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The use of antioxidants in the treatment of Graves' disease: evaluating the results

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ABSTRACT

Topicality. Accelerated metabolism in Graves' disease causes the development of oxidative stress, which significantly affects the clinical course and treatment results.
Purpose. This study was conducted to evaluate the effect of treatment with thyrosol and thyrosol in combination with antioxidants, in particular vitamins C and E, on indicators of thyroid hormone function (thyroid-stimulating hormone and thyroxine) and oxidative stress (malondialdehyde and total antioxidant capacity).
Material and method. The clinical study was performed on 41 patients with newly diagnosed Graves' disease of moderate severity, aged from 21 to 43 years, who were divided into two groups. The control group consisted of 19 patients who received thyrosol for treatment. The main group included 22 patients who were treated with thyrosol in combination with vitamins C and E. Examinations were carried out upon inclusion in the program and one and two months after the start of treatment.
Results. The conducted studies showed that in the course of treatment, the indicators of malic dialdehyde gradually decreased from 21.3±0.4 (17.3–29.2) to 10.31±0.1 (9.72–10.82) and thyroxine from 37.7±0.5 (31.2–42.7) to 15.31±0.2 (13.20–20.52) and the total antioxidant capacity increased from 0.69±0.04 (0.52–0.79) to 1.58±0.1 (1.48–1.61), thyroid-stimulating hormone from 0.01±0.004 (0.07–0.001) to 2.31±0.1 (0.90–3.52). These changes were more pronounced in the main group compared to the control group during the study one month and two months after the start of treatment.
Conclusions. Thus, antioxidant supplements can be used to improve thyroid function in hyperthyroid patients by enhancing antioxidants and restoring the oxidant-antioxidant balance.

Keywords: hyperthyroidism, antioxidants, malondialdehyde, total antioxidant capacity, oxidative stress

INTRODUCTION

Graves' disease (hyperthyroidism) is characterized by increased secretion of thyroid hormone triiodothyronine and tetraiodothyronine and lowering the level of thyroid-stimulating hormone.

Thyroid hormones are involved in oxidative metabolism, in the synthesis and degradation of non-enzymatic antioxidants, such as glutathione, vitamins C and E, uric acid, ceruloplasmin and ferritin, as well as enzymatic antioxidants [1]. An imbalance between the synthesis of prooxidants and antioxidants is defined as oxidative stress. Thyroid tissue has been found to have high levels of oxidative stress, which is associated with hyperthyroidism [2].

Pathological changes in the oxidant and antioxidant systems occur as a result of excessive production of thyroid hormones. It has been established that oxidative processes play a role in the development and clinical manifestations of Graves' disease, such as thyrotoxic myopathy and cardiomyopathy, orbitopathy [3]. Excessive production and/or inadequate deactivation of reactive oxygen species causes oxidative stress [4]. If an excessive amount of reactive oxygen species harmful to cell membranes is

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not disposed of by appropriate systems, they cause lipid peroxidation [5].

In the treatment of hyperthyroidism, antithyroid drugs are used, in particular, such as thyrosol, carbimazole, which prevent the iodination of tyrosine leading to a decrease in the synthesis of T3 and T4 [6]. At the same time, these drugs suppress the production of cytokines and eliminate or reduce the formation of radicals by thyroid cells, the activity of oxidative stress and its clinical manifestations [7]. There are individual experimental and clinical works in which the expediency of using antioxidants, in particular vitamins C and E in the treatment of hyperthyroidism and Graves' disease [8-10] is substantiated.

The purpose of the study: To evaluate the effect of antioxidants on the activity of oxidative stress by indicators of malondialdehyde and total antioxidant capacity, and the function of the thyroid gland in patients with Graves' disease.

MATERIAL AND METHODS

The planned studies were carried out on 41 patients aged 21–43 with newly diagnosed Graves' disease with a clinical course of moderate severity, who were divided into 2 groups. Group 1 (A) (control – 19 women) consisted of patients who received thyrostatic and symptomatic therapy. Group 2 – the main group (B) included 22 patients who received the same therapy as the patients of group 1 with the addition of antioxidants (vitamins C and E).

