Volume 2, Issue 12, December - 2024 **ISSN (E):** 2938-3811

Web of Scientists and Scholars: Journal of Multidisciplinary Research

CHARACTERISTICS OF THE PROCESSES OF FREE RADICAL OXIDATION AND THE ACTIVITY OF ANTIOXIDANT PROTECTION ENZYMES IN PATIENTS WITH DIFFUSELY TOXIC GOITER ON THE BACKGROUND OF CORRECTIVE THERAPY WITH IODINE-SACCHARIDE COMPLEX

Uktam Pirnazarovich Khamroev.
Bukhara Medical Institute. Uzbekistan

Abstract
Studies have been conducted to study and characterize the features of free radical oxidation processes and the activity of antioxidant protection enzymes in patients with diffusely toxic goiter on the background of corrective therapy with an iodine-saccharide complex. The study included 154 patients with a diagnosis of diffuse toxic goiter treated with mercazolil. It was revealed that against the background of corrective therapy, the functional state of the liver is impaired and oxidative stress increases depending on the duration of corrective therapy, manifested by the intensive involvement of the glutathione redox system in the process of antioxidant protection.

Keywords: Diffuse toxic goiter, lipid peroxidation, antioxidant system.

Introduction

Diffuse toxic goiter (DTZ) is an organ-specific autoimmune disease and is the cause of thyrotoxicosis in 80% of patients (20). Studies have shown that DTP accounts for approximately 5-6 cases per 100,000 population per year, and at the same time, women aged 18 to 60 are more likely to be ill (15, 25, 27, 34).

Diffuse toxic goiter is characterized by hyperproduction of thyroid hormones, a persistent increase in their serum levels combined with a uniform, diffuse increase in all parts of the thyroid gland, as well as changes in the functional state of various organs and systems. Experimental studies have shown that morphological abnormalities in the liver structure are noted against the background of DTP therapy. (9, 12, 21, 23, 42).

To date, there is no consensus on a single treatment strategy for thyroid diseases. During the treatment of DTH, thyrostatic drugs are effective only in the initial stages of thyrotoxicosis and in the absence of antibodies to thyroid-stimulating hormone (TSH) receptors (13,14,16,17). These drugs act on different stages of iodine metabolism (7,19,21,24). Thus, mercazolil, tyrosol, metisol, propylthiouracil inhibit two stages of thyroglobulin (TG) bio-synthesis: they reduce the activity of peroxidase, the insufficiency of which leads to a decrease in the rate and

organification of iodine and the peripheral conversion of thyroxine to triiodothyronine (1,2,4,5,6,35). The frequency of thyrotoxicosis recurrence after drug treatment varies from 35-80% depending on the duration of follow–up (3,8,10,11,32,33). Despite significant research in this area, there is still no consensus on the treatment of thyroid diseases. There are supporters of both radical and organ-preserving operations. Based on the above, the purpose of this study was to characterize the features of free radical oxidation processes and the activity of antioxidant protection enzymes in patients with DTP on the background of corrective thyrostatic therapy..

Research Materials and Methods:

The study included 154 patients with a diagnosis of diffuse toxic goiter (Graves-Bazedov disease) who were undergoing inpatient treatment at the Department of I-surgery of the Bukhara Regional Multidisciplinary Medical Center. Among the patients, there was a predominance of 138 women (89.6%), 26 men (10.4%). The average age of the patients was 42 years. Many patients were 140 (90.9%) at the age of work activity (from 25 to 50 years). In most cases of follow-up, patients suffered from concomitant diseases. The examined patients were conditionally divided into 2 groups. The first group consisted of 63 (40.9%) patients who received thyrostatic therapy (TST) for 1 year, the second group consisted of 91 (59.1%) who received thyrostatic therapy for 3 years.

The criteria for the effectiveness of TST, in addition to eliminating the clinical picture of thyrotoxicosis, were the normalization of laboratory parameters such as triiodothyronine-TK, tetraiodothyronine-T4, and thyroid-stimulating hormone-TSH. Among the patients of the first group studied, 45 (71.4%) achieved compensation for thyrotoxicosis against the background of TST (relief of the clinical picture of the disease-tachycardia, supraventricular arrhythmias, heart failure, weight loss due to increased appetite, muscle weakness, tremor, sweating, irritability, tearfulness, ocular symptoms of thyrotoxicosis, endocrine ophthalmopathy and normalization of laboratory parameters). Subcompensation of DTP was noted in 18 (28.6%) patients (relief of the clinical picture of the disease with the preservation of hormonal signs of thyrotoxicosis - a moderately elevated T4 content).

