at the same time. For the study, pieces were taken from the stomach, small intestine, large intestine and liver of control and experimental animals on the 3rd, 7th and 21st days of postnatal life. The isolated material from the organs was fixed in a 10% solution of neutral formalin and Carnoy's fluid. The obtained material was subjected to morphological, morphometric and electron microscopic methods of study. In the course of experimental studies, the effect of chronic liver pathology in the mother on the postnatal morphogenesis of the gastrointestinal tract organs of the offspring was revealed. Experiments have shown that toxic hepatitis of the mother will negatively affect the postnatal growth, development and formation and the morphofunctional state of the vascular-tissue structures of the gastrointestinal tract and liver of the offspring, causing pathomorphological changes in their vascular-tissue structures, which subsequently lead to a lag, a delay in the processes of postnatal development and their formation. All this determines the need to develop scientifically based therapeutic and preventive measures in relation to children born and nursed by mothers with liver pathology, in order to prevent the consequences of development.

Keywords: toxic hepatitis, mother-offspring, gastrointestinal tract, liver, ontogenesis.

Introduction

The processes of formation and development of internal organs of mammals begin in utero and end after birth. However, various pathological factors of the internal and external environment during pregnancy negatively affect the processes of development of the structure and function of organs. The rapid development of the chemical industry, improper disposal of waste from chemical and nuclear production, the widespread use of pesticides and other pesticides not only caused negative shifts in the environment, but also became the cause of acute and chronic toxic poisoning and damage to organs and tissues of humans and animals [1,2]. It is known that the birth and upbringing of healthy children primarily depends on the condition of the mother. Hence the relevance and importance of studying the effect of maternal pathology on offspring. The issue of the effect of maternal liver pathology on pregnancy and offspring has long attracted the attention of doctors, since it is often one of the causes of death in young children and often leads to a variety of severe injuries. [3, 4]. The question of the influence of chronic toxic hepatitis of the mother on the morphological aspects of early postnatal development and formation of the organs of the gastrointestinal tract and liver of the offspring has not been sufficiently studied to date. [5,6,7,8,9,10,11].

Purpose of the research

The aim of our work was to study the early postnatal development and formation of the organs of the gastrointestinal tract and liver of the offspring, under conditions of chronic toxic damage to the liver of the mother.

Materials and Methods

The experiments were conducted on sexually mature female white mongrel rats weighing 170-180 g. The model of heliotrin hepatitis in the experimental animals was obtained by weekly administration of heliotrin at a rate of 0.5 mg/100 g of animal weight for 6 weeks. Ten days after the last injection, males were added to the females. The experimental animals were rat pups aged 3, 7, 14, 21 days, born and nursed by female mothers with chronic toxic hepatitis. These study periods are consistent with the generally accepted division of age periods in rats: neonatal period (1-5 days), suckling

period (6-21 days). The work was carried out in accordance with the "Rules for Carrying Out Work Using Laboratory Animals". Animals were decapitated under ether anesthesia. The control group consisted of rat pups born and nursed by healthy intact females, which were given the same amount of isotonic solution instead of heliotrin at the same time. For the study, pieces of stomach, small intestine, large intestine and liver were taken from control and experimental animals on the 3rd, 7th and 21st days of postnatal life. The isolated material from the organs was fixed in 10% neutral formalin solution and Carnoy's fluid. The obtained material was subjected to morphological, morphometric and electron microscopic methods of study. All the obtained morphometric data were subjected to variational-static processing using the Fisher-Student method as modified by Ermolaeva-Biryukova using a software package on a computer. Differences satisfying $P \leq 0.005$ were considered reliable.

Results and Discussion

During the experimental studies, a negative effect of chronic liver pathology in the mother on the postnatal morphogenesis of the gastrointestinal tract organs of the offspring was revealed. The experiments showed that toxic hepatitis of the mother will negatively affect the postnatal growth, development and formation and the morphofunctional state of the vascular-tissue structures of the gastrointestinal tract organs and the liver of the offspring, causing pathomorphological changes in their vascular-tissue structures, contributing to the lag, delay in the processes of development and formation. Studies have shown that the stomach of the rats of the control group on the 3rd day of postnatal life is thin; the mucous membrane is light pink with a grayish tint. The surface of the mucous membrane has a small number of low folds. All 4 membranes are distinguished in the wall of the stomach: the mucous membrane is the most powerful in its thickness, the submucosa (loose, unformed connective tissue), serous (mesothelium) and muscular (thin, consists of smooth muscles) membranes. The surface of the mucous membrane and gastric pits are covered with a single-layer cylindrical epithelium; the gastric pits are less deep than in the control (intact) rats. The stroma of the interpit, fundic and pyloric glands contains a small number of connective tissue cells. The fundic glands have the largest number of proper glandular cells

