EFFECT OF HYPERTHERMIA ON THE RATE OF ELIMINATION OF I^{131} FROM THE THYROID GLAND AND THE BODY

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In rats exposed to hyperthermia, besides inhibition of the iodine-concentrating mechanism in the thyroid gland, the intrathyroid hormonal fractions are mobilized and their internal deiodination takes place intensively, nonhormonal iodine is actively discharged from the gland, and the elimination of extrathyroid iodine is stimulated. Exposure of man to hyperthermia gives a qualitatively similar effect. Transient hyperthermia after the accumulation of radioiodine by the thyroid gland reduces the absorbed dose for the thyroid gland and the body as a whole appreciably and it can be regarded as a promising constituent of the combined treatment of radioiodine poisoning.

KEY WORDS: hyperthermia; thyroid gland; iodine metabolism; radioprotective action.

Methods of protection of the thyroid gland when there is a threat of acute poisoning with radioactive iodine have been described in fair detail [1, 8]. However, after the accumulation of radioiodine by the gland these methods are inactive, for they only block the intake of iodide from the blood stream but do not stimulate the elimination of intrathyroid iodine. The known method of stimulating this process, by administration of thyrotropin [11, 12], is also ineffective because of the increased reutilization of radioiodine by the thyroid gland. Meanwhile data have been obtained to show the inhibitory action of a raised ambient temperature on the iodine-accumulating function of the thyroid gland [7, 9]. The mechanism of this effect remains unexplained.

The object of this investigation was to study the behavior of radioiodine in the thyroid gland and in the body of rats and man during exposure to brief hyperthermia.

EXPERIMENTAL METHOD

Experiments were carried out on 48 male Wistar rats with a mean weight of 240 g. A solution of NaI^{131} without carrier was injected intraperitoneally into the animals in a dose of 10 Ci/100 g body weight. The rats were decapitated 0.25, 0.5, 1, 3, 6, 11, and 24 h after injection of the isotope. The group of experimental rats was exposed to hyperthermia 6 h after injection of I^{131} by placing them in an incubator, ventilated with air, at 37°C for 2 h; the animals were killed 3 h after removal from the incubator. During the investigation of the animals, intravital whole-body radiometry was carried out by means of a special apparatus [3]. After sacrifice, radiometry was performed on the thyroid glands, the whole blood, and the hormonal fraction of serum isolated on an ion-exchange resin. A morphological analysis also was undertaken of the thyroid gland and the thyroid tissue homogenates were tested for incroporation of the label into thyronine radiochromatographically [5].

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TABLE 1. Values of Parameters of Curves Showing Change in Radioactivity on the Thyroid Gland, in the Whole Body, and Whole Blood of Intact Rats

	T'_{biol} (in h)	T''_{biol} (in h)	k_1	k_2
Thyroid gland	66	3,8	0,20	—0,20
Whole body	2,0	47	0,32	0,68
Whole blood	1,3	12	0,74	0,26

In experiments on six euthyroid volunteers (men aged 28-35 years) after enteral administration of an aqueous solution of NaI^{131} without carrier in a dose of 1 Ci the I^{131} content was measured (in percentages of the dose administered) in the body as a whole and in the thyroid gland in a low-background chamber with a γ-spectrometric counter [4]. The tests were carried out after 2, 7, 12, 25, and 36 h and 4, 13, and 35 days. Subjects of the experimental group were exposed to a temperature of 30-45°C 8 h after receiving the radioiodine (four exposures, each lasting 10 min, at 45°C, at 30°C in the intervals) and with a relative humidity of about 100% for 2.5 h.

EXPERIMENTAL RESULTS

Analysis of the curves of the change in radioactivity in the thyroid gland, in the whole body, and in the whole blood obtained in the experiments on rats (Fig. 1a, b) showed that they approximate sufficiently accurately to an equation of the form:

$$Q_t = Q_0 \cdot \left(k_1 e^{-\frac{0.693}{T'_{biol.}} \cdot t} + k_2 e^{-\frac{0.693}{T''_{biol.}} \cdot t} \right),$$

where Q_0 is the quantity of I^{131} administered, t is the time after administration (in h), and the corresponding values of k_1, k_2, T'_{biol}, and T''_{biol} are given in Table 1.

The curves in Fig. 1 show that the accumulation of the label in the thyroid gland of the intact rats reached a maximum 11 h after the injection, when it was 17.6 ± 8% of the injected dose. By the time of reaching the maximum the I^{131} concentration in the hormonal fraction of the thyroid tissue homogenate was 75%. After exposure to hyperthermia the I^{131} content in the thyroid gland was significantly lower ($P < 0.01$), and by 11 h it was 10.2 ± 0.8% of the administered dose or 57% of the normal level of accumulation. The I^{131} content in the hormonal fraction was reduced by more than three times, whereas in the nonhormonal fractions (MI, DIT, MIT) it was increased by 1.5 times.