Among the patients of the second group, 79 (86.8%) out of 91 patients had thyrotoxicosis compensation (relief of the clinical picture of the disease and normalization of laboratory parameters) on the background of TST. Subcompensation of DTP was noted in 12 (13.2%) patients (relief of the clinical picture of the disease with the preservation of hormonal signs of thyrotoxicosis - a moderately elevated T4 content).

Blood for analysis was taken from the ulnar vein on an empty stomach into vacutainers with heparin. The blood was centrifuged for 15 min at 3000 rpm. The plasma was carefully selected and stored at -20 °C until the study was performed. The hormone content in the blood plasma of the subjects was determined by enzyme immunoassay using standard commercial kits: thyroid-stimulating hormone, total thyroxine - T4, total triiodothyronine - T3, free thyroxine - T4 using HUMAN kits according to the attached instructions on the MINDRAY analyzer. The content of TBK-active POL products was determined spectrophotometrically [Stalnaya I.D.,

1977]. To determine the activity of SOD superoxide dismutase, the recommended method was used (Sirota T. V., 1999). Catalase activity was determined by the method (M.A.Korolyuk, 1988). The state of the glutathione redox system was judged by the amount of total, oxidized (OH) and reduced glutathione (VG), which were determined by Woodward and Frey in the modification of M.S. Chulkova, described by S.V.Travina. The activity of NADPH2–dependent glutathione reductase (GR) was determined by the method of S.N. Vlasova et al. The method for determining ceruloplasmin is based on the oxidation of the substrate para-phenylenediamine (Kamyshnikov V.S., 2003). The statistical analysis of the obtained results was carried out using modern statistical analysis packages: statgraphics Plusfor Windows version 4.0, Statisticafor Windows version 8.0. Statistical methods of descriptive statistics, correlation analysis, and establishing the reliability of the difference between data in the main and control groups based on the calculation of the Student's criterion were used for the work. The data in the text and tables are given as M±m (the average value ± the standard error of the average value). The results with a significance level of <0.05 (95% confidence interval) were taken as reliable).

Research Results and their Discussion

In clinical practice, the main markers of research in assessing the severity of diffuse toxic goiter are hormonal status, nervous system status, and metabolic status, which determine the symptom complex of the thyroid condition. However, against the background of this therapy, the functional state of the liver remains insufficiently studied in DTD, despite its crucial role in metabolic processes. As is known, biogenic amines are metabolized in the liver, enzymatic activation of steroid hormones, inactivation of insulin, glucagon, diuretic hormone, and extra-thyroid formation of T3 from T4 are carried out.

Studies have shown that after two months of mercazolil administration, liver mass was increased by 1.4 times (11,36,38). Necrosis foci were also detected, mainly centrolobular, a 2.8-fold increase in the mass of activated Kupffer cells with high acid phosphatase activity, which indicates an increase in the phagocytic function of the hepatic macrophage system, eliminating neurotic masses According to the authors, this is due to compensatory activation of intracellular blood flow, as evidenced by the expansion of sinusoidal capillaries and a 1.5-fold increase in their mass. At the same time, collagenogenesis is activated in parallel with destructive processes, the mass of newly formed collagen has increased by 2 times, which indicates a decrease in the regenerative capabilities of the liver during treatment of hypothyroidism with mercazolil.

Consequently, the introduction of mercazolil into the body for 2 months leads not only to the development of hypothyroidism, but also to changes in intracellular blood flow, dystrophic and necrotic lesions of hepatocytes, inhibition of cell proliferation and differentiation. To confirm the facts of liver dysfunction identified by the authors when using mercazolil, we examined some biomarkers for assessing the functional state of the liver against the background of using this drug for 1 and 3 years.

