

THE EFFECT OF THYROID PATHOLOGY ON THE DEVELOPMENT OF DISEASES OF THE LARGE SALIVARY GLANDS.

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Abstract

Salivary glands react to many physiological changes in the body, as well as to various pathological processes, including diseases of the endocrine systems. It is known that manifest forms of Hypo- and hyperthyroidism lead to irreversible changes in the salivary glands. Treatment of such patients is to compensate for the disease and achieve remission. The study of the morphological picture of the salivary glands in subclinical forms of thyroid disease would determine the etiotropic therapy of sialadenosis and sialadenitis.

Purpose of research. To study of morphological changes in the parotid salivary glands in subclinical forms of Hypo- and hyperthyroidism.

Materials and methods. The article presents experimental work on rats with modeling of preclinical forms of Hypo- and hyperthyroidism. 25 *Wistar* rats were divided into groups: I group – 10 rats with subclinical hyperthyroidism, II group – 10 animals with subclinical hypothyroidism, the comparison group consisted of 5 intact rats. To determine the level of free thyroxine and thyroid-stimulating hormone, blood was taken from the caudal vein. After setting the thyroid status, the salivary glands were taken, with following study of biological preparations.

Results. In animals of the I-th group on the 10th day on histological preparations of the parotid salivary gland functionally inactive lobules with severe lymphoid infiltration were visualized. On the 14th day in group II, retention cystic

transformation of salivary gland lobules with lymphoid infiltration was revealed. Thus, there are pathological changes in the salivary glands against the background of subclinical Hypo - and hyperthyroidism. This indicates the possibility of complex treatment: correction of thyroid status by an endocrinologist at this stage.

Key words Salivary gland, sialadenosis, sialadenitis, thyroid, subclinical hypothyroidism, subclinical hyperthyroidism.

Introduction

At the dentist's visit, patients with various pathologies of the large salivary glands (LSG) make up 11.7% of the total number of patients, with sialadenosis accounting for 29.4% of cases, and sialadenitis – 20.1%. [1]

Non-tumor diseases of LSG are predictors of various somatic disorders of the body. [2] The leading role in the development of sialadenosis is given to the pathology of the endocrine system. [3] Wiedzinski E., Chen Y. (2003) showed that in Hypo - and hyperfunction of the thyroid gland (TG) develops hypertrophy of the salivary glands and reduce the formation of secret. Hyposalivation and xerostomy is accompanied by changes in the chemical composition of saliva, its pH. The high acidity of the secret changes the charge of the micelle, which loses water, calcium and phosphates. All this contributes to demineralization and non-carious lesions of hard tissues of the teeth, as well as the development of diseases of the oral cavity. [3, 4, 5]

Dokleva M. N. et al. (2013) found that in 70% of cases, preclinical forms of Hypo - and hyperfunction of the thyroid gland are the cause of stone formation in LSG. [6] Without correction of thyroid status in the postoperative period, these patients with sialolithiasis had scar changes, and in 94% of cases the inflammatory process was associated. [7]

In the literature there are data on the presence of a correlation between hypofunction of the thyroid gland and parenchymal mumps, which is characterized by changes in the type of cysts formation in the salivary glands.

Currently, subclinical (preclinical) forms of thyroid dysfunction in the general population vary from 1.3 to 17.5% depending on gender and age. In epidemiological

studies, subclinical hypothyroidism is more common than manifest one, but in clinical practice it is less diagnosed. [8]

As a rule, patients with this form often contact to doctors of another specialty, including a dentist-surgeon. This is because hidden or preclinical forms of thyroid dysfunction are diagnosed by the dynamics of laboratory blood parameters: at normal concentrations of thyroid hormones, the level of thyroid stimulating hormone (TSH) changes. [9]

Currently, there are many methods of symptomatic treatment of inflammatory and dystrophic processes in the salivary glands, which are aimed at the removal of acute manifestations and the introduction of the disease into long-term remission. While retaining the practical need in the search etiotropic therapy of sialadenosis and sialadenitis. [10, 11, 12]

To date, the literature continues to discuss the need for correction of thyroid status in preclinical forms. [6]

The purpose of the study was to study the morphological changes in the parotid salivary glands (PSG) in subclinical forms of Hypo - and hyperthyroidism.

