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THE PROPHYLACTIC AND THERAPEUTIC ACTION OF SOMATOTROPIC HORMONE IN RADIATION AFFECTION

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Under the influence of ionizing radiation, processes of protein disintegration are intensified in the organism (1); the nitrogen balance becomes negative, the content of amino acid nitrogen in the blood is increased, and so forth. The somatotropic hormone (STH), as is known, hastens synthetic process in the organism. Upon injection of STH, positive nitrogen balance is achived, the synthesis of protein is increased, anabolic processes begin to predominate over catabolic processes. In other words, STH acts in contrary fashion to ionizing radiation. This has served as a basis for tests with STH as a prophylactic and therapeutic agent in radiation sickness.

There are few articles in the literature which touch on this problem, and those which do exist are contradictory. In a small number of animals it has been shown (7) that STH prevents loss of weight in irradiated animals, but does not influence their survival. It has also been noted (3) that STH prevents changes in the histologic structure and weight of the internal organs. At the same time, there are data indicating that STH induces an increase of weight in irradiated animals only when combined with streptomycin treatment (5). Radiation sensitivity is decreased in guinea pigs upon prophylactic injection of STH (6).

On the other hand, it has been shown that there is an increased mortality in irradiated mice (9) and guinea pigs (4) after injection of STH.

In our experiments, we used 422 adult male rats, weighing

125-160 gm at the beginning of the experiment (370 of these were irradiated). The rats were subjected to total body irradiation in the RUM-3 apparatus, at doses of 400, 500, 600, and 800 r. Preparations of STH were used which had been produced by the senior scientific worker of the biochemical division of the All-Union Institute of Experimental Endocrinology, T. S. Sakhatskaya, and by the production division (batches 3 and 20), and which were standardized in the division of experimental biology of the Institute.

The following series of experiments were run: (1) injection of STH after irradiation with minimum lethal doses of X-rays; (2) injection of STH after irradiation with sublethal doses; (3) injection of STH to irradiated rats, in conjunction with desoxycorticosterone-acetate (DOCA) and saline solution; (4) preliminary (before irradiation) injection of STH; (5) study of the influence of STH on the weight and histological structure of the endocrine glands and other organs in rats sacrificed 4 and 12 days after irradiation, and in control rats.

In four series of experiments, the blood leukocyte content was studied prior to irradiation and again on the 2nd, 4th, 7th and 10th days after irradiation and administration of STH and DOCA. The leukocyte count after irradiation with a minimum lethal dose of X-rays, or with sublethal doses, falls on the second day from control levels of 8000-21,000 to levels of 400-1400 per cu. mm.

We first determined the influence, of the preparations under study, on the body weight of normal rats (Fig.1) [page 32 of Source]. The gain in weight in rats receiving STH was greater than in the controls. The difference after 12 days averaged 14 gm, which is in accord with the effect of the international standard preparation of STH on increase of body weight in the intact animal.

The influence of STH on the weight and viability of the rats after irradiation with minimum lethal doses was studied six times in different groups of animals. Each group consisted of 20 irradiated rats: 10 received STH, and 10 served as controls. In all tests of this series, similar results were obtained. One of the typical curves of change in body weight and viability of the animals receiving STH (2 mg per rat per day) immediately after irradiation and during the ensuing days prior to death is shown in Fig.2 [page 32 of Source]. STH exerted a specific influence even with lethal doses of radiation. The weight curve of the rats receiving STH is higher than that of

the controls. Similar results were also obtained in other groups of tests. However, the survival rate in the group of irradiated animals receiving STH was the same as that of the controls in the tests in this series. Thus, the average duration of life of irradiated rats receiving STH (average figures) is 10 days, and of the control irradiated rats, 11 days.

The influence of STH in sublethal doses of irradiation was studied four times in various groups of animals. One of the typical curves of change in body weight and rate of survival is presented in Fig. 3 /page 32 of Source/. The irradiated rats receiving STH gained weight much more quickly than the controls, but there was no increase in the rate of survival in the tests of this series.

In the third series of experiments, studies were made of the influence of STH on the weight and survival rate of animals, when accompanied by a single injection of DOCA and the administration of saline solution. STH was given in the same doses (2 mg per rat per day), DOCA was given in a dose of one mg on the day after irradiation, followed by saline solution (in the drinking water).

The set-up of this series of experiments was dictated by the following considerations.

It has been shown (8) that STH does not act on the adrenalectomized animal, and that its effects can only occur with simultaneous administration of DOCA and salt solution. It has also been shown (2) that in irradiated animals, the mineralocorticoid function of the adrenals is disrupted and that injection of DOCA is capable, partially, of restoring this function. In irradiated rats, the syndrome of partial adrenal insufficiency develops. Hence we thought it expedient to combine the administration of STH with that of DOCA in the irradiated animals.

