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FEATURES OF REPRODUCTIVE DISORDERS IN WOMEN WITH HYPOTHYROIDISM AND HYPERTHYROIDISIS

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SUMMARY

This article examined the features of the problems of the relationship of reproductive disorders in women of reproductive age with thyroid gland pathologies. **Material and methods.** 220 women of reproductive age were examined, of which 78 (35.4%) were taken for research with various reproductive disorders. Patients were divided into 2 groups depending on the hormonal activity of the thyroid gland. Group 1 (33) of patients with hypothyroidism of various etiologies and group 2 (45) of patients with hyperthyroidism. The complex of laboratory and clinical examinations included: anamnesis, examination; clinical and biochemical research methods; a study in the blood plasma of hormones (thyroid stimulating hormone (TSH), prolactin, St.T3, St. T 4, antibodies to thyroid peroxidase (AT-TPO); luteinizing hormone (LH), follicle-stimulating hormone (FSH), estradiol, progesterone, testosterone); ultrasound of the thyroid gland (thyroid gland), mammary glands, pelvic organs; fine needle thyroid biopsy, pituitary MRI. The aim of the study was to study the features of the problems of the relationship of reproductive disorders in women of childbearing age with thyroid gland pathologies. **Results.** A comparative analysis of various pathologies of reproductive function in both clinical groups showed that menstrual dysfunction in the first clinical group was dominated by oligomenorrhea - 30%, and in the second group, opsenomenorrhea - 24% and dysmenorrhea-24.4%. In women with hypothyroidism (12%), I degree galactorrhea was detected. In the second group, pathology of the cervix was detected in 27% with a predominance of pseudo-erosion (33.3%), and in 12.5% - uterine fibroids. The presence of chronic salpingoophoritis was detected in 47.5%, cystic changes in the ovaries in 27% of women of the first clinical group. **Conclusions.** In women with a deficiency of thyroid hormones, a decrease in the pituitary gonadotropic function occurs with the development of hyperprolactinemia, a decrease in steroidogenesis, and a deficiency of the luteal phase of the menstrual cycle. With hyperthyroidism in women, hyperestrogenism is observed, which, according to the feedback mechanism, leads to a decrease in the concentration of FSH. At the same time, the level of progesterone remains quite low due to a decrease in the sensitivity of ovarian tissues to luteinizing hormone in conditions of FSH deficiency.

KEYWORDS: Thyroid gland, reproductive disorders, hormonal changes.

RELEVANCE

The woman's reproductive system consists of interconnected structural elements: the hypothalamus, pituitary, ovaries, and other target organs that provide the generative function, including the thyroid gland. The main function of the thyroid gland is to provide the body with thyroid hormones: triiodothyronine (T3) and thyroxine, or tetraiodothyronine (T4). Thyroid function is closely related to the hypothalamus – pituitary – ovary system due to the presence of common central regulatory mechanisms.[1,3] Such mechanisms are suprathypothalamic structures acting through neurosteroids, neurotransmitters and neuropeptides, and the hypothalamus, which affects the underlying links of the endocrine neuroregulation system through releasing hormones. Sexual and thyroid systems are regulated by tropic hormones of the anterior pituitary gland: follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin (PRL) and thyroid-stimulating hormone (TSH). The anterior pituitary is controlled by the thalamo-hypothalamic-cortical system. Thyrotropin-releasing hormone (TRH) stimulates the formation of not only TSH, but also prolactin. Therefore, the imbalance in the pituitary-thyroid system leads to a change in the synthesis of prolactin and gonadotropins.[1,3,5] Thyroid activity, synthesis and secretion of T3 and T 4 are monitored by TSH and autoregulation. TSH is a glycoprotein hormone consisting of 2 subunits: alpha and beta. It is known that TSH is synthesized in basophilic cells of the adenohypophysis[1,3,5] and TSH synthesis is regulated by TSH and by the principle of negative feedback by the level of thyroid hormones (free T3 and T 4).[1,3,5] The last variant of regulation occurs due to the effects of T3 on specific nuclear receptors in

