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PANCREATIC GLAND MORPHOLOGY IN EXPERIMENTAL HYPOTHYROIDISM

Norbek K. Niyozov [1]

Mirjalol I. Kukonboyev [2]

[1]Senior Lecturer, Tashkent Medical Academy,

E-mail. *norbekniyozov65@gmail.com* Tashkent, Uzbekistan.

[2]Student, Tashkent Medical Academy,

E-mail. *mirjalolqoqonboyev3@gmail.com* Tashkent, Uzbekistan.

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Abstract. *In our study, we examined white laboratory rats born from control and experimental mothers with hypothyroidism. As a result of morphological analysis of the pancreas in different periods of postnatal ontogenesis, significant changes in the delay in the development and formation of individual components of the vascular wall were revealed compared to the control group. From the first days after the start of the experiment, changes in the arterial wall were noted in all experimental animals. The results show that morphological changes in the cells of the pancreas and its blood vessels occur in the offspring born from mothers with hypothyroidism.*

Key words: *pancreas, acinus, mercazolil, share.*

МОРФОЛОГИЯ ПОДЖЕЛУДОЧНОЙ ЖЕЛЕЗЫ ПРИ ЭКСПЕРИМЕНТАЛЬНОМ ГИПОТИРЕОЗЕ

Аннотация. *В нашем исследовании мы обследовали белых лабораторных крыс, рожденных от контрольных и подопытных матерей с гипотиреозом. В результате морфологического анализа поджелудочной железы в разные периоды постнатального онтогенеза были выявлены существенные изменения в задержке развития и формирования отдельных компонентов сосудистой стенки по сравнению с контрольной группой. С первых дней после начала эксперимента у всех подопытных животных отмечены изменения артериальной стенки. Полученные результаты показывают, что у потомства, рожденного от матерей с гипотиреозом, происходят морфологические изменения в клетках поджелудочной железы и ее кровеносных сосудах.*

Ключевые слова: *поджелудочная железа, ацинус, мерказолил, доля.*

Introduction. Among endocrine diseases in the world, thyroid diseases occupy a high place in terms of incidence.

The incidence of manifest hypothyroidism is 0.2-1%, and latent primary hypothyroidism is 7-10%. Metabolic changes observed as a result of a deficiency or excess of thyroid hormones in the body also lead to morphological and functional changes in the gastrointestinal tract [1, 5, 8, 12]. According to the World Health Organization, studies conducted in Australia, Europe, Central Asia, the Middle East, and North America indicate that the prevalence of gastrointestinal diseases among the population is 7-41% and an average of 25%. In this case, in order to avoid negative impacts on people's life expectancy, it is necessary to expand modern diagnostic capabilities in identifying the disease, and the emergence of various conditions that lead to an increase in the disease leads to morphological and functional changes in the gastrointestinal system [2, 4, 7, 13]. 32% of patients under the supervision of the dispensary are patients with diseases of the digestive system. This disease in many cases causes significant material losses to the patient and the state budget due to the long-term temporary loss of working capacity, the high cost of treatment and rehabilitation processes [3, 6, 10]. In this regard, the prevention of thyroid diseases and their causes, the development of effective diagnostic and treatment methods are one of the urgent issues of modern medicine. In the last decade, a number of scientific studies have been conducted in the world to study thyroid diseases and their adverse effects on the gastrointestinal tract [9, 11]. In this regard, it is of particular scientific and practical importance to scientifically substantiate the morphological characteristics of the pancreas in offspring born from hypothyroid mothers, to determine that changes in the pancreas in hypothyroidism are mainly clinical, but given the paucity of information on morphological changes in the pancreas, scientific studies aimed at assessing the dynamics of changes in the pancreas are of particular scientific and practical importance. In modern domestic and foreign literature, there is no information on a comprehensive assessment of the morphofunctional characteristics of the development of the exocrine and endocrine parts of the pancreas in the postnatal period in offspring born from women with hypothyroidism. The increase in diabetes, the extreme importance of the problem of hypothyroidism in pregnant women, and the uncertainty and insufficient study of the structural and functional mechanisms of its negative impact on the postnatal development of the gastrointestinal system of the offspring, require a high level of relevance of research in this area.

