CYTOMORPHOLOGICAL ANALYSIS OF SECRETORY ACTIVITY IN NEURODYSTROPHIC PROCESSES IN THE LIVER

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Abstract: The article studies the differential analysis of tissue changes in the liver that occur in it with various types of denervation. To study the secretory activity of the denervated liver, experimental and intact animals were always killed at the same time of day - at 9-10 am, after a preliminary 24-hour fast. Denervation of the liver only limits the regulatory effect of nerve impulses on the liver parenchyma, causing a disorder of the entire secretory activity of hepatocytes.

Key words: cats, liver, denervation, hepatocytes, nerve transection, experiment, biliary pole, bile acids, Golgi apparatus.

ЦИТОМОРФОЛОГИЧЕСКИЙ АНАЛИЗ СЕКРЕТОРНОЙ ДЕЯТЕЛЬНОСТИ ПРИ НЕЙРОДИСТРОФИЧЕСКИХ ПРОЦЕССАХ В ПЕЧЕНИ

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Резюме: В статье изучены дифференциальный анализ тканевых изменений в печени, которые возникают в ней при различных видах денервации. Для изучения секреторной деятельности денервированной печени экспериментальные и интактные животные забивались всегда в одни и те же часы суток — в 9—10 часов утра, после предварительного их 24-часового голодания. Денервация печени лишь ограничивающая регулирующее

влияние нервной импульсации на паренхиму печени, вызывает расстройство всей секреторной деятельности гепатоцитов.

Ключевые слова: кошки, печень, денервация, гепатоциты, перерезки нервов,

эксперимент, билиарный полюс, желчных кислот, аппарат Гольджи.

Introduction. In an intact organism, a glandular cell functions as part of a whole. At the same time, like any other somatic cell, the glandular cell is an integrated system, meaning it cannot develop, function, or reproduce without any of its components [2,3]. Understanding the mechanisms of central regulation of intracellular regulatory systems is of great theoretical and practical interest and remains relevant at the current stage of scientific research [1,4]. Selective disruption of the afferent or efferent components of the reflex arc can serve as one of the possible methods to elucidate their role in the structural and functional organization of glands [5].

Study Objective. The object of study in this work was the denervated liver in an experimental setting.

Materials and Methods. The experimental animals used were male domestic cats. All experimental and intact animals were housed in a vivarium and maintained on a standard mixed diet. After surgical intervention, experimental animals were euthanized at various time points, ranging from 1 week to 6 months, always between 9–10 a.m. following a 24-hour fasting period. Control operations involved opening the spinal canal or abdominal cavity without subsequent nerve transection or removal of nerve ganglia. The secretory activity of hepatocytes in intact animals was studied at different time points after feeding and at various times of the day. A total of 20 operated and approximately 10 intact animals were examined. Tissue samples from the organs of intact and operated animals were analyzed using cytological, histochemical, and biochemical methods.

Results. The secretory activity of hepatocytes is manifested in their production of both protein (plasma proteins, enzymes secreted with bile) and non-protein (bile