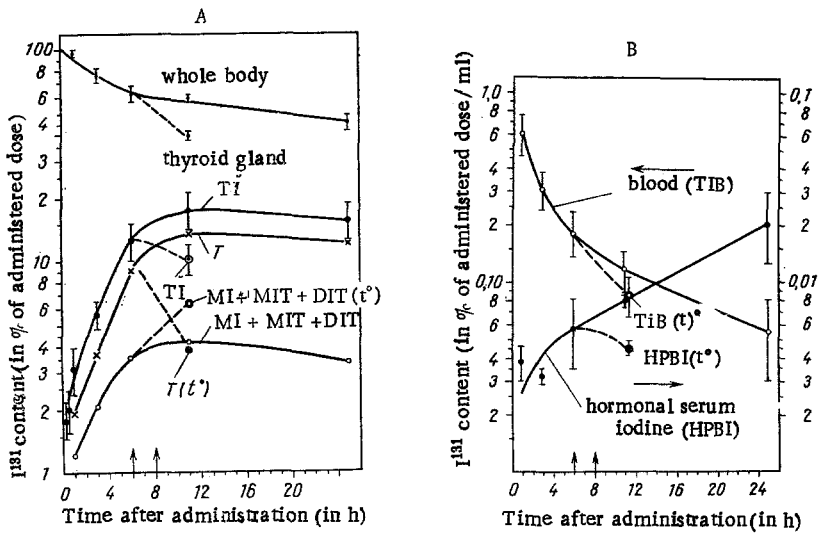

Fig. 1. Effect of brief hyperthermia on the kinetics of I^{131} in rats (continuous lines — control, broken lines — experiment): A) I^{131} content in whole body, thyroid gland, and its iodine-containing fractions; TI) total content of I^{131} in the thyroid gland; T) content of label in thyronines; MI + MIT + DIT) total content of label in the form of iodide and in tyrosines; B) content of I^{131} in 1 ml whole blood (TIB) and in hormonal, protein-bound iodine-containing fraction (HPBI) in 1 ml serum. Arrows mark beginning and end of exposure to hyperthermia.

TABLE 2. Values of Parameters of Curves of Radioiodine Elimination from the Human Body and Thyroid Gland under Normal Conditions and after Exposure to Hyperthermia

	Group	k_1	k_2	k_3	T'_{biol} (per diem)	T''_{biol} (per diem)	T'''_{biol} (per diem)
Thyroid gland	Control	$0,22 \pm 0,02$	$-0,140 \pm 0,007$	$-0,077 \pm 0,017$	94 ± 20	$0,32 \pm 0,03$	$0,13 \pm 0,012$
	Experimental	$0,18 \pm 0,02$	$-0,090 \pm 0,020$	$-0,087 \pm 0,016$	35 ± 9	$0,37 \pm 0,04$	$0,16 \pm 0,023$
		$0,2<P<0,3$	$0,1<P<0,2$	$0,6<P<0,7$	$0,05<P<0,1$	$0,6<P<0,7$	$0,3<P<0,4$
Whole body	Control	$0,387 \pm 0,014$	$0,40 \pm 0,06$	$0,22 \pm 0,05$	—	$0,45 \pm 0,06$	$0,16 \pm 0,02$
	Experimental	$0,34 \pm 0,04$	$0,45 \pm 0,04$	$0,21 \pm 0,02$	—	$0,28 \pm 0,012$	$0,19 \pm 0,02$
		$P=0,3$	$0,5<P<0,6$	$P=0,9$	—	$0,05<P<0,1$	$0,3<P<0,4$

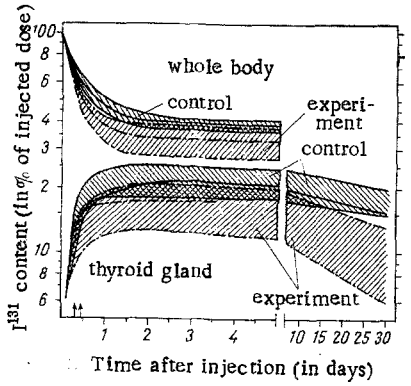

Fig. 2. Curves of change in radioactivity in the whole body and thyroid gland of normal subjects (control) and after brief exposure to hyperthermia (experiment). Period of hyperthermia indicated by arrows.

Under normal conditions 5 h after injection of I^{131} its elimination from the body took place with a biological half-life of 47 h; by 11 h the I^{131} concentration in the body of the rats was $59.1 \pm 2.2\%$ of the injected dose. After exposure to hyperthermia the residual radioactivity in the body was $39.7 \pm 1.8\%$ ($P < 0.001$). The half-elimination period was reduced to 8.4 h.