As can be seen from the presented research results presented in Table 1, the activity of alanine aminotransferase and aspartate aminotransferase enzymes in the blood of the examined individuals significantly increases relative to healthy individuals during treatment, which indicates damage to the membrane structures of hepatocytes, as well as impaired functional activity of the respiratory chain in the mitochondria of hepatocytes due to impaired intracellular blood flow. As is known, the enzyme gammaglutamyltransferase is a marker of a violation of the functional state of the bile-forming function of the liver. An analysis of the research results presented in the table indicates a significant increase in GGT in the blood plasma of the subjects on the background of mercazolil therapy, which indicates a violation of the bile-forming function of the liver. It should be noted that in the study we did not observe significant changes in thyroid-stimulating hormone, as well as the level of thyroid hormones in blood plasma.

Table 1 Plasma levels of liver markers and thyroid hormones in patients with diffuse toxic goiter during therapy

Indicators	Units of measurement	Group comparisons n=18	Patients on the background of treatment n=154	
			В течение 1 года n=63	В течение 3 лет n=91
ALT	ME /L	18,93±1,39	44,12±4,28*	48,74±3,52*
AST	ME/L	16,74±1,41	40,37±3,42*	42,43±2,68*
GGT	ME/L	34,18±2,39	78,25±5,87*	96,12±6,47*
TTG	mME/L	1,73±0,12	1,51±0,11	2,15±0,18
Free Tk	pmol/L	4,38±0,33	4,13±0,32	3,96±0,29
Free T4	pmol/L	18,25±1,18	17,4±1,33	18,9±1,24

Note: *-the significance of the differences is P <0.05 relative to the indicators of the comparison groups

As you know, glutathione is a key element of antioxidant protection, it is able to restore other antioxidants. The reactivity of thiol groups is affected by any effect, including hormonal effects, which can cause conformational changes in the protein molecule. As can be seen from the presented research results (Table 2), the level of all forms of glutathione increases in patients with DTZ, against the background of a decrease in the ratio of reduced glutathione to its oxidized form, which indicates the increased use of the reduced form of glutathione in the glutathione peroxidase system in patients with DTZ. This condition indicates the intensive use of the glutathione redox system for antioxidant protection in patients with DTP. Despite the ongoing mercazolil treatment, the VH ratio/The OH during 1 year of treatment was 5.5, and after 3 years it was 6.2 compared to 4.0 in the comparison group. The data obtained indicate a functional shift in the fluctuations of the thiol disulfide equilibrium towards an increase in the need for a reduced form of glutathione for the antioxidant protection of liver cells in patients with DTH against the background of mercazolil therapy. Consequently, with DTT on the background of therapy in the liver, there is an intensive involvement of the glutathione redox

system for antioxidant protection and intensive use of glutathione peroxidase for the formation of a reduced form of glutathione (VG).

Table 2 Glutathione reductase and glutathione redox system in the blood of patients with diffuse toxic goiter on the background of

Indicators	Units of measurement	Group comparisons n-18	Patients on the background of treatment n=154	
			Within 1 year n-63	Within 3 years n=91
Glutathione Reductase	micromole/ NADPH2/	2,39±3,57	3,54±0,21*	4,18±0,27*
Total glutathione	mmol/l	1597,3±16,41	2251,9±19,56	1811,3±14,68
Oxidized glutathione	mmol/L	254,4±8,05	219,3±12,19	207,5±14,61
Reduced glutathione	mmol/L	1019,2±18,57	1208,9±21,13	1293,2±19,28
Ratio		4,0	5,5	6,2

Note: * - the significance of the differences is P< 0.05 relative to the indicator's comparison groups

As is known, thyroid hormones can have a protective role, affecting the content of antioxidants; on the other hand, hypothyroidism during treatment can increase oxidative stress. Therefore, the study of markers such as malondialdehyde and lipid peroxidation products can provide a deeper understanding of the effect of mercazolil in autoimmune thyroid diseases.

It is known from literature sources that reactive oxygen species are generated in all cells of the body. The mitochondrial respiratory chain makes the greatest contribution [8]. According to the authors, lipid peroxidation begins with the introduction of a free radical into the lipid layer (initiation), which oxidizes fatty acids to form a lipid radical, which, in turn, reacts with molecular oxygen dissolved in the medium [23, 28,29]. Lipid peroxidation leads to polycondensation, polymerization of lipids, as well as the formation of secondary compounds, aldehydes, among which cytotoxic malonic dialdehyde (MDA) and diene conjugates (DC) are mainly isolated.).

