EFFECT OF OXYGEN INHALATION ON RESPIRATION AND OXIDATIVE PHOSPHORYLATION OF THE LIVER MITOCHONDRIA OF IRRADIATED ANIMALS

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After local irradiation of the liver in rabbits and whole-body irradiation of rats, tissue respiration and oxidative phosphorylation of the mitochondria are depressed in the liver. The most marked decrease is found after local irradiation of rabbits in a dose of 6240 R. The use of oxygen inhalations does not prevent this depression of respiration and oxidative phosphorylation, but the intensity of the decrease is much lower, indicating a beneficial effect of oxygen on recovery processes after irradiation.

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The beneficial effect of oxygen inhalations on the general condition of cancer patients receiving radiotherapy has been reported previously. There is no general agreement regarding the beneficial effect of oxygen on the state of animals with radiation injuries, and the treatment of irradiated patients with oxygen inhalations requires experimental justification.

In the present investigation respiration and oxidative phosphorylation of the liver mitochondria of animals receiving local or whole-body irradiation were studied.

EXPERIMENTAL METHOD

The effect of local irradiation was studied on 30 rabbits weighing 2000-2200 g. The rats (160) were divided into two groups: group 1 (40 rats) received whole-body irradiation in a dose of 600 R, and group 2 (120 rats) were similarly treated with a dose of 900 R. Each group was divided into two subgroups, one of which was irradiated only, while the second received irradiation and daily oxygen inhalations. The investigations were carried out in different orders depending on the dose. In the rats of group 1 (600 R) they were carried out on the day of irradiation and thereafter on the 7th, 14th, 21st, and 28th days; on the rats of group 2 (900 R) daily for 14 days. The animals were killed by decapitation. The liver mitochondria were isolated by differential centrifugation by the method of Hogeboom and Schneider as modified by V. P. Skulachev [1]; the pH of the solution was 7.4. After washing, the mitochondria were suspended in 0.25 M sucrose solution corresponding in volume to the weight of the liver tissue. Composition of incubation medium: K_2HPO_4 $1.5 \cdot 10^{-1}$ M; $MgSO_4$ $5 \cdot 10^{-2}$ M; ATP-Na $1.8 \cdot 10^{-2}$ M; glucose $1.5 \cdot 10^{-1}$ M. Yeast hexokinase obtained by Sol' method was used. To 0.2 ml hexokinase, 0.4 ml of mitochondrial suspension was added. The substrate was 0.025 M succinic acid in a volume of 0.1 ml. The final volume of the incubation sample was 1 ml. Respiration was determined by a manometric method. Incubation was carried out at 26°. Absorption of oxygen was determined after equalization of the temperature for 7 min for a period of 20 min. Phosphorus was determined by the method of Lowry and Lopez, based on the difference between concentrations of inorganic phosphate at the beginning and end of incubation [2].

EXPERIMENTAL RESULTS

The results of the study of respiration and oxidative phosphorylation of the liver mitochondria of rabbits after local irradiation in a dose of 6240 R are given in Table 1.

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TABLE 1. Respiration and Oxidative Phosphorylation of Liver Mitochondria of Rabbits after Local Irradiation in Dose of 6240 R

Index	Unirradiated rabbits		Irradiated rabbits		Rabbits receiving irradiation followed by oxygen therapy	
	abs.	%	abs.	%	abs.	%
Respiration (in μg · atoms O_2/10 mg protein)	4.05	100	2.45	60	3.09	76
Oxidative phosphorylation (in μg · atoms P/10 mg protein)	8.37	100	3.81	45	5.41	64
P/O ratio	2.06	100	1.55	75	1.75	85

