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R E P O R T

on the performed research work on the topic "Investigate the radioprotective properties of the drug VS-1 (tablets Donovit-VS)"

Topic section: "Research on the effect of the drug of the VS-1 preparation on the hematopoietic system of irradiated animals."

The work was carried out jointly in the Laboratory of Radiation Biochemistry (Leading Researcher, Doctor of Biology, Prof. Ya.I. Serkiz) and the Laboratory of Radiation Cytology (Head of the Laboratory, Doctor of Biology G.M. Chobotko) of the Institute of Experimental Radiology Scientific Center for Radiation Medicine of the Academy of Medical Sciences of Ukraine.

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Materials and methods.

Male Wistar rats were used in the experiments. Animals were irradiated with X-rays using a RUM-17 apparatus at the Institute of Oncology of the Academy of Medical Sciences of Ukraine. The exposure dose rate was 0.529 mA/kg. Animals were given VS-1 preparation once every day for 30 days before irradiation. The single dose was twice the dose recommended for humans and calculated on the body weight of the animal (150 ± 20 g). The drug was given to animals in the form of an aqueous solution in the amount of 10 ml per animal per day.

The animals in the experiment were divided into 9 groups, similarly to the previous section of the topic:

1 - control (intact) rats;

2 - irradiated at a dose of 3 Gy;

3 - irradiated at a dose of 3 Gy + preparation VS-1;

4 - irradiated at a dose of 5 Gy;

5 - irradiated at a dose of 5 Gy + preparation VS-1;

6 - irradiated at a dose of 6 Gy;

7 - irradiated at a dose of 6 Gy + preparation VS-1;

8 - irradiated at a dose of 7 Gy;

9 - irradiated at a dose of 7 Gy + preparation VS-1.

The initial number of animals in each group was 100 pcs. Later, as the animals died due to their radiation death, especially at lethal doses, the number of animals in the groups decreased (according to Table 1 of the previous report on this topic).

The state of peripheral blood was studied in all experimental groups of animals, as well as in the control (non-irradiated) group. The studies were performed in dynamics: before irradiation, then on the 1st, 4th, 8th, 16th and 30th days after irradiation - i.e. in critical terms of development of radiation changes, which are established in classical radiobiology /2.3.4/. Blood for the study was taken from the tail vein of the animals.

The following blood parameters were studied: the number of erythrocytes, leukocytes, neutrophils, monocytes and lymphocytes in 1 mm cube of blood, as well as the amount of hemoglobin - the indicators were expressed in absolute units

according to the generally accepted principle in terms of 1 liter of blood. In addition to the composition of peripheral blood, the mitotic activity of bone marrow cells was studied in terms of the mitotic index using the thymidine label /1.4./. Bone marrow for research was taken from the femur of rats /1/. Mitotic activity was expressed as a percentage of the total amount of cells.

The research results were statistically processed on a personal computer using the M8 Excel 2000 application package.

Research results.

The results of studies of the composition of peripheral blood and the mitotic activity of bone marrow cells of rats irradiated at different doses, as well as irradiated animals using VS-1, are presented in Tables 1-4. Experimental data make it possible to compile the following picture of radiation damage at specific doses of radiation used.

A dose of 3 Gy (Table 1) causes changes only in the average values of such indicators as the number of erythrocytes, hemoglobin and neutrophils. These changes are statistically unreliable in relation to the norm. However, the use of the drug VS-1 leads to the normal listed indicators. As for the other indicators (leukocytes, monocytes, lymphocytes and mitotic index), a dose of 3 Gy causes a statistically significant decrease on the 1st, 4th and 8th days after exposure to radiation. The VS-1 preparation leads to the norm of the indicated indicators (in the tables, an asterisk indicates statistically significant changes in these indicators associated with the action of the drug, in relation to the value of the indicators, the changes of which are due to radiation exposure). It should be noted that a dose of 3 Gy is minimally lethal and, according to our data, is LD 2/30. The use of VS-1 at this dose resulted in no death of the animals. At the same time, according to the data obtained, all the studied parameters of blood and mitotic activity of bone marrow cells are normalized.

A dose of 5 Gy (LD 17/30 - 17% of animals die by the 30th day after irradiation) causes more significant radiation disturbances in the content of all studied peripheral blood cells (Table 2):

a statistically significant increase in the number of erythrocytes and hemoglobin on the 1st day and a decrease in these indicators on the 16th day;

statistically significant and significant decrease in the content of other elements blood (leukocytes, neutrophils, monocytes and lymphocytes) in all periods of research with maximum deviations on the first day;

statistically significant decrease (by 3 times) in the ability of bone marrow cells to division according to the mitotic index.

