



"Mitochondrial Dysfunction in Women and How it is Related to Reproductive Impairment in Cushing's Syndrome"

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ABSTRACT:

The problem of deterioration of women's reproductive function remains extremely urgent all over the world, and mitochondrial dysfunction is one of the reasons leading to insufficient supply of oocytes with energy. In our study, 22 women had reproductive disorders of various origins, including infertility. The study of the anamnesis of patients showed, in terms of the cause of infertility, the body mass index and levels of basal serum hormones, unlike the group with Cushing's syndrome, had a number of changes.

INTRODUCTION

Cytological analysis showed a number of organelle damage in the oocytes of older women: many mitochondria were elongated or spherical in shape, with a disturbed internal ultrastructure; cases of rupture of the outer membrane were noted. At the same time, laser scanning confocal microscopy revealed a decrease of almost 2 times in the activity of biochemical processes even in intact mitochondria.

Diagnosis of Cushing's syndrome is the most difficult problem in clinical endocrinology. The clinical manifestations of the effects of excess glucocorticoids (endogenous or exogenous) are diverse and may be barely distinguishable. [1,2]. Since the clinical syndrome is not always obvious, screening is necessary at the slightest suspicion and certainly in high-risk groups. So, there are several clinical disorders, the presence of which should

prompt the idea of searching for SC among the clinical spectrum of metabolic syndrome, including obesity, diabetes, hypertension and gonadal dysfunction [5].

Since women with Cushing's syndrome may have menstrual irregularities or signs and symptoms of an excess of androgens, PCOS is often diagnosed. Kaltsas G A 1, Korbonits M, Isidori A M, Webb, etc. They showed that most women with SC also have PCOS and suggested that women with PCOS should be examined for hypercorticism [6]. Interestingly, the cycle disorders in these women are probably more related to the degree of excess cortisol than to the actual concentration of circulating androgens [7].

The problem of violation of the functional state of the vascular endothelium, which has been actively studied for more than 10 years and to which a significant number of publications have been devoted, has not lost its relevance



to this day. As is known, the endothelium is involved in the formation of vascular tone, smooth muscle cell growth, thrombosis, fibrinolysis and many other processes in the body. Endotheliocytes regulate the immune response, migration of blood cells into the vascular wall, synthesis of inflammatory factors and their inhibitors, and perform barrier functions [8]. Data on the involvement of the endothelium in immune and non-immune inflammation were obtained [9].

Endothelial dysfunction is currently understood as a violation of the balance between the production of vasodilating, angioprotective, antiproliferative and vasoconstrictive, prothrombotic, proinflammatory, proliferative factors. One of the reasons for the violation of regional blood supply and microcirculation is endothelial dysfunction. The causes of endothelial dysfunction may be such features as: the presence of cells in a state of ischemia and hypoxia, age-related disorders, free radical damage, an imbalance of proteins in the blood, an increase in cholesterol levels, the influence of cytokines, hyperhomocysteinemia, increased sugar levels, pressure, exogenous and endogenous intoxication [10]. An analysis of the literature has shown that research on the state of the endothelium in SC syndrome has been little studied.

There are only isolated descriptions of studies by foreign authors. The study of the state of the vascular wall and the search for targeted treatment of endothelial dysfunction are important clinical and experimental tasks of modern endocrinology. In addition, there are few papers devoted to the study of the ultrastructure of cells in patients with SC.

All of the above was the reason for this study.

The aim of the study was to evaluate the role of endothelial damage factors and electron microscopic examination of mitochondria in patients with Cushing's syndrome

Material and Methods of Research

As of January 1, 2021, only 324 patients with various forms of SC are registered, including 225 women (69.4%), 99 men (30.6%). The average age was 27.58 ± 3.4 years (from 17 to 49 years). The duration of the disease averaged 4.2 ± 0.2 years. 20 healthy women of the appropriate age made up the control group.