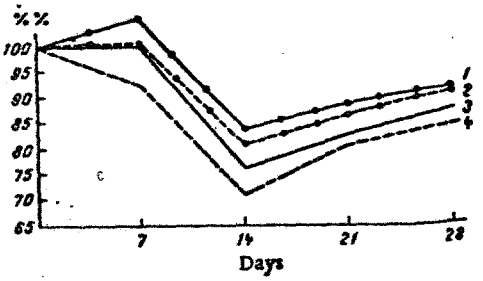

Fig. 1

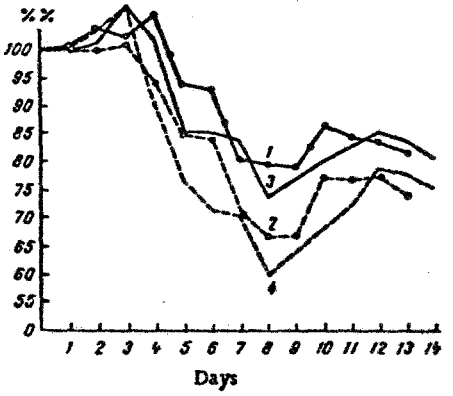

Fig. 2

Fig. 1. Changes in respiration and oxidative phosphorylation after whole-body irradiation in a dose of 600 R. 1) Respiration of animals receiving oxygen inhalations after irradiation; 2) oxidative phosphorylation of animals receiving oxygen inhalations after irradiation; 3) respiration of control animals; 4) oxidative phosphorylation of control animals.

Fig. 2. Changes in respiration and oxidative phosphorylation after whole-body irradiation in a dose of 900 R. Legend as in Fig. 1.

The results show that after local irradiation of the liver, the processes of tissue respiration and of associated oxidative phosphorylation in this organ are profoundly disturbed. Inhalations of oxygen had a beneficial effect on energy metabolism in the liver mitochondria after local irradiation.

Results showing changes in respiration and oxidative phosphorylation over a period of time after whole-body irradiation in a dose of 600 R are given in Fig. 1.

A gradual depression of respiration and oxidative phosphorylation was observed in the rats. During the first days respiration was almost unchanged, but after the 7th day it was diminished to reach a minimum by the 14th day, after which it rose slightly but had not regained its initial value by the 28th day.

In rats receiving oxygen inhalations, the index of respiration was much higher than in the control animals. During the first 7 days after irradiation the intensity of respiration rose slightly, then fell to reach a minimum on the 14th day, after which it again rose slightly but did not reach its initial level. Respiration in the animals receiving oxygen inhalations was thus slightly more intensive than in the controls.

Oxidative phosphorylation was depressed much sooner after irradiation than respiration. It was found to be depressed on the 2nd day after irradiation and reached a minimum also on the 14th day, after which it increased slightly without regaining its initial value. Administration of oxygen inhalations did not prevent depression of oxidative phosphorylation, which also fell to a minimum on the 14th day, after which it increased slightly but did not regain its initial level. However, oxidative phosphorylation in this group of animals was much higher than in the controls throughout the 28-day period, indicating a beneficial effect

of oxygen inhalations on coupled oxidative phosphorylation. Consequently, oxygen had a beneficial effect after whole-body irradiation of the animals in sublethal doses.

The pattern was somewhat different in rats receiving whole-body irradiation in a lethal dose (Fig. 2).

During the first days a slight increase in respiration and oxidative phosphorylation was observed, but by the 5th day both indices had fallen sharply in all groups of animals, to reach a minimum on the 8th day. After the 8th day a relative increase in respiration and oxidative phosphorylation began, and continued until death of the animals. However, despite this increase, they remained far below the initial level.

The fact that respiration and oxidative phosphorylation of animals receiving whole-body irradiation in a dose of 900 R began to increase on the 8th day although the animals were destined to die indicates that the disturbance of these processes in the liver mitochondria was not the cause of death. Death took place as a result of the progressive radiation pathology, the irreversible changes caused by the action of lethal doses of ionizing radiation. Oxygen inhalations under these conditions also had a beneficial effect on the indices of tissue respiration and coupled oxidative phosphorylation.

The experimental results demonstrate the value of oxygen administration to patients with cancer when ionizing radiation is used as one of the principal methods of treatment.

LITERATURE CITED

1. V. P. Skulachev, Relationship between Oxidation and Phosphorylation in the Respiratory Chain [in Russian], Moscow (1962).
2. O. H. Lowry and J. A. Lopez, J. Biol. Chem., 162, 421 (1946).