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CHARACTERISTICS OF STRUCTURAL COMPONENTS OF INTRAHEPATIC BILIARY TRACTS IN HUMANS

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Among the most common diseases of the hepatobiliary system are chronic cholecystitis, cholangitis, gallstone disease, and post-cholecystectomy syndrome, which are increasingly prevalent. Gallstone disease affects more than 10 % of the adult population in various countries around the world. There is a doubling of the number of patients every ten years in all economically developed countries. This pathology is found in women 3–4 times more often than in men. The incidence of the disease increases with age. The intrahepatic bile ducts of humans consist of two layers: an outer adventitial layer and an inner mucosal layer. In the initial part of the liver's biliary system, the biliary pathways in the mucous membrane are composed of cuboidal epithelium resting on the basal membrane. In the middle section of the human biliary system, not only cuboidal but also columnar epithelial cells appear. In the terminal section of the biliary system, the number of columnar epithelial cells in the inner lining increases. Epithelial cells change their shape from cuboidal to columnar. The outer layer is composed of loose connective tissue, with fibroblastic cell rows and an intercellular substance containing collagen fibers and amorphous material.

Key words: liver, bile ducts, cholecystitis, gallstone disease.

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ХАРАКТЕРИСТИКА СТРУКТУРНИХ КОМПОНЕНТІВ ВНУТРІШНЬОПЕЧІНКОВИХ ЖОВЧНИХ ШЛЯХІВ ЛЮДИНИ

До найпоширеніших захворювань гепатобіліарної системи включають хронічний холецистит, холангіт, жовчнокам'яну хворобу та постхолецистектомічний синдром, які зустрічаються дедалі частіше. На жовчнокам'яну хворобу страждає більш ніж 10 % дорослого населення в різних країнах світу. Спостерігається збільшення кількості хворих у 2 рази за кожні десять років у всіх економічно розвинених країнах. У жінок дана патологія зустрічається у 3–4 рази частіше, ніж у чоловіків. Відмічається зростання частоти захворюваності з віком. Внутрішньо печінкові жовчні протоки людини представлені двома шарами: зовнішній – адвентеційний та внутрішній – слизовий. На початку вивідної системи печінки жовчні шляхи у слизовій оболонці представлені кубічними епітелієм, який лежить на базальній мембрані. У середньому відділі жовчовивідної системи печінки людини, з'являються не тільки кубічні, а й призматичні епітеліоцити. У кінцевому відділі жовчовивідної системи кількості призматичних епітеліоцитів внутрішньої оболонки збільшується. Епітеліоцити змінюють свою форму з кубічної до призматичної. Зовнішня оболонка представлена пухкою сполучною тканиною, з клітин фібробластичного ряду і міжклітинна речовина з колагеновими волокнами та аморфною речовиною.

Ключові слова: печінка, жовчовивідні шляхи, холецистит, жовчнокам'яна хвороба.

The study is a fragment of the research project "Experimental Morphological Study of the Effects of Cryopreserved Preparations of Cord Blood and Embryoplacental Complex (EFPC), Diferelin, Ethalon, and 1 % Methacrylic Acid Ether on the Morphofunctional State of Several Internal Organs", state registration No. 0119U102925.

In modern clinical medicine, the treatment and prevention of biliary system pathology remain a relevant issue. Currently, the most common diseases of the hepatobiliary system include chronic cholecystitis, cholangitis, gallstone disease, and post-cholecystectomy syndrome, which are increasingly prevalent [2, 3, 7, 14].

Gallstone disease ranks third after cardiovascular diseases and diabetes and is one of the prevalent pathologies in humans. According to studies conducted by gastroenterologists, there is a doubling in the number of patients with gallstone disease every ten years in economically developed countries. The frequency of the disease increases with age. For instance, gallstone disease is diagnosed in 3.5 % of the population between 20 and 30 years old, 5 % between 40 and 50 years old, 20 % after 60 years old, and 30 % after 70 years old [6, 9, 11, 12].

According to the data from the Statistics Center of the Ministry of Health of Ukraine, the incidence of gallstone disease was 695 cases per 100,000 adult populations. Over the past 10 years, the number of affected individuals has increased by 70 %, and the number of cholecystectomy surgeries accounted for 10 % of the total number of surgical interventions. In 98 % of cases, the necessity for this surgical procedure was related to gallstones. However, surgical treatment does not always achieve the expected relief of symptoms and leads to a decrease in patients' quality of life. Quite often, within 6–12 months after the operation, the development of post-cholecystectomy syndrome is observed in 15 % of patients and, according to other data, even in 50 % of patients [1, 4, 5, 8].

