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ENGLISH VERSION: AGE FEATURES OF RADIOACTIVE IODINE (^{131}I) ABSORPTION BY RAT THYROID GLANDS IN CORRECTION OF THE DIETARY IODINE DEFICIENCY WITH ORGANIC IODINE*

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*The structure of endocrine morbidity is characterized by a significant spread of thyroid pathology. The insufficient efficacy of inorganic iodine drugs poses the problem of search for new means for iodine deficiency treatment and prevention. Given the progressive aging of the population in economically developed countries, the purpose of the study was to clarify the effect of organic iodine on the features of absorption and elimination of radioactive iodine from the thyroid glands of variously aged rats in the conditions of iodine deficiency in the diet. The study was performed on nonlinear white male rats in two series of studies that were kept on iodine-deficient isocaloric starch-casein diet for 60 days: the first series included two groups of old rats weighing 0.400-0.450 kg, the second series – two groups of sexually immature rats weighing 0.060-0.090 kg. There were 5 rats in each group. In animals of the experimental groups in each series, 10% of casein in the diet was replaced with organic iodine, which came with iodine-protein preparation from the red Black Sea algae *Phyllophora nervosa*. The functional state of the thyroid gland was studied using the Sodium Iodide Na ^{131}I Injection drug. The dosimetry was performed using the STS-6 Geiger-Muller Detector. Radioindication of the thyroid gland was carried out after subcutaneous administration of 0.1 ml of ^{131}I solution at the following time intervals: 0.5, 1, 2, 4, 6, 8, 10, 12, 24, 48, 72, and 96 hours after administration of ^{131}I . The study results were presented as a percentage of the radioiodine dose administered, adjusted for natural radioactivity background and the radioactive decay of the drug. It was found that in the iodine deficiency conditions, the thyroid glands of old rats have higher rates of radioiodine absorption and a lower rate of its excretion than the glands of immature rats, which indicates their lower iodine reserve and greater liability to iodine deficiency pathology. Intake of organic iodine regardless of the rats' age is accompanied by a decrease in radioiodine accumulation and acceleration of its excretion from the thyroid gland, which indicates a decrease in functional stress, but the glands of older rats absorb more iodine and excrete it more slowly, indicating less effective correction of iodine deficiency with age. Reduced functional activity of the thyroid glands in old rats can be used as a sensitive changes marker for the in-depth study of thyrotropic and thyroid disrupting effects.*

Key words: thyroid gland, functional activity, age, iodine deficiency, ^{131}I , organic iodine.

In the general system of control and regulation, which acts in the body with the direct participation of the endocrine system, one of the leading places belongs to the thyroid gland (TG) [18]. At the same time, in the structure of endocrine morbidity, about 47% is accounted for by thyroid pathology, which continues to grow [4]. Disorders of the TG cause the occurrence of clinical manifestations in many syndromes and severe health disorders [14].

An important reason for the growth of thyroid pathology is the decrease in the functional activity of the TG due to the impact of several environmental factors [2,3]. Although the morphofunctional state of the TG is the result of direct or indirect action of various natural, environmental, climatic, social, and other factors, the main affecting factor is the imbalance of biometals, the leading place in which is occupied by iodine deficiency [1]. Today, iodine deficiency is a global medical and social problem: according to the WHO, various health disorders caused by iodine deficiency are the third among 38 most common non-communicable diseases.

The insufficient efficacy of inorganic iodine drugs (iodides and iodates) traditionally used to correct iodine deficiency raises the problem of search for new drugs with pronounced thyrotropic properties. Organic iodine compounds can be considered such substances [9]. The use

of organic iodine compounds derived from seaweed is quite promising [10,11]. Thus, the iodine-protein drug obtained from the Black Sea red alga *Phyllophora nervosa* (DC.) Grev [13] contains a significant (up to 2%) amount of iodine in the form of bound amino acids (monoiodotyrosine, diiodotyrosine, thyroxine).

The territory of Ukraine is characterized by a mosaic combination of biogeochemical areas with reduced iodine content in the environment and areas with anthropogenic and industrial contamination of the environment with heavy metal ions, substances with thyroid disrupting, and radioactive properties. All these factors can affect various parts of the hypothalamic-pituitary-thyroid axis, which can disrupt the synthesis, secretion, and transport of thyroid hormones (TH), distort their local effects on target cells, cause functional and organic changes in the gland with subsequent disorders of the whole body.

