

Restructuring of the Thyroid Gland in Primary Hypothyroidism under the Influence of Intermittent Hypobaric Hypoxia

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We studied the effect of intermittent hypobaric hypoxia on morphofunctional characteristics of the thyroid gland during experimental hypothyroidism. Functional activity of the thyroid gland increased in the early period of hypoxia. Morphofunctional parameters reached a constant level with increasing the duration of hypoxia to 7-15 days. A new functional level was characterized by increased activity and normal function of glandular cells.

Key Words: *hypoxia; thyroid gland; hypothyroidism*

Hypothyroidism is a complex of symptoms developing as a result of drastic and sustained decrease in blood content of thyroid hormones. These changes are mainly associated with a pathological process in the thyroid gland (TG). Primary hypothyroidism is accompanied by dysfunction of various organs [3,4]. The incidence of primary hypothyroidism increased after reactor accident at the Chernobyl nuclear power plant [2,7]. The mechanisms of compensation and adaptation to hypoxia were studied in details. Hypobaric and normobaric hypoxia is extensively used in clinical practice [4,5]. However, little is known about the use of this method for the therapy of patients with hypothyroidism [1].

Here we studied the morphofunctional state of TG in experimental hypothyroidism under the influence of intermittent hypobaric hypoxia (IHH).

MATERIALS AND METHODS

Experiments were performed on male rats weighing 160-180 g. Hypothyroidism was induced by administration of mercazolyl in a dose of 2.5 mg per 100 g body weight. IHH (reduced oxygen supply)

was induced by elevation of animals to a simulated height of 6000-6500 m above sea level. The effect of IHH was studied on days 1, 3, 7, 15, and 30. The animals were decapitated under ether anesthesia.

TG tissue was treated routinely. Sections (5-7 μ) were stained with hematoxylin and eosin, picrofuchsin (van Gieson technique), and using periodic acid Schiff (PAS) reaction and poststained with hematoxylin. TG function was estimated by the histological algorithm [6] with the use of morphometric analysis of structural elements.

RESULTS

The relative weight of TG remained unchanged over the 1st day of IHH (Table 1). TG was morphologically similar in animals with hypothyroidism and intact specimens. The parenchyma of TG was presented by large round or oval follicles. Irregular follicles were found at the site of stromal thickening. Dense colloid adjacent to the wall of follicles was strongly stained with PAS. Follicles were lined with low cubical epithelium. The relative area of the thyroid epithelium significantly increased and the relative area of the colloid decreased (Table 1). Small amounts of the connective

tissue and lymphoid cells were seen between the follicles.

The relative weight of TG significantly increased on day 3 (Table 1). Morphological characteristics of TG reflected the increase in functional activity. Polymorphous follicles were present in the parenchyma. We found not only large follicles, but also medium and small follicles. The mean diameter of follicles decreased by 10.2% compared to the initial value ($p<0.05$). The cross-section area of follicles and colloid decreased by 19.4 and 27.1%, respectively. The height of the thyroid epithelium increased by 11.8%. The index of colloid accumulation decreased, while the follicle/colloid ratio increased. Small and medium follicles contained liquid and foamy light-rose colloid characterized by weak PAS reaction.

The weight of TG on day 7 was similar to that on day 3 (Table 1). The parenchyma was presented by medium and small follicles. The interfollicular epithelium proliferated between these follicles. The number of medium follicles increased. Morphometry revealed further decrease in the diameter and cross-section area of follicles and cross-section area of the colloid. The thyroid epithelium was presented by prismatic epitheliocytes. The height of these cells in rats differed from that in animals with primary hypothyroidism (by 23.4%, $p<0.05$). A correlation was found between the height of prismatic epitheliocytes and area of the epithelium. Vacuolization of the colloid manifested in the appearance of desquamated epitheliocytes. The relative area of the colloid decreased by 17.8%. The index of accumulation decreased, while the follicle/colloid ratio increased. Signs of plethora and stasis were revealed in vessels. We also revealed perivascular edema and focal diapedesis.