According to the etiological factor, the patients were divided into 3 groups: 1 gy. – patients with ACTH-dependent SC - 263 patients, of which 178 were women (67.7%) and 85 men, 2 gy. – with ACTH-independent SC – 53 patients, of which 42 were women (79.2%) and 11 (20.8%) men and 3 gy. – patients with ACTH-ectopic SC-8 (2.4%) patients, of which 3 (37.5%) men and 5 (62.5%) women.

In total, we observed 220 persons with SC of reproductive age, 153 of them women (69.5%). Then we selected these patients and conducted further studies.

Next, we selected women of fertile age (from 18 to 35 years), the number of which was 153.

According to the classification of the American Association of Endocrinologists from 2012, all 153 patients with SC who have been registered since 2000 (the deceased are not included) were distributed according to etiology as follows: 1 gr. – patients with ACTH-dependent SC– 115 (75.2%), 2 gr. – with ACTH-independent SC – 35 (22.9%) and group 3 were patients with ACTH-ectopic SC –3 (1.9%). The age of patients in group 1 ranged from 20 to 39 years and averaged 28.3 ± 0.64 years. In the 2nd group of 22-37 years, on average 30.4 ± 0.51 years and in the 3rd group – an average of 29.4 ± 0.51 years, respectively.

The second stage of this study was the selection of patients of the main groups and the control group.

Patients with SC were distributed by age according to the WHO classification of 2007 (Table 1.). Table 1 shows that the majority of patients were at a young reproductive age from 20 to 40 years.

Table 1. Distribution of patients by age (WHO, 2007)

Age, years	Female abs (%)
youth period	56 (36,6%)
17-21 years old	52 (33,9%)
22–29	45 (29,4%)
30-35	153

According to Narimova G.D. [26], the diagnosis of SC in most 87.5% of cases was established by the staff of the RSNPMCE of the Ministry of Health of the Republic of

Uzbekistan named after academician E.H. Turakulov, in 10.6% of patients, SC was established in regional endocrine dispensaries (OED), while 1.9% of patients



were diagnosed by specialists not according to their profile.

Inclusion criteria: Female patients, patients with SC (ACTH-ZSK, ACTH-NSK, ectopia), age – 11 years and older, absence of inflammatory diseases of internal and genital organs

Exclusion criteria: brain tumors, malignant neoplasms of any localization, patients with NAG, prolactinomas, somatotropinomas, gonadotropinomas, thyrotropinomas, acromegaly, acute critical conditions, severe chronic diseases of the liver, kidneys, gastrointestinal tract, patients with multiple endocrine neoplasia

The methods of treatment of ACTH-ZSC were surgical (TAG and AE, surgical treatment of ACTH of ectopic foci), radiation therapy (LT) and drug therapy (MT), as well as combination therapy (Cte).

All patients with SC received treatment in the Department of Neuroendocrinology and Neurosurgery of the Russian National Academy of Medical Sciences named after Academician E.H. Turakulov. Transnasal adenectomy of the pituitary gland (TAG) was performed initially in 93 patients, of which 14 were repeated (Prof. Powell M.P. (Great Britain, London), MD Makhkamov K.I.).

In the vast majority of cases, histological confirmation of corticotropinoma was obtained.

Adrenalectomy: was performed in 43 patients, 11 of them with ACTH-CSC (Department of Endocrine Surgery of the Russian National Center of Endocrinology of the Ministry of Health of the Republic of Uzbekistan named after Academician Ya.Kh. Turakulov, prof. Ismailov S.I.).

Drug therapy: was performed in 35 patients. This type of treatment was carried out in the absence of contraindications.

