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HORMONAL ANALYSIS IN THE DIAGNOSIS OF THYROID DISEASES

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Abstract: The creation of radioimmunoassay (RIA) methods for the determination of hormones had a decisive influence on the development of modern endocrinology and, above all, thyroidology. Since 1973, RIA methods have become routine diagnostic methods for the determination of thyroxine (T4), triiodothyronine (T3) and thyroid-stimulating hormone (TSH).

Key words: euthyroid state, hypothyroidism, thyrotoxicosis.

However, for a long time they made it possible to determine only fractions of hormones associated with transport proteins, and RIA methods for determining TSH did not allow the determination of its low (<0.1 mIU/l) concentrations. Later, variants of RIA were developed based on the immunometric principle, using solid-phase carriers and monoclonal antibodies. This made it possible to determine, along with general T4 and T3, their free forms.

Namely, free T4 and T3 provide the entire spectrum of biological activity. Their definition is the most informative in assessing the functional state of the hypothalamic-pituitary-thyroid system. The IRMA principle made it possible to increase the sensitivity of the TSH determination method to 0.16 mIU/l. This level of sensitivity satisfied clinicians in assessing the euthyroid state and hypothyroidism, but it did not allow differentiating normal from subnormal TSH levels in patients with thyrotoxicosis. In the last decade, fundamentally new non-isotopic technologies for hormonal immunoassays have been created. The sensitivity of this method in determining TSH was increased to 0.03 mIU/l.

Determination of total thyroxine (GT4).

The TT4 content in healthy people (euthyroid state) averages 104 nmol/l (65-160 nmol/l). Its concentration exceeds the level of T3 by 60 times. The main specific transport protein that has high affinity for T4 and T3 is thyroxine-binding globulin (TBG), although its affinity for T4 is 5 times higher than T3. TSH circulates in the blood at a concentration of 160 μg/ml and binds 75% T4 and 85% T3.

The second binding protein is prealbumin. It has a relatively low affinity and binds 15% T4 and only 3% T3, while its relatively high capacity is achieved at a significant concentration (250 μg/ml).

The third protein that binds T4 and T3 equally (10%) is albumin. Its content in the blood is 3.5 mg/ml, so albumin has a huge capacity for thyroid hormones.

Although the share of SG4 accounts for 0.03%, it is the fraction not associated with protein that provides the entire spectrum of its metabolic and biological activity, including providing a feedback mechanism for regulation of the hypothalamus - pituitary gland - thyroid gland.

Diagnostic significance of TT4 determination.

Until recently, quantitative determination of TT4 in blood serum served as the main hormonal parameter in assessing thyroid function. In the vast majority of cases, with clinically pronounced hyperthyroidism, the content of T4 in the blood of the general circulation is increased, and in hypothyroidism, it is decreased. The normal range for TT4 in the euthyroid state is 65,160 nmol/L with a mean value of 104 pmol/L.

These include:

- changes in the binding capacity of gyreoid-binding proteins. For example, the concentration of TT4 in the blood can be increased with an increase in their binding capacity. The latter may be due to a genetically determined increase in TSH content, as well as pregnancy, taking contraceptive drugs containing estradiol derivatives, and estrogen therapy.

Factors that distort the results of TT4 immunoassay.

1. Plasma samples from patients with lipemia can be used to determine TT4 if the triolein concentration does not exceed 60 mg/ml.

In hemolyzed plasma samples, determination can be made at hemoglobin levels up to 2.5 mg/ml. In patients with jaundice, high bilirubin levels (> 0.5 mg/ml) distort the results of thyroxine analysis.

2. Cloudy plasma samples should not be used.

3. Falsely elevated results when determining TT4 can be caused by some chronic blood diseases, in particular myelomas with high levels of IgG.

Determination of total triiodothyronine (TT3)

T3 is produced and secreted by the thyroid gland, but the majority of T3 is produced outside the thyroid gland by deiodination of T4. TT3 levels in healthy euthyroid people range from 1.04 to 2.5 nmol/L (mean value 1.7 nmol/L). About 99.5% of T3 circulating in the blood is bound to proteins. As for T4, the main transport protein. T3 is TSG. However, its affinity for T3 is much lower. Approximately 80% of plasma T3 is associated with TSH, the remaining 20% is transported by prealbumin and albumin (10% each). The share of free, not protein-bound T3 accounts for 0.3%. The free T3 fraction provides biological and metabolic activity and heme thereby maintains the euthyroid state.

Diagnostic significance of TT3

In most clinical cases, the level of TT3 correlates with the content of TT4. Determination of TT3 is more informative in case of thyrotoxicosis, since in some cases the level of TT4 does not change significantly, and the concentration of serum TT3 increases sharply. Therefore, T3 is a more adequate objective criterion in the diagnosis of thyrotoxicosis.

During pregnancy, TT3 levels increase, as does when taking estrogen-containing hormonal contraceptives. This. is known to occur in parallel with an increase in TSH concentration. In myeloma that produces large amounts of IgG, as well as in severe liver diseases, falsely elevated TT3 values are recorded. In newborns, T3 levels are also elevated. In older men, a slight decrease in its concentration is recorded. In women, TT3 levels do not depend on age. In half of the cases, there is a decrease in TT3 levels after various surgical operations. Chronic and acute diseases are also accompanied by a decrease in its level.

