

THEORETICAL MEDICINE: BASIC DEVELOPMENT TRENDS

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MORPHOLOGICAL CHANGES OF HEMOMICROCIRCULATORY FLOW OF THE OVARIES IN THE EARLY STAGES OF DIABETES MELLITUS UNDER STRESS

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Nowadays, diabetes mellitus (DM) occupies a leading position in the world among other diseases in terms of prevalence, continuous growth, complications and mortality [1, 2, 3]. In clinical and experimental studies, much attention is paid to the problem of diabetic polyendocrinopathies, which lead to impaired reproductive function in women. The scientific literature indicates that DM leads to development of partial types of gonadal dysgenesis, which can further cause menstrual irregularities leading to secondary amenorrhea of ovarian origin, which is confirmed by cases of diabetes in girls [4]. Therefore, the aim of the research was to study the histo-ultrastructural restructuring of the hemomicrocirculatory flow of the ovaries on the 14th day of streptozotocin-induced diabetes mellitus (SIDM) under stress.

Material and Methods. The study used 20 adult white male rats (body weight 180-200 g), which were equally divided into 4 groups: group 1 – rats with simulated SIDM and chronic immobilization stress, group 2 – rats with SIDM, group 3 – rats with immobilization stress, group 4 – intact animals. In groups 1 and 2, SIDM was simulated by a single intraperitoneal injection of streptozotocin «SIGMA» (USA), which was diluted in 0.1 M citrate buffer with a pH of 4.5 (at the rate of 6 mg per 100 g of body weight). In groups

1 and 3, immobilization stress was simulated by placing the animals in a closed plastic container for 5 hours a day. In group 1, SIDM was simulated and starting from the 14th day of the experiment chronic immobilization stress was simulated on a once-only basis. The material was taken on the 14th day from the beginning of the experiment. Histological, electron microscopic, biochemical and statistical research methods were used. Photographs of histological and semithin sections were used for morphometric studies (field of view of the light microscope Leica DM750 was photographed using a digital camera TouPCam 5.2M UHCCD C-Mount Sony). Morphometry was performed using ImageJ version 1.47t. The area of the profile field of arterioles, capillaries, venules, their walls and lumen was measured. In arterioles and capillaries, the Wagenworth index (WI) was determined by the formula [5]: $W=So/Spr \times 100$, where So is the vessel wall area (μm^2); Spr – the area of the lumen of the vessel (μm^2). Statistical analysis was performed using the statistical package StatSoft.Inc; Tulsa, OK, USA; Statistica 10.

Result. On the 14th day of the experiment, the level of glucose and glycated hemoglobin in the blood of rats in group 1 was the highest, compared to group 4, and was 15.61 ± 2.23 mmol/l ($p < 0.001$) and $7.21 \pm 0.72\%$ ($p < 0.01$), respectively; in group 2 – 13.53 ± 2.13 mmol/l ($p < 0.001$) and $6.12 \pm 0.48\%$ ($p < 0.01$); in group 3 – 5.45 ± 0.73 mmol/l ($p > 0.05$) and $2.18 \pm 0.32\%$ ($p > 0.05$); while in group 4 the above indicators were 4.35 ± 0.52 mmol/l and $2.03 \pm 0.17\%$. The level of cortisol in experimental groups 1-3 was probably higher than that of intact rats and was: in group 1 – 30.07 ± 2.93 ng/ml, in group 2 – 18.21 ± 2.09 ng/ml, in group 3 – 28.49 ± 2.34 ng/ml (in all cases, $p < 0.01$), in intact animals (group 4) it was 10.08 ± 1.13 ng/ml. Such biochemical changes in groups 1 and 2 indicate the development of decompensated DM, and in group 3 – the development of stress.

On the 14th day of the experiment, in 1-3 groups of animals, compared with group 4, there was a spasm of the vessels of the afferent link of the hemomicrocirculatory flow, which was confirmed by a decrease in the area of arterioles by 20-41% due to a decrease in their lumen by 35-56% (in all cases, $p < 0.05$). This morphometric rearrangement of arterioles led to an increase in the Wagenworth index in 1-3 groups of rats by 1.6-2.3 times ($p < 0.05$), which indicates a decrease in their capacity. In some lumens of capillaries of rats in groups 1, 2, erythrocyte sludges, adhesion of erythrocytes and platelets were noted. In the peripheral zone of endotheliocytes of capillaries of animals in groups 1-3 the thickened areas of the cytoplasm with organelles and an increase in the number of micropinocytic vesicles were observed; mitochondria with disorganized and partially destroyed crystals were visualized. In 1-2 groups of rats there was an increase in fenestration of

capillary endotheliocytes, and in group 1 the pores were formed in some places. This rearrangement of the capillaries indicates an increase in transendothelial metabolism. The lumen of the venules in group 1 animals, compared with intact rats, was probably increased by 18% and filled with formed elements of blood.

In the early stages of SIDM (14th day) on the background of hyperglycemia there was an increase in the functional activity of the pituitary-adrenal system [6], which leads to higher blood levels of adrenocorticotrophic hormone, catecholamines, glucocorticoids and increases the activity of the renin-aldosterone-angiotensin system, which cause vasoconstriction and raise blood thrombogenic activity, contributing to impaired microcirculation [2, 3]. According to our studies, the rearrangement of capillary endotheliocytes in 1-2 groups of rats (increased fenestration, pores and micropinocytic vesicles), in our opinion, on the one hand indicates increased transendothelial metabolism, and on the other hand – it is a response to hyperglycemia, which leads to higher levels of glycated hemoglobin, which in turn causes changes in blood flow (erythrocyte sludge, adhesion of erythrocytes and platelets to endothelial cells), which according to various authors indicates the development of diabetic microangiopathy [1, 3, 5].

Thus, in the early stages of SIDM there were initial signs of diabetic microangiopathy, manifested by: hemorheological disorders (erythrocyte sludge, adhesion of erythrocytes and platelets), spasm of the arterial link of hemomicrocirculatory flow, reactive changes in capillary endotheliocytes. These changes are more pronounced in comorbid pathology and lead to disruption of ovarian blood supply.

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MORPHOLOGICAL CHANGES OF THE MYOCARDIUM IN COMORBID PATHOLOGY

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The prevalence of heart failure in the population ranges from 1 to 4%, and in patients with diabetes mellitus (DM) it ranges from 12% in young people to 22% in people over 64 years [1]. According to the authors, almost a third of patients hospitalized with heart failure, have diabetes. Diabetic cardiomyopathy (DCMP) is diagnosed in approximately 4% of patients with type 1 diabetes at a young age, with a labile course, predisposition to ketoacidosis, low body weight and small vessel damage. DCMP has no specific clinical signs and often develops without subjective symptoms [2].

In view of the above, the aim of our research was to study the morphological changes in the myocardium of the heart of rats with streptozotocin-induced diabetes mellitus (SIDM) under chronic stress.

Material and Methods. The study used 15 adult white male rats (body weight 180-200 g), which were equally divided into 3 groups: group 1 – rats with simulated SIDM and immobilization stress, group 2 – rats with SIDM, group 3 – intact animals. In groups 1 and 2, SIDM was simulated by a single