All patients underwent the following range of studies, including general clinical and biochemical studies - general analysis of blood, urine, blood sugar, lipid spectrum, blood electrolytes (potassium, sodium,

chlorides, blood calcium), markers leptin, interleukin-6, assessment of plasma and platelet hemostasis, markers of endothelial dysfunction (Willebrand factor, VEGF and endothelin-1), radioimmunological hormonal methods of blood testing (adreno-corticotron hormone (ACTH), prolactin, cortisol, estradiol, progesterone, free testosterone, aldosterone, small and large dexamethasone samples, cortisol secretion rhythm), as well as instrumental studies – ECG, absorption X-ray densitometry, electron microscopic examination, ultrasound of the genitals (on days 7, 14, 21 of the cycle). All patients underwent magnetic resonance imaging of the pituitary gland (MRI) and computed tomography (CT) of the adrenal glands. If necessary, an oral glucose tolerance test was performed.

The quality of life was assessed using the Women's Health questionnaire – Women's Health Questionnaire – WHQ (author – M. Hunter). WHQ (Women's Health Questionnaire) – a special questionnaire for the study of women's quality of life (author – Dr. Myra Hunter, Department of Psychology Adamson Centre ST Thomas Hospital Lambeth Palace Road, London, UK

The obtained data were processed using computer programs Microsoft Excel and STATISTICA_6 (136-140). The reliability of differences in quantitative indicators ($n > 12$) was determined using the Wilcoxon method for unrelated ranges, the nonparametric criterion of randomization of Fisher components for independent samples was used to determine the reliability of small samples ($n < 12$), and the exact Fisher-Irwin criterion was used for qualitative values. The differences between the groups were considered statistically significant at $P < 0.05$. Research results. It was found that $82.4 \pm 5.63\%$ of women of fertile age had achieved remission, and $17.6 \pm 5.63\%$ of patients as a whole had not achieved remission. Table 2 shows the activity of the endogenous hypercriticism process in various forms of the disease.

Table 2 Characteristics of the condition of patients with SC according to the register (n=153)

№	The condition of patients n= 153	ACTG-ZSK (%±m) n= 115	ACTG-NSK (%±m) n= 35	ACTG ESC (%±m) n= 3	Total (%±m) n= 153
1	Remission n=126	n=89 77,4±3,22	n=34 97,1±4,12***	n=3 100,0±2,83	n=126 82,4±5,63
2	Active	n=26 22,6±2,63	n=1 2,9±1,83**	n=0	n=27 17,6±5,63

Note: - the significance of the differences compared to ACTH-dependent SC, where *** $p < 0.001$. (NDR-

patients who have not achieved remission, P- patients who have developed a relapse)



As can be seen from Table 2., a high remission rate was found in patients with ACTH-NSC, which amounted to $97.1 \pm 4.12\%$ of cases, and only in 1 case (2.9%) relapse of the disease developed due to an unfavorable outcome with the development of metastases after surgery for adrenal carcinoma.

According to the research results of Narimova G.D., in 2018, 71% of patients with SC in the Republic of Uzbekistan achieved remission [7]. Moreover, the lowest remission was observed in patients with ACTH-HSC and amounted to 65.3%, which is consistent with the literature data.

The next stage of our work was the clinical characterization of patients with SC. Patients were distributed according to the duration of the disease from the moment of manifest symptoms until the diagnosis of the disease (Table 3.). The results of this analysis showed that the duration of the disease up to one year was established in 42 patients (27.2%), the duration of the disease from one to 3 years was detected in 68 patients (44.4%), from 3 and It was detected for more than 43 years (28.1%).

Table 3 Prescription of the disease by group

The duration of the disease	ACTG –ZSK (n=115) abc (%)	ACTG –ZSK (n=35) abc (%)	ACTG –ZSK (n=3) abc (%)	ACTG –ZSK (n=153) abc (%)
is up to a year	28 (24,4%)	13 (37,1%)	1 (33,3%)	42 (27,2%)
from 1 year to 3 years	47 (40,7%)	19 (54,3%)	2 (66,7%)	68 (44,4%)
from 3 years and more	40 (34,9%)	3 (8,6%)	-	43 (28,1%)

Thus, it was revealed that the overwhelming majority of patients – 111 (72.5%) – had a disease prescription of more than one year, which causes a high incidence of complications in this category of patients.

