Thyperoxidase activity and cytochemical indices of blood neutrophils in autoimmune thyroiditis

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Objective: a study of the activity of thyroperoxidase and cytochemical indices of blood neutrophils during autoimmune thyroiditis and the establishment of their possible interrelations depending of the severity of the process.

Materials and methods. The material for histochemical studies was pieces of thyroid tissue taken from 27 patients with autoimmune thyroiditis after its subtotal resection. For cytochemical studies was used venous blood taken from the same patients at admission, as well as on the 2nd and 5th day after surgery. The control was venous blood taken from 10 healthy volunteers aged 20–45 years.

Materials and methods. In patients with autoimmune thyroiditis in the hypothyroidism stage, when formulating a reaction to thyroperoxidase in thyroid preparations, most of the visual field is occupied by large lymphocytic infiltrates.

Results. There are single follicles of small size with moderate and weak enzyme activity between them. Separate adenomatous foci, without visible lumen, contain a small amount of colored reaction products and in cases of severe course of the process only their traces are revealed. Myeloperoxidase activity in neutrophils with hypothyroidism is increased (P < 0.01). The content of glycogen and lipids in the neutrophils of the blood of this group of patients is also increased. The increase in the content of cationic proteins suggests that a significant increase in the cytochemical indices of neutrophils in this research variant is a consequence of the intensification of synthetic processes in cells at the stage of their development. The body responds as a stress to the decrease in the content of thyroid hormones in the form of activation of synthetic processes in cell structures, including blood cells.

Conclusion. Epithelial parenchyma of the gland in hypothyroidism is gradually replaced by lymphoid infiltrates. The activity of thyroperoxidase in autoimmune thyroiditis in the hypothyroidism phase is low and is directly dependenton the severity of the pathological process. The studied cytochemical indices of neutrophils in patients with autoimmune thyroiditis with hypothyroid syndrome were significantly elevated, which is especially pronounced in the last phase of the disease

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Despite the variety of diagnostic criteria that are available to determine thyroid function impairment, there are also littlestudied aspects of diagnostics, in particular, such as studying the cytochemical analysis of cellular enzymes that actively respond to hormonal imbalances at various sites. -the lesions of the thyroid gland [3, 9, 12]. It was shown that thyroxin (T4) and triiodothyronine (T3) can be deiodinated in the presence of hydrogen peroxide (H2O2) and myeloperoxidase, and the resulting iodine atoms affect the antimicrobial activity of neutrophil granulocytes (NG) [4, 6, 10, 19].

According to the authors, the deiodination of the thyroid hormones in NG is so intense that this can explain their accelerated exchange during bacterial infection in humans. Moreover, it has been shown that the anti-microbial effect of the myeloperoxidase - H₂O₂ system - iodide is largely associated with the process of deiodination, and the fixation of iodide with the phagocyte to some extent depends on the content of myeloperoxidase in it [15, 11, 16, 18]. It should be considered established that only part of T3 (about 20%) of human blood is of thyroid origin, and the rest of the hormone is formed in the blood by deiodinating thyroxin. Resting non-phagocytic leukocytes show low deiodinating activity, and during phagocytosis this process increases dramatically. The authors suggest that accelerated activation of the hormone and an increase in the rate of its disappearance from plasma in acute infections [2, 5, 7, 13, 20] apparently depend on the increased metabolism of tiroxine NG [2, 5, 7, 13, 20].

However, the concept of "antimicrobial system NG" includes not only myeloperoxidase. In particular, it is known that hereditary and acquired deficiencies of cationic proteins (CBs) also lead to a decrease in the microbial activity of NG and a weakening of the antimicrobial resistance of the organism [1, 8, 14, 17].

An important role in the implementation of anti-microbial functions of NG is played by glycogen and lipids. In particular, glycogen, which is the main energy material of leukocytes, is undoubtedly used both in phagocytic reactions and in the process of degradation of thyroid hormones.