By 11 h the I^{131} content in the whole blood of the intact rats had reached $0.118 \pm 0.011\%$ of the injected dose/ml. As a result of exposure to hyperthermia this index fell ($P < 0.05$) and reached $0.086 \pm 0.009\%$/ml. During the period of observation (0-25 h) a continuous increase in the quantity of label in the serum hormonal fraction was observed in the blood of intact animals. By 11 h the level of hormonal I^{131} was $7.3 \pm 1.4 \times 10^{-3}\%$/ml serum. In the experimental group the same index fell to $4.5 \pm 0.4 \times 10^{-3}\%$/ml.

The curves of elimination of radioiodine from the body and from the thyroid gland of the control and experimental groups of human subjects (Fig. 2) were described reasonably accurately by an equation of the type:

$$Q_t = Q_0 \left(k_1 e^{-\frac{0.693}{T'_{biol.}} \cdot t} + k_2 e^{-\frac{0.693}{T''_{biol.}} \cdot t} + k_3 e^{-\frac{0.693}{T'''_{biol.}} \cdot t} \right),$$

in which the corresponding parameters have the values showed in Table 2.

As a result of exposure to hyperthermia the elimination of radioiodine also was accelerated in man, but it was less marked than in the experimental animals. The half-elimination period of I^{131} from the thyroid gland (T'_{biol}), for instance, was shorter in the experimental group than in the control, whereas during the 24-30 h after the end of exposure to hyperthermia, more rapid elimination of I^{131} from the body also was observed. In addition, a more rapid relative increase in radioactivity in the thyroid gland from 6 to 12 h after injection of the label was observed in the control ($23 \pm 8\%$) than in the experimental series ($8.2 \pm 2.2\%$).

Hyperthermia, as the results show, led to the more rapid elimination of I^{131} from the thyroid gland and body of the rats. This is clear from the fact that the I^{131} concentration in the thyroid glands of the experimental rats was lower not only than in the intact rats, but also than at the beginning of exposure to hyperthermia. The decrease in the radioiodine concentration in the gland was due to a sharp decrease in the size of the labeled hormonal fraction. As the results of neutron-activation chromatography of thyroid gland homogenates show, under similar experimental conditions [5] the content of native iodine in the hormonal fraction is also reduced. As a consequence, an increase in the hormonal fraction in the blood might be expected. However, not only was it not increased but, on the contrary, it was reduced by 40%. This finding does not conflict with the postulated role of thyroid hormones in temperature adaptation [10, 13]. Since it is difficult to accept increased utilization or excretion of the thyroid hormones in an

unchanged form in this situation, it can only be postulated that the process of utilization of the hormonal fraction takes place at the thyrocyte level. The writers showed earlier that under similar conditions I^{131} passes rapidly and intensively from the colloid into the cells of the follicle [6]. Meanwhile the I^{131} content in the nonhormonal fraction increases significantly. It is reasonable to suggest that as a result of hyperthermia the intrathyroid deiodination processes are greatly activated, and their products are excreted from the thyroid gland. This explanation does not conflict with the possibility of maximal internal deiodination of thyroid hormones expressed previously [2].

The absence of an increase in the concentration of nonhormonal I^{131} in the blood was evidently the result of intensification of the elimination of extrathyroid iodide. This is confirmed by the fact that the difference between the I^{131} content in the control and experimental series 11 h after injection was $7.4 \pm 2.0\%$ in the thyroid gland and $19.4 \pm 2.8\%$ of the injected dose in the whole body. The morphological changes in the thyroid parenchyma (hypoplasia of the thyrocytes, an increase in volume of the follicles) indicate inhibition of the hormone-producing and iodine-concentrating functions of the thyroid gland.

Exposure to hyperthermia must thus be regarded not only as inhibitory with respect to thyroid function [7]. Besides inhibition of the iodine-concentrating mechanism, the intrathyroid hormonal fractions are mobilized and undergo intensive internal deiodination, with the active removal of nonhormonal iodine from the gland, and the pathways of elimination of extrathyroid iodine are stimulated.

Exposure of man to relatively weak hyperthermic action gave a qualitatively similar effect to that observed in animals. The elimination of radioiodine from the gland and from the body as a whole was accelerated. For instance, the averaged period of biological half-elimination of radioiodine from the gland was 35 ± 9 days in the experimental series and 94 ± 20 days in the control, and from the body the corresponding figures were 0.28 ± 0.012 and 0.45 ± 0.06 days. The absorbed dose for the thyroid gland under these circumstances was reduced on the average by 22% (observations for 35 days) and for the body as a whole by 13% (for 5 days).

Hyperthermia can thus be regarded as a promising constituent of the combined treatment of radioiodine poisoning.

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