Materials and methods

To solve this problem, an experimental model of the subclinical form of Hypo - and hyperthyroidism in animals was created, which meets the goal of the study. For this purpose, 25 laboratory *Wistar* rats weighing 320-340g were selected, which were in cells with free access to laboratory feed under standard lighting and temperature conditions. Animals were kept in accordance with the requirements of GOST R from 02.12.2009 53434-2009 "Principles of good laboratory practice (GLP)".

To simulate subclinical hyperthyroidism rats were administered per os drug levothyroxine sodium at a dose of 50 $\mu\text{g}/100\text{g}$ weight for 10 days. The state of subclinical hypothyroidism was achieved by the introduction per os tyrosol (thyrostatic) at a dose of 2.5 mg per 100 g of body weight for two weeks.

For the assessment of functional activity of the thyroid gland was performed blood sampling from the caudal vein in a volume of 2 ml into the microvette. Levels of

thyroid-stimulating hormone (TSH, mkME/ml), free thyroxine (T4 free, pmol/l) were determined by enzyme immunoassay using the Abbott 6C5032 kit on the “Architect” analyzer in the laboratory.

Subclinical hyperthyroidism was diagnosed with a decrease in the concentration of thyroid-stimulating hormone in the serum, in comparison with the control group; subclinical hypothyroidism was determined with an increase in the values of TSH, while the level of free thyroxine was within the normal range, at the level of the control group.

The animals were divided into three groups depending on their thyroid status:

I – 10 rats with subclinical hyperthyroidism model;

II – 10 with subclinical hypothyroidism;

III – 5rat individuals made a comparison group (control).

At the beginning and at the end of the experiment, as well as before taking blood at the stages of the study, the animals were weighed (Fig. 1).



Figure. 1. a - weighing animals, b - blood sampling from the caudal vein

After laboratory diagnosis of subclinical forms of Hypo - and hyperthyroidism in rats under endonasal anesthesia with diethyl ether, parotidectomy of parotid salivary glands was performed. Tissue samples were fixed in 10% neutral formalin (pH – 7.0-

7.2). Histological sections were mounted and straightened on slides, stained with hematoxylin and eosin. Hereinafter preparations were studied on the microscope Leica DMLS (Germany) at the Department of pathological anatomy of MGMSU named after Evdokimov A. I.

The obtained data were processed by the method of variation statistics. For the description of signs with normal distribution the average value with indication of standard deviation was used. Comparison of sets by quantitative characteristics (parametric analysis) is carried out using Student's t-test for unrelated sets. The reliability of the results was estimated at $p < 0.05$.

Results and discussions

In rats of the control group there was no refusal of feed and any other deviations in behavior. The external condition of the rats remained unchanged, the fur is bright and clean, the parotid glands were not visualized.

In the analysis of histological sections of the parotid salivary gland lobules were represented by densely located acinar secretory cells. Interlobular ducts with moderately extended lumen were lined with flattened epithelium. Salivary gland with moderate functional activity, with no damage of acinuses and unchanged stroma. (Fig. 2)