The use of lipid-containing compounds, which are a component of cellular membrane structures, is evident in the functional activity of NG, since it is performed by phagocytosis and endocytosis, i.e. with costly membrane structures.hese issues in the literature have been given insufficient attention, which determines the need for a comprehensive and in-depth study of the considered group of the antimicrobial components of Nitroglycerin in order to substantiate their important role in shaping the unspecified resistance of the organism and developing new approaches to regulating this important links of the defense mechanisms of the human body. And the objective determination of the level of nonspecific resistance of the organism by studying the cytochemical indices of NG is no less valuable in the sense that it becomes possible to correct them with thyroid hormones - the cofactor of the antimicrobial myeloperoxidase system. And this should be considered especially important in chronic and sluggish toxic-infectious pathologies. From the data presented, it follows that thyroid operoxidase, thyroid and myeloperoxidaseof neutrophil granulocytes are in the initial and final stages of the metabolism of thyroid hormones. However, the literature does not pay attention to their functional relationships, which, in our opinion, are undoubtedly present. This, in particular, is due to the fact that, to date, the method for determining the activity of thyroid operoxidase, which would be of great help in establishing the functional state of the thyroid gland, has not been worked out.

Given the above, it should be noted that the study of the functional relationships of the thyroid gland, regulating the main metabolic processes in the body, and NG, responsible both for the state of nonspecific resistance and the metabolism of thyroid hormones, is relevant both for the clinic and to solve common biomedical problems will first of all determine new diagnostic criteria that can be used not only for diagnostics, but also for predicting the functional state of the thyroid gland.

Hypothyroidism in the overwhelming majority of cases is a consequence of autoimmune thyroiditis, i.e. the last phase of the disease.

When autoimmune thyroiditis morphologically, proliferation and the associated increase in the thyroid gland take place first, and later atrophy of the parenchyma of the gland occurs, impairment of function and, as a result, hypothyroidism. In histological specimens, a characteristic infiltration with mononuclear cells (lymphocytes, monocytes) is observed. In this case, the normal structure of the gland is replaced by rapidly multiplying lymphocytes. Infiltrates contain a large number of B-lymphocytes, Tlymphocytes, macrophages. The process is accompanied by the destruction of follicles and attempts of the gland to regenerate, which leads to its increase. When the destruction of follicles reaches a certain level, hormone production decreases and, as a result, symptoms of hypothyroidism appear.

So, the cause of primary hypothyroidism, one of the most common endocrine diseases, is autoimmune thyroiditis. Less commonly, it is a consequence of surgery, in which there is a persistent deficiency of thyroid hormones in the body.

Purpose: to study the activity of thyroid operoxidase and cyto-chemical parameters of neutrophils of blood during autonomic insulin therapy and to establish their possible interrelationships depending on the degree of process expression

Material and methods

The material for histochemical studies was the pieces of thyroid tissue taken from 27 patients with autoimmune thyroiditis, operated on at the endocrine surgery department of the Republican Clinical Hospital.

For cytochemical studies used venous blood taken from the same patients at admission, as well as on the 2nd and 5th day after surgery. The control was venous blood of 10 healthy volunteers aged 20–45 years.

The activity of thyroid peroxidase (TPO) in the tissues of the thyroid gland was determined by the method developed at the Department of Histology of the Dagestan State Medical University (registration number 2015154203 dated December 16,2015).

Cytochemically in neutrophil granulocytes, myeloperoxidase activity was determined by the Graham-Knoll method using benzidine; the content of cationic proteins - according to the method V.E. Piga-rovskogo with methyl green; glycogen - according to J.F. MacManus; lipids using Sudan black B. The results were expressed as the average cytochemical coefficient.

Statistical data processing was performed using the Statistiks program. The significance of the differences between the groups was determined using the Kruskal – Wallis criterion; the significance of the differences before and after was evaluated by the Wilkox test.

Results and its discussion

In the postoperative thyroid material of patients with autoimmune thyroiditis in the stage of euthyroidism, when the reaction to thyroid operoxidase is established in the preparations, you are follicles of various sizes with moderate enzyme activity. The follicle wall is multilayered in some places as a result of proliferative activity. The distribution of reaction products in different parts of the follicles is uneven. In the interfollicular spaces there are multiple adenomatous and parenchymatous foci with moderate or high activity. Connective tissue propuffs expanded; they have numerous lymphocytic infiltrates without colored reaction products.

