## THE EFFECT OF THE THYROID GLAND ON THE FUNCTION OF REPRODUCTIVE SYSTEM OF WOMEN

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#### Resume,

This article presents the research data of 118 women aged 18 to 40 years with various disorders of reproductive function against the background of identified thyroid diseases. The results obtained indicate the undoubted role of the thyroid gland in the reproductive system, as evidenced by the positive results of treatment after correction of thyroid function.

Key words: reproductive system, hormones, thyroid gland, hypothyroidism.

# РОЛЬ ШИТОВИЛНОЙ ЖЕЛЕЗЫ В ЛЕЯТЕЛЬНОСТИ РЕПРОЛУКТИВНОЙ ФУНКЦИИ ЖЕНШИН

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#### Резюме,

В этой статье приведены данные исследования 118 женщин в возрасте от 18 до 40 лет с различными нарушениями репродуктивной функции на фоне выявленных заболеваний щитовидной железы. Полученные результаты свидетельствуют о несомненной роли щитовидной железы в деятельности репродуктивной системы, о чём свидетельствует положительные результаты лечения после коррекции функции щитовидной

Ключевые слова: репродуктивная система, гормоны, щитовидная железа, гипотиреоз.

## АЁЛЛАР РЕПРОДУКТИВ ТИЗИМИ ФАОЛИЯТИДА ҚАЛҚОНСИМОН БЕЗНИНГ ТУТГАН ЎРНИ

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## Резюме,

Ушбу мақолада репродуктив тизимнинг турли бузилишлари билан 18 ёшдан 40 ёшгача булган қалқонсимон без касалликлари бор аёлларнинг текшириш натижалари келтирилган. Олинган натижалар, қалқонсимон без функцияси коррекция килингандан сўнг даво натижаларининг ижобий бўлиши репродуктив фаолиятда қалқонсимон безнинг сўзсиз ўрни борлигидан далолат берди.

Калит сўзлар: репродуктив тизим, гормон, қалқонсимон без, гипотиреоз.

mong the endocrine glands that actively affect the A reproductive system, an important place is occupied by the thyroid gland. Endocrine disorders, along with inflammatory diseases, occupy one of the leading places in the structure of causes of infertility in women (29-43%) [7,9,12]. The decrease in thyroid activity of the thyroid gland in most women with mastopathy is associated with a violation in the system of the hypothalamus - pituitary - thyroid (thyroid) - hormonedependent organs. Thyroid insufficiency has a direct damaging effect both on the ovaries and on the peripheral organs - targets of the reproductive system, since thyroid hormones are the main regulators of the metabolic process at the level of the cell nucleus [3,6,8]. The frequency of hyperprolactinemia (GP) among endocrine pathology is 40-43%, and in the infertility clinic - 18.9%. Moreover, in 50% it has a pituitary origin and is manifested by microand macroprolactinoma, in the rest it is symptomatic due to hypothyroidism, polycystic ovary syndrome, liver, kidney diseases, and taking medications that cause a decrease in dopamine levels [2,4].

Of great interest is the study of the effect of the thyroid gland on the reproductive system of women. In studies of T. M. Varlamova, M. Yu. Sokolova (1999), it was found that thyroid dysfunction can lead to changes in the menstrual

cycle, infertility and miscarriage. So, with primary hypothyroidism, menstrual irregularities were detected in 33-80% of patients [3,10,14].

In 20% of women with hypothyroidism, an irregular menstrual cycle is observed from the moment of menarche (Ranrin I. et al., 2001). The most pronounced form of menstrual irregularities in hypothyroidism is amenorrhea, the frequency of which with this type of thyroid pathology ranges from 1.5 to 6%. The action of thyroid hormones on the mammary gland can be realized either directly or through other hormones, in particular prolactin (Prl)

On a huge number of examples, it was found that most somatic, nervous, infectious and other diseases are accompanied by a statistically significant violation of the optimal concentration of various trace elements (ME) at the subcellular, cellular, and organ levels [1,15,16]. Of the essential MEs, it would be advisable to single out those that significantly affect the reproductive function of the body. Iodine is important for the development and functioning of the thyroid gland, it is part of the hormones secreted by it, through these hormones it stimulates the metabolism of the whole body towards the breakdown of fats and carbohydrates and energy production; necessary for the normal development of the brain, fertilization

organs, skin, hair and teeth. Iodine deficiency leads to an increase in the thyroid gland (endemic goiter), inhibits human reactions, causes cretinism (with deficiency in childhood), slows down metabolic processes and lowers body temperature. With a lack of iodine, sexual development is delayed, physical and mental capabilities are reduced [1,3,4,13].

Elevated prolactin, thyroid disease with a change in the content of thyroid hormones in the blood serum can cause infertility, affect the maturation and ability of oocytes to fertilize.

