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The Influence of Potassium Iodide and Perchlorate on the Process of Thyroid Hormones Secretion

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Abstract

The effect of iodide and potassium perchlorate on the secretion of T3 and T4, the level of cAMP and the number of intracellular drops of colloid in the thyroid gland after stimulation with thyroid-stimulating hormone was studied. It was found that an excess of iodide suppresses the secretion, and the introduction of perchlorate prevents the inhibitory effect of iodide. The results support the opinion about the dependence of the adenylate cyclase system of the thyroid gland on the concentration of organic iodine.

Keywords: thyroid hormones; secretion; adenylate cyclase system; iodide; perchlorate

Thyroid hormone synthesis is dependent on normal iodine transport, and therefore knowledge of its regulation is fundamental to understanding the etiology and treatment of congenital and acquired thyroid conditions such as hypothyroidism and hyperthyroidism. The ability of the thyroid gland to concentrate iodine is also widely used as a tool for diagnosing thyroid diseases [1, 2].

It has now been established that iodide both in vitro [5, 10] and in vivo [3, 8] removes the activating effect of TSH on adenylate cyclase. In addition, it has been proven that for the implementation of this inhibitory effect, a preliminary transition of iodine to the organic form is required, since the use of agents that disrupt the organization of iodine removes it [8]. The inhibition by iodine of the stimulating effect of TSH on the adenylate cyclase system of the thyroid gland is also significantly weakened by perchlorate, which blocks the flow of iodine into the gland [4, 8]. The biochemical basis of this inhibitory effect is the subject of numerous studies that are carried out using an iodine-free diet, antithyroid substances, TSH and cyclic 3 ', 5'-AMP (cAMP).
This work is devoted to the study of the effect of iodide, its discrete intake and potassium perchlorate, separately and when administered together, on parameters characterizing the secretion of thyroid hormones, such as the level of cAMP in the gland tissue and the number of intracellular drops of colloid under conditions of stimulation with thyroid-stimulating hormone.

Research methodology. Potassium iodide at a dose of 0.5 mg and KCl04 at a dose of 6 mg were administered per os separately or in combination to rats under normal conditions and on a diet low

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in iodine. One day later, the animals were injected intraperitoneally with 50 IU of TSH, and after half an hour they were killed. The cAMP content in the gland tissue was determined using a Cyclic-AMP assay kit (England); for counting colloidal drops, thyroid sections (4–6 μm) were stained with Schiff's reagent and hematoxylin. Colloidal droplets were counted in 10 follicles containing from 20 to 30 cells of each preparation and expressed as the number of drops per 100 thyroid cells. The experiments were also carried out on rats kept on a diet with different iodine content, according to the previously described model [13], divided into 3 groups:

1 - rats of the second generation, receiving 40-45 μg of iodine per day per rat (control);

2 - rats of the second generation who received iodine at a dose of 4-5 μg / day per rat (iodine deficiency);

3 - rats of the second generation that received 3 times a 10-day load of iodide (up to the control level). The break between the loads was 10 days (discrete provision with iodine).

The animals under ether anesthesia were slaughtered 2 weeks, 2.5 and 5.5 months after the last iodide load.

All rats were injected with 20 mU of TSH 30 minutes before slaughter.

Research results. The results presented in Table 1 indicate that iodide significantly, without changing the basal concentration of cAMP in the gland tissue, sharply reduces the concentration of this substance under conditions of TSH stimulation in groups of animals kept both under normal conditions and on an iodine-free diet.

Table 1

The effect of potassium iodide and potassium perchlorate on the concentration of cAMP (pmol / g tissue) and on the content of intracellular (in 100 cells) in the thyroid gland of rats.

Animal groups	Intact animals		50 IU TSH		Iodine-free diet +50 IU TSH	
	cAMP	colloidal drops	cAMP	colloidal drops	cAMP	colloidal drops
the control	760±60 (n=6)	9±0,8 (n=4)	1088±47** (n=6)	149±23 (n=5)	1053±16 (n=6)	114±11 (n=10)
0.5 mg KI	1040±115 (n=6)	3±0,4* (n=4)	300±38* (n=6)	29±3* (n=5)	326±56* (n=6)	22±3* (n=10)
6 MG$KClO_4$	786±28 (n=6)	14±1,7* (n=4)	1900±128* (n=6)	184±14 (n=5)	973±38 (n=6)	177±15* (n=10)
0,5MG KI+ 6 MG$KClO_4$	760±23 (n=6)	10±1,3 (n=4)	1015±20 (n=6)	117±14 (n=5)	1453±152* (n=6)	130±8 (n=10)

*The differences between the groups of animals exposed and not exposed to iodide and perchlorate are significant (P <0.05).

** Differences in comparison with the group of intact animals, not exposed to iodide and perchlorate, are significant (P <0.05).

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The formation of intracellular colloidal droplets is suppressed by iodide both in the group of rats that did not receive TSH, and in the groups of animals stimulated with thyroid-stimulating hormone. The introduction of perchlorate, without affecting the basal concentration of cAMP, significantly increases it in animals that are only under the influence of TSH and does not change in animals kept on an iodine-free diet. The formation of intracellular colloidal drops under the influence of perchlorate is enhanced in all groups of animals. The introduction of perchlorate together with iodide completely removes the inhibitory effect of iodide on these parameters and indicators of the level of cAMP and the formation of intracellular colloidal drops remain close to the control in all groups of animals.