Domestic and foreign literature indicate that the increasing incidence of gallstone disease is influenced by environmental factors (dietary habits, food quality, eating patterns, water quality, lifestyle) and endogenous factors. This is particularly relevant in these challenging times when there is a war taking place in our country, which has disrupted the normal dietary patterns of many individuals [3, 10, 13].

Considering these circumstances, there is a need for comprehensive research on the biliary system. In our opinion, this is a pressing issue, and finding a solution to it will help in selecting more effective treatments for patients with hepatobiliary system pathology, as well as methods for prevention and intervention to mitigate the development of this condition.

The purpose of the study was to investigate the structural features of the components of the wall of the intrahepatic bile ducts in humans, which could help in addressing the issue of preventing cholecystitis and effectively treating inflammatory processes in the hepatobiliary system.

Materials and methods. General histological methods were used to study the structure of the wall of the intrahepatic bile ducts (staining of the specimens was performed with hematoxylin and eosin). To ensure proper fixation, the specimens were rinsed with a 12 % neutral formalin solution, and then the macro specimen was immersed in a 12 % neutral formalin solution.

The study was conducted on 15 liver specimens from deceased individuals aged 30 to 50 years without any detected hepatobiliary system pathologies. Organ collection was performed no later than 12 hours after death. The structural organization of the walls of the intrahepatic bile ducts was examined. The materials for the study were obtained from the Pathoanatomical Department based on Agreement No. 55 dated May 17, 2023, on scientific and practical cooperation between Poltava State Medical University and the Poltava Regional Pathoanatomical Bureau of the Poltava Regional Council. The scientific research complied with the moral and ethical norms in accordance with the principles of the Helsinki Declaration of Human Rights, the Convention on Human Rights and Biomedicine developed by the Council of Europe, the Order of the Ministry of Health of Ukraine “Procedure for conducting clinical trials of medicinal products and examination of materials from clinical trials” (Order No. 66 of February 13, 2006), the Ethical Code of the Physician of Ukraine, and the Ethical Code of the Scientist of Ukraine.

Microphotography was performed using the Biorex-3 VM-500T microscope, using the DCM 900 microphotography attachment. The obtained images were processed using the TSView software.

Statistical data analysis was conducted using the Statistic for Windows 7.0 software (StatSoft Inc., USA). The mean value was calculated, the standard error of the mean (m), and the results were considered reliable at $p<0.05$.

Results of the study and their discussion. Based on the application of a complex of objective morphological research methods and statistical analysis of the data, new information about the structure and development of the intrahepatic biliary system in humans was obtained. The obtained results of studying the elements of the intrahepatic biliary system provide sufficient evidence to state that, in addition to individual characteristics, the structural organization of the biliary system in humans largely depends on the type and nature of the diet, as well as the quantitative factor. Some individuals change their usual dietary habits and switch to a plant-based diet, completely eliminating fatty products, without considering the fact that the human body is omnivorous.

The intrahepatic biliary system in humans is composed of excretory ducts. The structural unit of the liver is the hepatic lobule, which contains non-muscular veins that collect mixed blood. Hepatocytes have a polygonal shape. This cell has multiple surfaces and two poles: sinusoidal and biliary. The sinusoidal pole faces the direction of the liver sinusoidal capillary and is lined with villi. The biliary pole, located between the two surfaces, is formed by the plasma membranes of hepatocytes that make up the wall of the bile capillary. Through the sinusoidal surface, various substances are absorbed from the blood, and then bile and other substances produced by hepatocytes pass into the biliary pole through the bile capillaries. Liver cells are surrounded by a double-layered circular protein-lipid plasma membrane that contains substances with high enzymatic activity, which catalyze the active transport of ions and molecules across the cell membrane into and out of the cell. The plasma membranes of hepatocytes are tightly interconnected near the bile capillaries. Between the liver cells and the wall of the sinusoidal capillaries, there is the space of Disse, which is almost completely covered by microvilli of hepatocytes. These cells form hepatic cords at the sides, which make up the segments and lobes of the liver.

