



MANIFESTATIONS OF VASCULAR COMPLICATIONS IN EXPERIMENTAL DIABETES MELLITUS

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Abstract

Objective to study the morphological and functional disorders of the pancreas and blood vessels of the lower limb of rats with experimental diabetes mellitus. The object of the study were 90 white rats at the age of 4-6 months. The morphological changes of the pancreas and the walls of blood vessels of the lower limb in experimental diabetes mellitus. Model of experimental diabetes reproduced by single intraperitoneal administration of streptozotocin Wistar rats at a dose of 60 mg / kg. Comparison of the mass of bodies of rat control and experimental group showed that during the experiment, the experimental group of rats had plenty in development compared to the control group by 1.7 times. In all the experiments in terms of pancreatic islets was observed moderate lymphocytic infiltration. Morphological examination of the vessels in different time postnatal ontogenesis demonstrated that compared with the control group in the form of changes in the delay of progression and formation of individual components vascular wall. Destructive changes in the arterial wall marked us all experimental animals from the early days after the experiment.

Keywords: diabetes, streptozotocin, pancreas, blood vessels

Introduction

The high prevalence of diabetes mellitus is recognized as a non-communicable epidemic and is a serious medical and social problem. This is due to the severity of its course, a large number of complications (1, 2). According to WHO, there are currently more than 220 million patients with diabetes in the world (1), 10-20% of them are patients with diabetes type 1 (4). In 2005, DM caused 1.1 million deaths worldwide (3), and between 2005 and 2030, WHO experts expect. Diabetic angiopathy is the main manifestation of diabetes mellitus. They represent a generalized lesion of arterioles, capillaries and venules, thereby determining the clinical course and prognosis of the disease and are the most common cause of death. Over 2.7-4.5 million high amputations are performed annually in the world for diabetic lesions of the lower extremities. Microvascular complications characteristic of diabetes mellitus are realized through the development of endothelial dysfunction. Understanding the





mechanisms of adverse changes that occur in the body in diabetes mellitus is an urgent problem of modern medicine. To develop methods of correction that could mitigate the consequences of complications of DM, it is necessary to know what mechanisms are violated in this case.

The aim of the work, was to study the morphofunctional disorders of the vessels of the lower limb of rats with experimental diabetes mellitus.

Material and research methods

The object of the study were 90 white rats (males) of the Wistar line with an initial weight of 180 ± 2.64 g at the age of 4-6 months. The model of experimental diabetes mellitus was reproduced by a single intraperitoneal administration of streptozotocin in 0.1 M citrate buffer, pH 4.5, to Wistar rats at a dose of 60 mg/kg. Determination of blood glucose from the tail vein was performed by the glucose oxidase method. From the direct action of streptozotocin, 3 rats died. 2 animals were not sensitive. Only rats with elevated glucose levels (>11 mmol/L) were used for further study. The rats were slaughtered 5,15,30,60,90 days after the start of the experiment. To study the pancreas and vessels of the hind limbs, both in intact animals and in ESD rats, histological preparations were stained with hematoxylin and eosin, according to Van Gieson and Weigert. As well as x-rays of blood vessels. For mathematical data processing, Microsoft Excel 2010 applications were used in the section of descriptive statistics, determination of standard deviations and comparison of samples with the determination of the arithmetic mean M , the average error of relative values m and the coefficient of reliability of the difference t .

Results of the study and their discussion

Comparison of the body weight of the experimental and control groups showed that at the beginning of the experiment there was no significant difference in both groups. During the experiment, the mass of rats of the experimental group remained in development compared to the control group by 1.7 times. At the same time, the growth rate of the control group was 50%, and in the rat pups of the experimental group it was 21%. The development of experimental diabetes mellitus in experimental animals was accompanied by persistent hyperglycemia. The level of glucose in the blood of rats with DM increased to 19.4 ± 4.3 mmol/l compared with 5.2 ± 1.1 mmol/l in the control group. The blood glucose level in rats with ESD on the 5th day after administration of streptozotocin was significantly higher by 3.2 times when compared with animals in the control group. During the following days of observation, the amount of sugar in



the blood of rats of the experimental group of animals also remained stably high - 15.9 mmol/l, practically unchanged (± 0.38 mmol/l) compared with the 5th day of the study. At the same time, the level of fasting glycemia reached its maximum value by the 30th the day of the study and amounted to 19.4 mmol/l.