In this variant of the thyroid pathology, it should be considered characteristic, along with the presence of these large interfollicular infiltrates, a weak delineation of the boundaries of the follicular cells, apparently related to the severity of the process of their destruction (Fig. 1.).In smears of blood leukomass of patients with autonomic instability in the stage of euthyroidism, in setting the response to myeloperoxidase, it can be seen that the percentage content of neutrophil granulocytes with moderate activity is reduced (55-60%, in normal - 80-85%). You are not cells with a high content of reaction products. Often determined neutrophil granulocytes with areas of the cytoplasm, free from activity. Increased percentage content of immature forms of neutrophils; their activity is higher. The cytochemical coefficient of the enzyme in blood NG is reduced in this group of patients (1.31 ± 0.08) , with a norm of $1.52 \pm$ 0.07).



Figure 1. The thyroid gland of a patient with autoimmune thyroiditis in the stage of euthyroidism. Reaction to thyroid operoxidase. 1 - follicles, the wall is multi-layered; 2 - adenomatous foci; 3 - lymphocytic infiltrates.

On the 2nd day of the postoperative period, the activity of myeloperoxidase in NG is not significantly changed. The quantitative content and distribution pattern of the reaction products are similar to the initial ones. However, by the end of the week, the number of band and young forms with high enzyme activity was sharply increased (Table 1).

The content of cationic protein in the neutrophil granulocytes blood of patients with autoimmune thyroiditis is similar to the control. Most of the cells have a moderate content of stained products and only 3-5% of phagocytes are saturated with them. In the postoperative period, due to the increase in the percentage of nonmature forms of NG, saturated with light green material, there is a slight increase in SCS - on the 2nd day 1.69 \pm 0.08, on the 5th day 1.71 0.04 (table 1).

In blood smears of leukomass of patients with autoimmune thyroiditis, the glycogen con-

tent in neutrophil granulocytes is moderately reduced (P <0.05); less percentage of cells with moderate and high content of Schiff reaction -positive material; in immature forms of phagocytes the number of stained products is also less.

The study of glycogen content in neutrophil granulocytes in the postoperative period showed that it corresponds to the original: less, compared to the control, the percentage of cells saturated with colored products, as well as with their moderate content. In the smears, cells with the distribution of stained products in the form of separate islands, or with areas of the peripheral zone free from them, are often detected.

Table 1. Cytochemical indices of blood neutrophil granulocytes in patients with autoimmune thyroiditis in the stage of euthyroidism before and after surgery (incl. Units) $M \pm m$

Index	Autoimmune thyroiditis in the stage of euthyroidism				
	Control	Initial	After surgery on		
			2nd day	5th day	
Myeloperoxidase	1,52±0,07	1,31±0,08*	1,35±0,06*	1,39±0,09	
Anodal Protein	1,62±0,09	1,65±0,05	1,69±0,08	1,71±0,04	
Glycogen	1,44±0,07	1,26±0,03*	1,28±0,04*	1,31±0,05	
Lipids	2,63±0,04	2,03±0,09**	2,13±0,07**	2,22±0,03*	

Note: the significance of differences (P) compared with the control (* - P < 0.05, ** - P < 0.01).

In the neutrophil granulocytes of the blood of patients with autoimmune thyroiditis, the lipid content is reduced with a high degree of reliability (P <0.01). In smears dominated by neutrophils with the location of colored products in the form of individual or plum-ish. Only the cytoplasm of single cells is completely filled by them.

In the postoperative period, on the 2nd and on the 5th day, the quantitative content and distribution pattern of the stained material corresponds to the baseline.However, it is possible to notice some features: the number of neutrophil granulocytes s with uneven islet arrangement of products has increased, the contours of cells completely devoid of sudan-positive material, or with their traces, are often revealed.

From the figure (2), it follows that the dynamics of the cytochemical indices of the IH of the blood of patients with autoimmune thyroiditis in the stage of euthyroidism, with moderate thyroid operoxidaseactivity, are not significantly changed, except for the content of lipids, the reliability of which is high.