Based on the notion that the hypothalamic-pituitary-thyroid complex is most sensitive to various impacts in sensitive periods of its development, the study of the impact of various substances on the functional state of the thyroid gland is usually performed on young laboratory animals [12]. At the same time, objective age-related changes in thyroid functional activity [20] and the progressive aging of the population in the vast majority of

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economically developed countries [15] make such a methodological approach insufficient, as it significantly narrows the ideas of the thyroid status and functionality.

Since the TG plays an important role in the processes of ensuring the vital functions of the body, the current situation encourages the intensified research aimed at the in-depth study of the age features in its activities. In this case, one of the most informative and accessible methods for studying the functional state of the TG is radioisotope diagnostics [7].

The aim of the research was to study the effect of organic iodine on the features of absorption and radioactive iodine elimination from the TG in variously aged rats under the conditions of iodine deficiency in the diet.

Materials and methods

Taking into account that the morphofunctional features of the TG and the nature of the rats' diet are the most relevant to those in humans, a 60-day subacute experiment was carried out under standard vivarium conditions on white nonlinear male rats in two series of studies. The first series of studies was performed on 2 groups of old rats weighing 0.400-0.450 kg, the second series – on 2 groups of sexually immature (growing) rats with an initial weight of 0.060-0.090 kg. Each group consisted of 5 rats; a total of 20 animals were examined. The rats were divided into groups in each series by random sampling. The animals were on a semi-synthetic isocaloric starch-casein diet.

Macro- and micronutrients came with a salt mixture of Jones J.H. & Foster C., from which iodine salts were extracted; background iodine content in the rats' diet of all groups was within the range of 1.6-1.8 µg/rat/day. The source of water-soluble vitamins was a standard vitamin solution made of distilled water; fat-soluble vitamins and α-tocopherol were added to the food mixture with unrefined sunflower oil. The source of dietary fibre was filter paper (0.1-0.2 g/rat/day). The food mixture was laid in the feeder once a day in the morning after cleaning the cages. All nutrients were included in the diet in accordance with the recommendations for animals of this species and age categories; drinking bowls were filled with distilled water, access to which was free. Animals of groups 1 and 2 served as controls for the first and the second series of studies, respectively. In the diet of rats in groups 3 and 4, 10% of casein was replaced by organic iodine, which came with an iodine-protein drug made of red Black Sea alga *Phyllophora nervosa* (DC.) Grev.

After 60 days of observation in rats of all groups, the functional state of the TG was determined by using the radiopharmaceutical ^{131}I "Sodium Iodide Na ^{131}I Injection" drug (Poland) with a half-life of 8.02 days. The solution for injection, which came in a hermetic container, was collected from the vial through a stopper with a disposable syringe and a needle, which, together with the remnants of the radioactive drug, were disposed of in accordance with the rules for radioactive waste management. Based on the fact that 1 ml of solution contains 37 MBq of the radioactive substance, rats were injected subcutaneously 0.1 ml of the drug at the base of the tail.

The dosimetric study was performed with laboratory equipment [5,8] using STS-6 Geiger-Muller Detector (Ukraine) and PP-16 recalculation device (RF) in compliance with the provisions of the "Basic Sanitary Rules for

Radiation Safety of Ukraine" No. z0552-05 of 02.02.2005. Radioindication of the TG in rats of all groups was performed at the following time intervals: 0.5, 1, 2, 4, 6, 8, 10, 12, 24, 48, 72, and 96 hours from the moment of ^{131}I introduction and was expressed in pulses per minute.

Before each indication, the radioactive background was determined, which was within the following limits during the study: before the indication – 64 pulses/min., after 2 hours – 94 pulses/min., after 4 h – 127 pulses/min., after 6 h – 123 pulses/min., after 8 h – 150 pulses/min., after 10 h – 172 pulses/min., after 12 h – 126 pulses/min., after 24 h – 119 pulses/min., after 48 h – 95 pulses/min., after 72 h – 99 pulses/min., after 96 h – 97 pulses/min. The results of the study were presented as a percentage of the injected radioiodine dose, adjusted for natural background and the radioactive decay of the drug. The obtained parameters were processed using Statistica 6.0 software. The study was carried out in compliance with the requirements of the "European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes" (Strasbourg, 1986; Kyiv, 2013).