The next step of the research was to analyze the nature of the course of the disease. It is known that the course of SC can be aggressive or torpid. With an aggressive course, the symptoms of the disease and complications increase rapidly (within a few months) There were 112 such cases (73.2%). The torpid course is characterized by the gradual development of the disease (over several years), which occurred in 41 (26.8%) of the total number of patients with SC. In most cases, it is the torpid course of the disease that causes late treatment of patients and, accordingly, late diagnosis, which causes severe complications that limit the choice of a treatment method for the disease.

Further, our analysis of the causal factors preceding the IC manifesto showed the dominant importance of stressful situations (34.4%), as well as TBI (7.8%), pregnancy (6.1%) and surgical interventions (4.5%) with infectious

diseases (3.2%). The proportion of births (3.3%), hepatitis (2.2%), and abortions (2.7%) was significantly lower than the other causes. 35.7% of patients did not associate the onset of their disease with anything.

The study of the burden on the life history of patients revealed that heredity for type 2 diabetes was burdened in 12 patients (7.8%), diabetes with hypertension in 35 (22.9%), while 43 (28.1%) had obesity in the genus, and 20 (13.0%) had infertility in the genus.

To further study this issue in order to determine the role of membrane pathology in the development of dyslipidemia and vascular wall lesions in patients with SC, we decided to study some aspects of disorders in the lipid metabolism system, hormonal status and the state of vascular endothelial cells.

As can be seen from the presented research results (Table 4), patients with SC have significantly high triglyceride levels, a slight increase in low-density lipoproteins (LDL) and a decrease in high density (HDL).

Table 4 Indicators of the pituitary-adrenal system in patients with SC

Indicator	Patients with SC n=25	Healthy people n=18
Cholesterol mmol/l	5,36±0,43	5,13±0,48



LDL mmol/l	3,68±0,29	3,41±0,24
HDL mmol/l	1,06±0,15	1,19±0,14
Triglycerides mmol/l	4,57±0,39*	0,87±0,11

Примечание: * - достоверность различий при сравнении группой контроля $P < 0,05$

Apparently, high blood triglyceride values stimulate adrenal steroidogenesis in vitro and in vivo. It should be noted that the stress state of LDL and VLDL directly transports cholesterol from the liver, which is necessary to ensure the synthesis of adrenal hormones.

As is known, adipocytes of adipose tissue secrete a large amount of free fatty acids, which activate macrophages that produce proinflammatory cytokines in patients with SC. Cytokines include adiponectin, which suppresses the increase in adipocytes and stimulates the production of leptin.

At the same time, the physiological role of leptin is to suppress appetite and increase energy consumption through the hypothalamus. However, as can be seen from the research results, the amount of circulating leptin

increases with an increase in the percentage of fat. Along with this, leptin receptor resistance develops and obese patients do not reduce their appetite.

Adipokines released from adipose tissue, as well as neuropeptides secreted from endothelial cells, are also involved in ACTH-independent activation of cortisol release by the adrenal cortex. In our studies, we observe an increase in the level of ACTH in the blood of the subjects. The analysis of the obtained research results presented in Table 5 indicates a significant increase in the level of adiponectin in the blood of patients with SC. As mentioned above, an increase in triglyceride levels and activation of the gluconeogenesis process contributes to an increase in white fat levels, which occurs against the background of a significant increase in leptin in the examined patients.