thyrotrophs.[1,3] It was also found that the level of thyroid hormones affects the hypothalamic production of TRH.[1,3,5] TSH stimulates the formation of TSH in the hypothalamus, which in turn stimulates the formation of thyroid hormones, and when thyrocytes reach TSH, it interacts with cell membrane receptors. The interaction of TSH with the membrane receptor leads to the activation of the adenylate cyclase cascade, as a result of which thyrocyte functions are induced, such as capture of iodine molecules, synthesis of thyroglobulin and release of T3 and T4.[1,6] LH, FSH and TSH are complex glycoproteins consisting of alpha A and beta-subunits. The structure of the alpha subunit is the same for all hormones, and the beta subunit is specific for each hormone. The beta subunit determines its luteinizing, follicle- stimulating or thyrotropic activity, however, only after combining with the alpha subunit. The structural similarity of hormones may indicate the presence of their common precursor during evolution.[1,4,6]

According to J. Nikolai et al., The close relationship between the thyroid gland and the reproductive system is also indicated by the occurrence of thyroid pathology after childbirth, the frequency of which is 11.3%. Thus, castration leads to a significant decrease in thyroxine secretion, and replacement therapy with estrogens contributes to its normalization.[4]

Thyroid hormones thyroxine (T4) and triiodothyronine (T3) affect the metabolic rate and energy, they enhance the absorption of oxygen by cells and tissues, stimulate the breakdown of glycogen, inhibit its synthesis, and affect fat metabolism. Especially important is the effect of thyroid hormones on the cardiovascular system. Increasing the sensitivity of the receptors of the cardiovascular system to catecholamines, thyroid hormones increase the heart rate and contribute to high blood pressure. Thyroid hormones are necessary for the normal development and functioning of the central nervous system, their deficiency in the antenatal period leads to the development of cretinism. Thyroxine stimulates the metabolism, accelerates biochemical reactions, affects all organs, supports the normal tone of the nervous system. The hormone thyroxine affects the activity of adrenaline and cholinesterase, water metabolism, regulating fluid reabsorption in the renal tubules, affects cell permeability, protein, fat and carbohydrate metabolism, the level of oxidative processes in the body, basic metabolism, hematopoiesis.[7,8]

Pathology of the thyroid gland can cause disorders in the reproductive system, such as premature or late puberty, amenorrhea, anovulation, infertility, galactorrhea due to hyperprolactinemia, miscarriage. Any long-term dysfunction of the thyroid gland affects the activity of the reproductive system until the termination of the last generative function.[1,7] In primary hypothyroidism, menstrual irregularities were detected in 33–80% of patients.[4] There is an opinion that primary hypothyroidism is accompanied by menstrual irregularities of the type of hypomenstrual syndrome or amenorrhea. However, a number of researchers point to primary hypothyroidism as one of the most common causes of polymenorrhea.[4] Estrogens have a stimulating effect on the thyroid gland by increasing the pituitary thyroid trophism to thyroliberin.[1,7] With hypoestrogenism, on the contrary, there is a decrease in the sensitivity of thyrotrophs, which can lead to secondary hypothyroidism in women with a lack of estrogen, for example, with natural and surgical menopause, depleted ovary syndrome, and resistant ovary syndrome.[1] Some experimental studies indicate the presence of TSH and T3 receptors in the ovary, which confirms the possibility of a direct effect of thyroid disorders on steroid and oogenesis.[1]

The purpose of the study was to study the characteristics of reproductive status in women with hypothyroidism and hyperthyroidism to optimize the diagnosis, treatment and management of infertility.

MATERIAL AND RESEARCH METHODS

For the period from 2017 to 2019 on the basis of the RSNPMC endocrinology named after Acad. Ya.Kh. Turakulova was examined 220 women of reproductive age (17-49 years) with various thyroid gland pathologies. Initial screening was performed to determine the concentration of hormones in the anterior pituitary, thyroid, ovary, ultrasound (ultrasound) of the thyroid and pelvic organs, and pituitary MRI.