containing mucous secretory granules. These cells subsequently differentiate into additional cells. Edema and swelling, infiltration of mononuclear cells is detected in the mucous membrane. Electron microscopy in the parietal cells shows closure of intracellular secretory canals, delayed secretion (Fig. 1).

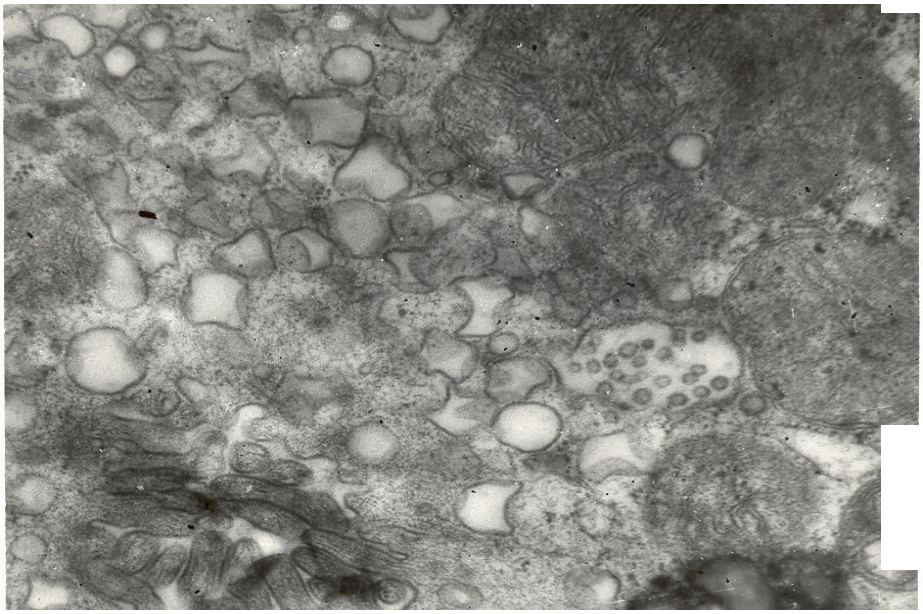

Fig. 1. Parietal cells of the gastric mucosa of 3-day-old rats. Closure of intracellular secretory canals, delay in secretion. TEM. 145000×

Some thinning of the small intestinal mucosa was observed compared to the control animals. The mucosa is represented by numerous folds and villi. Its cover consists of squamous epithelium, on the surface of which a moderate content of mucus is determined. Moderately pronounced dystrophic changes in the villi were established: their tortuosity, abundant vacuolization of the cytoplasm of the cells of the integumentary epithelium, deformation of its nuclei. In the stroma of the villi, foci of lymphohistocytic infiltration are often found. The length of the villi and the depth of the crypts, the number of mitotically dividing cells are less than in the control. In the apical part of the cytoplasm of the cells, there is a large number of secretory granules. A vacuolated Golgi complex, expanded profiles of the granular endoplasmic reticulum, a large number of mitochondria and vesicles are revealed. The submucosa is loosened in places due to edema and lymphohistiocytic infiltration. There are foci of connective

tissue micronecrosis. The vessels of this layer are sometimes filled with blood and with perivascular hemorrhages. The muscular layer consists of two layers: the inner one is circular, the outer one is longitudinal. It is edematous, swollen and loosened, has an uneven thickness. Vacuolated muscle cells are determined in places. Electron microscopy in the apical part of the cytoplasm of superficial pit cells reveals a large number of secretory granules, a vacuolated Golgi complex and expanded profiles of the granular endoplasmic reticulum of mucocytes. In the parietal cells there is a large content of mitochondria with a dense and increased content of vesicles; intracellular secretory canals are closed in the cytoplasm, a delay in secretion in the parietal cells is noted.

Ultrastructural studies of microvessels also indicate a tendency for some lag, a slowdown in the differentiation processes. (Fig. 2).