Table 5. Indicators of adipocyte hormones and IL-6 in the blood of patients with SC

Indicator	Patients with SC n=25	Healthy people n=18
Adiponectin ng/ml	15,46±0,19*	18,23±0,12
Leptin ng/ml	44,91±3,24*	8,73±0,76
Aldosterone pg/ml	179,58±9,68*	96,53±8,24
IL-6 pg/ml	3,98±0,29*	0,41±0,03

Note: * - the reliability of the differences when compared by the control group $P < 0,05$

An increase in serum aldosterone concentration in patients with SC is probably associated with obesity and metabolic disorders. This condition may also be due to increased activity of the renin-angiotensin-aldosterone system (RAAS).

At the same time, the increased content of IL-6 in the blood of the examined patients, in our opinion, is an unfavorable risk factor for the development of not only

obesity, but also cardiovascular disorders.

Against the background of an increase in ACTH levels in patients with SC, as can be seen from the presented research results (Table 6), there was a significant increase in cortisol levels at various times of the day. In addition, the examined patients showed a significant increase in the level of free cortisol in saliva, where its concentration exceeded the baseline level in the comparison group by an average of 6 times.

**Table 6.** Indicators of the pituitary-adrenal system in patients with SC

Indicator	Patients with SC n=25	Healthy people n=25
ACTH at 9 h, pg/ml	33,5+3,7	29,5+2,3
Cortisol at 9 h, nmol/l	678+48	384+17
Cortisol at 21 h, nmol/l	610+56	144+6,5
Free cortisol in saliva, nmol/l	21,7+3,7	3,7+0,5

Note: * - the reliability of the differences when compared by the control group $P < 0,05$

Diagnosis of endothelial dysfunction is an important task today, however, despite numerous studies and applied techniques, there is still no single standard, both among instrumental and laboratory methods. The works devoted to the relationship between the parameters of endothelial

dysfunction in patients with SC, as well as the influence of components of lipid metabolism and hormonal status on their occurrence are few and contradictory [200-202].

An analysis of the results of the study presented in Table 7 showed an increase in the level of Willebrand factor in patients with SC.

Table 7. Concentration of markers of endothelial dysfunction in patients with SC

Indicator	Patients with SC n=25	Healthy people n=28
The Willebrand factor %	114,47±9,78*	106,13 ±8,79
VEGF, pg/ml	187,26±11,23*	71,47±6,98
Endothelin -1 fmol/ml	2,83±0,24 **	0,31±0,026

Note: * - reliability of differences when compared by the control group $P < 0,05$, ** - $P < 0,001$

The study of endothelial dysfunction revealed an increase in markers of Willebrand factor, VEGF and ET-1 in the group with SC compared to the comparison group, especially ET-1. All of them are recognized markers of endothelial dysfunction and correlate with each other. It has been proven that obesity and hyperglycemia, dyslipidemia and hypertension contribute to the progression of markers of endothelial dysfunction. In obesity, the Willebrand factor plays a certain role in the increased endocrine activity of adipose tissue along with leptin.

ET-1 is a powerful vasoconstrictor, and its increase is shown in obesity, as well as in obesity in combination with hypertension or disorders of carbohydrate metabolism, which is completely consistent with our data. We also found an association of ET-1 with leptin levels, the leptin/adiponectin ratio, which is explained

by the fact that increased leptin production contributes to endotheliocyte damage by peroxides and free oxygen radicals and an increase in endothelin-1 expression. The relationship between the level of VEGF and IL-6 was also revealed. There is evidence that in obese patients, the level of VEGF is significantly increased compared to the indicators of the comparison group, which is regarded as a reaction to the activation of angiogenesis. The connection of VEGF with IL-6 is explained by its pathological effect, which is manifested by the premature development of atherosclerosis, which is realized through the activation of endothelial cells, as well as the proliferation and migration of smooth muscle cells, which leads to the development of endothelial dysfunction.

Electron microscopic examination was performed on 68 patients with SC.

It is known that mitochondria perform the following functions:



respiration, ATP synthesis, participation in iron metabolism, redox process, oxidation of amino acids with the help of metals: copper, iron, cobalt and manganese. Participation in the regulation of calcium, NO synthesis in membrane structures. Generation of reactive oxygen species and regulates apoptosis.