Table 1 The content of products of the LPO and AOS system in blood plasma in patients with diffuse toxic goiter during therapy

Indicators	Units of measurement	Group comparisons n-18	Patients on the background of treatment n=154	
			В течение 1 года n-63	В течение 3 лет n=91
DC	mmol/l	0,37±0,02	0,58±0,04	0,79 ±0,08*
YEAH	mmol/L	1,27±0,11	2,09±0,18	2,48±0,21*
СОД	Ед /мин/л	179,6±12,19	394,8±12,19	433,2±12,19
Каталаза	мкмоль/мин/л	169,5 ±9,05	503,8±12,05	619,2± 24,05*
Церулоплазмин	мг/дл	23,93±1,59	28,47±2,07	29,62±1,34*

Note: * - the significance of the differences is P< 0.05 relative to the indicators

MDA can promote cross-linking and polymerization of membrane components, damaging them, which leads to disruption of properties and functions such as fluidity, ion transport, enzymatic and receptor activity, the aggregating ability of cell surface determinants, etc. [A. Ayala, 2014].

As can be seen from the presented research results (Table 3), the level of MDA and DC in the examined patients against the background of mercazolil use tends to increase, especially pronounced in the group of patients who have been using the drug for 3 years. The revealed fact is probably due to the activation of glutathione-Z-transferase, an enzyme for which malondialdehyde is one of the substrates. Superoxide dismutase (SOD) and catalase form a tandem of enzymes that neutralize such reactive oxygen species as superoxide anion radical and hydrogen peroxide, the product of the reaction catalyzed by SOD, at the initial stages of nucleation. An analysis of the obtained research results presented in Table 3 indicates a high level of SOD in blood plasma in patients with DTD using mercazolil for 3 years, which is probably due to the accelerated synthesis of antioxidant enzymes (glutathione peroxidase) in response to oxidative stress in the examined patients. Another antioxidant enzyme in the blood plasma is ceruloplasmin, synthesized and secreted by the liver. Its antioxidant properties are mainly due to its ferroxydase activity. An increase in the activity of this enzyme, observed in our studies by 19% in the group of patients treated with mercazolil for 1 year and by 24% in patients treated with an iodine-saccharide complex for 3 years, which apparently aims to oxidize divalent iron to trivalent iron, thereby providing iron with tranferrin and inhibiting peroxidation processes. It should be noted that the signal for the induction of ceruloplasmin synthesis is an increase in IL-6, where the role of ceruloplasmin is to reduce the content of certain (pro-inflammatory cytokines I.L.Klaritskaya, 2010).

Thus, summing up the analysis of the presented materials, it should be emphasized that the introduction of mercazolil into the body for 3 years leads not only to the development of hypothyroidism, but also disrupts the structure and function of the liver, which is expressed in changes in markers of hepatocyte cytolysis and bile formation function, as well as increased indicators of the pro-oxidant and antioxidant system against the background of intensive involvement in the process of the reduced form of glutathione (VG).

Conclusions:

1. Against the background of corrective therapy with mercazolil, patients with diffusely toxic goiter experience a violation of the functional state of the liver and increased oxidative stress, depending on the duration of corrective therapy, manifested by the intensive involvement of the glutathione redox system in the process of antioxidant protection
2. Taking mercazolil for 3 years leads not only to the development of hypothyroidism, but also disrupts the structure and function of the liver, which is expressed in changes in markers of hepatocyte cytolysis and bile formation function, as well as increased indicators of the pro-oxidant and antioxidant system against the background of intensive involvement of the reduced form of glutathione in the process.