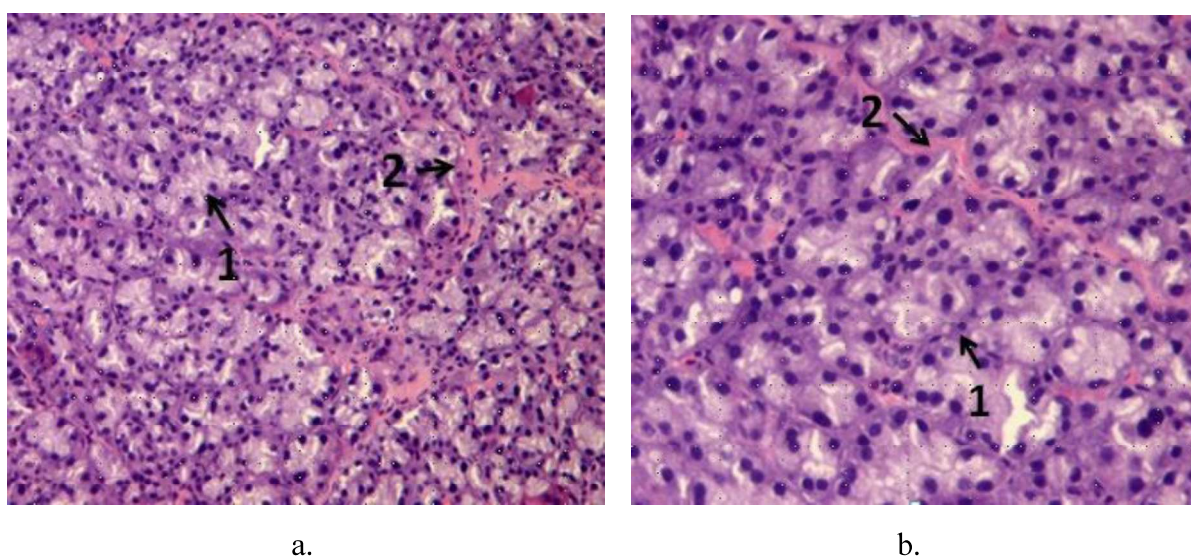


Figure. 2. Histological preparations of parotid salivary glands of the control group. Stained with hematoxylin and eosin. a – zoom x100, b – zoom x200; 1 – acinar secretory cells, 2 – lumen of the interlobular ducts

On the tenth day in animals of the first group receiving levothyroxine sodium at a dose of 50 µg / 100g, the average body weight was 290±14.8 g, which was lower than the control group by 35.2 ± 1.7 g. No changes in animal behavior were observed. External examination of 8 rats showed an increase in parotid salivary glands. In blood tests at normal values of T4, the free level of thyroid stimulating hormone was significantly reduced, compared with the control group by 32.36%, which corresponded to subclinical hyperthyroidism (tab.).

Table

The level of TSH and free T4 in the blood serum of laboratory animals, (M±m)

Value	I group (n=10)	II group (n=10)	Control (n=5)	<i>p</i>
TTF (мкМЕ/мл)	0,096±0,04	0,437±0,05	0,294±0,03	*0,002 **0,030
T ₄ free (pg/ml)	0,83±0,04	0,79±0,05	0,80±0,03	*0,560 **0,867

*Note: * Difference with control group I*

*** Difference with control group II*

In 8 out of 10 histological preparations, certain changes in the structure of the parotid salivary glands were revealed.

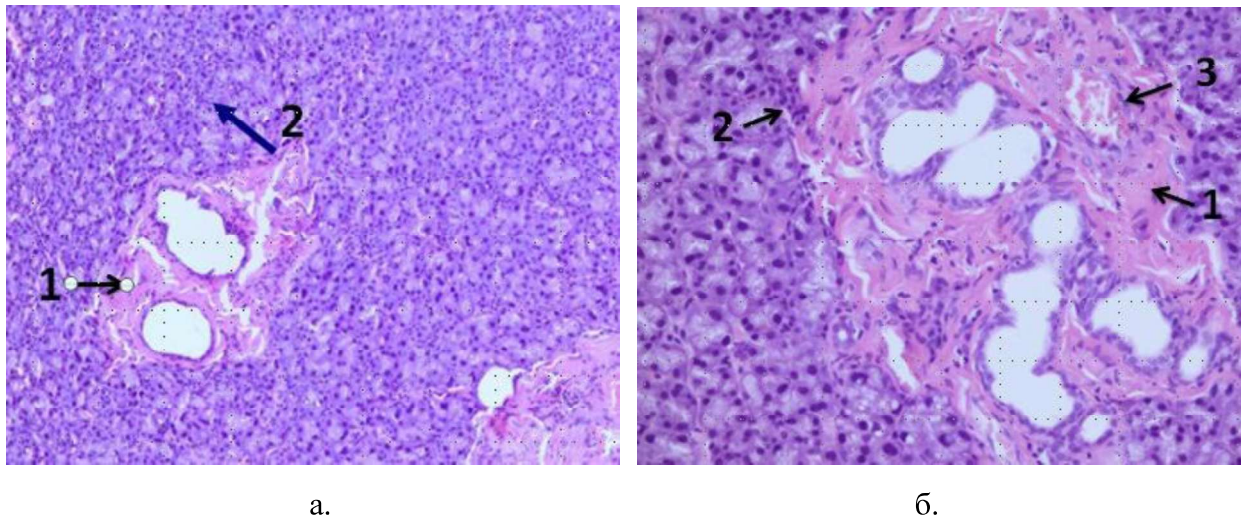


Figure.3. Histological preparations of parotid salivary glands of animals of group I (subclinical hyperthyroidism). Stained with hematoxylin and eosin. a – zoom x120, b – zoom x200; 1 - sclerosis of periductal and interlobular stroma, 2 – lymphoid infiltration, 3 – blood vessels plethora

Rats of the second group (per os tyrosol at a dose of 2.5 mg per 10 g) satisfactorily tolerated the drug. It is important that the animals did not abandon their usual food, noted their calm and balanced behavior, adequate (without signs of aggression) reaction to oral administration of thyreostatics. The color of the animals did not change, the fur did not shed, was clean and shiny.