Table 2.

Thyrocyte sensitivity and thyrotropic function of the pituitary gland

rats with iodine deficiency and discrete iodine supply

Time after the last iodide load	Animal groups (n = 10 in each group)	The number of colloidal drops in 100 thyrocytes	% thyrotropic cit in pituitary gland
2 weeks	The control	20,0 ± 1,08	19,9 ± 2,0
	Iodine deficiency	94,2 ± 7,80*	24,0 ± 1,1*
	Discrete iodine supply	37,9 ± 4,0**	23,6 ± 1,3*
2, 5 months	The control	60,0 ± 7,0	10,2 ± 1,0
	Iodine deficiency	106,8 ± 11,0*	27,1 ± 1,8*
	Discrete iodine supply	95,6 ± 9,0**	22,0 ± 2,5*
5, 5 months	The control	29,1 ± 3,1	9,8 ± 1,3
	Iodine deficiency	121,1 ± 14,0*	27,4 ± 1,8*
	Discrete iodine supply	12,0 ±8,0*	29,2 ± 3,4*
* - reliable difference from the readings in the control ** - significant difference from the indications and the control and iodine deficiency groups			

From the data (Table 2), it follows that in rats of all groups with iodine deficiency, the reaction of the formation of intracellular colloid drops in response to TSH administration is significantly increased. In the rats kept on discrete iodine supply, this reaction was higher than in the control, but lower than in animals with iodine deficiency. Analysis of the histostructure of the thyroid gland showed that there were differences in rats from groups with iodine deficiency and rats from groups with discrete iodide supply. So, with a discrete iodine intake, the structure is heterogeneous: along with small follicular zones, there are medium and large follicles with less active thyrocytes, and it is in them that the thyrotropic reaction is much weaker than in small ones.

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The percentage of thyrotrophs in the pituitary glands of rats from these two groups was approximately the same and significantly higher than in the control at all studied periods. These data indicate the natural involvement of the thyroid-stimulating function of the pituitary gland in the correction of the iodine deficiency state in experimental animals, and the absence of significant differences between the groups with iodine deficiency and those with discrete iodine supply supports the prevailing idea that it is the stable iodine supply that is a necessary condition for the normal functioning of the pituitary gland. thyroid axis. The results obtained correspond to the prevailing idea that thyroid cells, which are in different functional states, react differently to the influence of thyroid-stimulating hormone, as well as that their thyroid-stimulating reaction is highly associated with iodine supply [14].

Our results on the inhibitory effect of excess iodide on the secretion of thyroid hormones in response to TSH stimulation are consistent with the data of Yamamoto et al. [12], who showed the suppression of the level of colloidal endocytosis by iodide, as well as data indicating a decrease in the level of cAMP under the influence of iodide [9]. A necessary condition for the manifestation of the inhibitory action of iodide is both its active entry into the gland and the binding of iodine with some organic substances [9, 15]. Based on the data obtained, the authors draw a conclusion about the classical autoregulatory effect of iodide on the thyroid gland and suggest that the thyroid gland is capable of responding to an increase in the content of organic iodine inside it by modulating a decrease in the sensitivity of adenylate cyclase and TSH, and vice versa ... Our findings on the stimulatory effect of perchlorate on thyroid hormone secretion are consistent with those of Greer et al. [6], who studied the effect of perchlorate on the secretion of labeled iodide from the previously labeled 131I rat thyroid gland using the method of intravital gland perfusion. According to them, perchlorate causes a sharp increase in the secretion of iodine from the thyroid gland, and the secretion of hormones also increases. The authors believe that the increase in the secretion of the thyroid gland is due exclusively to the suppression of the iodine pump and that under these conditions iodine is more likely to be leached out of the cell than used for organic binding. On this basis, it can be assumed that perchlorate removes the suppressive effect of excess iodide on TSH-induced cAMP synthesis and the level of colloidal endocytosis by reducing the concentration of organic iodine in the gland. This conclusion is consistent with that of Rousset et al. [10], who found that the administration of perchlorate to mice increases the secretion of the thyroid gland in response to TSH stimulation by 1–2 times. When discussing the mechanism of action of perchlorate on the thyroid gland, the authors associate two processes: an increase in the secretion of hormones and the release of iodine. The authors believe that perchlorate, by unloading the space for intrathyroid iodide, is able to control the processes of stimulation of the thyroid gland; moreover, iodide or iodinated compounds in this regard can play an autoregulatory role.

Thus, our results testify in favor of the concept of the sensitivity of thyroid adenylate cyclase to the concentration of organic iodine in it. It becomes clear how the secretion of thyroid hormones is maintained within normal limits with the combined use of iodide and perchlorate: apparently, an excess of iodine reduces the ability of perchlorate to influence its concentration in the gland, and thus the process organification of iodine and secretion of thyroid hormones is maintained at an optimal level. The reaction of an animal organism to a change in iodine supply is carried out with the participation of all links of the pituitary-thyroid system. Iodine deficiency, as well as its discrete content in the diet, increase the sensitivity of thyrocyte secretion to the administration of thyroid-stimulating hormone, while the thyroid-stimulating reaction is more pronounced in thyroid follicular cells that are in an active functional state.

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