Microscopic examination of the pancreas of rats of experimental rats revealed degenerative and destructive changes in its tissue, especially the endocrine part - the islets of Langerhans. Already on the 5th day of ESD, edema of the interlobular connective tissue was observed. On the 60th day of the experiment, necrotic changes in β -cells were noted, which increased by the 90th day of the experiment.

In all periods of the experiment, moderate lymphocytic infiltration was noted in the pancreatic islets. The capillaries of the islets were sharply plethoric, the endocrinocytes located in the central zones were necrotic, and those located in the peripheral parts of the islet were hypertrophied. The volume fraction of islets decreased by 25% in comparison with rats in the control group. Insulin-positive cells were located singly or in the form of small clusters in the central sections of the islets around full-blooded capillaries. There was a significant decrease in the area occupied by endocrinocytes in all areas of the pancreas compared with the control group of animals.

X-ray vasography data established that in all animals of the experimental group within 5 days after the experimental modeling of diabetes mellitus, there was a noticeable expansion of intramuscular arterial vessels in the muscles of the leg and skin. So, in the early stages (5-15 days) of observation, inflammatory-destructive changes progress in combination with unexpressed atrophic processes.

Morphological studies of vessels at different times of postnatal ontogenesis showed that, compared with the control group, there were changes in the form of developmental delay and the formation of individual components of the vessel wall. We noted destructive changes in the arterial wall in all experimental animals from the first days after the experiment. They were characterized by thinning of the wall and expansion of the lumen of the vessel, a rare arrangement of endothelial nuclei, and desquamation of individual endothelial cells into the lumen of the vessel. The muscle layer is stretched, stands for 1 rows of cells. Fragmentation of the internal elastic membrane is also noted. On the 30th day of the experiment, sclerotic and destructive changes predominate in the walls of microvessels. The wall of the arterioles is thickened as a result of an increase in the basement membrane and wide surrounding connective tissue. In the middle shell of intramuscular vessels, a network of thin fibers connecting the inner and outer elastic membranes is revealed. Fragments of elastic membranes are replenished with new elastic elements. The membranes themselves





thicken somewhat. The wall of venules is also thickened and deformed due to hyperchromasia of endothelial cells and basement membrane.

On the 60th day of postnatal ontogenesis, morphological changes in the walls of blood vessels acquire a chronic course and are manifested by sclerotic and degenerative changes. The endothelial layer of the intima is represented by flattened cells, in others it forms a layer and a significant protrusion towards the lumen of the vessel. The basement membrane is tortuous, unevenly thickened and intensely stained with eosin, in some places due to thin and merges with the fibrous structures of the interstitial connective tissue. In the later stages of the experiment, hair loss and desquamation of the epidermis are observed on the foot of the limb. On the 90th day after the start of the experiment, trophic ulcers of various sizes appeared in the heel area or on the dorsum of the foot and toes.

Histological and histochemical studies show that all experimental animals have destructive changes in the walls of intramuscular vessels from the first days after ESD. Blood-filling vessels, their walls are thinned, the lumen is expanded. Many endothelial cells are swollen, cell nuclei are rarely located, some of them desquamate into the lumen of the vessel. The muscular layer of the vessels is stretched, consists of 1-2 rows of cells. The internal elastic membrane is thinned and fragmented in places. Moreover, in animals in the initial days of the experiment, destructive changes in the walls of intramuscular vessels are less pronounced. CHIC - reaction in animals of the experimental group is positive. Especially in 30 and 90 day old animals of the experimental groups, it is sharply positive. In subsequent periods (up to 30-60 days), the above vascular and tissue changes progress. An increase in the number of spastically narrowed vessels is observed. Often there are few and avascular zones, blind capillaries, especially in areas subject to atrophic changes. However, it should be noted that congestion in the venous bed is markedly pronounced. Such a picture of hemodynamic disorders leads to pronounced morphological changes in tissue structures.

Thus, the results obtained indicate that type 1 diabetes mellitus leads to changes in the vessels and muscles of the extremities. In the early period of the experiment that we studied, the development of diabetes mellitus leads to functional changes, and in the subsequent periods of the experiment, structural changes associated with impaired tissue metabolism.

Conclusion

The results indicate that the type 1 diabetes the pancreas causes changes and limbs.





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