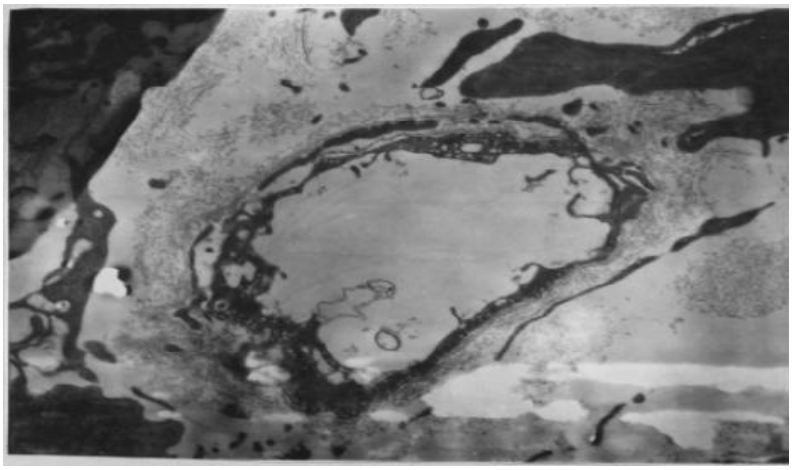

Fig. 2. Blood capillary of the jejunal mucosa of 21-day-old rats. The basement membrane is loosened, endotheliocytes are thinned. TEM. 10500×

In some places, the vessels in the mucosa are dilated. The architecture of the microvessels of all layers and sections of the stomach is unchanged. In some places, the vessel walls are edematous and tortuous. Dilation, tortuosity, and blood filling of the collecting venules were noted; the walls of individual vessels were edematous, with blurred contours.

In the mucosa of the small intestine, some thinning was observed compared to the control group of animals. The mucosa is represented by many folds and villi. Its cover

consists of squamous epithelium, on the surface of which a moderate mucus content is determined. In some places they are tortuous, with deformed nuclei. Lymphohistocytic infiltration foci are common in the stroma of the villi. The length of the villi, the depth of the crypts, and the number of mitotically dividing cells are reduced from the control value. Intraorgan vessels sometimes showed dilated, tortuous, full-blooded venous vessels with microstagnation phenomena. The study of postnatal development and formation of the small intestine of offspring born and nursed by mothers with CTG showed that maternal liver damage disrupts the morphofunctional state of the gastrointestinal tract, causing destructive changes in them: the growth rates of the components of the crypt-villus system were delayed, the number of mitotically dividing cells decreased, and the processes of proliferation and differentiation of cells slowed down. These changes subsequently led to a delay and lag in the growth and formation of vascular-tissue structures of the stomach and intestine. Although these disorders are gradually compensated for in the postnatal period of development, they were persistent in most animals and were observed until the end of the study.

Similar pathomorphological changes were also noted in the large intestine: in the early stages of development (3-7 days after birth) the wall of the large intestine is morphologically quite well expressed. The mucous membrane in the proximal sections is represented by pronounced villous folds of various shapes and sizes. The integumentary epithelium in all sections consists of flat cells, the nuclei of which are located in the basal part of the cells. The boundaries between the cells are unclear, the cytoplasm of the cells is wide and light. The crypts are shallow, their stroma is edematous, infiltrated with mononuclear cells. The morphometric indices of the crypt depth in the proximal, middle and distal sections of the intestine were somewhat less than the control figures. In the upper sections of the crypts, the bordered cells are swollen in places, their boundaries are erased. Deformation of the nuclei and vacuolization of the cytoplasm are observed in individual cells. The lumens of the crypts are dilated. The crypt stroma is loosened and infiltrated with mononuclear cells. The number of mitotically dividing cells is lower than in the control animals. Electron microscopically, the cell cytoplasm is light and contains a complex of organelles.