Results and discussion

Studies have shown that in older rats of control group 1, the maximum absorption of ^{131}I occurred 2 h after administration and was within $16.42 \pm 2.77\%$ of the administered dose. After 24 h, the level of radioactive iodine accumulation in the animals' TG decreased slightly and amounted to $12.65 \pm 2.01\%$. After 72 hours it was at the level of $5.90 \pm 0.56\%$, and at the end of the fourth day decreased to $3.91 \pm 0.43\%$ of the administered dose. In sexually immature rats of control group 2, the picture of ^{131}I accumulation and excretion was different.

The highest level of radioactive isotope accumulation was observed 1 h after its introduction and was $10.62 \pm 2.19\%$. At the end of the first day, it decreased sharply by 2.7 times ($4.00 \pm 1.12\%$ of the administered dose; $p < 0.01$). Subsequent excretion of the isotope occurred less rapidly – $2.43 \pm 0.09\%$ at 72 hours and $0.83 \pm 0.11\%$ at the end of the fourth day. Summarizing the results of the presented study fragment, it can be noted that in the conditions of alimentary iodine deficiency, the thyroid glands of old rats have higher absorption of radioactive iodine and are characterized by a lower rate of excretion than the thyroid glands of growing animals (Fig. 1). The findings indicate that the thyroid glands of older animals have a smaller iodine reserve, as a result of which they are more susceptible to goitrogenic effects of iodine deficiency.

Correction of iodine deficiency in the diet of rats in experimental groups with organic iodine changed the nature of absorption and excretion of ^{131}I thyroid in both old and sexually immature rats. Although in older animals of experimental group 3, the maximum absorption of radioactive iodine did not differ statistically in magnitude from that in the control ($15.68 \pm 2.77\%$ as compared to $16.42 \pm 2.77\%$; $p > 0.05$), it occurred much faster – in 0.5 hours after the isotope administration. At the end of the first day, the level of ^{131}I accumulation in the thyroid glands of rats in this group decreased as compared to the maximum by 2 times and was $7.43 \pm 0.87\%$ of the administered dose, whereas in animals of the same age in control group I who did not consume organic iodine, it only decreased by 4% during the same period.

Fig. 1. Dynamics of ^{131}I absorption and elimination by thyroid glands of variously aged rats under conditions of iodine deficiency in the diet.

We found a reliable (as compared to the control indices to the discussed series of studies) decrease in the level of radioactive iodine accumulation in the thyroid glands of old rats in group 3 after 72 hours from the moment of administration ($4.16 \pm 0.39\%$; $p > 0.05$). After 96 hours, the content of ^{131}I in the TG of rats in group 3 was $3.39 \pm 0.40\%$, which almost did not differ from that of rats in the control group ($p > 0.05$).

In general, when correcting alimentary iodine deficiency with organic iodine, the excretion of radioiodine

from the thyroid glands of old rats was more accelerated than that from the thyroid glands of the same age animals that did not consume organic iodine (control group 1). The graphic curve, which depicts the rate of radioactive iodine absorption and excretion from the thyroid glands of old rats, whose diet was enriched with organic iodine, was smoother than in the control for this series of studies (Fig. 2). The findings may indicate that the intake of organic iodine significantly reduces ("mitigates") the manifestations of iodine deficiency.

Fig. 2. Dynamics of ^{131}I absorption and elimination by thyroid glands of old rats under conditions of iodine deficiency in the diet and its correction with organic iodine.

In sexually immature rats of group 4, which consumed organic iodine, the numerical values of the maximum ^{131}I absorption and the time of its onset did not differ from those in animals of the control for this series of studies (2nd) group. Thus, the maximum radioactive isotope absorption reached $11.53 \pm 0.59\%$ of the administered dose and occurred during the first hour after its introduction.

At the end of 24 hours, the radioactive iodine accumulation in the TG of rats in this group decreased as compared to the maximum by almost 4 times and amounted to $3.09 \pm 0.49\%$ of the administered dose, which did not differ from the rats in the control group. Thus, during the first day of indication, we did not find differences

in the ^{131}I absorption rates by the thyroid glands of sexually immature animals in the experimental and control groups ($p > 0.05$). At the same time, after 48 and 72 hours, the levels of iodine radioactive isotope accumulation in the thyroid tissue of rats, whose iodine deficiency was corrected with organic iodine, decreased to $2.00 \pm 0.08\%$ and $1.70 \pm 0.12\%$, which was significantly lower than the value of similar parameters in the control for this series of studies (in both cases $p < 0.001$).

