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Pathomorphologic and Morphofunctional Changes of Pancreatic Parenchyma under Experimental Influences (Review Article)

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Abstract The article considers the problem of changes occurring in the pancreas in thyrotoxicosis. The ultrastructural changes of cells of exocrine and endocrine part of the pancreas were analyzed. The results can be used in endocrinology and gastroenterology. Disturbance in the functional activity of the thyroid gland leads to systemic disorders of most organs and the whole organism. However, there are very few works devoted to the study of pathomorphological and Morphofunctional changes of pancreatic parenchyma in thyrotoxicosis. It is known that the function of the pancreas is under the regulatory influence of a number of hormones, and thyroid hormones occupy not the last place in this series.

Keywords Hormon, Pancreatic parenchyma, Experimental influences, Pathomorphologic and morphofunctional changes, Thyrotoxicosis

The pancreas is an unpaired organ that is involved in digestion and regulation of metabolic processes in the body. This gland has exocrine and endocrine parts, and its functioning is subject to regulation. Different types of laboratory animals are often used for research on the pancreas, which have a similar structure and function of this organ. However, there are some differences that may affect the results of experiments. There are literature data designed to determine the similarities and differences in the structure of the pancreas in humans and laboratory animals. Major features of similarity have been found in both the anatomical and histologic structure of this organ. However, there are differences in the anatomical structure of the gland as well as in the ductal system and cell composition of the islet apparatus. These data may be useful for pharmacologists, toxicologists, histologists, physiologists and pathologists studying the pancreas and its pathologic processes [4].

Studying reactive morphological changes in endocrine and exocrine parts of the pancreas under the influence of different temperatures in experimental rats scientists indicate that in conditions of hypothermia elements of the endocrine part of the pancreas do not undergo sharp morphological changes, while in the exocrine part ultrastructural changes indicate an increase in protein and transcapillary exchange. When analyzing the changes in pancreatic cells under hyperthermia, it can be stated that these changes are more serious than under hypothermia and are characterized by significant heterogeneity, equally affecting secretory processes in both exocrine and endocrine parts of the organ [15].

The study of the effect of cryomodeling in pancreatic pathology showed that local morphological changes depended on the temperature at which cooling was performed. The study concluded that modeling of pancreatic pathology by cryovaporization provides high specificity and stability for studying the mechanisms and methods of treatment of this pathology. The results obtained allow us to recommend this experimental model for further studies of the occurrence and treatment of pancreatic pathology [5].

When studying the effect of cryo-influence on the pancreas of white rats, the features of alterative, dyscirculatory and regenerative processes were found. Exposure of the pancreas at -20℃ and for 1 minute causes pathomorphologic changes. Hypothermia causes necrosis in the pancreas and disruption of microcirculation, which is manifested as dilated capillaries and hemorrhages. A perifocal reaction is seen in the area of cryoinfection. The hypothermia zone is eventually replaced by proliferating connective tissue, which leads to scarring atrophy of the parenchyma [6].

The combination of intermittent normobaric hypoxia and melatonin affects morphologic indices of both exocrine and endocrine parts of the pancreas. The exocrine function of the gland may decrease due to a reduction in the size of the acinus, exocrinocytes and epithelial height. At the same time, morphologic changes in the endocrine part of the gland indicate its activation, as the islets of Langerhans become larger and the number and density of endocrinocytes in them increase. The combined effects also lead to a decrease in

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connective tissue layers between the acinus and lobes, which facilitates oxygen transport to the gland and improves metabolic processes and hormone penetration into the blood. These results may be useful when using intermittent normobaric hypoxytherapy and melatonin to increase the activity of endocrine function of the gland in individuals with diabetes mellitus and hypertension [20].

During experimental modeling of diabetes mellitus by a single intravenous injection of streptozotocin (50 mg/kg), morphometric studies of the endocrine apparatus of the pancreas of rats with experimental streptozotocin-induced diabetes mellitus showed a significant decrease in the area and perimeter of pancreatic islets, which allowed us to consider the above morphometric parameters as basic parameters for characterizing the islet apparatus of the rat pancreas during modeling of this pathology.

