EFFECT OF POTASSIUM IODIDE AND PERCHLORATE ON THE SECRETION OF THYROID HORMONES

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The effect of potassium iodide and perchlorate was studied on parameters characterizing the secretion of thyroid hormones: the cyclic AMP level in the thyroid gland tissue and the number of intracellular colloid drops during stimulation with thyroid hormones. Excess of iodide was shown to depress these indices whereas perchlorate prevented the inhibitory effect of iodide. The results support the view that the adenylate-cyclase system of the thyroid gland is sensitive to the organic iodine concentration. Excess of iodide evidently reduces the ability of perchlorate to affect its concentration in the gland, so that the process of organification of iodine and the secretion of thyroid hormones are maintained at the optimal level.

KEY WORDS: thyroid hormones; secretion; adenylate-cyclase system; iodide; perchlorate.

An excess of iodide is known to depress the stimulating action of thyrotropic hormone (TTH) on various aspects of thyroid function [5, 10], including on the secretion of organic iodine [2, 6].

The biochemical basis of this inhibitory effect has been the subject of much research, in connection with which an iodine-free diet, antithyroid substances, TTH, and cyclic AMP have been used. The central position of adenylate cyclase (ACase) in the mechanism of TTH-induced stimulation has led several workers to concentrate their attention on the study of the effect of iodide on this system. It has recently been shown that iodide, both in vitro [3, 11], and in vivo [1, 7] abolishes the activating effect of TTH on ACase. It has also been shown that for this inhibitory effect to take place, the iodine must first be converted into the organic form, for the use of methimazole or other agents disturbing the organification of iodine abolishes it [8]. The depression of the stimulating action of TTH on the adenylate-cyclase system of the thyroid gland by iodine is also considerably weakened by perchlorate, which blocks the entry of iodine into the gland [8].

The object of this investigation was to study the effect of potassium iodide and perchlorate, separately and in combination, on parameters characterizing the secretion of thyroid hormones, such as the cyclic AMP level in the thyroid tissue and the number of intracellular colloid drops during stimulation with thyrotropic hormone.

EXPERIMENTAL METHOD

Potassium iodide (0.5 mg) and $KClO_4$ (6 mg) were given per os separately or in combinations to rats kept either under ordinary conditions or on a diet with a low iodine content. After 24 h the animals were given an intraperitoneal injection of 50 milliunits TTH, and killed 30 min later. The cyclic AMP concentration in the thyroid gland tissue was determined by means of a "cyclic AMP Assay Kit" (England), and to count the colloid drops sections (4-6 μ) through the thyroid gland were stained with Schiff's reagent and hematoxylin. Colloid drops were counted in 10 follicles containing from 20 to 30 cells in each section, and expressed as the number of drops per 100 thyroid gland cells.

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TABLE 1. Effect of Potassium Iodide and Potassium Perchlorate on Cyclic AMP Concentration (pmoles/g tissue) and on Number of Intracellular Colloid Drops (in 100 cells) in Rat Thyroid Gland

Group of animals	Intact animals		50 milliunits TTH		Iodine-free diet + 50 milliunits TTH	
	cyclic AMP	colloid drops	cyclic AMP	colloid drops	cyclic AMP	colloid drops
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* ($n = 10$)
0.5 mg 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 ($n = 10$)

*Differences between groups of animals receiving and not receiving iodide and perchlorate are significant ($P < 0.05$).

†Differences compared with group of intact animals not receiving iodide or perchlorate are significant ($P < 0.05$).

EXPERIMENTAL RESULTS

The results given in Table 1 show that iodide did not significantly change the basal cyclic AMP concentration in the thyroid tissue but sharply reduced its concentration during stimulation with TTH in groups of animals kept either under ordinary conditions or on an iodine-free diet.

The formation of intracellular colloid drops was inhibited by iodide both in the group of rats not receiving TTH and in the groups of animals stimulated by thyrotropic hormone.

Administration of perchlorate, while it had no effect on the basal cyclic AMP concentration, considerably increased it in animals treated with TTH only but left it unchanged in animals kept on an iodine-free diet. The formation of intracellular colloid drops was stimulated by perchlorate in all groups of animals.

Administration of perchlorate together with iodide completely abolished the inhibitory action of iodide on these parameters, and the cyclic AMP level and number of intracellular colloid drops formed remained close to the control values in all groups of animals.

The present results regarding the inhibitory action of an excess of iodide on the secretion of thyroid hormones in response to stimulation by TTH agree with those of Yamamoto et al. [12], who showed that iodide depresses the level of colloid endocytosis, and also with evidence that the cyclic AMP level falls under the influence of iodide [8, 11]. Essential conditions for the manifestation of the inhibitory action of iodide are, first, its active entry into the gland and, second, binding of the iodine with certain organic substances [8]. From their results the authors draw a conclusion on the classical autoregulatory effect of iodide on the thyroid gland and postulate that the gland can respond to an increase in the content of organic iodine in its tissues by modulating the decrease in the sensitivity of AC-ase to TTH and vice versa.

The present results regarding the stimulating action of perchlorate on the secretion of thyroid hormones agree with those of Greer et al. [4], who studied the effect of perchlorate on the secretion of labeled iodide from the thyroid gland, previously labeled with ^{131}I, of rats by a method of intravital perfusion of the gland. According to their findings, perchlorate sharply increases the secretion of iodine from the thyroid gland; hormone secretion also is increased. These workers consider that the increase in secretion from the thyroid gland is due entirely to inhibition of the iodine pump and that, under these circumstances, iodine is washed out of the cell rather than being utilized for binding with organic compounds.

It can accordingly be postulated that perchlorate abolishes the inhibitory action of an excess of iodide on TTH-induced cyclic AMP synthesis and on the level of colloid endocytosis by reducing the organic iodine concentration in the gland. This conclusion is in agreement with the opinion of Rousset et al. [9], who found that administration of perchlorate to mice increases secretion from the thyroid gland in response to stimulation by TTH by 1-2 times. In a discussion of the mechanism of action of perchlorate on the thyroid gland these workers bring the two sides together: an increase in secretion of hormones and in the outflow of iodine. They consider that perchlorate, by emptying the intrathyroid iodide space, is able to control the stimulation of the thyroid gland; iodide or iodinated compounds may play an autoregulatory role in this respect.

The results of the present experiments thus support the concept that ACase of the thyroid gland is sensitive to the organic iodine concentration in the gland.

It is becoming clear how the secretion of thyroid hormones is maintained within normal limits following the combined administration of iodide and perchlorate: The excess of iodine evidently reduces the ability of perchlorate to affect its concentration in the gland, and consequently the process of organification of iodine and the secretion of thyroid hormones are maintained at the optimal level.

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