In the center of the hepatocyte, there is a nucleus with one or possibly two nucleoli. Approximately 75 % of liver cells contain a single nucleus, with 70 % of all hepatocytes being triploid, around 2 % being octaploid, and 25 % being diploid. Hepatocytes have well-developed granular and agranular endoplasmic reticulum. The granular endoplasmic reticulum contains numerous ribosomes, while the agranular reticulum does not contain ribosomes. Hepatocytes have a well-developed Golgi apparatus and a large number of mitochondria. In addition to the aforementioned organelles, hepatocyte cytoplasm contains lysosomes, peroxisomes, glycogen particles, lipid droplets, and other structures.

Hepatocytes in the hepatic lobule form hepatic cords in two rows, between which bile and sinusoidal capillaries are formed. The sinusoidal capillaries converge radially towards the center of the lobule and drain into the central vein. The wall of the bile capillaries is formed by the plasma membranes of hepatocytes, which are anchored to each other by intercellular contacts. This capillary is part of a complex network that opens into the bile duct at the periphery of the lobule. The short duct connecting the bile capillaries to the bile duct is called a cholangiolar, and its inner lining consists of epithelial cells.

The human biliary system consists of intrahepatic bile ducts, where bile secretion begins, starting from small ducts and ending with larger ducts. Subsequently, the right and left hepatic ducts emerge. They then merge to form the common hepatic duct. The gallbladder, in turn, connects to the common hepatic duct through the cystic duct, forming the common bile duct, which empties into the duodenum. The proper functioning of the entire biliary system depends on how smoothly each link of this vital chain operates, without interruptions.

To conduct a more objective study, the investigation of the state of intrahepatic bile ducts in different areas of the human liver was proposed. The first section was the initial section located at the top of the liver, 2 cm away from the edge. The middle of the liver was then examined. Finally, material for investigation was collected near the liver's hilum, 1 cm away from the edge (Fig. 1).

In the initial segment of the liver's biliary system, the mucous membrane of the bile ducts is composed of cuboidal epithelial cells. They are arranged side by side in a single row and rest on the basement membrane. On a transverse section of one duct, an average of approximately 17.7±2.58 epithelial cells can be observed. The cytoplasm exhibits basophilic staining and contains general-purpose organelles such as ribosomes, which synthesize proteins for the epithelial cells themselves, granular endoplasmic reticulum associated with the Golgi complex, and mitochondria that carry out energy synthesis, thereby supporting cellular viability. The cell nuclei are predominantly located in the center and exhibit a large Gertwig index, indicating that the nucleus occupies a significant portion of the cytoplasm. The outer membrane is composed of connective tissue, within which fibroblast cells and collagen fibers are present. Arterioles and venules are observed near the duct (Fig. 2).

In the middle section, the mucous membrane of the intrahepatic bile ducts in humans is composed of both cuboidal and columnar epithelial cells. The average number of cuboidal epithelial cells is 7.29±1.82, while columnar cells amount to 7.87±1.82. The nuclei are mainly located near the apical surface, but there are also cells where the nucleus is localized in the center. A significant Gertwig index is also observed. The outer membrane remains unchanged. Arterioles and venules are localized near the duct, forming a triad together (Fig. 3).

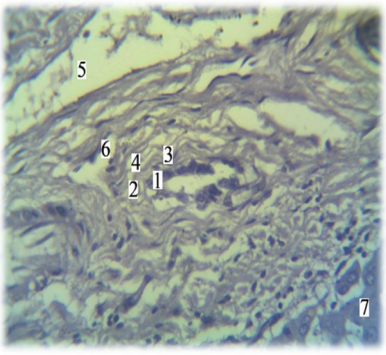

Fig. 1. Intrahepatic bile duct of a human at the beginning of the biliary system. 1 – mucous membrane epithelium; 2 – fibroblasts; 3 – fibrocytes; 4 – collagen fibers; 5 – venules; 6 – capillary; 7 – hepatocytes. Staining: hematoxylin-eosin. Magnification: x40.