When studying structural and functional changes in the endocrine apparatus of the pancreas in white rats and mice with alloxan- and streptozotocin-induced diabetes, it was found that the development of diabetes in animals was accompanied by necrobiotic processes in B-cells, a decrease in the area of endocrine islets and degranulation of insulinocytes. However, some islets were in a state of increased functional activity, which was accompanied by cell hypertrophy and activation of regenerative processes. The formation of new islets from ductal epithelium was also noted. In this regard, the number of insulin-producing elements decreased, resulting in absolute insulin deficiency. Comparative analysis showed that alloxan- and streptozotocin -induced diabetes causes degeneration of B-cells and a decrease in the number of islets, which limits the functional capabilities of the endocrine apparatus [8].

Studying the morphology of rat pancreas under the influence of dimefosfon, its normalizing effect on the structure of rat pancreas was determined. The use of dimefosfon leads to changes in the structural organization of acinuses, reduction of destruction of the terminal secretory compartments and normalization of connective tissue. In the endocrine part of the gland, there is a thickening of insulocyte arrangement in pancreatic islets and a decrease in interlayers of loose connective tissue. There is also an increase in the size of islets, indicating an increase in the number of endocrine cells in the gland. These results indicate a positive effect of dimefosfon on the structure and function of the pancreas [3].

Administration of polyoxidonium to rats in different doses showed that polyoxidonium has different effects on the pancreas and the level of total protein in blood serum depending on the dose. The drug normalizes the microstructure of endocrine and exocrine sections of the gland, as well as the structure of connective tissue and blood vessels. The level of total protein in blood serum in rats increases under the influence of polyoxidonium. The experiment also revealed changes in rat pancreas associated with normalization of acinus structure, maintenance of fibrotic component and reduction of blood vessel edema. In the endocrine part of the gland, thickening of insulocytes in islets, an increase in their size and, probably, an increase in the number of endocrine cells and the activity of hormoneogenesis were observed. Administration of polyoxidonium to rats increases the level of total protein in serum by 7.8-15.6% compared to the control group [2].

Studying the effect of congenital hypothyroidism on the state of glycopolymers in the pancreas, conducted on Wistar rats administered mercazolil to model hypothyroidism, it was found that hypothyroidism affects carbohydrate determinants of the pancreas through the binding of three lectins (WGA, PNA, LCA). Lectin receptor expression was detected in the exocrine part of the pancreas. Further experiments showed that exposure of hypothyroid animals to carbohydrate determinants at different periods of the experiment induced a weak response in the endocrine part of the organ. It was also found that all lectins (WGA, LCA, PNA) showed selective binding to different structures of the pancreas. It is noted that, as a result, the decrease in metabolic processes in congenital hypothyroidism leads to a slowdown in pancreatic morphogenesis and changes in the number of receptors for lectins [13].

Magnesium plays an important role in regulating pancreatic function. However, the effectiveness of magnesium preparations to activate pancreatic function may depend on the age of the individual. Changes in the morphofunctional state of rat pancreas after long-term administration of magnesium chloride were investigated. In 3-month-old rats there were observed signs of decrease in functional activity of the pancreas, both in its exocrine and endocrine parts. At the same time, in 15-month-old rats magnesium chloride increased the activity of the exocrine part of the gland. In addition, changes in the endocrine part corresponding to the age of the rats were observed. Thus, magnesium administration had different effects on morphologic changes in the pancreas in rats of different ages. Taking into account these differences, the administration of magnesium in preparation should be considered especially for pancreatic dysfunction in people of different ages. This is especially important in adulthood, when pancreatic activity decreases [21].