The complex of laboratory and clinical examinations included: anamnesis, examination; clinical and biochemical research methods; a study in the blood plasma of hormones (TSH, St. T 3, St. T4, AT-TPO; luteinizing hormone (LH), follicle-stimulating hormone (FSH), estradiol, progesterone, testosterone); Ultrasound of the thyroid gland, mammary glands, pelvic organs; Pituitary MRI; fine needle thyroid biopsy if necessary.

During the screening study, the control and main groups were determined, which were subsequently examined in depth. The main contingent of follow-up was 78 women, of which two groups were subsequently formed: the first clinical group - 33 women with hypothyroidism; the second clinical group - 45 women with hyperthyroidism. To compare the data, a control group was formed, which consisted of 20 healthy women of reproductive age without any endocrine and somatic pathologies.

Since menstrual irregularities and infertility are clinical signs of a number of gynecological diseases, we used the following selection criteria to include and exclude other causes.

Table 1: Inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
infertility in planning a desired pregnancy for more than one year after regular sexual intercourse	lack of male factor infertility
menstrual irregularities	tubal peritoneal forms of infertility
the presence of changes in the concentration of pituitary hormones in the blood (thyroid stimulating hormone (TSH), prolactin (PRL)	endometriosis (examination of the pelvic organs using ultrasound with a vaginal probe in the dynamics of the menstrual cycle)
the presence of changes in the concentration of thyroid hormones in the blood (triiodothyronine (St. T 3), thyroxine (T4), free thyroxine (St. T4), as well as the presence of antibodies (AT) to thyroglobulin (TG) and thyroid peroxidase (TPO)	other forms of endocrine infertility
lack of tubal-peritoneal form of infertility	immunological forms of infertility.
the absence of positive titers of class G immunoglobulins for opportunistic infections (herpes simplex virus, cytomegalovirus, mycoplasma, ureaplasma, toxoplasma, chlamydia).	

The following research methods were used in the work

1. Anamnesis was collected: the form and duration of infertility, the nature of menstrual irregularities.
2. Objective examination: determination of the weight-height index - the ratio of body weight in kilograms to body length in meters squared; body type was determined; the degree of hair growth, changes in the skin and mucous membranes (striae, greasiness, etc.); the degree of development of the mammary glands, palpation examination of the mammary glands (structure of the mammary glands, seals, discharge from the mammary glands); galactorrhea was assessed as grade I with drip colostrum during palpation of the mammary glands, grade II - jet excretion of colostrum during palpation of the mammary glands and grade III - spontaneous excretion of colostrum from the mammary glands; gynecological examination: reproductive status was assessed jointly with a TMA gynecologist from the Department of Gynecology (Professor G. Babadzhanova).
3. Instrumental research methods. Ultrasonic research methods: pelvic organs - with an ultrasound machine Aloka - SSD 500 with a 7.5 Hz sensor, thyroid and mammary glands with a 3.0 Hz sensor. Ultrasound examination of the thyroid gland and determination of its volume were carried out on the basis of RSNPMC endocrinology using the Fukuda U-2000 ultrasound machine (Japan). Pituitary MRI (8 women). Studies of the fundus and visual fields (8 women). Electrocardiography (for everyone).

The material was processed by the method of variation statistics on an HP PC using the program developed in the EXCEL package, using a library of statistical functions, with calculation of arithmetic mean (M), standard deviation (y), standard error (m), relative values (frequency, %), student criterion (t), with the calculation of the probability of error (P). Differences in mean values were considered significant at a significance level of $P < 0.05$. At the same time, we adhered to the existing guidelines for the statistical processing of the results of clinical and laboratory studies (Zaitsev V.M. et al., 2003).