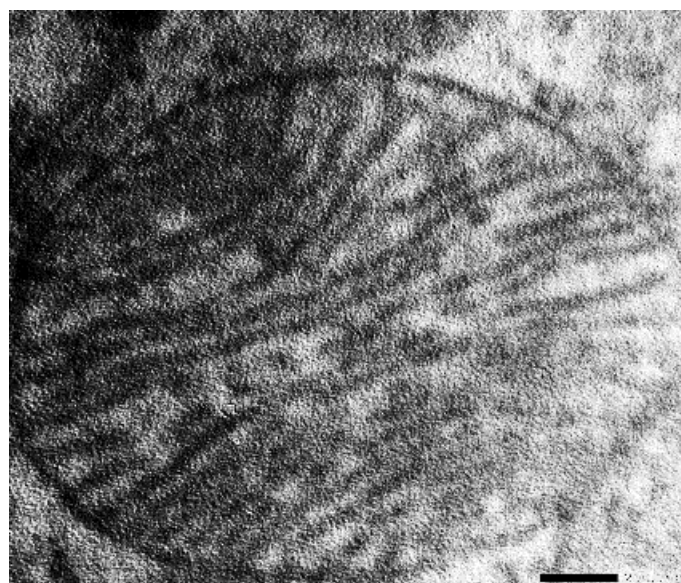
Our study showed that the mitochondria of women of fertile age have rounded and oval shapes, sizes range from 600 nm to 1200 nm. All mitochondria have two membranes, the outer membrane is lipoprotein and impermeable, the inner one forms crystals that pass through the mitochondrial matrix in the form of osmophilia membranes (Fig. 2). The outer membrane of the mitochondria with a thickness of 20 nm consists of osmophilia protein substances, which evenly surrounds the mitochondrial matrix. The inner membrane moves away from the outer membrane towards the matrix and forms crystals, which also have a thickness of 20 nm and form a large number of smooth osmophilia partitions. Between them there is a moderately osmophilia matrix, which contains carbohydrates, microelements and enzymes. Crystals in their composition contain amino acids and trace elements and dehumidifies respiration, ATP synthesis, participation in iron metabolism, redox process. With the help of metals, in particular copper, iron, cobalt and manganese, amino acids are oxidized and leads to the reduction of nicotinamide or NADH. Also, crystals are involved in the regulation of calcium, synthesis of NO in membrane structures. When the respiratory substrates or proteins

of the mitochondrial Crist are oxidized, carbon dioxide and water are formed, while the electrons are taken by NADH and reduced nicotinamide or NADH (nicotinamide-adenine dinucleotide) and give its electron to oxygen and water is formed. Due to the oxidation of protein substrates and NADH, ATP is synthesized.

In this scientific study, the second group consisted of patients with SC in remission, in which the amount of cortisol in the blood of patients has average values and, therefore, pathological changes form gradually over a long period.

We also studied the mitochondria of white blood cells isolated by ultracentrifugation.

The study of the mitochondrial ultrastructure showed that in patients with SC in remission, all membrane structures, both the outer shell and the crystals were presented in a curved form. The adhesion of ribosomes and polysomic to the outer membrane of mitochondria was noted (Fig. 2), while the colic of ribosomes and polysomic were changed and there was a violation of the osmophilicity of ribosomal grains. These submicroscopic changes in mitochondria and other organelles of the cytoplasm of nucleated blood cells indicate lipophilic glucocorticoids penetrate by diffusion through the membranes of mitochondria and increases the permeability of membranes and water and protein substrates of the cytoplasm, in particular ribosome proteins, penetrate into the mitochondrial matrix



Rice 2. The ultrastructure of the mitochondria is represented by an external osmiophilic membrane and long crosses on the background of the matrix. Electron microscopy. Uv: 35,000.