During acute exposure to tetrachloromethane, morphological changes in the pancreas were less pronounced than in the liver and were manifested only in peripheral parts. Moreover, they were similar in all groups of animals exposed to tetrachloromethane. The effect of correction by both compounds was ineffective, but signs of reparative (restorative) processes were observed during correction by Heptor preparation. Consequently, the corrective effect of Heptor preparation is more pronounced than that of the studied composition. The obtained data indicate the absence of gross morphological changes in the structure of the pancreas under acute exposure to tetrachloromethane [14].

The expression of tumor necrosis factor alpha receptors (TNFαR1) in rat pancreatic tissue was found to be altered in pancreatopathy induced by nimesulide administration. TNFαR1 expression was detected in endocrine islets of Langerhans, and the intensity of expression was dependent on the dose of nimesulide. In animals receiving the therapeutic dose of the drug, the area of expression was increased, which

may be related to the effect of TNF-α on endocrine islets cells and indicate readiness for apoptosis. In animals treated with high doses, a decrease in the expression area was observed, which may be related to the deterioration of islet trophism and increased toxic effects of nimesulide. These factors may lead to disruption of the structure or reduction in the number of cellular receptors, which is consistent with the literature. The study showed changes in the expression of TNFαR1 receptors in nimesulide-induced pancreatopathy [7].

Studying changes in the pancreas of mice under the influence of pulsed and isko-intensive laser radiation with different parameters. showed improvement of blood flow and relieved the stress vascular component associated with venous stasis. At a frequency of 150 Hz, increased secretory activity was observed in the cells of the insular apparatus, which increased at higher frequencies; however, at a frequency of 300 Hz and an exposure of 15 minutes, dystrophic cells appeared. Increasing the frequency to 1500 Hz caused an increase in synthetic processes, but had an unfavorable effect on cells at the stage of intracellular synthesis. Frequency of 3000 Hz decreased synthesis of zymogen granules and morphological changes in the organ. Increasing the exposure and the number of irradiation sessions enhanced the effects of laser irradiation on pancreatic tissues at all irradiation frequencies. The study showed that low-intensity laser radiation can have a positive effect on pancreas functioning [19].

When studying the relationship between the endocrine and exocrine parts of the pancreas, the mechanisms of regulation of endocrine cells affecting the production of exocrine secretion were found. The study concluded that the pancreas, due to its hormonal function, participates in the adaptive reactions of the organism to changes in the external environment and plays an important role in maintaining homeostasis. Local changes in the level of insular hormones in the area of transition between endocrine and exocrine tissue may be the cause of morphologic changes in the exocrine part of the pancreas. Understanding of these relationships is important in studying clinical aspects of various pancreatic diseases [9].

There are works on heterogeneity of the exocrine part of the pancreas, also on morphological and functional differences between acinuses and acinar cells. These works confirm the heterogeneity of peri- and teleinsular acinuses under different conditions. To date, at least three types of heterogeneity in the exocrine portion of the pancreas have been demonstrated: differences in enzyme content, antigens, and blood group. In the process of digestion, there are rhythmic fluctuations in the secretory activity of the gland. In 15 minutes after a meal there is a partial release of previously accumulated secretion from the zymogenic zone. After 2 hours, most of the pancreatic cells begin to maximally secrete secretion and enter the synthesis phase. It is also noted that areas of parenchyma surrounding the islets of Langerhans do not undergo cyclic changes, but instead contain zymogen granules. Such cell heterogeneity is important for metabolic processes and pancreatic secretion [10].

The study of structural and metabolic changes of endocrine system and exocrine parenchyma of pancreas at complete external drainage of bile showed that periinsular acinuses were more resistant to the absence of bile than teleinsular ones. While the rest exocrine parenchyma underwent dystrophic processes, periinsular acinuses retained their size and metabolic activity corresponding to the control group. This, was explained by the active relationship between exocrine parenchyma and the state of the insular apparatus of the pancreas. The pancreas, due to its hormonal function, participates in adaptive reactions to environmental changes and is part of the general adaptive complex of the organism regulating homeostasis. The mechanisms of paracrine influence of endocrine islets and the organization of microvascular networks connecting islets with the exocrine part are also important when considering various pancreatic diseases [11].