RESEARCH RESULTS AND DISCUSSION

Of 220 women of reproductive age from 17 to 49 years with various thyroid pathologies, 78 patients with hypothyroidism and hyperthyroidism were selected, who underwent a complete clinical and hormonal study. Of the 78 patients, 33 (42.3%) were with hypothyroidism and 45 (57.7%) with hyperthyroidism. Of 33 women with hypothyroidism, 10 (30%) had hypothyroidism associated with autoimmune thyroiditis (Hashimoto's thyroiditis), 16 (48.4%) had hypothyroidism associated with iodine deficiency, and 13 (39.3%) due to nodular goiter and U 4 (12.1%) had mixed goiter. Of the 45 patients with hyperthyroidism, 20 (44.4%) had AIT associated with hyperthyroidism, 29 (64.4%) had iodine deficiency, 9 (20%) had nodular goiter, and 8 (17.7%) there was a mixed goiter.

Ultrasound of the thyroid gland in healthy women did not reveal a significant difference in volume between the lobes, and on average it amounted to 14.80 ± 0.71 cm3. In patients, depending on the degree of thyroid enlargement, the volume also increased. The main percentage was women with I degree of thyroid enlargement (67.5%), which corresponded to a volume of 19.30 ± 0.66 cm^3. At the second degree of increase (29.7%), the volume was 22.4 ± 0.9 cm^3. In the first group, in women with hypothyroidism, signs of autoimmune thyroiditis (AIT) were found in 30.3% of women, diffuse goiter in 18.1%, nodular goiter in 24.4% (nodular colloid to a different degree proliferating goiter), in 15.1% of multinodular goiter and mixed goiter - found in 12.1% of women. And in the second group, signs of autoimmune thyroiditis (A IT) were found in 44.4% of women, diffuse goiter in 26.6%, nodular goiter in 8.8% (nodular colloid to a different degree

proliferating goiter), in 6, 6% of multinodular goiter and mixed goiter are found in 13.3% of women. Studies of blood supply to the thyroid parenchyma with nodular pathology showed that the total volumetric blood flow is 2 times greater in sick women than in healthy women, and specific blood flow is reduced by 30%. At the same time, thyroid puncture followed by histological characterization did not reveal malignant transformation of thyroid cells.

To assess the hormonal state of the thyroid gland in order to confirm subclinical and manifest forms of the state of hypo - and hyperthyroidism, we conducted a study, namely, determination of the content of TSH hormones in blood, St. T 3, St. T4. (Table 2)

Table 2: Indicators of thyroid hormones in blood plasma in women in the control (n = 20) and the examined groups (n = 78) before treatment.

Groups	TSH mIU / ml	St. T4 pmol / l	St.T3 pg / ml	AT-TPO ME / ml
1. With hypothyroidism (n = 33)	8.5 ± 10.5 p <0.05	10.9 ± 2.8 p <0.05	2.3 ± 0.04 p <0.05	107.5±21.5 p <0.05
2. With hyperthyroidism (n = 45)	0.09 ± 0.03 p <0.05	26.3 ± 5.3 p <0.05	5.05± 1.2 p <0.05	150.9±24.7 p <0.05
3. Healthy (n = 20)	1.81 ± 0.074	14.4 ± 1.7	3.4 ± 0.6	19.4 ± 2.6

Note: p <0.05 - reliability in relation to control.