Purpose of the Research. To determine the nature of morphological changes in the pancreas in experimental hypothyroidism.

Materials and Methods. To achieve the goal of the study, the pancreas of 80 sexually mature white laboratory rats was studied. White laboratory rats were divided into 2 groups.

Group 1 consisted of 30 healthy rats as a control group. In the experimental group 2, 50 female white laboratory rats were given 0.5 mg of mercazolil per 100 g of body weight for 14 days to induce experimental hypothyroidism. Subsequently, the rats were given 0.25 mg of mercazolil per 100 g of body weight for 1 month. After the rats became pregnant and gave birth to their offspring, the mother rats were continued to be given 0.25 mg of mercazolil per 100 g of body weight during lactation. Blood was taken from the tail vein of the mother and offspring rats, and the amount of thyroid hormones was studied. The baby rats were euthanized by decapitation on days 3, 7, 14, 21, and 30 after birth. Tissues from the head, body, and tail of the pancreas were removed for histological examination. The pancreatic tissue was fixed in 10% formalin, dehydrated in alcohol, and paraffin blocks were prepared. Histological preparations of 8-12 μm were prepared from the prepared paraffin blocks and stained with hematoxylin-eosin.

Experiments and euthanization of animals by decapitation were carried out in accordance with the “European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes” (Strasbourg, 1985). Histological sections prepared on a rotor microtome with a thickness of 8-10 microns were stained with hematoxylin-eosin by the standard method [Volkova O. V. V., Yeletsky Yu.K., 1982].

Results. The body and pancreas weights of rat pups, the relative weight of the pancreas to body weight, length, width, and thickness vary with age (Table 1). From 3 days to 30 days, the pancreas increased by 1.9 times in weight, 1.4 times in length, 3.9 times in width, and 3.0 times in thickness. The anatomical dimensions of the pancreas reached their maximum growth rate by 21 days. It can be seen that the pancreas of 3-day-old rat pups is fibrous in shape. Gradually, the shape of the pancreas becomes triangular, and later becomes prismatic triangular. The pancreas is the most important organ of the digestive system, structurally consisting of three parts, the first part is the duodenal part, located in the U-shaped bend of the duodenum, caudal to the place of its confluence with the common bile duct. The second part is the pyloric part, consisting of many separate segments located along the common bile duct. The third part is located in the duplication of the gastrosplenic ligament, and is called the gastrosplenic part.

Morphofunctionally, the pancreas consists of exocrine and endocrine parts (Fig. 1). The pancreas of the control group of rats is covered externally with connective tissue.

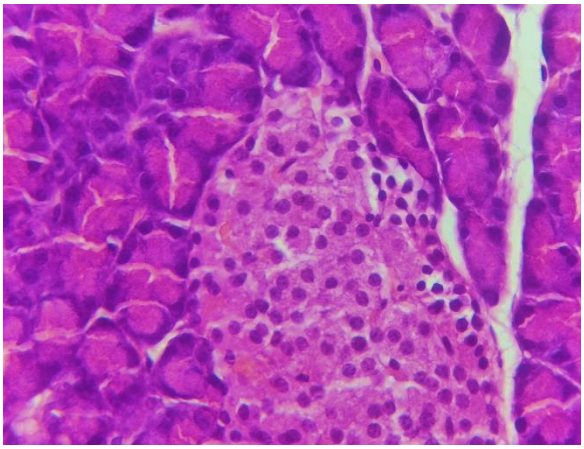

Figure 1. *Pancreas of a 14-day-old control rat. Appearance of the acinus and islets of Langerhans. Staining: hematoxylin-eosin. Magnification: 10x40.*

The capsule, consisting of connective tissue, forms thin layers and penetrates deep into the gland. Trabeculae divide the gland into separate compartments, the thickness of the trabeculae increases from 0.62±0.022 μm at 3 days to 0.72±0.036 μm at 30 days. They are covered with a single-layer prismatic epithelium. The connective tissue contains blood vessels, excretory ducts, and nerve vessels. The structural and functional unit of the exocrine part of the pancreas is the acinus, which contains the final secretory compartment and the ducts, from which the excretory ducts begin (Fig. 2). The acini consist of 7-12 large exocrine pancreatocytes, or acinocytes, and several small tubular cells, or centroacinar cells. The acini are pyramidal in shape, with a wide base resting on the basement membrane and a narrowed apex. The volume of the acini was found to be 8696.3±23.5 μm3, and the number of cells in the acini was 11.3±1.2.

