PHASIC CHANGES IN THE REACTIVITY OF IRRADIATED ANIMALS TO ANESTHETICS

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Changes in the reactivity of animals subjected to the action of ionizing radiation to anesthetics are of both practical and theoretical importance. In spite of the importance of this problem, however, it has not received its due attention in the literature. The investigations which have been carried out in this field [1, 2, 3, 5, 6, 7] are incomplete, for they do not take sufficiently into consideration the individual characteristics of the various anesthetics or their dose, and also the severity of the radiation sickness.

The object of the present investigation was to study the reactivity of irradiated animals to anesthetics in different periods of acute radiation sickness, and its dependence on the factors enumerated.

METHOD

The research was carried out on 4000 white mice of both sexes, weighing 15-22 g.

In each series of experiments the animals were divided into two groups: one group of animals was not irradiated, and acted as controls; the other group received whole-body irradiation with x-rays and developed radiation sickness.

The study of the reactivity was conducted in three forms of radiation sickness: in moderately severe radiation sickness (dose of irradiation 360 r) causing death of from 5 to 10% of the irradiated animals within 30 days of exposure; in a severe form of the disease (dose of irradiation 720 r) leading to death of 100% of the animals on the fifth to seventh day after irradiation; finally, in a very severe form of the disease (dose of irradiation 1440 r), causing death of all the animals on the third or fourth day after exposure.

The reactivity of the irradiated animals was investigated, paying consideration to the individual properties of the different anesthetics: the action of a type I anesthetic – ether – and of a type II anesthetic – hexobarbital – was studied [4].

Each of these anesthetics was investigated in narcotic and toxic doses.

Ether was administered by inhalation in a glass exsiccator for 15 minutes. Changes in reactivity were studied in relation to feebly narcotic (concentration in air of 0.2 ml/liter), narcotic (0.4 ml/liter) and toxic (0.6 ml/liter) doses of ether.

Hexobarbital was injected subcutaneously in the form of a 2% solution. The reactivity of the animals was investigated in relation to feebly narcotic (90 μg/g), narcotic (150 μg/g) and toxic (250 μg/g) doses of the drug.

The indices of reactivity were: the latent period of anesthesia, the duration of the anesthetic state and the percentage of animals which slept and died.

Not less than 20 mice were used in each series of experiments. The results obtained were treated statistically.

RESULTS

The observations showed that the reactivity of the irradiated animals in relation to anesthetics was significantly altered. The changes in reactivity bore a phasic character which depended on the period of the disease.

A feature common to all the anesthetics investigated was the presence of a phase of lowering of resistance to the narcotic action of the agents at the climax of the sickness, quite irrespective of the individual properties of the anesthetic and the severity of the radiation sickness. It is clear from Fig. 1 that the duration of ether and hexobarbital anesthesia in the irradiated animals at the climax of the radiation sickness was considerably increased over the control values. An increase in the duration of anesthesia was observed in all the forms of radiation sickness studied: in moderately severe, severe and very severe forms. This increase in the duration of anesthesia is one of the indices of a change in the resistance of the irradiated animals in relation to anesthetics. Similar results were obtained by other authors in their investigations [1, 2, 6].

At other periods of the disease the reaction of the irradiated animal to anesthetics was dependent on a whole series of factors. The first of these factors is the specific properties of the anesthetics.

For instance, at the beginning of the latent period of moderately severe radiation sickness, i.e., immediately after irradiation with a dose of 360 r, a transient rise in resistance to the narcotic action of ether was observed – the duration of anesthesia in the irradiated animals was considerably shorter than in the controls.

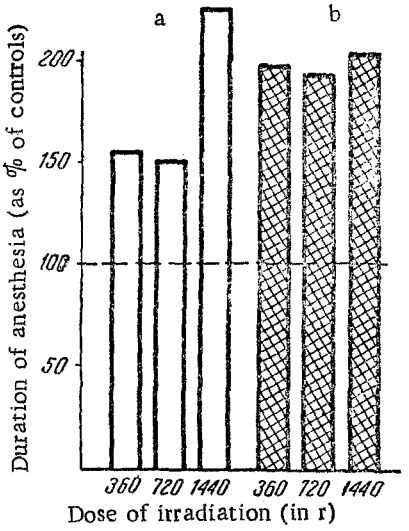

Fig. 1. Duration of ether and hexobarbital anesthesia during the climax of radiation sickness. Legend: white columns – duration of ether anesthesia; shaded columns – duration of hexobarbital anesthesia. Controls taken as 100%.

At the same time the resistance to the narcotic action of hexobarbital was unchanged (Fig. 2). On the other hand, 24 hours after irradiation a sharp rise in the resistance to the narcotic action of hexobarbital was observed (the irradiated animals were not plunged into a narcotic state after administration of hexobarbital in a dose of 90 μg/g, whereas control animals were in a state of narcosis). The resistance to ether, however, was indistinguishable from the controls at this period. Later, in the recovery period (28 days after irradiation with a dose of 360 r), however, in addition to the increased resistance of the irradiated animals to the narcotic action of hexobarbital, a fall was observed in the resistance to the narcotic action of ether (see Fig. 2). It should be pointed out that a relationship between the reaction of irradiated animals and specific, or perhaps group, characteristics of the anesthetic agent [4] has been observed by other investigators [1, 3, 5, 7].