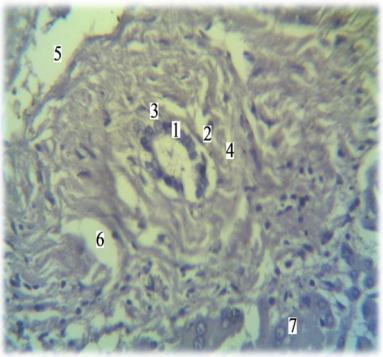

Fig. 2. Intrahepatic bile duct of a human, middle section of the biliary system. 1 – mucous membrane epithelium; 2 – fibroblasts; 3 – fibrocytes; 4 – collagen fibers; 5 – venules; 6 – capillary; 7 – hepatocytes. Staining: hematoxylin-eosin. Magnification: x40.

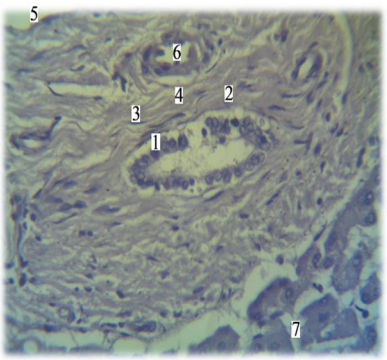

Fig. 3. Human bile duct. Terminal portion of the intrahepatic biliary system. 1 – mucous membrane epithelium; 2 – fibroblasts; 3 – fibrocytes; 4 – collagen fibers; 5 – venules; 6 – capillary; 7 – hepatocytes. Staining: hematoxylin-eosin. Magnification: x40.

In the terminal section of the intrahepatic bile ducts, which are closest to the liver hilum, the epithelial cells have a columnar structure. The number of cells increases and averages 28.12±4.02. The nuclei are mainly located on the apical surface and have an oval shape. The outer membrane remains unchanged, and there are also fibroblastic cells and intercellular substance with collagen fibers and amorphous material. The adventitial layer is represented by dense fibrous connective tissue, and in fibrotic areas, there is a small number of vessels of the microcirculatory system. In peripheral areas of the adventitial layer, small deposits of adipose tissue can be observed. Within these adipose tissue deposits, neurovascular bundles are present.

The efficiency of fluid absorption and drainage processes is enhanced by a well-developed microvascular system. Vascular elements of the mucous membrane form numerous anastomoses, which also contribute to the reabsorption of water and other components of bile.

In the initial section of the hepatic bile ducts, the mucous membrane is composed of cuboidal-shaped epithelial cells. In the middle section, the mucous membrane of the intrahepatic bile ducts in humans is composed of both cuboidal and columnar epithelial cells. In the terminal section of the intrahepatic bile ducts, which are closest to the liver hilum, the epithelial cells have a columnar structure.

At the beginning of the biliary system, cell nuclei are predominantly located in the center. In the middle section, they are more often positioned near the apical surface. Cells with nuclei located in the center are also observed. In the terminal section, nuclei are predominantly located on the apical surface and have an oval shape. The Gertwig index varies. In the beginning and middle sections, it was high, with nuclei occupying a larger area. In the terminal section, a low nuclear-cytoplasmic ratio was observed. The outer membrane remains unchanged. Arterioles and venules are located next to the duct.

The structure of all structural elements of the human biliary system is fully adapted to ensure the efficient functioning of this organ. The occurrence and development of pathology in the human biliary system can be caused by various factors: diet type, eating habits, quality of consumed food, functional state of adjacent organs, overall internal state of the body, and external environmental factors. The simultaneous cumulative effect of such diverse factors influences the adaptive responses of the human body [2, 6, 9, 13].

Knowledge of the anatomy and ultrastructure of the biliary pathways is necessary for a proper understanding of the hepatobiliary system and its pathology. Hepatocytes are arranged in rows and form dense cellular plates. They are separated from bile capillaries by the basolateral membrane and from sinusoids by the sinusoidal membrane. Due to the differences in the structure of the sinusoidal membrane and the membrane facing the bile capillary, hepatocytes are polarized cells. Adjacent hepatocyte plates are separated by sinusoids lined with endothelial cells. Extensions of endothelial cells form pores that allow direct contact between plasma and hepatocytes with the sinusoidal membrane. Unlike other types of endothelium, sinusoidal endothelium does not have a basal membrane. This facilitates the transfer of protein-bound substances (bilirubin and bile acids) from sinusoids to the space of Disse and further into hepatocytes, as well as accelerates the excretion of lipoproteins from hepatocytes into sinusoids [5, 8, 11, 14].

Conclusions

By applying a complex of objective morphological research methods, new data on the features of the structure and development of intrahepatic bile ducts in humans have been obtained.