Inclusion criteria: patients with Graves' disease, first diagnosed with a clinical course of moderate severity.

Exclusion criteria: patients with relapsed Graves' disease, with serious comorbidities (diabetes mellitus, hypertension, dyslipidemia, kidney disease) and those with a history of using such drugs as glucocorticoids, oral contraceptives or vitamin supplements, pregnant and nursing mothers.

Treatment for control (A) included the use of thyrosol according to the scheme: 30 mg per day for two weeks, then 20 mg per day for three weeks, then 10 mg per day; anaprilin 20 mg three times a day for two weeks. Patients of the main group (B) received treatment according to the program of the control group supplemented with antioxidants: vitamin C 1 g in tablets three times a day and vitamin E in a dose of 100 mg in one capsule twice a day for two months.

The content of thyroid-stimulating hormone, free thyroxine, malondialdehyde and total antioxidant capacity in the blood was studied in the periods when taken for the study and one month and two months after the start of treatment.

The content of malondialdehyde in blood serum was determined by the reaction with Thiobarbituric acid. The ELIZA method was used to find total antioxidant capacity. The obtained digital data of the studied indicators are presented as the average value and standard deviation. T-test was used to compare the mean value of quantitative variables in both groups, and Pearson's correlation coefficient was used to investigate the relationship between quantitative variables. The level of statistical significance was defined as $P < 0.05$.

RESULTS

The conducted studies showed that the control and main groups were identical in terms of age, laboratory characteristics of hyperthyroidism and oxidative stress.

During the examination after a month of treatment, it was noted that the indicators of hyperfunction of the thyroid decreased in patients of both groups – the level of thyroid-stimulating hormone increased and the indicator of free thyroxine decreased. These changes were more pronounced in patients of the main group and in comparison, with the control group they were reliable ($p<0.05$). The level of malondialdehyde also decreased: according to average indicators in the control group by 20% and in the main group by 39 % ($p<0.05$). The index of total antioxidant capacity increased: in the control group from 0.72±0.05 (0.53–0.81) to 1.08±0.15 (0.81–1.21), i.e., by 50 % and in the main group from 0.69±0.04 (0.52–0.79) to 1.29±0.16 (1.11–1.39) – by

TABLE 1. Changes in indicators of thyroid-stimulating hormone, free thyroxine, malondialdehyde and total antioxidant capacity during the specified examination periods

Indicators \ Examination terms		Initial data	After a month of treatment	After two months of treatment
Thyroid hormone	A	0.01±0.004(0.07-0.001)	0.28±0.05 (0.1-0.9)	1.21±0.3 (0.21-3.19)
	B	0.01±0.005(0.05-0.001)	0.42±0.05 (0.3-1.6) *	2.31±0.1 (0.90-3.52) *
Free thyroxine	A	37.7±0.5(31.2-42.7)	29.3±0.7 (24.7-32.2)	22,21±0.3 (17.20-28.52)
	B	36.5±0.4(32.8-45.3)	26.1±0.5 (20.7-29.2) *	15.31±0.2 (13.20-20.52) *
Malondialdehyde	A	20.5±0.5(16.5-28.9)	16.3±0.3 (14.3-21.7)	11.51±0.2 (10.80-13.92)
	B	21.3±0.4(17.3-29.2)	13.1±0.4 (11.9-18.5) *	10.31±0.1 (9.72-10.82) *
Total antioxidant capacity	A	0.72±0.05(0.53-0.81)	0.98±0.11 (0.81-1.21)	1.32±0.08 (1.21-1.49)
	B	0.69±0.04(0.52-0.79)	1.29±0.12 (1.11-1.39) *	1.58±0.1 (1.48-1.61) *

Note: *- changes are reliable due to the indicators of the control group ($P < 0.05$)

86%. Compared with the control group, the changes are reliable (p<0.05) (Table 1).

The study of the determined indicators after two months of treatment showed their improvement comparing with the data obtained after one month of treatment. TSH in both groups was determined within the limits of euthyroidism: in the control group it was 1.21±0.3 (0.21–3.19) and in 3 patients it was below normal, i.e., in indicators of mild thyrotoxicosis, and in patients of the main group –2.31±0.1 (0.90–3.52) and in all cases within the limits of euthyroidism.