Ultrastructure of pancreatic parenchyma and its capillaries was studied after ischemia, the greatest changes were observed when creating ischemia of the inferior vena cava basin organs. At creation of plator in the inferior vena cava basin the changes were insignificant and did not affect the histofunctional state of the pancreas in the postoperative period. When stasis was created, activation of secretory process in the pancreatic parenchyma cells was observed. Our observations allow us to conclude that acute circulatory disorders in the abdominal aorta basin are more pronounced and stable with selective occlusion of the arterial system leading to ischemization of organs and tissues [1].

During longitudinal resection of the splenic part of the pancreas in male rats at different periods of the experiment they note that in response to partial resection of the splenic part of the pancreas reparative processes in the pancreas in experimental animals develop in all its parts: both at the site of resection and far from it. On the basis of the analysis of 3 H-thymidine incorporation, mitotic coefficient and index of degenerated nuclei, they concluded that the duct epithelium, along with the epithelium of the end sections, makes a very noticeable contribution to the formation of epithelial tubes, some of which are secondarily differentiated into typical end sections and typical islet cells. The number of DNA-synthesizing cells in both exocrine and endocrine epithelium increases in the part of the PG remote from the resection site early after the injury. Ultrastructural characteristics of exocrine and endocrine epithelium testify to the intensification of synthetic processes in epithelial structures of the PG. The increase in the total volume of islet tissue in experimental animals by 30 days of experience testifies in favor of compensation of the endocrine component of pancreatic epithelium lost during resection. At the same time, the compensation is associated not only with the increase in proliferative activity of islet cells in the early terms after resection, but to a large extent occurs due to the process of acino-insular transformation, as evidenced by numerous findings of "mixed" cells at the periphery of the PA and in the peri-islet acinuses [18].

The study of morphofunctional features of the pancreas

in pregnant rats under different conditions of nutrition and chronic stress has shown that hyper- and hypocaloric nutrition and stress have a negative effect on pancreatic exocrinocytes, causing cytoplasmic hydropic dystrophy, chronic inflammation, atrophy and sclerosis. The endocrine part of the gland also undergoes rearrangement expressed by dystrophic changes in cytoplasm, hyperchromatosis, chromatin margination, apoptosis, lipomatosis and fibrosis. The level of morphofunctional activity of exo- and endocrinocytes is also reduced under these conditions. Hemodynamic and hemorheologic abnormalities are also found. These changes indicate a high risk of developing chronic pancreatitis and secretory insufficiency, as well as type I diabetes mellitus in animals [12].

Morphological studies of the structure of the pancreas of rabbits in experimental atherosclerosis and its treatment with various drugs, in rabbits, which experiment was induced using the classical Anichkov technique for three months, after which the rabbits were given the following drugs for four months: vinboron, polysorb and polysponin. Morphologic study of the pancreas of rabbits showed that atherosclerosis develops hypofunction of the insular apparatus, which is manifested by a decrease in the size of insulocytes and their nuclei, as well as in the amount of aldehyde-fuchsinophilic granularity. However, in rabbits treated with vinborone, polysorb and polysponin, these phenomena of hypofunction are reduced. The findings of the study indicate the potential efficacy of these drugs not only for the treatment of atherosclerosis, but also for further study in experimental diabetes [17].

Conclusions

Thus, the need to use experimental animal models of thyrotoxicosis to study morphofunctional changes in cellular structures of both exocrine and endocrine parts of the pancreas is of great theoretical and practical importance. A considerable amount of information concerning various aspects of pathogenesis and etiology was obtained as a result of preclinical studies. Unfortunately, despite the wide range of available possible ways of induction in the study of thyrotoxicosis problem, we have not found exhaustive data reflecting pathomorphologic and morphofunctional changes of pancreatic parenchyma in thyrotoxicosis. The available data are scarce, few in number and the problem is insufficiently studied. Morphologic changes in the pancreas in thyrotoxicosis have not been described. Further in-depth study of structural changes in the pancreas in thyrotoxicosis is required.

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