1. At the beginning of the hepatic biliary system, the mucous membrane of the bile ducts is represented by epithelial tissue. The cells have a cuboidal shape and are arranged in rows. On a cross-section of a single duct, there are approximately 17.7±2.58 cells. Nuclei are predominantly located in the center of the cell, but they can also be found on the apical surface.

2. In the middle section of the human hepatic biliary system, there are some differences in the structure of the inner membrane. In the intrahepatic bile ducts, not only cuboidal but also prismatic forms of epithelial cells can be present. Their number is approximately 21.87±1.82. Nuclei have some differences in their localization, being situated not only in the center of the cell but also near the apical surface.

3. The intrahepatic bile ducts that are closest to the liver hilum have a prismatic structure, and their nuclei are predominantly located on the apical surface. They have an oval and bean-like shape. They undergo a transition from cuboidal to prismatic shape, and their number increases to approximately 28.12±4.02 cells. The outer membrane is composed of connective tissue containing fibroblastic cells and collagen fibers.

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REMODELING OF THE WALL OF THE ASCENDING COLON IN RATS UNDER THE INFLUENCE OF THE FOOD ADDITIVES COMPLEX

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Food additives are substances added to raw materials, finished products and medicines to extend the shelf life of the product, prevent the development of pathogenic microflora, and improve taste and organoleptic qualities. Monosodium glutamate, sodium nitrite and ponceau 4R are among the most widely used food additives. The experiment involved 84 mature male rats. The animals received 0.6 mg/kg sodium nitrite E250, 20 mg/kg monosodium glutamate E621 and 5 mg/kg ponceau 4R orally. Samples of the ascending colon of rats for histological examination were taken at 1, 4, 8, 12 and 16 weeks. It was found that oral administration of the food additives complex MSG, ponceau 4R and sodium nitrite for 16 weeks causes significant changes in the morphometric parameters of the wall of the ascending colon in rats. A pronounced reaction of the intestinal mucosa is characterized by the destruction of intestinal epithelial cells and disruption of the crypt structure with subsequent incomplete recovery at late follow-up.

Key words: food additives, monosodium glutamate, sodium nitrite, ponceau 4R, ascendenig colon.

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РЕМОДЕЛЮВАННЯ СТІНКИ ВИСХІДНОЇ ОБОДОВОЇ КИШКИ ЩУРІВ ЗА УМОВ ВПЛИВУ КОМПЛЕКСУ ХАРЧОВИХ ДОБАВОК

Харчові добавки – це речовини, які додаються до сировини, готових продуктів та лікарських препаратів з метою подовження терміну зберігання продукту, запобігання розвитку патогенної мікрофлори, поліпшення смакових та органолептичних якостей. Monosodium glutamate, sodium nitrite and ponceau 4R є одними з найбільш широко вживаних харчових добавок. The experiment involved 84 mature male rats. Тварини отримували 0.6 mg/kg sodium nitrite E250, 20 mg/kg monosodium glutamate E621 and 5 mg/kg ponceau 4R перорально. Відбір зразків висхідної ободової кишки щурів for histological examination was carried out at 1, 4, 8, 12 and 16 weeks. Встановлено, що пероральне застосування комплексу харчових добавок MSG, понсо 4R та нітриту натрію упродовж 16-ти тижнів зумовлює достовірні зміни морфометричних показників стінки висхідної ободової кишки у щурів. Характерною є виражена реакція слизової оболонки кишки, що характеризується деструкцією кишкових епітеліоцитів та порушенням структури крипт з подальшим неповним відновленням на пізніх термінах спостереження.

Ключові слова: харчові добавки, глутамат натрію, нітрит натрію, понсо 4R, висхідна ободова кишка.

The study is a fragment of the research project "Restructuring of the organs of the immune, respiratory and excretory systems under the effect of various exogenous factors (monosodium glutamate, sodium nitrite, ethanol, methacrylate)", state registration No. 0121U108234.

The main purpose of using food additives is to extend the shelf life of the product, prevent the development of pathogenic microflora, and improve taste and organoleptic qualities. Monosodium glutamate, sodium nitrite and ponceau 4R are food additives that have different purposes and are widely used in combination in food, medicines and animal feed. All three substances are sodium salts by their chemical nature. The use and acceptable daily intake of food additives in Europe is regulated and periodically reviewed by the European Food Safety Authority. It should also be noted that for children, the