The volumetric ratios of tissues in different parts of the pancreas were as follows: in the spleen, acinar tissue accounts for 77.3% of the total tissue volume, and endocrine tissue accounts for 3.5%, and in the duodenal part of the organ, 88.3% and 0.35%, respectively.

In order to substantiate the induction of experimental hypothyroidism in rats, the levels of triiodothyronine (T3), unbound thyroxine (T4), and thyrotropin-releasing hormone (TRH) were determined in the blood of rats on different days of the experiment.

Analysis of the data obtained showed that on the 7th day of the experiment, the T3 and T4 hormones of the hypothyroid and control group rats were practically not different from each other.

On the 14th day of the experiment, a pronounced decrease in the T4 indicator and a less pronounced decrease in the T3 indicator were observed.

On the 21st day of the experiment, a decrease in the T4 hormone indicator was found to be 2 times, and T3 - 1 time. The thyroid hormones in the blood of 30-day-old rats changed as follows: T4 indicator was observed to decrease by 4 times, and T3 - by one and a half times.

Thus, the analysis of the hormone indicators revealed a significant decrease in the thyroxine (T4) hormone in the blood of rats with experimental hypothyroidism. The decrease in the T4 hormone was clearly visible from the 14th day, and by the last days of the experiment, its reliability decreased to 4 times.

The level of thyroid hormones in the blood is controlled by thyrotropin hormone. A decrease in the level of T3 and T4 hormones in the blood led to an increase in the TTG hormone.

On the 3rd and 7th days of the experiment, the level of TTG was the same as in the control group. By the 14th day of the experiment, a gradual increase in TTG was noted, and by the 21st day, it was 2 times higher than in the control group.

In experimental hypothyroidism, changes were observed in the morphological structure of the pancreas. Morphological changes in the structure of the pancreas On the 7th-14th day of the experiment, the segmental structure of the gland was preserved, edema was visible on the periphery (Fig. 2). Already in the first days of the experiment, edema developed in the gland tissue, collagen fiber twitching, changes in blood vessels, and dystrophic changes in cells were observed.

Despite the development of the above changes, it is evident that the segmental development of the gland was preserved. In the first days of the experiment, engorgement of venous vessels, plasmarrhagia due to increased permeability in the blood vessel wall were observed, and foci of peripheral hemorrhage (Fig. 3), focal edema were detected in the stroma.

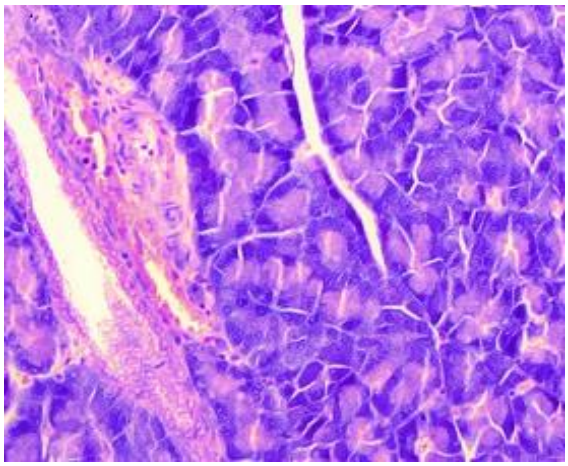

Figure 2. *Histological appearance of*

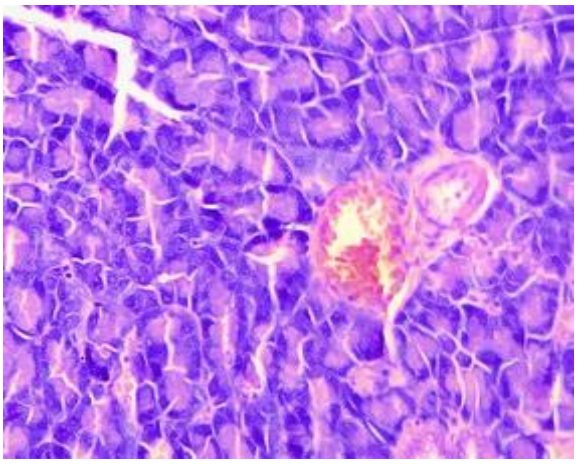

Figure 3. *Histological appearance of*

the pancreas of a 7-day-old experimental rat. Disturbance of acinocyte architecture. Interstitial edema. Staining: hematoxylin-eosin. X: 10x20.

the pancreas of a 14-day-old experimental rat. Hemorrhages. Staining: hematoxylin-eosin. X: 10x20.