Swollen mitochondria with a light matrix are encountered. A vacuolated Golgi complex is detected, and lymphocytes are found between the epithelial cells. The basal membrane is of moderate density and somewhat thinned. The number of goblet cells exceeds the control values. They are at different stages of secretion. The indices of the microvessel distribution density in 3-7-day-old rats are somewhat lower than in the control animals. The wall of the venules is varicose and tortuous in places. The diameter of the lumen of the venous vessels is larger than in the control. Short elastic fibers and single smooth muscle cells are determined among poorly differentiated cells in their wall. Mucopolysaccharides and mast cells are concentrated around the vessels. Due to the close morphofunctional and neurohumoral relationship of the digestive organs with each other, pathological changes in one organ cause disturbances in another. After 14 days of postnatal development of the rats, the indices of the thickness of the mucous and serous-muscular membranes of the large intestine, the depth of the crypts and the number of cells in the crypts were less than in the control animals. The integumentary epithelium is flattened, in places with pycnotic altered nuclei. Detachment of the epithelial layer was observed. The cells are polymorphic, in places swollen, with light cytoplasm. Individual crypts in the middle and lower thirds are dilated, their stroma is infiltrated with lymphohistiocytic cells. In the middle and lower thirds of the crypts, a large number of goblet cells are observed, the total number of which exceeds the control figures. In the epithelial layer of the crypts, intercellular edema, vacuolization of the cytoplasm, with reduced microvilli are detected. In the submucosa and muscular membranes, there are areas loosened and infiltrated by mononuclear cells. Lymphoid tissue appears in the submucosa and crypt stroma. The serous membrane is a layer of mesothelial cells. They are located close to each other, their cytoplasm is fine-grained and relatively light. All of the above pathomorphological changes in tissue structures in all parts of the colon were often focal.

The studies after 21 days of postnatal life of animals showed that in some animals the revealed pathomorphological changes gradually leveled out, due to which the organ microstructure gradually approached the control groups, but the morphometric indices did not finally reach the control figures. However, in most animals the

pathomorphological changes persisted, and sometimes progressed. The morphometric indices of the wall of all the studied sections were lower than in the control animals. The crypt epithelium was represented by prismatic cells with and without borders, as well as a large number of goblet cells. In some places, the lumen of individual crypts in the middle and lower third was widened. The stroma of some crypts was infiltrated with lymphohistiocytic cells. The studies after 30 days of postnatal life of animals showed that in some animals the revealed pathomorphological changes gradually leveled out, due to which the organ microstructure gradually approached the control groups, but the morphometric indices did not finally reach the control figures. However, in most animals the pathomorphological changes persisted, and sometimes progressed. Morphometric indices of the wall of all studied sections are lower than in the control animals. The crypt epithelium is represented by prismatic cells with and without borders, as well as a large number of goblet cells. In some places, the lumen of individual crypts in the middle and lower third is widened. The stroma of some crypts is infiltrated with lymphohistiocytic cells. The formation of the muscular plate of the mucous membrane lags behind that of the animals of the control groups. The number of mitotically dividing cells in the proximal, middle and distal sections of the intestine is 1.5; 1.2 and 1.1 times lower than in the control. In the capillary network of the mucous membrane of the large intestine, tortuosity and some expansion of the diameter are noted. The efferent postcapillaries are widened and have a sinusoidal character. Several postcapillaries, merging, form venules, which have varicose dilations in some areas of the mucous, submucosa and serous-muscular membranes. Morphometric indices of the venule lumen diameter are greater than those of control animals. Aggregated blood cells are detected in their lumen; the basement membrane is edematous and loosened (Fig. 3).