Purpose of the study: study of the etiopathogenetic factors of infertility in women with thyroid diseases and develop methods for treating this pathology from the perspective of correcting microelementosis of the body.

## Materials and methods

Clinical and laboratory observations in women with menstrual irregularities and infertility were carried out together with an endocrinologist at the Department of Obstetrics and Gynecology, Bukhara Medical Institute. The main group consisted of 118 women with GP aged 18 to 40 years. For comparison and interpretation of the results, 56 women were considered to be "practically" healthy (control group).

All women were subjected to a comprehensive examination, which included collecting an anamnesis, studying past and present extragenital diseases, the nature and characteristics of the formation of menstrual function, gynecological diseases; general examination, examination and palpation of the thyroid gland and mammary glands, clinical and laboratory tests, including determining the level of gonadotropic and thyroid-stimulating hormones in the blood, microelement status of blood. The study included only those patients who, after a thorough examination by a therapist, were found to be practically healthy or suffering from various menstrual irregularities, hyperprolactinemia and infertility.

Hormone levels were determined by enzyme-linked immunosorbent assay (ELISA) on a HUMAREADER SINGLE analyzer (Germany, 2005). Standard reactive kits were used to determine (luteinizing, follicle-stimulating hormones, prolactin, progesterone, testosterone and thyroid) hormones in the blood serum. The microelement status of the organism was determined by mass spectrometry on an Agilent 7500 a analyzer. inductively Coupled Plasma Mass Spectrometer (Japan, 2001). The level of 10 essential and 5 toxic MEs in blood serum was determined.

### Results and discussion

64% of women had endemic goiter, of which 33% had a subclinical form of hypothyroidism. However, only 16.8% of women were observed by an endocrinologist and received iodine preparations to correct thyroid pathology. Noteworthy is a high percentage of thyroid diseases as a causative factor of secondary GP. This factor was detected in 38 (32.2%) patients. So, endemic goiter was found in 23 (19.5%) patients. A subclinical form of hypothyroidism was detected in 12 (10.2%) and hyperthyroidism in 3 (2.5%) women.

Therefore, in more than half of the examined patients, hyperprolactinemia was combined with such clinical manifestations as galactorrhea, menstrual-ovarian cycle

disturbances of the type of amenorrhea and oligomenorrhea, as well as signs of premenstrual syndrome, etc.

Emotional-personality disorders, as a rule, a tendency to depression, sleep disturbance are noted in 20-30% of patients. Non-specific complaints of increased fatigue, weakness, memory loss, pain in the heart without clear localization and irradiation are observed in 15-25% of patients.

The TSH, T3 and T4 indices in women of both groups were within the normal range: TSH -  $2.18 \pm 0.13$  mIU, ml in healthy women and  $3.13 \pm 0.14$  mIU / ml in women with GP (P < 0.001) However, there is an increase in TSH in women with endemic goiter, with GP. This outcome probably indicates the compensatory mechanism of the body in response to a relatively reduced concentration of the hormones T3 and T4 in this category of women. So, there is a negative correlation between TSH and the hormones T3 (r = -0.65), T4 (r = 0.73) and iodine in red blood cells (r = 0.88), which indicates the antagonism of the hormone T3 and T4. As noted above, the level of hormones T3 and T4 was within the normative values in both groups. However, in women with endemic goiter, with GP, these indicators approached the lower threshold of normal: the content of T3 was 139  $\pm$  0.08 nmol / E, T4 - 94.7  $\pm$  4.1 nmol / E. In healthy women, the hormones T3 and T4 were respectively  $1.75 \pm 0.2$  and 108.7 $\pm$  5.3 (P < 0.05). Indicators of TSH, T3 and T4 in women with a subclinical course of hypothyroidism, suffering from GP, were characteristic of hypothyroidism. The level of TSH was  $5.1 \pm 0.15$ , T3 -  $1.1 \pm 0.051$ , T4 -  $52.1 \pm 1.6$  (P <0.01-0.01). Interesting results were obtained in the analysis of the correlation matrix. In this category of women, a negative correlation of T3 (r = -0.58) and T4 (r = -0.64) with prolactin level is observed. A direct correlation occurred with iodine (r = 0.77), zinc (r = 0.62) and iron (r = 0.56).

The concentration of TSH in women with hyperthyroidism was significantly lower (1.3  $\pm$  0.07 mIU / ml) than in healthy ones (2.18  $\pm$  0.13 mIU / ml; P <0.001). On the contrary, the level of hormones T3 and T4 significantly exceeded the values in healthy: 2.5  $\pm$  0.03 and 144  $\pm$  5.6 mIU / ml, respectively (P <0.001).

Most of the iodine in the blood in healthy women is found in red blood cells. The level of this bioelement in the blood serum is  $14.8 \pm 1.1 \, \mu g\%$ , in red blood cells -  $37.4 \pm 2.4 \, \mu g\%$ .