By the 21st day of the experiment, the lobular structure of the gland is preserved, but a slight decrease in the size of the lobes is detected. An increase in the intensity of the edema in the stroma of the pancreas is observed, which spreads throughout the gland and acquires a diffuse character. Swelling and local fragmentation of collagen fibers are observed. In the preserved parts of the stroma, reparative processes are intensified, intensive proliferation of fibroblasts and the formation of fibrils are detected. In the acini of exocrine cells, the location and structure of the nucleus and nucleoli change, vacuolization of the cytoplasm, zymogenic granules decrease, and the structure of the endoplasmic reticulum is disrupted. Loss of degranulation is observed in the cytoplasm of endocrine cells. The interlobular venous vessels are dilated, leukocyte accumulation is detected, and myxomatosis of the vessel wall and myxomatosis is detected. We can see that the diameter of the pancreatic acini lags behind the control group by up to 4%, and their height by up to 18%. The acini are irregularly shaped, with a clear boundary between the zymogenic and basophilic areas. Signs of destruction are visible in the peripheral areas of the acinar part of the pancreas.

On day 30, characteristic structural changes were detected in the pancreas, namely, atrophy and deformation of the lobes, the intensity of the swelling in the gland storm increased and spread to the entire gland. In the lobes, a decrease and atrophy of the epithelium of the acini, dystrophic changes in the endocrine cells α, β cells, and an irregular change in their number were detected. In the lobes located on the periphery of the pancreas, the architectonics of the acini was disturbed. It can be seen that some acinocytes around the areas of blood transfusion have moved away from each other and are compressed. Discomplexation is observed in the acini, and vacuolization of the cells is detected. The boundaries of the cells are unclear. It was found that the interlobular and intralobular ducts are widened. α-type cells are slightly enlarged. α-cells are less damaged than β-cells, since they are covered with a denser cytoplasmic membrane. The islets of Langerhans were edematous (Fig. 3), changes were observed in the blood vessels.

Increased permeability of microvessels and venous vessels in the form of visible vascular dilation led to the release of the liquid part of the blood through the vessel wall into the surrounding connective tissue.

The appearance of edema was noted in the stroma, mainly in the perivenular and pericapillary spaces. Collagen fibers were swollen, loose, the capsule was unevenly located, and connective tissue edema was observed. The average area of \u200b\u200bthe β-cell nuclei decreased and karyopyknosis occurred. The area of \u200b\u200bthe α-cell decreased by 8.5% compared to the control group. The acinus lagged behind in diameter by up to 3%, and its height by up to 12%.

Conclusion. The results of the study showed that in hypothyroidism, negative changes were observed in the pancreas of offspring born from the mother rat. These changes were hemomicrocytic in nature, manifested as edema of the intermediate stroma, destructive and dystrophic changes in the cell. The changes were more pronounced on the 14th day of the experiment, and ultrastructural changes were manifested as destabilization of membrane structures in the acini. Destructive changes were detected in the mitochondria of the acini.

Disorganization of the acini and their structures indicates a violation of the contractile function of acinocytes. The obtained data prove that changes in the acini at the cellular and subcellular levels lead to chronic pancreatitis. It was found that the diameter and height of the acini cells of the experimental group of rats were smaller than those of the control group. The diameter and height of the pancreatic acini cells of the experimental group of rats at 3 days of age did not differ from those of the control group. The diameter and height of the acinus cells of 7-day-old rat pups were found to be significantly smaller. By 14 days of age, this indicator gradually decreased and was found to be 1.2 times smaller than in the control group, and by 21 days of age, it was 1.3 times smaller. By 30 days of age, this indicator was noted to be 1.5 times smaller.

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