References

1. Almakaeva L.F. Cognitive functions and oxidative balance in the offspring of rats with experimental hypothyroidism with correction by an iodine-saccharide complex // Abstract by K.M.N.,Yekaterinburg, 2021, p. 26.
2. Biryukova, E.V. Hypothyroidism: clinic, diagnosis, approaches to therapy / E.V. Biryukova, M.V. Shishkin // Therapy. - 2017. - No. 7. - P. 110-115.
3. Bueverov A. O. Oxidative stress and its role in liver damage/A.O.Bueverov // Russian Journal of Gastroenterology, Hepatology, Coloproctology. - 2002. -No. 4. -pp. 21-25.
4. Interrelation of TSH, cortisol and prolactin parameters in patients with autoimmune thyroiditis / E.V. Popova, P.K. Akella, Yu.V. Popova [et al.] // Bulletin of medical Internet conferences. - 2015. - Vol. 5, No. 12. - pp. 16471649.
5. Khamdamov B.Z., Dekhkonov A.T., Khamdamov A.B., KhAkimbayeva K. A. Characteristics of the immune profile in wound infection in patients with diabetes mellitus // Biology and problems of medicine. - Samarkand, 2022. - № 3 (136). - Pp. 112-117.
6. Khamdamov B.Z., Dekhkonov A.T., Khamdamov A.B. Immunological profile of wound infection in patients with diabetes mellitus //LXXVI International Scientific and Practical Conference. London, United Kingdom - 2022. - P. 70-71.
7. Karbyshev, M. S. Biochemistry of oxidative stress: an educational and methodical manual / M. S. Karbyshev, Sh. P. Abdullaev; under the general editorship of A.V. Shespopalov. - Moscow : Publishing House XX, 2018. - 60s.
8. Khamdamov A.B., Khamdamov I.B., IMPROVED METHOD OF BARIATRIC SURGERY FOR PATIENTS WITH METABOLIC SYNDROME DUE TO GASTRO-ESOPHAGEAL REFLUX DISEASE// New day in medicine. - 2024. - №12 (74). - C. 541-456.
9. Konoplyanko, V.A. Pathophysiological processes in hypothyroidism in experiment / V.A. Konoplyanko, R.D. Klebanov // Health and environment. - 2015. - Vol. 2, No. 25. - pp. 102-105.
10. Toirov A. S., Khamdamov A. B. Experimental – morphological justification of the antiparasitic effect of photodynamic therapy on germinative elements in the terminal fibrosis capsule layer from hepatic exinococcectomy // doctor newsletter. – 2022. – №3(106). – C.121-126.
11. Nekrasova T.A., Shcherbatyuk T.G., Davydenko D.V. and others. Features of lipid and protein peroxidation in autoimmune thyroiditis without and with minimal thyroid dysfunction. Clinical and experimental thyroidology. 2011;7:4:38-43.
12. Khamdamov B.Z., Isamutdinov A.Z., Khamdamov A.B. Character and analysis of changes in clinical and immunological parameters in patients with anastomositis after mini-bypass surgery // New day in medicine. - Bukhara, 2024. - № 6 (68). - P. 76-85.
13. Oxidative stress /E.B. Menshikova [et al.] // Prooxidants and antioxidants, Moscow: Slovo Publishing House, 2006. 554c.
14. Khamdamov B.Z. Complex treatment of diabetic foot syndrome with critical lower limb ischemia. // Journal of Biomedicine and Practice. Tashkent 2020, Special Issue; 5:801-

814.
15. Popov S.S. Catalase activity in experimental thyrotoxicosis in rat tissues / S.S. Popov, A.V. Semenikhina, T.I.Rakhmanova // Bulletin of the Russian State Medical University. - 2006. - No. 2. - pp. 414-415.
16. 16. Khamdamov B.Z. Optimization of methods of local treatment of purulent-necrotic foot lesions in diabetes mellitus. // Magazine. New day in medicine. 2018;4(24):112-115.
17. Pavlyuchenko, I.I. Comparative analysis of indicators of the antioxidant protection system in patients with hypothyroidism and COPD / I.I. Pavlyuchenko, E.I. Dydyshko, O.S. Okhremenko // Kuban Scientific Medical Bulletin. - 2017. - Vol. 24, No. 5. - pp. 59-62.
18. Khamdamov B. Z., Akhmedov R. M., Khamdamov A. B. The use of laser photodynamic therapy in the prevention of purulent-necrotic complications after high amputations of the lower limbs at the level of the lower leg in patients with diabetes mellitus. // Scopus Preview. International journal of Pharmaceutical Research. July-Sept, 2019;11(3).
19. Khamdamov B.Z. Morphological changes in the use of photodynamic therapy in the treatment of wound infection in an experiment. Journal of Morphology. Saint Petersburg, 2020. Volume 157 (2-3). –pp. 223-224.
20. Tapbergenov S.O., Sovetov B.S., Bekbosynova R.B. Glutathione redox system and antioxidant protection enzymes in hypothyroidism and adrenalectomy // Successes of modern natural science. - 2015. – No. 1-2. – pp. 192-194.

Web of Scientists and Scholars: Journal of Multidisciplinary Research