CHANGES OF IODINE ABSORPTION IN THYROID GLAND AT EXPERIMENTAL 2,4-DMA INTOXICATION IN RATS

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Introduction

The phenoxy herbicide 2,4-D still using in agriculture and manufacturing at some chemical plants, particularly in Ufa, Russia, causes toxic influence on the organism resulting in metabolic disorders, and pathology of endocrine system, especially thyroid gland[1,2,3]. We previously reported on the changes of thyroid hormonal spectrum in rats at experimental 2,4-D action[4]. Some reduction of iodine absorption by thyroid gland, decrease of serum T4 level and T4 hepatic clearance was found in workers regularly contacted to 2,4-D-sodium salt[5]. In another investigation the experimental action of 2,4-D micro-doses on animals was accompanied by activation of thyroid iodine absorption, not dependent on TSH serum level[6]. The aim of the present study was to determine the changes of thyroid iodine accumulation (both basal and under action of exogenous thyroxin) as one of the possible reasons of thyroid hormonal disturbances.

Methods and Materials

The experiments were carried out on 72 male rats of 180-230 grams body weight. The animals received the water solution of 2,4-D-dimethylamine salt (2,4-DMA) intragastrally every day during four weeks in total dose equivalent to LD_{50} and 1/10 LD_{50} for all period. Control animals received 0.9% sodium chloride solution. Upon the termination of intoxication period all rats were injected intraperitoneally with sodium ^{131}Iodide (10 kBq/100 g body weight). The accumulation of ^{131}I in thyroid gland was determined 72 hours later by decapitation of rats, extraction of the gland and its radiometry on the gamma counter. At the same time the samples of liver tissue and blood serum of the animals were also taken and its gamma activity was measured. For evaluation of thyroxin blocking influence on iodine accumulation in thyroid gland the separate animals were additionally injected intraperitoneally with L-thyroxin solution ("Sigma", 1 mg/100 g body weight) 24 hours after ^{131}I injection and 48 hours before decapitation. The control animals in all cases received 0.9% sodium chloride by the same way. All statistic data processing was performed using Student t-criterion.

Results and Discussion

The results of the study presented in Table 1 show the significant dose-dependent decrease of iodine accumulation in thyroid gland of rats intoxicated by 2,4-DMA to 76.1 – 67.9% of the control level. This effect could be mediated either through central influence (meaning reduction of TSH level[4]), or local thyroid mechanisms (meaning inhibition of iodide peroxidase found out in our experiments). In our case 2,4-DMA showed similar effect on iodine absorption as high doses of iodide, perchlorate or thiocyanate. Taking the view that the herbicide in 4-month intoxication was similar way influenced the hypothalamic and pituitary sections if integrated thyroid axis resulted in simultaneous decrease of TSH level and hypothyroxinaemia[4], we consider it possible to assume the partial substitution of base

receptor ligands (probably T4, T3 or iodine) running as back-way regulators in pituitary and thyroid glands, with 2,4-D or its metabolites, meaning some general structural details of thyroid hormones and the herbicide (halogenated phenol ring)[1]. This influence could lead to disorders of back-way links in thyroid system and decrease of hormonal sensitivity of its regulatory mechanisms.

Table 1. ^{131}Iodine accumulation in thyroid gland of rats at 28-day intoxication by 2,4-DMA (M±m; n=12).

Group of animals	Control	1/10 LD_{50} 2,4-DMA	LD_{50} 2,4-DMA
Whole thyroid gland, pulses/min	24180 ± 1613	18395 ± 495	16441 ± 637
% of control level	—	76,1*	67,9 *
Liver, pulses/min×g of tissue^{o}	45,3 ± 1,2	53,3 ± 4,8	86,1 ± 24,0
% of control level	—	117,6	190,0 *
Serum, pulses/min×ml	102,3 ± 3,9	104,3 ± 47,9	129,3 ± 47,5
% of control level	—	101,9	126,4

*- P<0.05

The total activity of the liver and serum samples was lower than 0.7% of the thyroid level and was not changed significantly, except some elevation of liver iodine accumulation. The last effect was probably connected to accelerated deiodination and conjugation of de novo synthesized ^{131}I-contained hormones in liver of intoxicated rats[1,7].

For determination of regulation disorders we tested the effect of exogenous thyroxin as blocking agent of iodine absorption on the control and intoxicated animals. The results showed in Table 2 testify the 6 times decrease of ^{131}I accumulation in thyroid gland of the control animals. The action of 2,4-DMA enforced this effect: further 3 times reduction of iodine absorption was found. In contradiction to above data the action of increased 2,4-DMA dose has resulted in deblocking effect on ^{131}I absorption: iodine accumulation was about 1.5 times higher than in animals received lower dose of toxicant. This phenomenon seems to be probably connected with metabolic effects of 2,4-D (some activation of iodothyronine synthesis as a result of evaluated conjugation and excretion of T4).

Table 2. ^{131}Iodine accumulation in thyroid gland of rats treated with L-thyroxin at 28-day intoxication by 2,4-DMA (M±m; n=12).

Group of animals	Control + T4	1/10 LD_{50} 2,4-DMA + T4	LD_{50} 2,4-DMA + T4
Whole thyroid gland, pulses/min	3585 ± 1458	1205 ±193	1728 ± 329
% of base control level	14,8 *	4,98 *	7,14 *
Liver, pulses/min×g of tissue	39,0 ± 6,2	40,5 ± 3,6	38,5 ± 3,5
% of base control level	86,1	89,4	85,0
Serum, pulses/min×ml	55,0 ± 11,6	39,0 ± 5,0	58,3 ± 22,0
% of base control level	53,8	38,1*	57,0

* - P<0.05

Thus, the results of our investigation show the significant decrease of iodine absorption in thyroid gland of rats in conditions of 28-day 2,4-DMA intoxication. The mechanisms of this reduction seem to include both changes of hormone-receptor interaction in back-way regulation loops in hypothalamic-pituitary-thyroid axis and accompanying intra-glandular metabolic disorders.

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