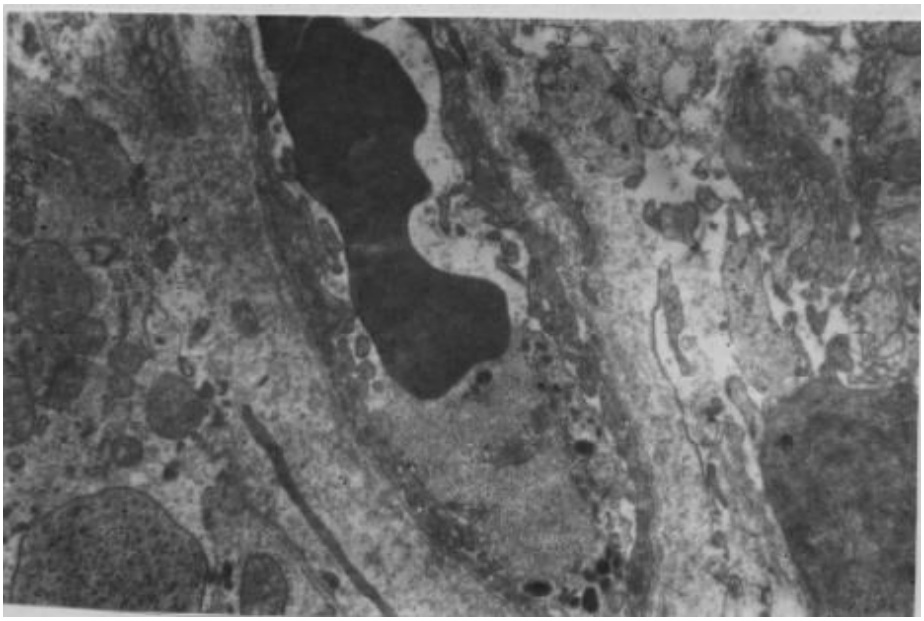

Fig. 3. Venule of the submucosa of the colon in 21-day-old rats. Aggregated blood cells in the lumen of the vessel. TEM. 10500×

It should be noted that all of the above morphological changes in the vascular-tissue structures of the small and large intestines were focal.

Significant disturbances were found in the microstructure of the liver in newborn rats (3-7 days). Hepatocytes were loosely and randomly located, separated by wide and full-blooded sinusoidal hemocapillaries. Hydrolytic dystrophy was observed in many hepatocytes. Pycnosis and lysis of nuclei were observed in individual cells. On the 3rd-7th day of postnatal development of rat pups born and nursed by mothers with chronic toxic hepatitis, the following picture was observed in the vascular-tissue structures of the liver: in the microstructure of the liver in newborn rat pups (3-7 days), hepatocytes were located loosely and randomly, separated by wide and full-blooded sinusoidal hemocapillaries. In some hepatocytes, hydropic dystrophy was noted, in individual cells, pyknosis and lysis of nuclei were observed. The size of hepatocytes increased 18.5 ± 0.8 compared to the parameters of the control group of animals (in the control 12.0 ± 0.4). The number of binuclear liver cells is relatively greater, 2.7 ± 0.3 (in the control 1.2 ± 0.04). The liver lobules and beams are poorly contoured. Electron microscopic examination revealed that the cytoplasm of liver cells was finely granular, and the nuclei of many hepatocytes were oval. Mitochondria were abundant, with an

electron-dense matrix. In some places, infiltration and expansion of sinusoidal hemocapillaries were detected in the interlobular connective tissue.

After 21 days of postnatal development, some increase in the severity of the pathomorphological changes described above was observed in the animals of the experimental group. In some places, against the background of a distinct beam-lobular structure of the liver, areas with disintegration of the liver parenchyma were detected, and liver cells were distributed randomly. Infiltration by mononuclear cells was observed in the interlobular connective tissue. In the animals of the control group, a distinct beam-lobular structure of the liver was noted at this time.

Electron microscopically, the nuclei of hepatocytes were round, often oval in shape, with two or three nucleoli located closer to the membrane of the nucleus. The nuclei are unchanged with a delicate network of finely lumpy chromatin. Kupffer cells are single. The Disse space is slightly expanded in places. In some centers of the lobules, a decrease in hepatocytes is noted, a slight increase in granulomas and small-cell nodules adjacent to the portal tracts is noted. The endoplasmic reticulum is often represented by vacuoles, vesicles of various sizes. The perilobular veins are full-blooded and around the liver triads the vessels are highly branched, a change in the angioarchitectonics and foci of capillarization are noted (Fig. 4).