With GP, the concentration of iodine in the whole decreases: up to  $9.6 \pm 0.6$  µg% in blood serum (P <0.001) and up to  $23.6 \pm 2.1$  µg% in red blood cells (P <0.001), while maintaining its ratio in these two environments. There is a direct close correlation of the decrease in iodine in red blood cells with hormones such as T3 (r = 0.74) and T4 (r = 0.7) and an increase in thyroid size (r = 0.8) in women with GP. There is an average correlation with progesterone (r = 0.38) and FSH (r = 0.35) and a high negative relationship of iodine with prolactin (r = -0.61). The results obtained indicate the advisability of prescribing iodine preparations to women with GP.

Indicators of TSH, T3 and T4 in women of both groups were within the normal range: TSH -  $2.18 \pm 0.19$  mIU / ml in healthy women and  $3.13 \pm 0.28$  mIU / ml in women with GP. However, there is an increase in TSH in women with endemic goiter, with GP (P < 0.01). Apparently, this indicates the inclusion of compensatory mechanisms of the body in response to a decrease in the concentration of hormones T3 and T4 in this category of patients. So,

there is a negative correlation between TSH and the hormones T3 (r = -0.65), T4 (r = 0.73) and iodine in red blood cells (r = 0.88), which indicates the antagonism of the hormones T3 and T4.

As noted above, the level of hormones T3 and T4 was within the normative values in both groups of patients. However, in women with endemic goiter, with GP, these indicators were approaching a low threshold: T3 was 139  $\pm$ 0.18 nmol / E, T4 was  $94.7 \pm 7.3 \text{ nmol}$  / E, and in healthy it was 1, respectively,  $75 \pm 0.2$  and  $108.7 \pm 8.6$  nmol / E (P <0.05-0.01). Indicators of TSH, T3 and T4 in women with a subclinical course of hypothyroidism, suffering from GP, were characteristic of hypothyroidism. The level of TSH was  $5.1 \pm 0.39$ , T3 -  $1.1 \pm 0.053$ , T4 -  $52 \pm 3.1$  (P < 0.05-0.01). In the analysis of the correlation matrix with GP, a negative correlation of T3 (r = -0.58) and T4 (r = -0.64) with prolactin level was observed. A direct correlation occurred with iodine (r = 0.77), zinc (r = 0.62) and iron (r = 0.56).

The TSH concentration in women with hyperthyroidism was significantly lower (1.3  $\pm$  0.1 mIU / ml) than in healthy women (2.18  $\pm$  0.19 mIU / ml; P < 0.01). On the contrary, the hormones T3 and T4 were significantly higher -  $3.3 \pm 0.22$  and  $184 \pm 13.3$  mIU / ml, respectively.

The history of drug therapy for GP has more than 4 decades. Even before 1970, endocrinologists and gynecologists used thyroidin with success to treat certain forms of the syndrome of galactorrhea-amenorrhea and hypothyroidism. It can be assumed that the GP in patients with successful thyroidin therapy was due to primary hypothyroidism and the stimulating effect of thyroliberin, therefore, the appointment of thyroidin was justified and contributed to the correction of thyroid function and normalization of prolactin synthesis, which was confirmed by laboratory data after 10-20 years. With GP combined with primary hypothyroidism, thyroidin is used at 0.1 g / day, triiodothyronine hydrochloride at 20 µg. These drugs block the release of TRH, which reduces the secretion of Prl

Such patients, as a rule, do not need additional treatment with Prl blockers. G. A. Melnichenko, N. I. Marova (1998) argue that the drug of choice for this form of GP is L-thyroxine.

In general, indicators of thyroid hormones, (TSH, T3, and T4) in women with GP suffering from thyroid diseases simultaneously were characteristic of the pathology of the latter. We have identified regular relationships with both prolactin, LH and FSH, and with a number of essential MEs, which indicates the community of hormones and MEs in the body that make up a single homeostasis. Thus, the inclusion in the complex therapy of ME - containing the drug iodomarin, along with dostinex, significantly increased its effectiveness in women with thyroid diseases. Moreover, an increase in the blood level of a number of essential MEs directly correlated with the normalization of hormonal indices.

#### **Findings:**

1. Among the examined women with infertility in 37.5% of cases, hyperprolactinemia of functional origin was revealed and was secondary, which was mainly caused by thyroid diseases.

- 2. In women with hyperprolactinemia, a decrease in the content of FSH and LH was characteristic, among which women with an euthyroid increase in the thyroid gland against the background of an increased TSH content and a low level of T3, T4 predominated, which necessitates the correction of the thyroid function in the treatment of hyperprolactinemia.
- 3. For women with menstrual irregularities and infertility, the presence of pronounced microelementosis is characteristic, which manifests itself 1.5 times as a decrease in the concentration of essential and conditionally essential trace elements. The above dictates the need for the correction of microelementosis in the complex treatment of hyperprolactinemia in women with thyroid diseases.

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