Short-term adaptation of animals with hypothyroidism to IHH for 15 days was followed by a decrease in the relative weight of TG (Table 1). Microscopy showed that TG mainly contains medium follicles. The diameter of follicles did not differ in this period and previous stage. No differences were found in the diameter of medium follicles in treated and intact animals. The epithelium was presented by prismatic cells with oval hyperchromic nuclei. They were oriented perpendicularly to the basal membrane. The relative area of the colloid and epithelium significantly differed from the baseline value. The follicle/colloid ratio and index of colloid accumulation remained unchanged in this period. Colloid was regularly distributed in follicles and moderately stained with eosin and pyronin. Desquamation of the epithelium was revealed in some follicles. Resorption vacuo-

TABLE 1. Effect of Hypoxia on Morphometric Characteristics of TG in Experimental Hypothyroidism ($M\pm m$)

Parameter	Intact animals	Animals with hypothyroidism (baseline value)	Period, days				
			1	3	7	15	30
Relative weight of gland, mg	18.20±0.19	40.30±0.22 ⁺	41.10±0.13 ⁺	43.80±0.18 ⁺	42.40±0.24 ⁺	43.70±0.19 ⁺	24.10±0.21 ⁺
Diameter of follicle, μ	40.10±0.21	48.00±0.24 ⁺	46.90±0.19 ⁺	43.10±0.12 ⁺	41.20±0.15 ⁺	40.60±0.13 ⁺	41.30±0.17 ⁺
Sectional area of follicle, μ^2	1269.90±19.16	1808.60±20.14 ⁺	1726.70±17.39 ⁺	1458.20±23.11 ⁺	1332.50±19.11 ⁺	1293.90±20.23 ⁺	1338.90±18.61 ⁺
Sectional area of colloid, μ^2	690.10±16.13	1253.50±24.09 ⁺	1163.60±13.20 ⁺	913.90±17.24 ⁺	768.10±19.93 ⁺	732.20±14.06 ⁺	769.00±15.32 ⁺
Height of thyroid epithelium, μ	5.22±0.13	4.02±0.03 ⁺	4.20±0.05 ⁺	4.49±0.05 ⁺	4.96±0.09 ⁺	5.03±0.06 ⁺	5.01±0.04 ⁺
Index of colloid accumulation	5.22±0.05	5.97±0.06 ⁺	5.58±0.07 ⁺	4.80±0.06 ⁺	4.25±0.05 ⁺	4.03±0.06 ⁺	4.13±0.04 ⁺
Follicle/colloid ratio	1.29±0.05	0.85±0.04 ⁺	0.95±0.06 ⁺	1.19±0.05 ⁺	1.30±0.04 ⁺	1.27±0.05 ⁺	1.21±0.04 ⁺
Sectional area of nucleus, μ^2	16.23±0.60	11.04±0.50 ⁺	13.10±0.40 ⁺	14.1±0.5 ⁺	14.9±0.3 ⁺	14.6±0.3 ⁺	15.0±0.4 ⁺
Relative area of epithelium, %	47.1±0.4	37.2±0.2 ⁺	39.7±0.6 ⁺	44.2±0.3 ⁺	47.0±0.6 ⁺	46.8±0.5 ⁺	46.2±0.5 ⁺
Relative area of colloid, %	36.4±0.6	43.9±0.5 ⁺	41.8±0.9 ⁺	37.1±0.6 ⁺	36.1±0.4 ⁺	36.7±0.4 ⁺	38.1±0.4 ⁺

Note. ⁺ $p<0.05$ compared to intact animals; * $p<0.05$ compared to animals with hypothyroidism.

les were localized in peripheral region of the colloid. Layers of the connective tissue were found between some follicles. Vascular plethora was accompanied by mild diapedesis and edema in the surrounding tissue.

On day 30 of hypoxia, the tissue of TG contained medium follicles and small number of large follicles. Large follicles had dense colloid and were rose colored. The positive PAS reaction was revealed. Morphometric parameters of follicles in treated rats significantly increased on day 15 ($p < 0.05$ compared to the baseline value) and did not differ from those in intact specimens (Table 1). The cell cytoplasm was eosinophilic. The nuclei were located in the central area. The height of the epithelium correlated with the relative area, follicle/colloid ratio, and index of colloid accumulation. Resorption vacuoles were preserved in the majority of medium follicles. Layers of the connective tissue and microfocal or diffuse polymorphonuclear cell infiltration were identified in the interfollicular space. Signs of erythrosthesis were revealed in individual vessels.

Morphological study and morphometry showed that morphological changes in TG reflect an increase in functional activity during the early stage of IHH. They are stabilized after short-term adaptation and correspond to a new functional level by the end of the first month.

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