On the fourteenth day, the average body weight of animals was $360,8 \pm 21,9$ g, which increased by $20,1 \pm 1,5$ g compared to the control group. External examination showed an increase in parotid salivary glands in all 10 animals. Blood serum concentrations of thyroid-stimulating hormone were 48.64% higher than those of the control group at normal levels of free thyroxine, which corresponded to subclinical hypothyroidism (tab.).

In 9 out of 10 histological preparations of parotid salivary glands reactive retention cystic transformation of parotid salivary gland lobules was revealed, as well as functionally inactive lobules with the accumulation of secretion. Intra- and interlobular retention dilated ducts lined with flattened epithelium. Sclerosis of

interlobular and periductal stroma with severe lymphoid infiltration. In the stroma there is uneven the blood vessels plethora (Fig. 4).

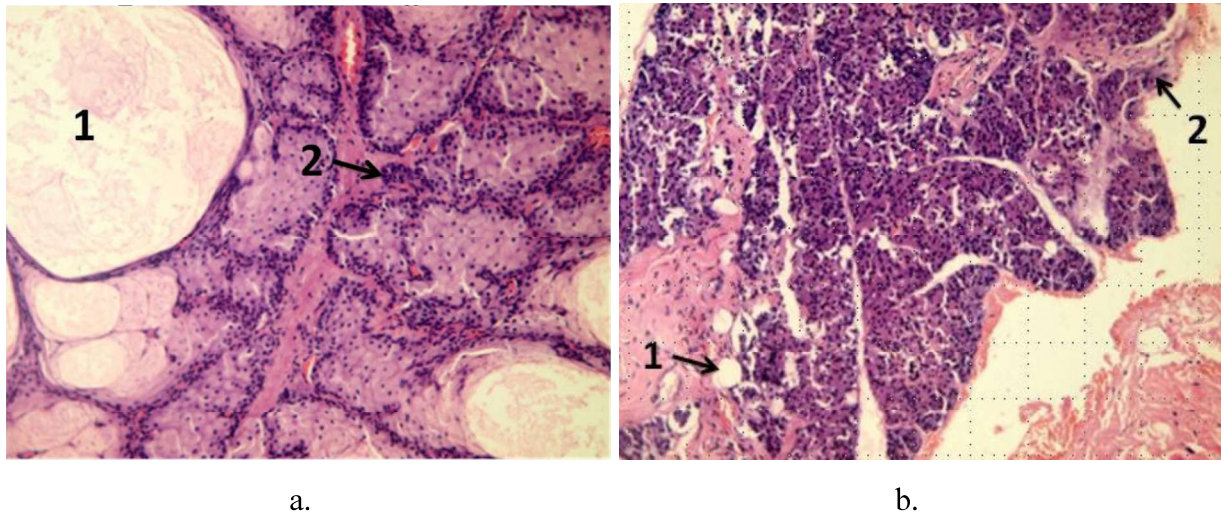


Figure. 4. Histological picture of parotid salivary glands in animals of group II (subclinical hypothyroidism). Stained with hematoxylin and eosin. a – zoom x200; b – zoom x75; 1 – cystic transformation of salivary gland lobules; 2 – lymphoid infiltration

Conclusion

In experimental animals (*Wistar* rats) with subclinical hypothyroidism, morphological changes in the parotid salivary glands in the form of cystic transformation in gland tissues with lymphoid infiltration are observed.

Already at this stage, thyroid dysfunction is a trigger for the development of pathological processes in the parenchyma of the salivary gland, which further lead to irreversible changes.

The study confirms the need for etiotropic therapy of sialadenosis and sialadenitis together with an endocrinologist at the stage of subclinical forms of thyroid dysfunction.

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