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MODERN ASPECTS OF MORPHOLOGICAL CHARACTERISTICS OF THE THYROID GLAND IN POLYPHARMASY

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Summary. Pathology of the thyroid gland is considered a marker of environmental distress. The most significant morphophysiological structure of the thyroid gland is a tissue microregion that combines a group of follicles and interfollicular space with an autonomous system of blood and lymph circulation. It is the structures of the tissue microregion that suffer the most under the action of pathogenic factors on the thyroid gland, reducing its role in providing morphological and metabolic changes in tissues and organs [Borodin Yu.I., et al., 2018]. But morphological and morphometric changes in the thyroid gland during polypharmacy with anti-inflammatory drugs are poorly understood. The article presents a review of the literature on structural changes in the thyroid gland during polypharmacy with anti-inflammatory drugs.

Key words: polypharmacy, thyroid gland, morphology, anti-inflammatory drugs.

Relevance. According to the World Health Organization (WHO), among endocrine disorders, thyroid diseases occupy second place after diabetes mellitus. According to statistics, up to a third of the entire population of the planet suffers from disorders of the thyroid gland. More than 740 million people in the world have endemic goiter or suffer from other thyroid pathology; 1.5 billion people are at risk of developing iodine deficiency diseases. Moreover, according to statistics, the increase in the number of thyroid diseases in the world is 5% per year [N.Yu. Kryuchkova, et al., 2018].

In recent decades, the functional state of the thyroid gland in patients of various profiles has been actively studied. It is known that thyroid hormones regulate the state of all organs and systems in the human body, primarily the processes of growth, maturation and differentiation of cells [A.R. Volkova, 2018].

The issues of thyroid gland morphology receive much attention due to the growth of endocrine pathology throughout the world. Pathology of the thyroid gland ranks second after diabetes mellitus [O. V. Gorchakova., 2019].

Pathology of the thyroid gland is considered a marker of environmental ill-being. The most significant morphophysiological structure of the thyroid gland is the tissue microregion, which unites a group of follicles and the interfollicular space with the autonomous blood and lymph circulation system. It is the structures of the tissue microregion that suffer the most when pathogenic factors act on the thyroid gland, reducing its role in ensuring morphological and metabolic changes in tissues and organs [Borodin Yu.I., et al., 2018].

The thyroid parenchyma itself is formed by a system of thyrocytes, among which there are two main types - follicular and interfollicular cells. The former form follicles with the ability to extracellularly accumulate hormonally active substances. The latter are involved in the proliferation of thyroid parenchyma, forming interfollicular islands between follicles. The morphogenetic potencies of stromal-parenchymal relationships are determined by the ratio of follicular epithelial tissue, colloid and

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interstitium. The importance of the thyroid gland (TG) for the life of the body is difficult to overestimate [Starkova I., 2012].

In addition to thyrocytes - the main cell population that makes up the follicular compartment of the gland, it contains the second largest cell group - calcitoninocytes (parafollicular or C-cells) [Solyannikova D.R., Bryukhin G.V., 2009]. They are of neurogenic origin and belong to the so-called APUD system [Smirnova T.S., 2009], which is a cell population scattered in various organs and producing various biologically active substances, which is considered as a diffuse neuroendocrine system [Sazonov V.F., 2014].

Parafollicular cells are located in small groups in the thyroid interstitium and/or lie on the basement membrane between thyrocytes (intraepithelial), but never border the lumen of the follicle. Their maximum number is concentrated in the central sections of each lobe of the thyroid gland, which are called the “C-cell region”. Parafollicular cells make up no more than 1% of the thyroid epithelium. They are 2-3 times larger than thyrocytes, polyganal or slightly elongated in shape, have larger and lighter nuclei with 1-2 dense nucleoli and pale cytoplasm containing small argyrophilic granules [Volkov V.P., 2014].

The term “polypharmacy” (from poly – many and pragma – object, thing) means the simultaneous and often unreasonable prescription of many medications or medical procedures [E.A. Panova, et al., 2019]. Polypharmacy is nothing more than pharmaceutical pressure exerted on the patient as a result of an irrational integrated approach.

In outpatient and inpatient settings, patients are most often prescribed more than two medications at the same time. Moreover, the doctor does not always know what the patient is actually taking and in what doses; incompliance often occurs. Polypharmacotherapy can occur not only due to a large number of concomitant diseases and conditions in the patient, but also due to the wrong choice of medications, when the patient takes unidirectional, mutually exclusive or optional medications. There is a failure or distortion of the effect of the prescribed drug due to changes in metabolic processes in the elderly body. This often leads to incorrect correction of treatment tactics towards increasing the number of medications or replacing them with stronger ones. The results of polypharmacy are a decrease/absence of treatment effect, unwanted side effects, frequent hospitalizations, and large financial costs for both the patient and the healthcare system as a whole. The scientific medical community offers evidence-based methods to combat polypharmacy in the form of various analytical algorithms for prescribing pharmacotherapy. These are the Drug Appropriateness Index (Medication Appropriateness Index, USA, 1992), Beers criteria (American Geriatrics Association, 2003, 2012), STOPP/START criteria (UK National Health Service Guidelines, 2013, 2015), FORTA (Germany, 2011), PINCER criteria (UK, 2012) [Guthrie B., Yu N., Murphy D., 2015]. Unfortunately, at present, the frequency and consequences of irrational polypharmacy in outpatient clinics in our country remain insufficiently studied [E.A. Panova, 2019].

