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Ionizing radiation, carbophos, and T-2 toxin combined effect on animals

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Abstract.

Rapid development of industry, including nuclear industry, intensification, and chemicalization of agriculture cause a sharp increase in the anthropogenic load on the biosphere with the impact of biological and toxicological factors in conditions of the increased radiation background. These factors combined, additive, synergistic, and inhibitory effects can be expected. The work is aimed to study the features of the combined effects of ionizing radiation, carbophos, and T-2 toxin, as well as to find the ways of animals' protection under their combined effects. The experiments studied the clinical condition, life expectancy, and peripheral blood picture. The features of ionizing radiation, carbophos, and T-2 toxin combined effect on the sheep were specified and the mutual strengthening of their influence on the body was shown. Clinical, hematological, immunological parameters, and pathoanatomical picture are more vivid in the case of a combined lesion than in the case of an isolated exposure to damaging factors.

Keywords: Ionizing radiation; carbophos; T-2 toxin; combined lesion; treatment

INTRODUCTION.

The increasing use of various sources of ionizing radiation in energy, industry, agriculture, and science was naturally predetermined by the scientific and technical process. Unfavorable environmental factors and the possibility of damage by biological agents pose a threat and probability of combined animal lesions under these conditions [1,2,3].

Combined radiation lesions occur with the simultaneous or sequential exposure to damaging factors characterized by mutual influence and differ in their course from the isolated lesions by the same factors. At the same time, the disease acquires qualitatively new signs as a result of the strengthening effect.

Combined lesions are usually severe. The time of the hidden period shortens and the pick period of the radiation sickness significantly prolongs, the hemorrhagic syndrome becomes more vivid, and the percentage of complications increases.

Violations of the neuroendocrine system and in hematopoiesis are recorded. Overall and local resistance to infection reduces. The activity of the bone marrow and lymphoid system elements is suppressed. The phagocytic activity of leucocytes and the function of immunobiological protective mechanisms are inhibited. Tissues barrier properties weaken. There is an increase in their permeability, weakening, or distortion of the inflammatory reaction, etc.

There are limited data on animal lesions by ionizing radiation and T-2 toxin in the literature. It was found that doses of T-2 toxin and ionizing radiation which do not cause mouse death under isolated exposure can cause deaths if used combined [4,5,6].

The animals' sensitivity to gamma rays is reduced in various ways. In particular, it is the use of radioprotective medicines causing the formation of endogenous radioresistance background. The immune system mobilization activates both humoral and cellular immunity factors. It has both local and general effects on the body, blocks the development of conditionally pathogenic microflora. The efficiency and optimal conditions for the hemosorption procedures application have been investigated to remove the early manifestations of the affected intoxication and to facilitate the subsequent course of acute radiation sickness [7,8,9] and immunocorrection [10,11].

Animals' treatment with mycotoxicosis includes the use of tonic agents, symptomatic therapy, and sorbents whose beneficial effect is associated with participation in the mineral metabolism regulation [12]. Therapy of poisoning by organophosphorus pesticides (OP) is based on the use of two groups of therapeutic medicines—cholinolytics and cholinesterase reactivators. It is successful if the complex therapy started in time, including measures to restore the function of breathing and blood circulation, symptomatic treatment, prevention of relapses and complications. The means of non-specific therapy include adrenolytics, antibiotics, vitamins, antihistamines, etc. However, methods of animals' combined lesions treatment by radiation, OP, and mycotoxins are hardly developed. They are either not always available or their dosage forms are not suitable for their effective use. Therefore, the search for methods and means of the body combined lesions treatment is relevant both theoretically and practically.

MATERIAL AND METHODS.

Thirty sheep of "Prekos" breed were used in the experiments. The average live weight is 37.5 ± 0.5 kg. Clinical conditions, life expectancy, and peripheral blood picture have been tested. Sheep blood was taken from the jugular vein. The degree of lipid peroxidation intensity (LPI) was defined by the malondialdehyde accumulation. The immune status of animals was determined by the state of cellular immunity.

Organophosphorus pesticide-malathion (ADV 50%) was used as a toxic substance. Crystalline T-2 toxin was added

as a 5% aqueous solution at the doses of 1/5 and 1/10 LD_{50} orally by means of a probe.

To solve the tasks, 30 sheep were divided into six groups of five animals each. Animals of the first group received T-2 toxin at a dose of 1/5 LD_{50}; sheep of the second group were irradiated at a dose of 2.0 Gy; in group 3, T-2 toxin was given at a dose of 1/5 LD_{50} + irradiation at a dose of 2.0 Gy; there was an inoculation with malathion at a dose of 1/5 LD_{50} in group 4; there was an inoculation with priming of T-2 toxin at a dose of 1/5 LD_{50} + irradiation at a dose of 2.0 Gy + priming with malathion at a dose of 1/5 LD_{50} in group 5; the sixth group served as a biological control.