acids, plasma phospholipids, cholesterol) secretory products. Additionally, unlike muscle cells, hepatocytes can freely absorb glucose from the blood and store it in their cytoplasm as glycogen granules. The liver, as a digestive gland, functions through the biliary pole of hepatocytes by secreting bile acids, alkaline phosphatase, and small amounts of other enzymes into the duodenum. Through their vascular pole, hepatocytes receive raw materials from the blood and release finished secretory products back into the bloodstream. It is in this region of the liver lobules that complex structural and functional relationships between the circulatory system and the vascular pole of hepatocytes are established. Our data indicate that cellular organelles are involved in the secretion of bile acids. Biochemical data show that structural changes in mitochondria and their movement within the cell during different phases of bile acid secretion suggest that mitochondria not only provide the bioenergetic support for bile formation but also participate directly in bile acid secretion. To study the secretory activity of the denervated liver, both experimental and intact animals were euthanized at the same time of day (9–10 a.m.) after a 24-hour fasting period. In intact animals, during these hours, most cells in the liver lobules are filled with secretory granules (the phase of bile acid accumulation). In mixed denervation (removal of celiac plexus nodes or transection of vagus nerves), the degree of impairment in liver secretory activity depends on the extent of denervation. The most extensive denervation in our experiments was achieved by removing the semilunar nodes of the celiac plexus or simultaneously removing the celiac and superior mesenteric plexus nodes and transecting both vagus nerves below the diaphragm. However, despite vascular disturbances in the liver with mixed denervation, glycogen never completely disappears, although its levels typically decrease. In contrast, with deafferentation of the liver, hepatocytes completely lose their ability to accumulate glycogen. Mixed denervation results in more extensive necrotic foci in the liver compared to pure deafferentation. In the preserved areas of the lobule parenchyma, some hepatocytes retain secretory activity, while others show clear signs of impaired

secretory processes. Structural changes in cellular organelles are also observed: the Golgi apparatus becomes significantly hypertrophied, bile canaliculi appear dilated and fragmented in many places, and small amorphous areas are found in some hepatocytes. Biochemical analysis of plasma proteins (albumins and globulins) using paper electrophoresis revealed a sharp decrease in total serum protein two weeks after liver denervation, primarily due to a reduction in the albumin fraction. Five months after mixed denervation, there was a tendency toward normalization of the levels of various protein fractions in the serum. Thus, the experimental data presented in this study indicate that even partial denervation of the liver, which only limits the regulatory influence of nerve impulses on the liver parenchyma, disrupts the entire secretory activity of hepatocytes. Our experiments clearly distinguish the effects of pure deafferentation of the liver from mixed denervation. In the latter case, the overall pattern of denervation changes is compounded by intensified vascular and circulatory disturbances due to complete vascular denervation. Liver denervation triggers a series of chain reactions that underlie all physiological mechanisms of the organism and ensure the interaction of its various parts. To understand the complex interplay of factors affecting the secretory activity of denervated hepatocytes, we briefly consider the main changes observed in liver denervation. Deafferentation of the liver was achieved in our experiments by removing spinal ganglia. We noted that deafferentation leads to the loss of hepatocytes' ability to absorb glucose and store it as glycogen granules. In intact fasted animals, glucose induces the synthesis of glucokinase in the liver, whereas in fasted animals with denervated livers, glucose does not affect the reduced activity of this enzyme. Fasting induces the synthesis of glucose-6-phosphatase in a normal liver but does not produce this effect in a denervated liver. Similarly, insulin administration restores glucokinase synthesis in the liver of diabetic organisms, but in denervated livers, insulin does not alter the reduced activity of this enzyme. In our experiments, the glycogen storage function of hepatocytes did not recover even six months after deafferentation. In other words, hepatocytes

denervated in the sensory aspect lose their ability to respond to many external factors, including hormonal ones. It should also be considered that impaired glucose metabolism in the liver alters the intracellular energy resources of hepatocytes, ultimately leading to disrupted ATP synthesis in their mitochondria. It can be hypothesized that impaired ATP synthesis alters the conformational state of proteins in mitochondrial membranes. Our experiments clearly demonstrate the dynamics of structural and functional impairments in the mitochondrial apparatus of denervated hepatocytes.

Conclusion. In the later stages of deafferentation, a reduction in the number of mitochondria in liver cells is observed, and in some hepatocytes, mitochondria disappear entirely. In the early stages of denervation (two weeks post-operation), hepatocytes are notably overloaded with secretory granules, which often appear swollen with blurred contours. Sometimes, these granules merge into large fuchsinophilic conglomerates interspersed with vacuoles of varying sizes. One and three months after deafferentation, the number of secretory granules and mitochondria in hepatocytes is significantly reduced, and in some cells, they disappear completely.

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