THEORETICAL MEDICINE: BASIC DEVELOPMENT TRENDS

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MORPHOLOGICAL CHANGES IN GRANULOSA CELLS IN EXPERIMENTAL DIABETES UNDER CONDITIONS OF CHRONIC STRESS

МОРФОЛОГІЧНІ ЗМІНИ ЗЕРНИСТИХ ФОЛІКУЛОЦИТІВ ПРИ ЕКСПЕРИМЕНТАЛЬНОМУ ЦУКРОВОМУ ДІАБЕТІ ЗА УМОВ ХРОНІЧНОГО СТРЕСУ

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According to the Ministry of Health, the psychological consequences of the war, including post-traumatic stress disorder, will affect our health even 7-10 years after its end. Stress and constant psychological pressure in girls and women are the main causes of multifollicular changes in the structure of the ovaries, which lead to polycystic ovary syndrome [3, 4]. The cause of multifollicular transformation of the ovarian structure can be diseases of the endocrine system, in particular diabetes mellitus (DM). Scientific data indicate that with diabetes mellitus, erased forms of gonadal dysgenesis develop, which can further cause menstrual cycle disorders, in particular, leading to secondary amenorrhea of ovarian genesis, which is confirmed by cases of DM in girls [1, 2]. The relevance of the problem of diabetes mellitus (DM) is determined not only by its prevalence. Chronic lifelong course, early

disability, high mortality rate put this disease on a par with such catastrophic illnesses as AIDS and cancer [5].

Based on the above-mentioned, the goal of our work is the study of morphological changes in the ovarian granulosa cells of sexually mature female rats with streptozotocin (STZ)-induced diabetes mellitus under conditions of chronic stress.

Material and Methods. The study used 20 adult white female 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 SDM, group 3 – rats with immobilization stress, group 4 – intact animals. In groups 1 and 2, SDM 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, SDM 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. Statistical analysis was performed using the statistical package Stat.Soft.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±0.72% ($p<0.01$), respectively; in group 2 –13.53±2.13 mmol/l ($p<0.001$) and 6.12±0.48% ($p<0.01$); in group 3 – 5.45±0.73 mmol/l ($p>0.05$) and 2.18±0.32% ($p>0.05$); while in group 4 the above indicators were 4.35±0.52 mmol/l and 2.03±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, an increase in the number of granulosa cells was observed in animals of groups 1 and 2. At the ultrastructural level, destructive changes are observed in the membrane organelles of these cells: the inner membrane of mitochondria is destroyed with the subsequent

formation of vacuoles of various sizes, the tubules and vesicles of the Golgi complex expand and collapse. Most of the cells are filled with lipid droplets with a blurred periphery. Hyperplasia of the smooth endoplasmic reticulum is noted. Such changes in granulosa cells indicate their increased functional activity. In the ovaries of rats in groups 1 and 2, granulosa cells with pronounced signs of vacuolar dystrophy and colliquative necrosis were observed. Individual cells were filled with lipid droplets with a blurred periphery and were half-empty. In the ovaries of rats of group 3, in the granulosa cells of the internal theca of the follicle, reverse morphological phenomena of the vacuolar dystrophy type prevailed. Whereas autophagosomes and apoptotic bodies were detected in granulosa cells of the outer theca of the follicle.

Conclusions. Experimental diabetes leads to an increase in the functional activity of ovarian granulosa cells, which is confirmed by a visual increase in their cytoplasm of lipid droplets and hyperplasia of the smooth endoplasmic reticulum. Along with functionally active granulosa cells, granulosa cells with pronounced signs of vacuolar dystrophy and colliquative necrosis, which are usually found in animals with comorbid pathology, are visualized. Chronic immobilization stress leads to apoptosis and vacuolar dystrophy of ovarian granulosa cells.

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