Radiation sickness simulation was carried out by sheep irradiation on a gamma-ray machine (radiation source ^{137}Cs) at a dose of 2.0 Gy at an exposure dose rate of 6.2 R/minute.

Zoocarbum was used as the sorbent of T-2 toxin at the rate of 2 g/kg of body weight.

Sulfotozifan injected subcutaneously at a dose of 38 mg/kg was used to prevent acute radiation disease. Antidote AL-5, including cholinolytic A-2 (25 mg/kg), dipiroksim (12 mg/kg), sodium bromide (8 mg/kg), and glucose (10 mg/kg) were used in cases of malathion poisoning.

The tested agents' protective efficiency was evaluated by the survival of animals after irradiation and priming them with malathion and T-2 toxin.

RESULTS AND DISCUSSION.

Priming with T-2 toxin (group 1) and sheep irradiation at a dose of 2.0 Gy (group 2) caused rapidly passing nervous disorders—general inhibition and excitement. Body temperature, heart rate, and respiration fluctuated slightly within the physiological norm. There was a dilution of fecal masses for some animals. The palatability of feed did not change. There were no remarkable changes in the skin and visible mucous membranes. Periods of radiation damage and toxicosis were very weak clinically and only for some animals. There were no cases of animals' death in the group.

The animals injected with T-2 toxin and exposed to ionizing radiation (group 3) felt well, short-term periods of oppression were replaced by a rapidly passing excitation, feed palatability did not change at the beginning of the first week. A sharp deterioration in the general condition was recorded starting from the seventh day. Some sheep had shortness of breath and cough. The visible mucous membranes were hyperemic, with a bluish tinge. Serous effusions which later turned into serous-purulent were noticed from the nasal openings. Sheep were oppressed, refused to feed, and were lying for the most part. The survival rate in this group was 50%, the average life expectancy of the dead animals was 9.0 ± 1.5 days.

T-2 toxin, ionizing radiation, and malathion combined effect on sheep (group 5) led to an increase in the damaging factors which was characterized by a decrease in survival (25%), the average life expectancy of the dead animals (7.5 days), and changes in hematological parameters. Thus, the number of erythrocytes in all five experimental groups was within the biological control on the third day. The content of the red blood cells in groups 3 and 5 decreased and amounted to 77.1% and 76.3% from the control on day 7. There was a tendency to reduce their number in the subsequent terms of the study. There was a decrease in hemoglobin from day 7, which was 8.4% and 9% in groups 3 and 5. The hemoglobin level in these groups decreased in the subsequent study period and it was 78.3 ± 0.6 g/l and 77.2 ± 0.4 g/l at 95.2 ± 0.4 g/l in the biological control group on the 21st day.

The dynamics of the total protein content in the group of the combined affected sheep was characterized by a significant decrease in its level by the 21st and 28th days of the experience. The change in the number of leucocytes in the peripheral blood of the experimental sheep was more remarkable. Their number was 5.73 ± 0.23 in the group of combined lesions with T-2 toxin and ionizing radiation (group 3), while it was 5.60 ± 0.22 × 10^9/l at 8.78 ± 0.40 × 10^9/l for the healthy animals in the group of combined lesions with three pathogenic factors (group 5) on the third day. The decline in this indicator continued on the 14th day and amounted to 80.2 in groups; 75.6%; 53.3%; 80.6%, and 51.0% from the control group.

The amount of malondialdehyde (MDA) increased by 1.8–3.2 times after the combined exposure from the third day. A significant increase in this indicator was noted in the third and fifth groups. The MDA content in erythrocyte hemolysate was 6.88 ± 0.36 and 7.92 ± 0.37 on the third day at 2.23 ± 0.17 μmol/ml. It was 8.56 ± 0.77 and 9.12 ± 0.37 at 4.57 ± 0.27 in blood plasma in the control group. The level of MDA in the hemolysate of the red blood cells has reached the original values by the end of the term of studies. The third group of sheep where it exceeded the control by 3.3 and 2.4 times was an exception. This index in the erythrocyte hemolysate and in the blood plasma exceeded the one in the biological control group by 4.7 and 2.9 times in the fifth group on the 28th day.

Experiments for tools testing and the development of the animals' protection scheme at the combined lesion of ionizing radiation, malathion, and T-2 toxin performed on 12 sheep were divided according to the principle analogs into three groups (Table).