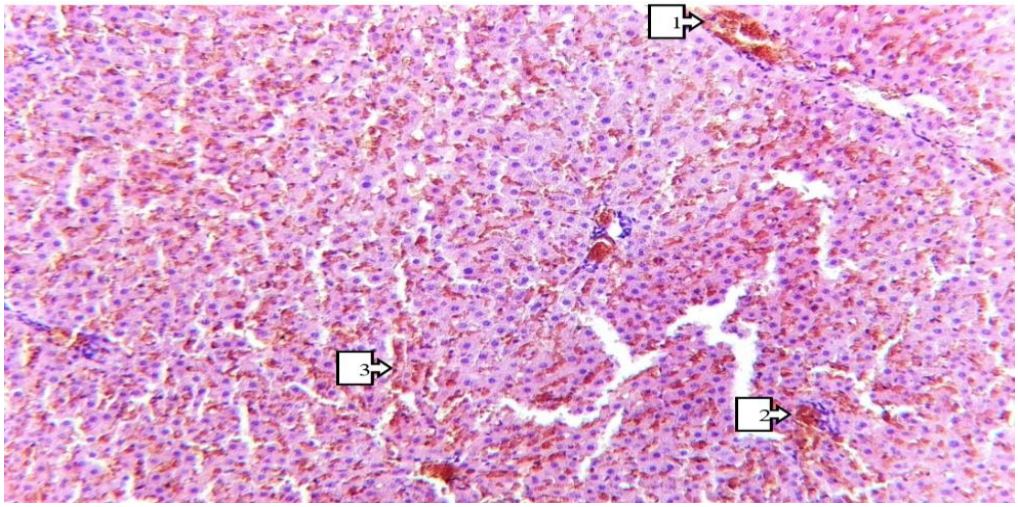

Fig. 4. Liver of rat pups on the 21st day of postnatal life. Perilobular veins are full-blooded (1) and around the liver triads the vessels are multi-branched (2), changes in angioarchitectonics and foci of capillarization are noted. Hematoxylin and eosin staining. 10x10.

Our studies once again prove that due to the close relationship of the functional system "mother-fetus", any pathology of the mother before and during pregnancy leads to pathology of the organs of the offspring not only in the prenatal, but also in the postnatal period of development.

Thus, the data of our studies showed that liver pathology in the mother will negatively affect the postnatal growth, development and formation and the morphofunctional state of the gastrointestinal tract and liver of the offspring. Analyzing these processes, we believe that the violation of the detoxifying function of the mother's liver is of great importance here. The liver of the fetus is not yet ready for sufficient detoxification of metabolic products. It is clear that in this case accumulation of substances (pyruvic acid, lactic acid, free radical oxidation products, metabolites, etc.) with cytotoxic effect is possible in tissues, including the liver. Damaging effect on the internal organs of the developing fetus can also be caused by such products that penetrate to the fetus when the permeability of the placenta is impaired, but are normally detoxified in the mother's liver and do not reach the fetus. [12,13, 14,15,16,17,18]. Consequences of such effects are observed already in the early postnatal period of development in the form of a gradual dystrophic process in the vascular-tissue structures of the organs under study. Another reason for pathomorphological changes in the offspring is apparently due to certain immunopathological shifts in the body, since protein products of decaying hepatocytes cause an autoallergic reaction, the possibility of such a mechanism is indicated by destructive changes in the internal organs of the offspring. In addition, the structural disorders of the digestive system organs and their microcirculatory bed in rats born to mothers with chronic hepatitis B may be a consequence of a deficiency of plastic and a number of biologically active substances for the fetus during the embryonic period of development. This deficiency occurs when the maternal liver function is impaired, placental insufficiency occurs, and when exposed to products of impaired metabolism. As a result of the suppression of the liver's antitoxic function, perverted metabolic products accumulate in the mother's blood, which affect the embryos during the intrauterine period of development. On the other hand, developing hepatocellular

insufficiency [19,20,21,22,23,24,25] leads to changes in the mother's body - this is reflected in a change in the quantitative and qualitative composition of the mother's breast milk, and subsequently these factors affect the processes of postnatal growth, development, and formation of the offspring's organs. The combination of the above factors, in our opinion, causes the disruption of histogenesis and morphogenesis in the fetus's body, gradually developing dystrophic processes in postnatal ontogenesis, slowing down and lagging behind the processes of growth, development and formation of organs and systems. Considering that the animals were implanted on the 10th day after the administration of the drug to the females (during this period there is no hepatotoxin in the blood of the females), we believe that the cause of the above pathomorphological changes in the vascular-tissue structures of the stomach, small and large intestines and liver is, first of all, the deficiency of plastic, trophic and energy material in the fetus during the intrauterine period of development, due to the pathology of the mother's liver, and not the direct effect of the hepatotropic poison on the fetus. At the same time, other factors are not excluded, such as a violation of the liver's antitoxic function and the resulting products of impaired metabolism and their metabolites in the mother's blood, entering the fetus's body through the placenta, a change in the quantitative and qualitative composition of the mother's breast milk. All this determines the need to develop scientifically based therapeutic and preventive measures to prevent pathology in children born and nursed by mothers with liver pathology.

Conclusion

1. Chronic toxic liver damage in the mother has a negative effect on the processes of postnatal development and the formation of tissue structures of the gastrointestinal tract and liver of the offspring.

2. Hepatotoxins introduced into the mother's body before pregnancy and formed in it during hepatitis, entering the blood and then into the mother's milk, contribute to the development of inflammatory-reactive changes in the vascular-tissue structures of the gastrointestinal tract and liver in the offspring's body in the early periods of life, postnatal development and growth.