In this series, an even greater difference in weight was noticed between the animals receiving STH and DOCA, and the controls (Fig.4) /page 32 of Source/. Thus, the weight difference between animals irradiated with sublethal doses (control) and those receiving STH was 17 gm, and the difference between control rats and those receiving STH and DOCA and salt solution was 34 gm. However, the irradiated rats receiving STH and DOCA and salt solution died in greater numbers than did the controls, and sooner after irradiation (Fig.4) /page 32 of Source/.

In the fourth series of experiments, STH was given over a period of 10-14 days prior to irradiation (various sublethal doses of X-rays). In this series there were three groups of experiments. The results of one of the groups of experiments are presented in Fig. 5 [page 33 of Source]. The upper curve represents the weight changes and survival rate of a group of rats receiving STH prior to irradiation, and the lower curve is that of the controls. The difference in weight of the animals before irradiation was very slight in this group; however, the rats receiving STH lost weight to a lesser extent than did the controls, and died in fewer numbers. Thus, of 10 animals receiving STH before irradiation, nine survived, while of those not receiving STH, only six survived. In two other groups, the findings were similar. The results of this series are presented in:

Table 1

Survival rate of rats receiving STH for 10-14 days prior to irradiation

No. of group	STH (2 mg per rat per day, given in two divided doses)		Control (physiologic saline solution at pH 3.0)	
	No. of animals in test	No. surviving	No. of animals in test	No. surviving
I	10	8	10	4
II	10	4	10	2
III	10	9	10	6
Total	30	21	30	12

As can be seen from these figures, of 30 rats receiving STH prior to irradiation, 21 survived, while of 30 rats not receiving STH before irradiation, only 12 survived. Hence, STH as a preventive measure, given prior to irradiation, exercises a decidedly protective effect.

In the fifth series of experiments, studies were made of the influence of STH on the weight of the endocrine glands and other organs in normal and irradiated rats. In Table 2, data are

presented on the changes of weight of the endocrine glands and other organs in normal rats receiving, over a period of four or twelve days, STH in doses of 2 mg per rat per day.

If one compares the changes of absolute weight (in mg), it is apparent that, with the exception of the weight of the pituitary (it diminishes slightly after injection of STH), certain glands of internal secretion and other organs increase in weight. Obviously, the weight difference in the experimental and control animals is due to increase in weight of the internal organs. This was observed in the groups of animals receiving STH for four and for twelve days (the difference was somewhat greater in the latter case). However, the relative weights of the endocrine organs (with the exception of the adrenals) and other organs did not change under these conditions.

The influence of STH on the weight of the endocrine glands and other internal organs is slightly more obvious in the irradiated animals. In the irradiated animals (Table 3), the weight of the glands of internal secretion and of all the internal organs was much reduced by four days after irradiation (except the adrenals, which increased in weight). STH increases the weight of the adrenals and normalizes the absolute weight of all the endocrine glands and internal organs. The relative weight of the adrenals is increased, in comparison with the irradiated controls, as is that of thyroid and the testes (statistically significant differences). Hence, the irradiated animals, apparently, are slightly more sensitive to the action of STH than are normal animals.

As can be seen from these findings, STH is only prophylactic in its effects, and not therapeutic. Injection of STH after irradiation produces decrease in the loss of weight in the animals but does not increase their survival periods. Apparently, STH normalizes only the disrupted metabolism in the irradiated animals, but does not alter other factors which lead to death of the animals from radiation injury. Hence, it is necessary to study the possibility of using STH in radiation sickness in combination with other measures.

The protective effect of STH may be explained by the fact that this hormone is one of the substances which, by influencing the level of metabolism of the organism, expecially the oxygen consumption of the tissues, reduce the oxygen tension in the tissues and thereby exert a protective effect.

Table 2 - Changes of body weight and of the weight of the respectively

Group	No. of animals	Body weight in gm		Weight gain in gm	Weight (mg and mg percent)
		initially	at autopsy		
Normal	14	150	166	+16	Absolute (in mg) Relative (mg per 100 gm body weight)
Normal plus four days of STH	9	150	173	+23	Absolute (in mg) Relative (mg per 100 gm body weight)
Normal	5	148	185	+37	Absolute (in mg) Relative (mg per 100 gm body weight)
Normal plus 12 days of STH	5	148	196	+48	Absolute (in mg) Relative (mg per 100 gm body weight)

internal organs in normal rats receiving STH for 4 and 12 days (2 mg per rat per day)