The second factor influencing the reactivity of the irradiated animals to anesthetics is the severity of the radiation sickness.

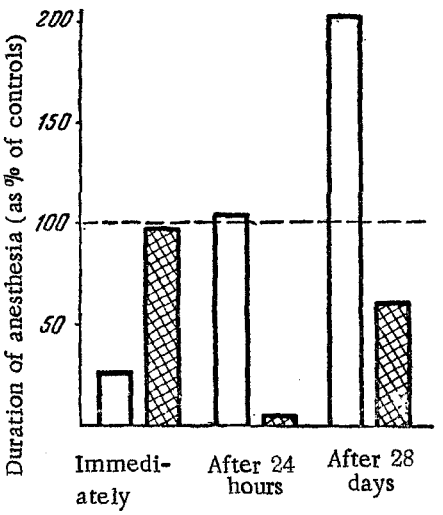

Fig. 2. Change in the reactivity of animals irradiated with 360 r to different anesthetics at various periods after irradiation. Legend: white columns – duration of ether anesthesia; shaded columns – duration of hexobarbital anesthesia.

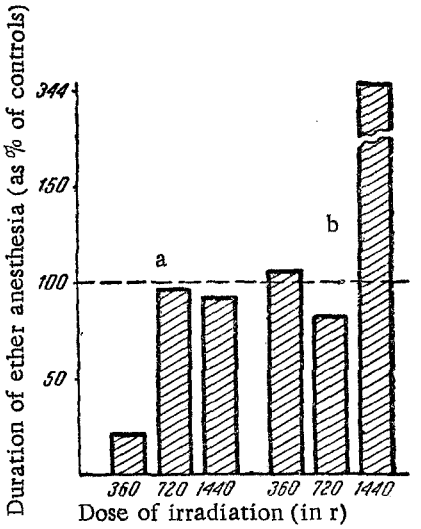

Fig. 3. Change in the reactivity of irradiated animals to ether, depending on the severity of the radiation sickness. a) Immediately after irradiation; b) 24 hours after irradiation.

By way of example, we may cite the data on the change in the resistance of the irradiated animals to the narcotic action of ether. The increased resistance to the narcotic action of this agent, found at the beginning of the latent period of radiation sickness of moderate severity, was not observed in the more severe forms of sickness (Fig. 3).

Differences were also found in the change in reactivity, especially in relation to ether, in severe and very severe forms of radiation sickness. For instance, 24 hours after irradiation, in the severe form of radiation sickness (720 r) the reactivity of the animal to ether was indistinguishable from that of the controls. In the very severe form of radiation sickness (1440 r), however, a considerable increase in the sensitivity to the narcotic action of ether was observed – the irradiated animals were much longer in a state of narcosis than the animals of the control series (see Fig. 3).

The third factor determining the character of the reaction of the irradiated animal is the dose of the anesthetic.

The increase in the resistance of the animals to the action of ether, already observed in the latent period of radiation sickness of moderate severity, for instance, was much more pronounced after the action of a feebly narcotic dose of the anesthetic than after the action of a dose producing a state of deep narcosis. The subsequent fall in the resistance of the irradiated animals by comparison with the controls in the recovery period was also much more obvious when a feebly narcotic dose of ether was given.

This state of affairs may also be illustrated by the results obtained from an investigation of the reactivity of the irradiated animals to hexobarbital.

For example, 24 hours after irradiation with a dose of 1440 r, i.e., in the latent period of the very severe form of radiation sickness, a much greater increase in the duration of the latent time of anesthesia was observed after administration of a feebly narcotic dose (90 μg/g) of hexobarbital than after injection of the drug in a dose producing a state of deep anesthesia (150 μg/g). After the injection of hexobarbital in a toxic dose (250 μg/g) the duration of the latent time of anesthesia in the irradiated animals was the same as that in the controls.

In conclusion it must be stressed that the resistance of the irradiated animals to narcotic doses of anesthetics, and their resistance to toxic doses of the same agents, did not always change in a parallel manner. At the height of the severe and very severe forms of radiation sickness, for instance, a fall in the resistance to the narcotic action of ether was accompanied by an increase in resistance to its toxic effect. For example, after administration of ether in a toxic concentration, in the control series 90.9% of the animals died, whereas in the experimental series (3 days after irradiation with a dose of 1440 r) under the same conditions only 28.6% of the mice died.

SUMMARY

As shown in the work there is a marked change in the reaction of x-ray-irradiated white mice to anesthetics. These changes are phasic in character and depend upon the stage of the disease. At the height of the disease there is a rise of the sensitivity to anesthetics, irrespective of the animal's individual peculiarities and the severity of the disease. During other stages of radiation sickness the changes in the reactivity depend upon the specific features of the anesthetic used, its dose and the severity of the disease.

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