3. Pathomorphological changes in the vascular-tissue structures of the gastrointestinal tract and liver of the offspring subsequently lead to a delay in the processes of postnatal formation and development of organs and systems as a whole.

4. All this determines the need to develop scientifically based therapeutic and preventive measures to prevent pathology in children born and nursed by mothers with liver pathology.

References

1. Шубина О.С., Киреева Ю.В. Морфологические особенности печени потомства белых крыс в условиях свинцовой интоксикации. //VII конгресс международ. ассоц. морфологов; Морфология. – 2006. – Т.129, №4. – С. 143. [Smekalina O.U., Bryuhin G.V. Morfofunktsionalnaya harakteristika endokrinnyih i tuchnyih kletok slizistoy obolochki dvenadtsatiperstnoy kishki potomstva samok kryis s hronicheskim esperimentalnyim porajeniem pecheni. Vestnik Ujnouralskogo gos. universtiteta. 2011; 26 (7): 120-124.
2. Яковлева Л.М., Любовцева Л.А. Морфофункциональные изменения подвздошной кишки крыс при интоксикации этанолом. Морфология. 2012; 141 (1): 62-65. [Yakovleva L.M., Lyubovtseva L.A. Morfofunktsionalnie izmeneniya podvzdoshnoy kishki kryis pri intoksikatsii etanolom. Morfologiya. 2012; 141 (1): 62-65.
3. Ильиных М.А., Брюхин Г.В. Структурно функциональное становление поджелудочной железы потомства животных с хроническим экспериментальным поражением гепатобилиарной системы различного генеза. Вестник Челябинского гос. педагогического университета. 2006; 4 (6): 113-123. [Ilinyh M.A., Bryuhin G.V. Strukturno funktsionalnoe stanovlenie podjeludochnoy jelezy potomstva jivotnyh s hronicheskim eksperimentalnym porajeniem gepatobiliarnoy sistemi razlichnogo geneza. Vestnik Chelyabinckogo gos. pedagogicheskogo universtiteta. 2006; 4(6): 113-123

4. Серышева О.Ю., Брюхин Г.В. Морфофункциональная характеристика эпителия крипт двенадцатиперстной кишки у потомства самок крыс с экспериментальным поражением печени. Морфология. 2013; 144(4): 36-41. [Serysheva O.U., Bryuhin G.V. Morfofunktsionalnaya harakteristika epiteliya kript dvenadtsatiperstnoy kishki u potomstva samok kryis s eksperimentalnyim porajeniem pecheni. Morfologiya 2013; 144(4): 36-41

5. Смекалина О.Ю., Брюхин Г.В. Морфофункциональная характеристика эндокринных и тучных клеток слизистой оболочки двенадцатиперстной кишки потомства самок крыс хроническим экспериментальным поражением печени. Вестник Южноуральского гос. университета. 2011; 26 (7): 120-124. [Smekalina O.U., Bryuhin G.V. Morfofunktsionalnaya harakteristika endokrinnyih i tuchnyih kletok slizistoy obolochki dvenadtsatiperstnoy kishki potomstva samok kryis s hronicheskim esperimentalnyim porajeniem pecheni. Vestnik Ujnouralskogo gos. universtiteta. 2011; 26 (7): 120-124.

6. Медведь В.И. Грицай И. Нарушение функций печени у беременных: Влияние на течение беременности, состояние плода и исход родов \\ Здоровье Украины. – 2015 –Спец. Вып. – С. 24-27 [Medved V.I. Gritsay I. Narushenie funktsiy pecheni u beremennyih: Vliyanie na techenie beremennosti, sostoyanie ploda i ishodov rodov\\ Zdorovie Ukrainyi. – 2015 –Spets. Vyip. – S.24-27

7. Воробёва В.А. Новопольцева Е. Г. Красильникова Н. Е. Особенности поражения ЖКТ у недоношенных при внутриутробных инфекциях и методы их коррекции // Вопросы современной педиатрии. – 2006; 4: 120-125. [Vorobieva V.A. Novopoltseva E.G. Krasilnyikova N.E. Osobennosti porajeniya JKT u nedonoshennyih pri vnutriutrobnyih infektsiyah I metodyi ih korrektsii // Voprosyi sovremennoy pediatrii. – 2006; 4: 120-125.