Thus, the study of the mitochondrial ultrastructure showed that in patients with Cushing's syndrome in remission, there is a thickening and an increase in osmophilicity of membrane structures, showing an increase in protein and

carbohydrate metabolism and an increase in their content in submicroscopic mitochondrial structures, which shows an increase in respiration, redox processes and ATP synthesis in mitochondria.



Submicroscopic examination of the mitochondria of white blood cells at the stage of acute SC showed the development of destructive changes in all ultrastructural components of the mitochondria. The outer membrane is unevenly thinned with foci of decay and lysis, especially in the areas of vacuolization of the cytoplasm of the cell, the osmophilic contours of both the outer and inner membrane are not determined. In the circumference of the mitochondria, the presence of tightly adjacent structureless osmiophilic masses is determined, which are apparently

due to the decay and destruction of other cellular organelles. In the zone where there is a structureless mass, the contours of the outer mitochondrial membrane are not determined due to the fusion of membrane substrates with a structureless mass. Mitochondria are enlarged in size due to matrix edema. Some of the cristae are in a state of decay and destruction (Fig. 3) and form moderately osmiophilic structureless contents with foci of vacuolization and increased osmiophilicity of granules.

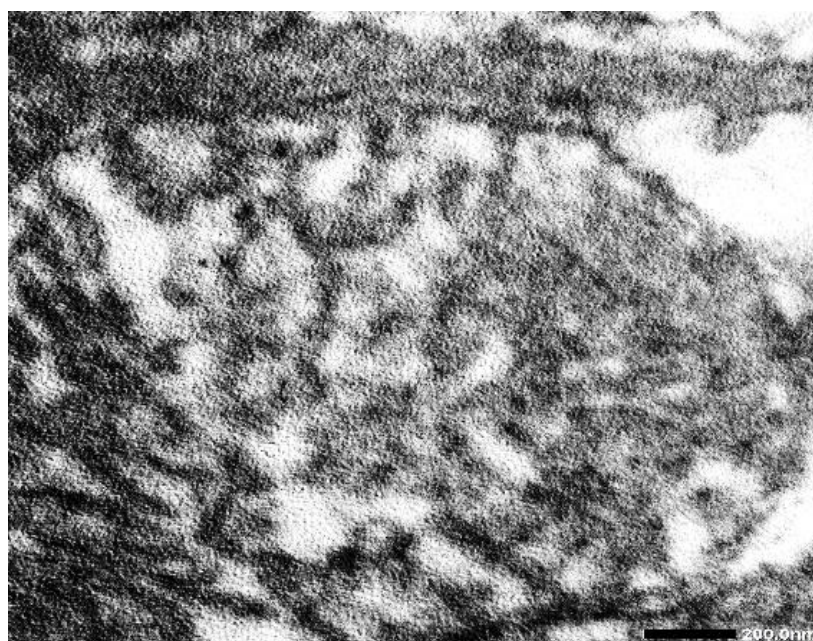


Fig. 3. Destruction of membrane structures and edema of the mitochondrial matrix. Electron microscopy. Figure 3. Destruction of membrane structures and edema of the mitochondrial matrix. Electron microscopy. Uv: 40 000 40 000.

The other part of the cristae are located closely and closely adjacent to each other, the membrane structures are thickened and strongly osmophilic. These submicroscopic changes in mitochondria under the action of cortisol are explained by the fact that in the membrane structures and matrix, the exchange of proteins, lipids and carbohydrates is disrupted, which, due to the hydrophobic and hydrophilic properties, stabilize ultrastructural components and carry out ion transmission, disruption of redox processes and ATP synthesis.

With the exacerbation of Cushing's syndrome in some mitochondria of lymphocytes, there is a marked thickening of the outer membrane and cristae. At the same time, the outer membrane of the mitochondria is significantly thickened, strongly osmiophilic, intermittent in places, merges with the ribosomes of the shell, crystals from the inner side. The crystals are also thickened, osmiophilic and

arranged randomly (Fig. 4). Between the crystals, the mitochondrial matrix is moderately osmiophilic and has a finely granular background.