Figure 2. Dynamics of cytochemical indices of blood neutrophil granulocytes in patients with autoimmune thyroiditis in the stage of euthyroidism with moderate thyroid peroxidase (TPO) activity before and after surgery.

When setting the response to thyroid operoxidase in the thyroid of patients with autoimmune thyroiditis in the stage of hypothyroidism of moderate severity, most of the field of vision is occupied by largelyphocytic in-filtrates. Between themare single follicles of small size with moderate or weak enzyme activity (Fig. 3).



Figure3. The thyroid gland of the patient autoimmune thyroiditis in the stage of hypothyroidism of moderate severity.

Reaction to thyroid operoxidase. 1- lymphocytic infiltrate; 2 - follicles with a moderate content of the enzyme; 3 - adenomatous foci with weak activity. H. × 400.

Separate adenomatous foci, without visible lumen, contain a small number of colored reaction products and in cases of severe course of the process only their traces are revealed.

The activity of myeloperoxidase in the NG of the blood of patients with autoimmune thyroiditis in the stage of hypothyroidism of moderate severity is increased compared withcontrol with a high degree of confidence (P <0.01). The percentage of NG with a moderate amount of reaction products was significantly increased. Only single cells have either a small number of stained granules, or are over saturated with them.The study in the postoperative period showed a gradual decrease in the activity of the enzyme: on the 2nd day - 2.03 ± 0.09 , on the 5th day - 1.85 ± 0.07 , with baseline values of 2, 12 ± 0.11 . At the same time, a decrease in the percentage of neutrophil granulocytes with moderate activity and parallel growth of cells with a low content of stained and saturated granules can be traced.

In the NG of the blood of patients with autoimmune thyroiditis in the stage of hypothyroidism of moderate severity of the process, the content of cells is significantly increased.

Most segmented cells are saturated with colored granules. However, most often, the granules weakly contour due to the severity of the diffuse component. The colored material is evenly distributed in the cells. However, in smears, cells, often segmented toonuclear, with the location of reaction products in the form of separate thickenings with degranulation sites are often detected. In the postoperative period, the content of cells tends to decrease mainly due to a decrease in the percentage of neutrophil granulocytes with high enzyme activity.

The glycogen content in blood neutrophil granulocytes of patients with autoimmune thyroiditis in the hypothyroid stage is increased with a high degree of confidence (P <0.01). The overwhelming majority of cells are saturated with Schiff reaction -positive material. Only single segmented neutrophils have a small amount of stained material located in the form of individual thickeners.

Table 2. Cytochemical indicators of neutrophil granulocytes in the blood of patients with autoimmune thyroiditis in the stage of hypothyroidism of moderate severity before and after surgery (in conventional units). $M \pm m$

Index		Autoimmune thyroidi	litis in hypothyroidism		
· · · · · · · · · · · · · · · · · · ·	Control	Initial	After surgery on		
			2nd day	5th day	
Myeloperoxidase	1,54±0,08	2,12±0,11**	2,03±0,09*	1,85±0,07*	
Anodal Protein	1,62±0,06	1,98±0,08**	1,83±0,07*	1,71±0,06*	
Glycogen	1,44±0,07	2,22±0,12**	2,01±0,11	1,63±0,09	
Lipids	2,62±0,11	2,92±0,12**	2,88±0,11*	2,75±0,09	

Note: the significance of differences (P) compared with the control (* - P < 0.05, ** - P < 0.01).

In the postoperative period, on the 2nd day a significant decrease in the number of stained

products takes place. This tendency is even more pronounced on the 5th day: the amount

of NG with moderate content of Schiff reaction positive material is reduced to 70-75%, the number of cells saturated with reaction products is also reduced. However, even by the end of the week, the SCP content of glycogen only approaches the control figures (1.63 \pm 0.09, with the control - 1.44 \pm 0.07).

As follows from the above data (Table 2), the content of lipids in neutrophil granulocytes of the blood of patients with autoimmune thyroiditis in the hypothyroid stage is significantly higher than the control values. In the maz-kakh most of the NG is saturated with dark sudanpositive material, the nucleated parts of the cells are clearly outlined; In these enlightened areas, the granular component of the reaction products is well seen.