As can be seen from the data table. 2, in women of the first clinical group, compared with the control group, there is a significant decrease in the level of St. T 4 (p <0.05). In group II, in the analyzed thyroid parameters, the opposite picture is observed, that is, a significant increase in plasma concentration of St. T 3, St. T4 relative to the indicators of the control group and clinical group I (p <0.05). Therefore, an analysis of the thyroid condition in women with hypothyroidism showed that 45.5% (15 women) had a subclinical version of hypothyroidism. In the group of women with hyperthyroidism, in all cases there was a manifest variant of the course of hyperthyroidism, that is, an increased content of St. T3 and St. T 4. Determination of antibodies to thyroid cells showed that women with hypothyroidism there is a significant increase in the level of antibodies to TPO relative index control group s (p <0.05). In women with hyperthyroidism, the concentration level of AT-TPO is high compared to the control group and the first clinical group (p > 0.05), and tends to increase. Analysis of the detected antibodies in women showed that in the second group in 44.4 % of cases an increased titer of antibodies to A T- TPO is detected. In clinical group I, an increased titer of antibodies to AT-TPO is manifested in 30% (10 women). Therefore, thyroid hypofunction is caused mainly by the autoimmune component (30%), and the rest, apparently, due to metabolic disturbances in the thyroid gland. Moreover, an increase in the titer of antibodies to TPO can be accompanied by both an increase and a decrease in thyroid function (10 women with hypothyroidism and 20 with hyperthyroidism). Most women with hyperthyroidism show diffuse toxic goiter**,** which develops as a result of unregulated stimulation of the initially normal thyroid gland with thyroid- stimulating immunoglobulin that activates thyroid TSH receptors, as it has an affinity for the same membrane receptors as TSH. A change in the thyroid condition naturally affects the menstrual and reproductive functions of women, as it is in close interaction with the hypothalamic-pituitary-ovarian system, primarily due to the presence of common central regulation mechanisms.[1,2]

A comparative analysis of various reproductive dysfunctions in both groups showed that oligomenorrhea, 30%, and opsenomenorrhea, 24%, and dysmenorrhea, 22%, prevailed in the first group of NMFs. In 12% of women with hypothyroidism, grade I galactorrhea was detected. Pathology of the cervix was detected in 27% with a predominance of pseudo-erosion (33.3%), and in 12.5% - uterine fibroids in the first group. The presence of chronic salpingoophoritis was detected in 47.5%, cystic changes in the ovaries in 27% of women in the second group.

Table 3: Comparative analysis of menstrual irregularities in women with hypothyroidism and hyperthyroidism.

Menstrual irregularities	With hypothyroidism (n = 33)	With hyperthyroidism (n = 45)
Normal cycle	-	-
Hypermenorrhea	4 (12.2%)	5 (11.1%)
Amenorrhea	8 (24.2%)	7 (15.5%)
Polymenorrhea	-	6 (13.3%)
Opsomenorrhea	8 (24.2%)	11 (24.4%)
Hypomenorrhea	3 (9%)	5 (11.1%)
Dysmenorrhea	-	11 (24.4%)
Oligomenorrhea	10 (30%)	-

In studies conducted by GE Krassas (2000), out of 214 women suffering from DTZ, a violation of MC was detected only in 46 (21.5%), which in our study was detected in 78 (100%). Among them, 24 patients had hypomenorrhea, 15 - polymenorrhea, 5 - oligomenorrhea, 2 - hypermenorrhea, while in our study there were: hypomenorrhea- 5, polymenorrhea-6, dysmenorrhea-11, opsenomenorrhea -11, hypermenorea-5 amenorrhea -7 out of 45 of all examined patients with hyperthyroidism. A study conducted by GE Krassas (2000) in no patient revealed amenorrhea, while in our case it was 15.5% of 45 patients with hyperthyroidism. In the control group consisting of 214 women with euthyroidism, only 18 (8.4%) had some type of menstrual irregularity, of which 12 had oligomenorrhea.[2,3] Thus, menstrual irregularities with thyrotoxicosis are noted 2.5 times more often than in a healthy population.

In turn, the state of the reproductive system has a pronounced effect on the function of the thyroid gland. In the 'group of women with hypothyroidism, in terms of hormones, there is an increase in the plasma of prolactin and testosterone compared with the control group ($p < 0.05$). Indicators of progesterone (2.0 ± 3.5 ng / ml), estradiol (39.4 ± 30.5 pg / ml) LH (3.0 ± 6.2 IU / ml) and FSH (3.50 ± 1, 12 IU / ml) are significantly reduced compared with healthy women ($p < 0.05$). In women with hypothyroidism, prolactin level (21.6 ± 14.4 ng / ml) significantly exceeds the value in the control group ($p < 0.05$).