We performed a correlation analysis between the stage of SC, the level of cortisol, ACTH, leptin, ED markers, indicators of the vascular-platelet link of the hemostasis system and electron microscopic examination (Table 8). As can be seen from Table 10, significant correlations of the SC stage by EMI (remission/activity) were revealed and a number of laboratory-hormonal indicators. A direct correlation was found between the stage of SC according to EMI with the levels of ACTH, cortisol, leptin, ET-1 and indicators of the hemostasis system, which confirms the high prognostic value of this indicator in the prognosis of fertility recovery in patients with SC. At the same time, the greatest correlation between the stages of EMR was observed with the level of ET-1.

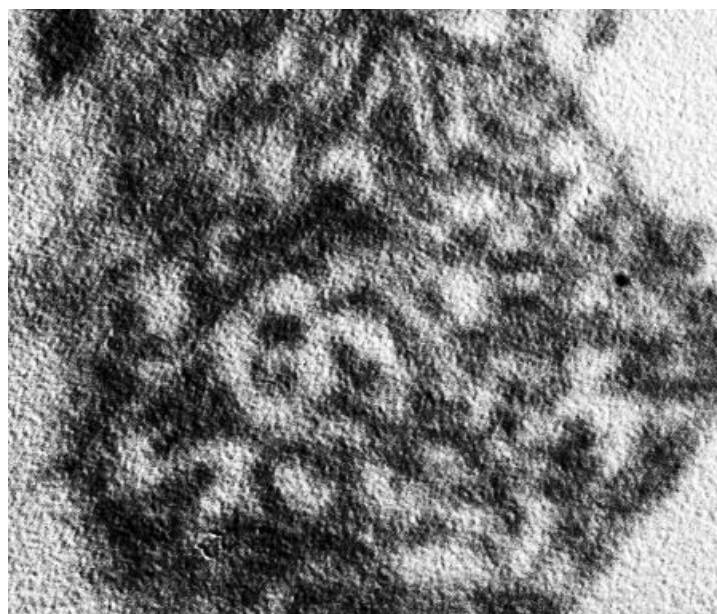


Fig. 4. Cushing's syndrome, the stage of exacerbation. The outer membrane and the crystals are thickened, fragmented, and arranged randomly. Electron microscopy. Uv: 35,000

Table 8. Correlation analysis between the SC stage, cortisol level, ACTH, leptin, ED marker, indicators of the vascular-platelet link of the hemostasis system and electron microscopic examination

Stage by EMI	ACTH, pg/ml	Cortisol, nmol/l	Leptin, ng/ml	SDE 1x10 ⁴ /l	IAP, unit /l	Endothelin -1 fmol/ml
Remission stage	0,52	0,82	0,68	0,70	0,82	0,89
Active stage	0,56	0,89	0,72	0,71	0,77	0,93

Note : The content of desquamated endotheliocytes in the blood, – SDE, Plasminogen activator inhibitor – IAP, electron microscopic examination –EMI

Conclusions

1. In order to achieve effective fertility restoration in patients with SC, it is recommended to conduct an electron microscopic examination of the myochondria or an assessment of Endothelin-1 in the blood during treatment: in the active stage, pathogenetic treatment should be performed, and in the remission stage, appropriate cycle restoration should be performed with subsequent induction of ovulation. 2. Significant correlations of the stage of SC according to EMI (remission/activity) were revealed and a number of laboratory-hormonal indicators. A direct correlation was found between the stage of SC according to EMI with the levels of ACTH, cortisol, leptin, ET-1 and indicators of the hemostasis system, which confirms the high prognostic value of this indicator in the prognosis of fertility recovery in patients with SC. At the same time, the greatest correlation between the stages of EMR was observed with the level of ET-1.

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