On the 2nd day after the surgical intervention, the decrease in the content of the colored material is not reliable. Only a decrease in the number of neutrophil granulocytes saturated with Sudan-positive material is characteristic; cells with moderate content

prevail. The growth of neutrophil granulocytes with a low content or with traces of reaction products is also noted.

By the end of the week after the operation, the decrease in the lipid content in neutrophil granulocytes compared with the initial one was noticeable (2.75 ± 0.09 , with the initial - 2.92 ± 0.12). However, in comparison with control, the figures of the indicator are significantly higher.

The cytochemical indices of neutrophil granulocytes in the blood of patients with autoimmune thyroiditis in the hypothyroidism stage with weak thyroid operoxidase activity, as compared with the options described above, have features. The initial figures, compared with the control, were significantly increased (P < 0.01); in the postoperative period, they tend to decrease (Fig. 4).



Figure 4. Dynamics of cytochemical parameters of neutrophil granulocytes (NG) in the blood of patients with Autoimmune thyroiditis in the hypothyroid stage with weak thyroid peroxidase (TPO) activity before and after surgery.

As follows from the above illustrative material, in the thyroid gland in patients with autoimmune thyroiditis in the hypothyroidism stage, when setting the response to thyroid operoxidase in preparations, most of the visual field is occupied by large lymphocytic infiltrates. Between them are single follicles of small size with moderate and weak enzyme activity. Separate adenomatous foci, without visible lumen, contain a small amount of colored reaction products, and in cases of severe course of the process only their traces are revealed. It is necessary to assume that in this variant of the pathological process there is an intensive degradation of follicular cells according to the scheme mentioned earlier, and this is clearly seen in cases of severe (far gone) degree of disease development, i.e. the epithelial parenchyma of the gland is gradually completely, or almost completely, replaced by lymphoid infiltrates. The latter in appearance and cellular composition resemble peripheral lymphoid organs. The consequence of these processes is that the thyroid gland ceases to perform the function of the endocrine organ. The results of parallel cytochemical studies of neutrophil granulocytes in the blood of patients with autoimmune thyroiditis in the pre-operative period are similar to those in adenomatous nodular goiter. In particular, the activity of myeloperoxidase in NG is increased compared with the control with a high degree of confidence (P <0.01) due to a significant increase in the percentage of cells with moderate and high enzyme activity. The content of glycogen and lipids in blood neutrophil granulocytes of this group of patients is also higher. In either case, an increase in the content of the reaction products is associated with an increase in saturation by the diffuse component.

The peculiarity of the cytochemical pattern of blood neutrophil granulocytes in this group of patients should be considered as a significant increase in the content and cationic protein. This suggests that the substantial growth of all the studied cytochemical indices of neutrophil granulocytes in this variant of research is a consequence of the intensification of synthetic processes in cells at the stage of their development. And in the case of adenomatous nodular goiter, and even more so with autoimmune thyroiditis, one should look for a stimulator of myo-loocytopoiesis in the red bone marrow. The peculiarities of the correlation interrelations between the activity of thyroid operoxidase and the cytochemical indices of blood neutrophil granulocytes in patients with autoimmune thyroiditis in the hypothyroid stage are shown in Figure 4.

It can be assumed that the organism reacts as to stress to a transcendent decrease in the

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content of hormones with a broad spectrum of action, such as thyroid ones. And, apparently, one of the protective reactions of the body, aimed at preserving homeostasis, is the activation of synthetic processes in cell structures, including blood cells.

Findings

1. In thyroid patients with autoimmune thyroiditis in the stage of euthyroidism, the activity of thyroid operoxidase, as well as the cytochemical indices of neutrophil granulocytes, were not significantly changed. Their stability is maintained in the postoperative period.

2. The activity of thyroid operoxidase in autoimmune thyroiditis in the phase of hypothyroidism is low and is directly dependent on the severity of the pathological process.

3. The studied cytochemical indices of neutrophil granulocytes in patients with autoimmune thyroiditis with hypothyroidism syndrome were significantly increased, which is especially pronounced in the last phase of the development of the disease.

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