Factors distorting the results of determining TT3

These include:

- hemolyzed serum with hemoglobin level > 1.25 mg/ml:
- lipemic serum with lipid (triglyceride) levels > 15 mg/ml;

- serum bilirubin content > 0.25 mg/ml.

High levels of TT4 and TT3 can also occur with an overdose of iodine preparations in people living in goiter-endemic regions.

Definition of sT4.

In free form, the blood of the general circulation contains no more than 0.03% T4. The concentration range characteristic of a normally functioning thyroid gland is 9.0-25 pmol/l with an average value of 15.7 nmol/l. Currently, c'G4 is one of the main determining markers in assessing thyroid function.

Initially, a special method was created to determine fT4, which is based on the principle of balanced dialysis. The method is highly reliable and accurate.

Thyroid diseases

1. Hyperthyroidism (T3 toxicosis) Possible overdose of T3

2. Euthyroid state with autonomously functioning thyroid tissue:

3. Compensatory increase in T3 content due to:

Factors influencing the results of sT3 analysis..

With a normally functioning thyroid gland, the mechanisms that regulate its function are designed in such a way that the content of fT4 does not depend on the concentration of binding proteins. It is this circumstance that makes it possible to use the determination of cT4 as the most adequate and direct marker in assessing the hormonal function of the thyroid gland.

In the case of hyperthyroidism, the 6G4 level increases (>25 pmol/l). In hypothyroidism it decreases (<9 pmol/l). An increase in the level of circulating fT4 is recorded in patients receiving thyroxine replacement therapy.

Factors influencing the results of determination of fT4.

Heating samples of the test material due to denaturing proteins leads to an increase in the content of 'cT}, as well as: triglyceride content >3.75 mg/ml, hemoglobin content in a hemolyzed sample >1.25 mg/ml, bilirubin content in patients with jaundice >0.125 mg /ml.

Definition of cT3.

T3 is the main biologically active thyroid hormone. About 99.7% of T3 is bound to proteins and only 0.3% circulates in free form. The cT3 fraction provides the entire spectrum of metabolic activity. cT3 is a metabolic product of T4 outside the thyroid gland. It must be emphasized that deiodination of T4 with the formation of T3 occurs more intensely in the anterior pituitary gland than in peripheral tissues.

A low basal TSH level and the absence of its release under the influence of TRH confirm the diagnosis of hyperthyroidism, and a slight surge indicates possible hypopituitarism. Hypothyroidism is always accompanied by an unusually high (20-100 mIU/L) TSH level when TRH is administered.

It should be borne in mind that some neurotropic pharmacological drugs, especially those of a dopaminergic nature, can significantly change the response of the adenohypophysis to the administration of TRH. Drugs that reduce the response of the pituitary gland to the introduction of TRH include: corticosteroids, L-DOPA, acetylsalicylic acid, and those that potentiate the release of TTT include amidarso, theophylline.

Negative test results clearly indicate the ineffectiveness of the conservative therapy used. Diseases in which the pituitary gland's response to TRH is significantly reduced include Yatsenko-Cushing's disease, severe chronic kidney disease, diabetic ketoacidosis coma, mental depression, and fasting.

Determination of thyrostimulating hormone (TSH).

Determination of TSH, along with cT'4, is one of the leading “strategic” markers in assessing the status of the thyroid gland. TSH belongs to the group of glycoprotein hormones. Its molecular weight is 28,000. It consists of two subunits. At the same time, the p-subunits of all glycoprotein hormones have their own individual chemical structure, which determines their biological specificity.

The synthesis and secretion of TSH are vertically regulated by the hypothalamic triptatide, thyrotropin-releasing hormone, or thyrotropin-releasing hormone (TRH). In turn, TSH acts on the thyroid gland, ensuring the synthesis and secretion of T4 and T3. The regulation of TSH secretion is based on a negative and positive feedback mechanism: high concentrations of free T4 and T3 inhibit, and low concentrations stimulate the release of TSH.

The diagnosis is confirmed by low concentrations of T4 and T3. In the case of subclinical mild hypothyroidism, when the level of cT4 and TT4 in the blood is within the normal range, the detection of elevated TSH levels becomes crucial. A low TSH level in hypothyroidism indicates insufficiency of the pituitary gland or hypothalamus and excludes a primary dysfunction of the thyroid gland.

In hyperthyroidism, the synthesis and secretion of TTT are suppressed, so the determination of very low concentrations of TSH using ultrasensitive methods is of fundamental importance in the diagnosis of various forms of hyperthyroidism. TSH analysis is also important for therapeutic monitoring of patients with hypothyroidism receiving daily thyroxine replacement therapy. By determining the TSH level, you can optimize the dose of L-thyroxine taken.

Factors distorting the results of TSH determination.

These include:

- cloudy whey;
- the presence of blood cells in the serum;
- triolein level > 60 mg/ml;
- hemolysis (hemoglobin level > 0.3 mg/ml);
- bilirubin content > 0.04 mg/ml.

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