The indicator of free thyroxine in patients of the control group was 22.21±0.3 (17.20–28.52) and in 3 patients it exceeded the reference indicator of the norm, and in patients of the main group – 15.31±0.2 (13.20–20.52). In both groups, in comparison with the indicators of the month of treatment, the level of malondialdehyde decreased. In the control group, it was 11.51±0.2 (10.80–13.92), and in the main group – 10.31±0.1 (9.72–10.82), that is, in comparison, the changes are reliable (p <0.05). The index of total antioxidant capacity continued to grow. Compared with the month of treatment in patients of the control group, it increased from 1.08±0.15 (0.81–1.21) to 1.32±0.1 (1.21–1.49) and in the main group – from 1.29±0.16 (1.11–1.39) to 1.58±0.08 (1.48–1.61), that is, the average improvement in both groups was 22 %. However, in the final result, compared to the initial data, that is, before treatment, this indicator increased by 83.3 % in the control group, and by 128.9 % in the patients of the main group.

DISCUSSION

The main thesis of the study was an assumption that the combination of a thyrostatic drug and antioxidants in the treatment of thyrotoxicosis can reduce oxidative stress, increase the overall antioxidant capacity and contribute to the achievement of euthyroidism faster than a single thyrostatic drug.

The conducted studies showed that the levels of malondialdehyde and total antioxidant capacity in the blood serum make it possible to assess the severity of oxidative stress and its changes in the treatment of thyrotoxicosis. According to the results of the study, we believe that hyperproduction of thyroid hormones and excessive activation of metabolic processes with the formation of reactive oxygen species play an important role in the occurrence and progression of oxidative stress. For the first time, the importance of hyperproduction of thyroid hormones in the development of oxidant-antioxidant imbalance was reported by Lien A.P.H. et al. (2008) [11].

The results of our research showed a pronounced decrease in the level of malondialdehyde and an increase in the total antioxidant capacity in the treatment of thyrotoxicosis with thyrosol in combination with antioxidants compared to thyrosol. We also established an inverse relationship between the level of malondialdehyde and the level of total antioxidant capacity (-0.602, p<0.001), malondialdehyde and thyroid-stimulating hormone (-0.659, p<0.001) and a positive correlation between total oxidative capacity and thyroid-stimulating hormone (-0.597, p<0.001). The results of our research are consistent with those published by Dr Razia Sultana et al. (2022) with the data they presented in their work on indicators of oxidative stress and total antioxidant capacity in patients with hyperthyroidism after treatment with carbimazole and an antioxidant [12]. It is worth noting that in none of the previous studies devoted to this problem published before 2022 in patients with hyperthyroidism, no correlation was found between malondialdehyde and total antioxidant capacity. Olia et al. (2019) published data on indicators of total antioxidant capacity and malondialdehyde in patients with thyrotoxicosis compared to healthy ones [5]. There are publications of a similar plan in which the level of malondialdehyde was correlated with several antioxidants [3,13]. Similar research, devoted to the topic of oxidative stress and antioxidant status in patients with hypo- and hyperthyroidism, was conducted in 2011 by Petrulea et al. (2011). Their findings indicate that excess thyroid hormone has a profound effect on oxidative stress and the antioxidant system. They expressed the opinion that antioxidant supplements in patients with hyperthyroidism can have a beneficial effect on reducing the level of thyroid hormones [14]. The positive effect of antioxidants on the results of treatment of patients with hyperthyroidism was previously reported by other authors [10,15,16].

CONCLUSIONS

Summarizing the discussion of the results of the study, the following conclusions can be drawn:

1. Restoration of the oxidant-antioxidant balance is an important factor in the treatment of patients with thyrotoxicosis.
2. To achieve a positive treatment result, the use of antioxidants is pathogenetically justified, useful and necessary.
3. Supplementation of thyrostatic therapy with antioxidants must be implemented in the practice of treating patients with toxic goiter.

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