The table shows that the tested medicines use resulted in 100% survival rate of the poisoned animals and 50% death of untreated sheep poisoned with toxicants.

The use of therapeutic and preventive agents greatly facilitated the course of the combined lesion, smoothed its clinical manifestation, reduced shifts in the blood system, such as fewer changes in the number of red blood cells, hemoglobin level, hematocrit, and total protein content.

As it was stated in the leucogram, the decrease in the total number of leucocytes due to lymphocytes with a simultaneous increase in the percentage of neutrophils, especially their young forms—young and rod cells—followed immediately after the combined exposure. The content of lymphocytes both for the treated and untreated animals decreased from the third up to the seventh days inclusively. More vivid changes occurred in the first group of animals (combined effect of ionizing radiation, malathion, and T-2 toxin). Treated animals' differences in outcomes have not been traced on the 21st day. Its rate was 43.5 ± 2.3 in the group of combined lesions without

treatment, while it was 66.0% ± 2.6% in the group of biological control. Treated animals did not differ from the control ones and it was 64.4% ± 1.5% by the 28th day.

The content of MDA and cellular immunity factors for the sheep of the second group were at the level of initial rates. The increased level of MDA in the first group was observed on the 14th day twice exceeding the control rates. The level of MDA in erythrocyte hemolysate and blood plasma in group 1 was 2.22 and 2.06 times higher, respectively, by the end of the study period. Thus, MDA content in the blood of the treated sheep exposed to combined lesions was less obvious and returned to the normal state faster.

There was a significant decrease in T-lymphocytes (by 23.7%) in the peripheral blood of the affected sheep in the initial period. Subsequently, there was a decrease in the number of T-cells, which on the 14th day was 23.05 ± 0.11 at 28.5 ± 0.51 for the treated animals and 37.13% ± 0.45% for the biological control group. There was an increase in the number of T-lymphocytes from the 21st day.

Sheep exposed to the combined effect of the damaging agents showed a significant decrease in B-cells on the seventh day and their gradual recovery began from the 14th day (especially in the group of protected and treated animals). At the same time, a fast rate of B-cell recovery compared to T-cells was noted at an early stage.

Thus, high efficiency of the product sulfotozifan, antidote AL-5, zoocarbum and their positive effect on survival, life expectancy, the rate of hematological parameters recovery, and the number of T- and B-cells in the sheep combined lesion have been obtained during the experiments.

CONCLUSION.

The damaging effect of mutual strengthening of physical (ionizing radiation), chemical (malathion) and biological (T-2 toxin) factors in their combined application was revealed. The combined effect of ionizing radiation at a dose of 5.0 Gy, T-2 toxin, and malathion at a dose of 1/5 LD_{50} compared with a separate lesion led to changes in clinical and hematological (decrease in the number of leucocytes by 58%, erythrocytes by 24%, and hemoglobin by 26%), biochemical (increase in MDA content by 4.2 times) and immunological (decrease in the number of T-lymphocytes by 3.5 times, for B-cells it was by 65%) indicators. It reduces survival and the average life expectancy of the dead animals.

The optimal scheme of animals' protection exposed to the combined lesions has been worked out for the first time. It is aimed at the prevention of radiation injuries, treatment of malathion poisoning, binding and excretion of T-2 toxin, and provides animals' protection.

The use of the sulfotozifan (subcutaneously) at a dose of 38 mg/kg, antidote AL-5 (intramuscularly) at a dose of 2–3 ml and zoocarbum at a rate of 2 g/kg of animals live weight with a combined lesion by ionizing radiation, malathion, and T-2 toxin has a positive effect on the clinical conditions. It normalizes clinical and hematological parameters, increases the number of T- and B-lymphocytes, and inhibits the processes of LPI. The use of the specified means allows to expand the animals' protection means from the combined lesion for the purpose of receiving environmentally safe livestock products.

Table - Sheep survival exposed to combined ionizing radiation (2.0 Gy), malathion (1/5 LD_{50}), T-2 toxin (1/5 LD_{50}) and the use of treatment.

Group	Exposure	Dose	Qty of animal, heads	Died-off (heads)	Survived (heads)	Survival rate, %	Medium lifespan (days)
1	Irradiation + malathion + T-2 Toxin	2.0 Gy + 1/5 LD_{50} + 1/5 LD_{50} +	4	2	2	50	9.0 ± 1.0
2	Sulfotozifan + irradiation + malathion + AL-5 + T-2 toxin + zoocarbum	38 mg/kg + 2.0 Gy + 1/5 LD_{50} + 3 мл 1/5 LD_{50} + 2 g/kg	4	-	4	100	-
3	Biol. control	-	4	-	2	100	-

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