Endocrine glands						Internal organs				
pituitary	thyroid	adrenals	goiter /?/ "zobnaya zheleza"*	testes	seminal vesicles and prostate	heart	lungs	liver	kidneys	spleen
7.6	22.9	32	398	2086	733	629	1155	8079	1472	1023
4.6 ±0.22	13.7 ±0.57	18.7 ±0.96	241.7 ±19	1258 ±33.4	420 ±30.6	393 ±14.2	693 ±26.2	4856 ±209.6	886 ±58.3	646 ±63
6.0	24	42.9	446	2176	656	663	1217	7836	1587	1164
3.4 ±0.1	13.9 ±0.5	24.0 ±1.05	250 ±19.8	1269 ±67	376 ±72	382 ±9.1	650 ±45	4540 ±347	867 ±85	671 ±65
8.6	18.4	47.4	374	2170	785	698	982	6320	1558	1040
4.5 ±0.14	10.0 ±0.98	25.6 ±1.1	157 ±36	1153 ±43	475 ±63	399 ±14	535 ±44	3315 ±194	840 ±27	565 ±28
7.8	19.2	636	412	2190	864	740	1204	6704	1612	1302
3.9 ±0.14	9.8 ±0.75	32.5 ±1.8	209 ±25	1118 ± 62	441 ±58	377 ±18	611 ±45	3615 ±147	821 ±12	663 ±12

* /"zobnaya zheleza" usually refers to the thyroid or to goitrous disease thereof, but since the thyroid has already been included in this list under its more frequent designation of "shchitovidnaya zheleza", the meaning of "zobnaya zheleza" is uncertain/

Table 3 - Changes of weight of the body and of internal organs irradiation

Group	No. of animals	Body weight in gm		Weight change in gm	Weight in mg and mg percent
		initially	at autopsy		
Normal	14	150	166	+16	Absolute (in mg)
					Relative (in mg per 100 gm body weight)
Irradiated	16	152	138	-14	Absolute (in mg)
					Relative (in mg per 100 gm body weight)
Irradiated plus somatotropic hormone (STH)	17	153	145	-8	Absolute (in mg)
					Relative (in mg per 100 gm body weight)

in irradiated rats (600-800 r) receiving STH for 4 days after (2 mg per rat per day)

Endocrine glands						Internal organs				
pituitary	thyroid	adrenals	goiter/?/ "zobnaya zheleza"	testes	seminal vesicles and prostate	heart	lungs	liver	kidneys	spleen
7.6 ±0.3	22.9 ±1.04	32 ±1.3	398 ±34.0	2086 ±48.4	733 ±52.6	629 ±21.2	1155 ±46.7	8079 ±318	1472 ±223	1089 ±100.8
4.6 ±0.22	13.7 ±0.57	18.7 ±0.96	241.7 ±19	1258 ±33.4	420 ±30.6	393 ±14.2	693 ±26.2	4856 ±209.6	886 ±58.3	646 ±63
5.8 ±0.15	17.3 ±1.06	39.8 ±1.6	53.5 ±3.6	1594 ±75.5	571 ±56.7	537.5 ±13.8	920 ±62.6	6950 ±398	1395 ±53.1	255 ±38.6
4.1 ±0.12	12.4 ±0.86	25.5 ±1.22	38.1 ±2.78	1187 ±49.7	265 ±37.6	384 ±14.3	665 ±41.8	5049 ±287.9	1013 ±31.9	182 ±32.5
6.5 ±0.28	18.5 ±0.6	49.5 ±1.8	81.3 ±5.3	1976 ±47.9	550 ±45.2	578 ±13.9	866 ±21.9	7932 ±240	1497 ±33.4	274 ±33.5
4.5 ±0.2	13.1 ±0.6	34.2 ±1.16	55.7 ±3.86	1354 ±36.7	382 ±23.2	399 ±10.1	598 ±16.5	5162 ±164.2	1039 ±25.9	188 ±23.3

/"zobnaya zheleza" usually refers to the thyroid or to goitrous disease thereof, but since the thyroid has already been included in this list under its more frequent designation of "shchitovidnaya zheleza", the meaning of "zobnaya zheleza" is uncertain/

Conclusions

(1) STH facilitates the maintenance of weight in animals irradiated with sublethal and minimum lethal doses of X-rays, but does not increase their survival times.

(2) Joint administration of STH, DOCA and salt solution exerts a significant influence on the weight of the animals and hastens their death.

(3) The administration of STH prior to irradiation with sublethal doses of X-rays exhibits a definite protective effect.

(4) In irradiated animals, STH increases the weight of the adrenals and normalizes the absolute weight of the endocrine glands and internal organs. In control rats, the weight of the adrenals, thyroid and testes is increased in comparison with that of the irradiated animals.

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