In 96 hours after the ^{131}I isotope administration, the level of its absorption by the TG in the group of sexually immature rats receiving organic iodine, as compared to the maximum decreased by 15 times and was

0.76±0.12%, that did not differ from the control for the discussed series of studies in a ($p>0.5$). Analysis of the nature of the graphical curves of absorption and excretion of ^{131}I in rats of this series of studies showed that the intake of organic iodine contributed to lower absorption of

thyroid iodine and greater rate of its excretion from the glands than in rats of the control animal group for this series (Fig. 3). This indicates the ability of organic iodine to "mitigate" the effects of iodine deficiency and to improve thyroid function.

Fig. 3. Dynamics of ^{131}I absorption and elimination by thyroid glands of sexually immature rats under conditions of iodine deficiency in a diet and its adjustment by organic iodine.

Comparison of the functional state of the thyroid gland in animals of different ages, whose iodine deficiency in the diet was corrected with organic iodine, revealed that the TG of old rats was characterized by greater iodine absorption capacity and a lower rate of radioactive isotope excretion than the TG of immature animals. Thus, the maximum absorption of ^{131}I by the TG in

old rats of group 3 occurred 0.5 hours after the administration and reached 15.68±2.77% of the administered dose, whereas in sexually immature rats of group 4 it occurred later (after 1 h) and was less (11.53±0.59%; $p<0.05$). The excretion of the iodine radioactive isotope from the TG of old rats in group 3 was less dynamic than from the TG of sexually immature rats in group 4 (Fig. 4).

Fig. 4. Dynamics of ^{131}I absorption and elimination by thyroid glands of variously aged rats under conditions of iodine deficiency correction in the diet with organic iodine.

Thus, in 24 h after administration, the content of ^{131}I in the glands of group 3 rats decreased as compared to the maximum by 2 times, after 48 hours – by 3 times, after 72 hours – by almost 4 times (7.43±0.87%, 5.08±0.67% and 4.16±0.39%, respectively, as compared to the control group, $p<0.01$). In contrast, in sexually immature rats of group 4, the excretion of the ^{131}I isotope from the TG occurred almost by 2 times faster (3.09±0.49%, 2.00±0.08% and 1.70±0.12%; respectively, as compared to indices of the control group and group 3 rats $p<0.01$).

Particularly significant differences in the functional activity of the TG were found in 96 hours after the isotope administration: the ^{131}I content in the TG of old rats decreased more than by 4 times (3.39±0.41%), while in sexually immature rats it decreased more than by 15 times (0.76 ± 0.12%; $p<0.01$). The above indicates that the correction of similar thyroid disorders depends on age: in older individuals, it is less effective than in young rats.

Thus, the results of studying the absorption and elimination of the ^{131}I radioactive isotope in the iodine de-

iciency correction in the diet with organic iodine confirm the dependence of the functional activity of the thyroid gland on age: thyroid glands of older rats are more affected by iodine deficiency than the glands of growing animals. The obtained data confirm the study [6], which found the lower functional activity of the TG in older animals and studied its causes.

Age fluctuations in the levels of the thyrotropic pituitary hormone, free and total thyroxine, and triiodothyronine have also been established in publications [16,17,19], which indicate age-related changes in the "hypothalamic-pituitary-thyroid" system as one of the probable causes of thyroid pathology growth. For a total, the identified features of the functional activity of the thyroid gland may be due to the different needs of the body in thyroid hormones at different periods of life, i.e. they may be a manifestation of adaptive response.

Conclusions

1. The effect of organic iodine on the functional state of the thyroid gland under the conditions of iodine deficiency is due to age: the glands of sexually immature experimental rats have lower iodine accumulation capacity and are characterized by a higher elimination rate than the glands of older rats.

2. Reduced functional activity of the thyroid glands in old rats is promising to be used as a sensitive marker of changes in the in-depth study of the thyrotropic and thyroid disrupting effects.

3. Consuming organic iodine in the conditions of iodine deficiency in the diet helps to increase the functional activity of the thyroid gland, regardless of age, as evidenced by a decrease in the degree of ^{131}I absorption and accelerates its excretion from the glands.

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