Akande and Hockaday[10] found that the average levels of LH both in the follicular and luteal phases of the menstrual cycle are significantly higher in women with hyperthyroidism than in normal women. We found (Tab. 4) the same tendency when comparing the values of testosterone (4.5 ± 2.1 nmol / ml) increased compared with the control group ($p < 0.05$) and in the group with hyperthyroidism ($p < 0.05$).

Table 4: Indicators of hormones of reproductive status in blood plasma in women of the control and clinical groups before treatment.

Hormones	With hypothyroidism (n = 33)	P	With hyperthyroidism (n = 45)	P	Healthy (n = 20)
LH (IU / ml)	3.0 ± 6.2	p <0.05	24.9 ± 7.5	p <0.05	15.8 ± 3.4
FSH (IU / ml)	3.5 ± 1.2	p <0.05	2.9 ± 2.0	p <0.05	8.5 ± 2.3
Estradiol (pg / ml)	39.4 ± 30.5	p <0.05	134.8 ± 6	p <0.05	72 ± 8.7
Progesterone (ng / ml)	2.0 ± 3.5	p <0.05	5.2 ± 16.5	p <0.05	11.3 ± 6.5
Prolactin (ng / ml)	21.6 ± 14.4	p <0.05	20.7 ± 18.6	p <0.05	13.7 ± 4.9
Testosterone (nmol / ml)	4,5 ± 2,1	p <0.05	0.9 ± 0.5	p <0.05	0.33 ± 0.2

Note: p <0.05 - reliability in relation to control.

The opposite dynamics is observed in the content of estradiol in the blood plasma (39.4 ± 30.5 pg / ml, $p < 0.05$), the level of estradiol is relatively reduced compared to the control group, and in the group with hyperthyroidism it is reliably high (134.8 ± 6.36 pg / ml,). LH level (18.60 ± 1.21 IU / ml, $p < 0.05$) is relatively increased in the studied groups, and FSH (1.80 ± 0.72 IU / ml, $p > 0.05$) is reduced. (tab. 4)

Table 5: Indicators of hormones that regulate the reproductive function of women against the background of conservative treatment.

Hormones	With hypothyroidism (n = 33)	P	With hyperthyroidism (n = 45)	P	Healthy (n = 20)
LH (IU / ml)	3.0 ± 6.2	p <0.05	24.9 ± 7.5	p <0.05	15.8 ± 3.4
FSH (IU / ml)	3.5 ± 1.2	p <0.05	2.9 ± 2.0	p <0.05	8.5 ± 2.3
Estradiol (pg / ml)	39.4 ± 30.5	p <0.05	134.8 ± 6	p <0.05	72 ± 8.7
Progesterone (ng / ml)	2.0 ± 3.5	p <0.05	5.2 ± 16.5	p <0.05	11.3 ± 6.5
Prolactin (ng / ml)	21.6 ± 14.4	p <0.05	20.7 ± 18.6	p <0.05	13.7 ± 4.9

Note: p <0.05 - reliability in relation to control.

Thus, with a deficiency of thyroid hormones in women, a decrease in the pituitary gonadotropic function with the development of hyperprolactinemia and a decrease in steroidogenesis was revealed. Failure of the luteal phase of the menstrual cycle develops. Apparently, impulse secretion of gonadoliberin is impaired, which leads to a decrease in the level of gonadotropins, the absence of an ovulatory peak of LH, which is manifested by luteal phase insufficiency or anovulation (65%). Violation of the secretion of gonadotropins could cause the development of secondary hyperandrogenism, in which the growth and development of follicles is impaired, hypofunction of the corpus luteum occurs. At the endometrium, estrogen and progesterone receptors are