8. Буданов П.В. Стрижаков А.Н. Этиология, патогенез, диагностика и лечение внутриутробной инфекции // Вопросы гинекологии, акушерства и перинатологии. – 2010; 9(3): 61-71. [Budanov P.V. Strijakov A.N. Etiologiya, patogenez, diagnostika i lechenie vnutriutrobnoy infektsii // Voprosyi ginekologii, akushertsva i perinatologii. – 2010; 9(3): 61-71.

9. Горячёва Л.Г. Шилова И.В. Течение хронического гепатита В у детей, рождённых от матерей с HB-Вирусной инфекцией // Детские инфекции. – 2015. [Goryacheva L.G. Shilova I.V. Techenie hronicheskogo gepatita B u detey, rojdennyih ot materey s HB-Virusnoy infektsiey // Detskie infektsii. – 2015.
10. Kowalska-Kanka A. The concentrations of bile acids and erythropoietin in pregnant woman with intrahepatic cholestasis and the state of the fetus and newborn // Medycyna Wieku Rozwojowego. – 2013; 17(3): 103-109.
11. Bonney. J.H. Kwa M.E.-Aryee. Fatal hepatitis E viral infections in pregnant in woman in Ghana: a case series. // BMC Res Notes – 2012; 5: 478.
12. Knight L., Todd G., Stevens Johnson. Syndrome and Toxic Epidermal Necrolysis: Maternal and Foetal Outcomes in Twenty-Two Consecutive Pregnant HIV Infected Women // Plos One. 2015; 10(8): P. e0135501.
13. Chełchowska M, Gajewska J., Ambroszkiewicz J., Laskowska-Klita T. Exposition of pregnant women and their children on toxic effect of lead from tobacco smoke// Przeglad Lekarski. 2009; 66(10): 869-72.
14. Yin Y, Department of Obstetrics and Gynecology, the Third Affiliated Hospital of Sun Yat-Sen University, Guangzhou, Guangdong Province, China.//Plos One.-2017; 12(6): P. e0178671
15. Chen Zhao Z. Course-, dose-, and stage-dependent toxic effects of prenatal dexamethasone exposure on fetal articular cartilage development.//Toxicology Letters. 2018; 286: 1-9.
16. Mirderikvand N, Mohammadzadeh Asl B. Embryo toxic effects of depleted uranium on the morphology of the mouse fetus.//Iranian Journal Of Pharmaceutical Research. 2014; 13(1): 199-206.
17. Zhu Y, Pang Y. Association Between Chronic Exposure to Tobacco Smoke and Accumulation of Toxic Metals in Hair Among Pregnant Women.//Biological Trace Element Research. 2018 Mar 01.
18. Zhao Y. Zhang X. Viral hepatitis vaccination during pregnancy.//Human Vaccines & Immunotherapeutics . 2016; 12(4): 894-902.

19. Page C.M. Hughes B.L. Hepatitis C in Pregnancy: Review of Current Knowledge and Updated Recommendations for Management// Obstet Gynecol Surv. 2017; 72(6): 347-355.
20. Schanche M, Avershina E, Dotterud C. High-Resolution Analyses of Overlap in the Microbiota Between Mothers and Their Children.//Current Microbiology [Curr Microbiol] 2015 Aug; 71(2): 283-90.
21. Ban L., Gibson J.E., West J. Association between perinatal depression in mothers and the risk of childhood infections in offspring: a population-based cohort study.//BMC Public Health. 2010; 31(10): 799.
22. Avershina E; Storrø O. Johnsen R. Major faecal microbiota shifts in composition and diversity with age in a geographically restricted cohort of mothers and their children.// FEMS Microbiology Ecology. 2014 Jan; 87(1): 280-90.
23. Gurnee E.A., Ndao I.M; Gut Colonization of Healthy Children and Their Mothers With Pathogenic Ciprofloxacin-Resistant Escherichia coli.//The Journal Of Infectious Diseases. 2015; Dec 15; 212(12): 1862-8.
24. Lu L.L, Chen B.X. Maternal transmission risk and antibody levels against hepatitis B virus e antigen in pregnant women.//Int J Infect Dis] 2014 Nov; 28: 41-4.
25. Julsgaard M. Christensen L.A; Concentrations of Adalimumab and Infliximab in Mothers and Newborns, and Effects on Infection.//Gastroenterology. 2016 Jul; 151(1): 110-9.