Thyroid diseases are one of the most common types of endocrine pathology, which is caused by many factors, among which the most important are iodine deficiency, increased background radiation, unfavorable environmental conditions and psycho-emotional stress. Acute and chronic stress can disrupt the secretion of thyroid hormones and significantly change the morphology of the gland, causing changes of varying severity and direction [S.N. Styazhkina, 2015].

Drug effects on the immune system often lead to the development of undesirable phenomena such as autoimmune diseases. Moreover, of all the organs of the endocrine system, the thyroid gland is

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most often affected, an organ whose embryonic development features predispose to both spontaneous and induced lesions under various autoimmune influences [G.A. Melnichenko, 2016].

The term "polypharmacy" is often used in the medical literature, but there is no generally accepted definition. In domestic literary sources, polypharmacy is defined as the simultaneous prescription of a large number of drugs, including their unjustified use. In foreign literature, the term “polypharmacy” is used (polypharmacy, from the Greek poly- and pharmacy - medicine). In other literary sources, there is a qualitative definition of polypharmacy - prescribing a patient more drugs than the clinical situation requires, and a quantitative definition - prescribing 5 or more drugs to a patient [D.A. Sychev, V.A. Otdelenov, N.M. Krasnova, 2016].

The reason for the simultaneous prescription of several drugs may be the presence of concomitant diseases (multimorbidity), the availability of drugs, as well as clinical recommendations, guidelines of professional medical societies, treatment standards, which in some cases contain recommendations for the use of complex therapy with more than 5 drugs for only one indication, the effectiveness of which corresponds to high levels of evidence. An analysis of the literature shows that today the fight against polypharmacy with anti-inflammatory drugs is one of the important tasks in providing medical care to patients of any age. This emphasizes the need to develop strategies that improve the quality of medical care and reduce adverse reactions to drugs [Shekunova E.V., Kovaleva M.A. 2020 Yil Annuar Fazalda, Adam Quraisiah, Mohd Fahami Nur Azlina. 2018, Arthur J. Kast L, Natalie A. Terry, Gaary D. Albenberg, 2019].

At the end of the twentieth century, P.J. Davis et al. non-genomic mechanisms of TH action were discovered and subsequently studied, which originate from plasma membrane receptors for T3 and T4 located on the αVβ3 integrin [Davis P.J., Glinsky G.V., Lin H.Y. et al., 2015]. This integrin is expressed on the surface of leukocytes, platelets and epithelial and endothelial cells, ensuring interaction between cells, as well as leukocytes with biological surfaces. Non-genomic mechanisms include stimulation of TH without the participation of transcription of the mitogen-activated protein kinase, phosphatidyl-inositol 3-kinase and serine-threonine kinase genes, thereby promoting tumor progression: angiogenesis, cell proliferation and cell migration. Also, iodothyronines, in a dose-dependent manner, are able to stimulate the expression of tissue-specific pro-inflammatory genes, thereby providing a systemic pro-inflammatory effect, which at the tissue and organ level leads to an immunopathological process. Considering the systemic pro-inflammatory effect of TH, it is assumed that long-term hyperthyroidism can contribute to the emergence of a chronic inflammatory response, which makes cells more susceptible to malignancy [Glushakov R.I., Vlaseva O.V., Sobolev I.V. et al. 2015].

Cytokine-induced thyroiditis (in 50–70% of cases occurs as a destructive variant), thyroid lesions when using check-point inhibitors (check-point inhibitors) are known (use of a combined treatment regimen CTLA-4 + PD-1/PD-L1 leads to an increase in the incidence of hypothyroidism to 20%). Some researchers see an impact on immune processes even in such iatrogenic thyropathies as lithium-induced glandular disorders. The authors describing these lesions note that the predisposition to autoimmune lesions of the thyroid gland or the very nature of the disease for which treatment is being carried out (lithium for bipolar affective disorder; interferon B for hepatitis C) are also based on autoimmune mechanisms [Melnichenko G .A., Glibka A.A., Demicheva O.Yu., 2019].

From the above literature review, it is clear that there is insufficient research on polypharmacy and its effect on the endocrine system, especially the thyroid gland. There are some inconsistencies among the available data that require further morphological and morphometric studies.

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