blocked, and the endometrium becomes thin with the absence of a full phase of secretion. A leading cause of reproductive system disorders with a decrease in thyroid function is a violation of monoaminergic control of the secretion of luliberin by the hypothalamus and damage to the mechanisms of positive feedback between the ovaries and the pituitary gland (15%). Hyperprolactinemia, most likely, develops as a result of a slowdown in the conversion of DOPA to dopamine with a deficiency of thyroid hormones. Another reason may be related to the stimulating effect of thyroliberin on lactotrophic cells of the anterior pituitary gland (12%). Due to the excess production of prolactin, the gonadotropin release cycle is disrupted, LH production decreases, ovulation stops. A decrease in the level of estradiol and progesterone can be considered as one of the mechanisms of menstrual dysfunction. In this case, an increase in the frequency of hyperproliferative processes in target organs is possible. In women with hyperthyroidism, hyperestrogenia is observed, which, according to the feedback mechanism, leads to a decrease in the concentration of FSH, which was also increased in women with hyperthyroidism in our study (80%). At the same time, the level of progesterone remains quite low due to a decrease in the sensitivity of ovarian tissues to LH under conditions of FSH deficiency. In response to a change in the level of progesterone, the concentration of LH in the blood plasma also increases by the feedback mechanism. An increase in LH can also be caused by a decrease in the level of free testosterone. Thyroid function disorders in the form of hyper-or hypothyroidism are accompanied by most diseases - endemic or sporadic goiter in the form of a diffuse or nodular form, thyrotoxic goiter, chronic AIT and others, while nodular sporadic goiter often occurs without impaired function. Violations of the relationship between the thyroid and reproductive systems determine the violation of the menstrual cycle, infertility, the development of hormone-dependent tumors, and in the case of a subclinical course, they can be considered risk factors for fetal loss and abnormalities of its development. On the other hand, functional disorders of the reproductive system with a change in the content of sex steroid and gonadotropic hormones, in turn, can be one of the factors in the development of thyroid pathology. The mechanisms of dysregulation of menstrual function in thyroid pathology are complex, need to be clarified and specified. Menstrual dysfunction is a serious medical and social problem, closely associated with a decrease in fertility. Full compensation of thyroid function is an indispensable condition for the management of patients with menstrual dysfunction, one of the most important sanogenetic factors and a pathogenetically substantiated method of immunocorrection. Treatment of women in the clinical group was aimed at restoring thyroid function, menstrual function, surgical removal of nodules, stopping galactorrhea and restoring fertility. The main treatment methods include the use of hormone replacement therapy, antithyroid drugs, surgical treatment of nodules, the use of dopamine agonists, as well as symptomatic treatment. For all forms of hypothyroidism, levothyroxine replacement therapy was carried out, the dose of the drug and the duration of treatment were selected individually (1.6-1.8 μg per 1 kg of body weight). To date, there is no consensus on the advisability of appointing replacement therapy for subclinical hypothyroidism. Based on the clinical manifestations of the state of the reproductive system, we considered it necessary to conduct replacement therapy at this stage of the disease. For the treatment of hyperprolactinemia, a dopamine agonist Bromocriptine was prescribed to 9 women, with strict control of hormones in the blood (1/4 tablet 2 times a week in the evening). To compensate for the lack of the luteal phase was prescribed progestogens (utrozhestan, djufaston from 14 to 25 days of the menstrual cycle, according to 2 pills a day, 10 days, 3 cycles). In order to stimulate ovulation, clomiphene, chorionic gonadotropin. In hyperthyroidism appointed tireostatika merkazolil while beta-blocker atenolol (1/2 tablets in the morning). Indications for surgical treatment were large goiter sizes, intolerance to thyreostatics, retrosternal arrangement of goiter, presence of a palpable node in the thickness of the thyroid gland (10 women were operated on).

As a result of treatment in women with hypothyroidism, hormonal indicators show an increase in St. T 4 blood content (21.1 ± 3.6 nmol / L, p <0.05) compared with the period before treatment, a decrease in TSH concentration (2, 1 ± 0.5 mIU / L, p <0.05).

Table 6: Indicators of thyroid hormones in blood plasma in women examined and in the control group after treatment.

