DOI https://doi.org/10.30525/978-9934-26-260-9-20

MORPHOFUNCTIONAL CHANGES OF CORTICOTROPIC EDOCRINOCYTES UNDER CONDITIONS OF COMORBID PATHOLOGY

МОРФОФУНКЦІОНАЛЬНІ ЗМІНИ КОРТИКОТРОПНИХ ЕДОКРИНОЦИТІВ ЗА УМОВ КОМОРБІДНОЇ ПАТОЛОГІЇ

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Elucidation of the peculiarities of the morpho-functional reorganization of the pituitary-adrenal system in diabetes mellitus is an important medical and social problem nowadays. Because the dysfunction of the hypothalamic-pituitary-adrenal system plays a central role in the pathogenesis of this disease [1, 5]. Thus, hyperproduction of contrainsular hormones (glucocorticoids, aldosterone) leads to the development of micro– and macroangiopathy as a compensatory reaction in response to metabolic stress. [4].

In clinical and experimental studies, a lot of attention is paid to the problem of diabetic polyendocrinopathies [4, 5]. While it should be noted that these works don't explain on the issue of comorbidity in diabetes, in particular, the influence of long-term chronic stress on its course. Considering that there is currently a war in Ukraine, the majority of the population is in terms of constant stress. 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 [3].

Considering the above, the aim of our study was to establish the histo-ultrastructural changes of corticotropic endocrinocytes of the adenohypophysis in streptozotocin diabetes mellitus (SDM) under conditions of chronic immobilization stress (CIS).

For testing were used 20 sexually mature white male rats (whose body weight is 180-200 g), which were equally divided into 4 groups: 1 – with simulated SDM and chronic immobilization stress, 2 – with SDM, 3 – with immobilization stress, 4 – intact animals. In the 1st and 2nd groups of rats, SDM was modeled 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). CIS was modeled by immobilizing animals in a sealed plastic container (Ukrainian patent for the invention No. 125623). In the 1st group of animals, SD was simulated and starting from the 14th day of the experiment, chronic immobilization stress was simulated one-time. Histochemical (azan staining according to Hendenhain), ultramicroscopic, biochemical and statistical research methods were used. The material was collected on the 14th day of the experiment. Statistical analysis was carried out using the statistical package Stat.Soft.Inc; Tulsa, OK, USA; Statistics 10.

Result. On the 14th day of the experiment, the level of glucose and glycated hemoglobin in the blood of the 1st group of rats is the highest compared to the 4th group and is 15.24±2.67 mmol/l ($p<0.001$) and 7.54± 0.69% ($p<0.01$), in the 2nd group – 13.74±1.29 mmol/l ($p<0.001$) and 6.08±0.59% ($p<0.01$), in the 3rd group – 5.15±0.83 mmol/l ($p>0.05$) and 2.24±0.31% ($p>0.05$), while in the 4th group of animals the above indicators are 4.85±0.47 mmol/l and 2.13±0.15%. The level of cortisol in experimental groups 1-3 was probably higher than that of intact rats and was: in the 1st – 31.54±3.03 ng/ml, in the 2nd – 17.39±2.24 ng/ml, in the 3rd – 29.42±2.86 ng/ml (in all cases $p<0.01$), in intact animals (4th group) 10.17±1.21 ng/ml. Such biochemical changes in the 1st and 2nd groups of rats indicate the development of subcompensated diabetes, and in the 3rd, the development of stress.

On the 14th day of the experiment, hyperemia of the adenohypophysis and vacuolar dystrophy of individual basophils were noted in groups 1-3 of rats. The number of corticotropic endocrinocytes per 0.01 mm 2 of adenohypophysis area probably increases in the 1st group of animals to 4.8±0.13, in the 2nd – to 4.3±0.12, in the 3rd – to 4.6 ±0.07 (intact – 2.8±0.07, in all cases $p<0.05$). In the cytoplasm of most corticotropic endocrinocytes of animals of groups 1-3, a large number of secretory granules (SG) can be visualized, which fill it and the processes of the cell. Among (SGs), young

forms with a matrix of moderate and high electron density prevail in animals of the 2nd group, while in rats of the 1st and 3rd groups, bordered (SGs) («haloed granule») prevail, which indicates active processes of adrenocorticotropic hormone release from cells. The nuclei of corticotropic endocrinocytes of animals of groups 1-3 have an irregular shape and a marginal arrangement of chromatin. The perinuclear space is defined by sites. There are few mitochondria, some of them are represented by vacuoles due to the destruction of their cristae. Hypergranulated and moderately granulated corticotropic endocrinocytes predominate in the adenohypophysis. In most of them, there is hypertrophy of the components of the Golgi complex and the granular endoplasmic reticulum. The cisterns of the latter are expanded, and in the intercisternal hyaloplasm free ribosomes are visualized. Volume density of SG, compared to the 4th group of animals, increases in the 1st group of animals to 7.44±0.12%, in the 2nd to 6.98±1.21%, in the 3rd to 6.78±0.73% (in all cases $p<0.05$). Such morpho-functional changes in corticotropic endocrinocytes in SCD and ICS indicate adaptive and compensatory processes that are associated with hyperglycemia and stress. The development of a stress reaction, manifested by an increase in the functional activity of corticotropic endocrinocytes of the adenohypophysis, which coincided with the functional stress of the cells of the bundle zone of the adrenal glands and was accompanied by an increase in the level of cortisol in the peripheral blood, was described by other researchers in diabetes [5, 6]. These authors believe that adenocorticotropic hormone through its receptors on B-cells of pancreatic islets stimulates Ca^{2+}-dependent processes of insulin secretion and protein activation. Other researchers noted an increase in the level of corticoliberin in the blood in the fourth week of the development of streptozotocin diabetes [7], and immunohistochemical methods proved that the neurons of the paraventricular and arcuate nuclei are most involved [2, 6].

Thus, the morpho-functional changes in corticotropic endocrinocytes in (DM), (HIS) and their combination indicate an increase in their functional activity and the development of adaptive and compensatory processes in them.

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