Groups	TSH mIU / ml	St. T4 pmol / l	St. T3 pg / ml	AT-TPO ME / ml
1. With hypothyroidism (n = 33)	2.1 ± 0.5 p <0.05	21.1 ± 3.6 p <0.05	3.1 ± 0.06 p <0.05	30.8 ± 2.5 p <0.05
2 .With hyperthyroidism (n = 45)	2.64 ± 0.7 p <0.05	15.6 ± 1.2 p <0.05	4.02 ± 0.9 p <0.05	56 ± 8.5 p <0.05
3 . Healthy (n = 20)	1.81 ± 0.074	14.4 ± 1.7	3.4 ± 0.6	19.4 ± 2.6

Note: p <0.05 - reliability in relation to control.

In women with hyperthyroidism at the end of treatment compared with the period before treatment, there is an increase in the concentration of TSH in the blood (2.64 ± 0.7 mIU / ml), a decrease in St. T 4 (15.6 ± 1.2 pmol / L)

AT-TPO (56 ± 8.5 IU / ml, p <0.05). Moreover, the values of indicators of St. T 4, AT-TPO reached the corresponding indicators of the control groups (tab. 6). The physiological dimensions of the thyroid gland with hypothyroidism were achieved in 77.2% of women, the restoration of menstrual function in 63.3%, and signs of galactorrhea in 85.7%. During the observation period, pregnancy occurred in 9 women (31%) of 29 suffering from infertility. The frequency of pathology from the mammary glands decreased by 47.6%. In women with hyperthyroidism, these rates were 66.6, respectively; 71.4; 87.5; 41.6 and 75%.

Consequently, the effectiveness of treatment was slightly higher in the group of women with hyperthyroidism. Apparently, there is a more pronounced decrease in metabolic processes in the woman's body with a functionally reduced thyroid condition and a decrease in the sensitivity of the ovaries to gonadotropins in conditions of reduced metabolism, as well as a decrease in estrogen metabolism with a deficiency of thyroid hormones. The choice of therapeutic tactics for nodular thyroid formations is one of the complex and debatable problems. Different approaches are primarily due to the heterogeneity of the structure of nodes. But even with certain nosological forms of thyroid nodules, modern tactics are ambiguous. In our studies, total thyroidectomy was performed in 9% of women with nodular goiter. The entire fraction was removed. The presence of bilateral multinodular goiter in 6% of women, diffuse toxic goiter was the basis for subtotal thyroid resection in 3% and in 19% total resection. In this case, the stump was left on the sides of the trachea. Subsequently, all patients were prescribed hormone replacement therapy with thyroid hormone preparations, dopamine antagonists, estrogen-progestogen drugs.

Thus, our studies have shown that, despite the presence of hypothyroidism and hyperthyroidism, the correct and timely conservative and surgical treatment allows you to restore reproductive function.

CONCLUSIONS

1. Women with a deficit of thyroid hormone is a decrease of gonadotropic pituitary function with the development of hyperprolactinemia (27.2%), lack of lutein howling menstrual cycle phase (78.7%).
2. With hyperthyroidism, women have hyperestrogenia (80%), which, by the feedback mechanism, leads to a decrease in the concentration of FSH (75.7%). At the same time, the level of progesterone (77.7%) remains quite low due to a decrease in the sensitivity of ovarian tissues to luteinizing hormone in conditions of FSH deficiency.
3. The state of menstrual function is an integral indicator of women's reproductive health. When studying menstrual dysfunctions in a comparative analysis of various pathologies of reproductive function in both clinical groups, it was shown that menstrual dysfunction in the first clinical group was dominated by oligomenorrhea - 30%, and in the second group - opsenomenorrhea - 24% and dysmenorrhea - 22%. In the first clinical group, 10 (30%) women suffered from infertility, and in the second group, 19 women (42.2%).
4. During the period of treatment and observation in patients in both groups, pregnancy occurred in 9 women (31%) out of 29 suffering from infertility. The frequency of pathology from the mammary glands decreased by 47.6%.

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