The use of the drug VS-1 at this dose reduces the death of animals by 3 times to LD 5/30. This is accompanied by a statistically significant normalization of the number of erythrocytes, hemoglobin and lymphocytes in the blood. There is also a statistically significant increase in the content of leukocytes, neutrophils and monocytes in relation to their significant decrease associated with the action of radiation. However, these indicators do not return to normal, which is especially characteristic in the earliest post-radiation periods - the 1st and 4th days. The VS-1 preparation significantly increases the mitotic activity of bone marrow cells in all periods of research - in the most critical periods for the body on the 1st and 4th days, this indicator improves (almost doubles).

A dose of 6 Gy (LD 50/30 - 50% of animals die by the 30th day after radiation exposure) causes significant radiation disturbances in the hematopoietic system (Table 3). The use of the BC-1 drug only leads to a tendency to normalize individual blood parameters. However, these changes, although directed towards normalization, are statistically unreliable and insignificant in magnitude. Despite the fact that at this dose of radiation, the VS-1 drug still increases the survival rate of animals by 24%, but in terms of the composition of peripheral blood and the mitotic activity of bone marrow cells, its anti-radiation efficacy is insignificant.

After irradiation of animals at a dose of 7 Gy (LD 83/30), the radioprotective properties of the VS-1 preparation in terms of blood and mitotic activity of bone marrow cells (Table 4), as well as in terms of animal survival, do not appear.

Table 1. Changes in the cellular composition of peripheral blood and mitotic activity of bone marrow cells in rats irradiated with X-rays at a dose of 3 Gy and also irradiated after the action of the VS-1 preparation.

Experience conditions. Time after irradiation,	Erythrocytes, 10^{12} /l.	Hemoglobin, g/l	Leukocytes, 10^9 /l	Neutrophils, 10^9 /l	Monocytes, 10^9 /l	Lymphocyte, 10^9 /l	Mitotic index, %
Control (non-irradiated)	8,4 ± 0,5	139±12	14,5±1,8	3,7±0,5	5,1±0,4	11,3±1,7	6,3±+0,7
Irradiated 3 Gy 1 day	8,9±0,7	145±14	6,0±0,5	3,3±0,4	3,6±0,2	8,2±0,8	4,5±+0,3
4 days	8,5±0,9	138±15	6,3±0,4	3,5±0,5	3,5±0,4	9,7±1,1	4,9±+0,4
8 days	7,4±0,8	125±13	9,4±1,1	3,6±0,5	3,8±0,3	10.3±1,2	5,5±+0,6
16 days	8,3±0,8	138±16	11,6±1,2	3,7±0,3	4,1±0,5	10,8±0,9	5,8±+0,7
30 days	9,0±1,1	141±17	13,9±1,4	3,6±0,5	4,4±0,4	11,1±1,3	5,7±+0,6
Irradiated 3Gr+VS-1 1 day	8,5±0,9	138±15	12,9±1,4*	3,5±0,5	5,0±0,7*	10,9±1,2*	5,6±0,6*
4 days	8,4±0,9	139±11	13,4±1,3*	3,8±0,3	4,8±0,4*	11,4±1,3	6,5±0,7*
8 days	8,2±1,1	140±12	14,5±1,5*	3,6±0,4	5,1±0,6*	11,2±1,1	6,2±0,8
16 days	8,3±1,0	141±14	13,9±1,6	3,7±0,4	5,5±0,5*	12,5±1,4	6,9±0,6
30 days	8,7±0,8	139±13	14.4±1,4	3,8±0,3	5,2 ± 0,6	12,2 ± 1,3	7,0± 0,8

Table 2. Changes in the cellular composition of peripheral blood and mitotic activity of bone marrow cells of rats irradiated with X-rays at a dose of 5 Gy and also irradiated after the action of the VS-1 preparation.

Experience conditions. Time after irradiation, days	Erythrocytes, 10^{12} /l.	Hemoglobin, g/l	Leukocytes, 10^9 /l	Neutrophils, 10^9 /l	Monocytes, 10^9 /l	Lymphocyte, 10^9 /l	Mitotic index, %
Control	8,4 ± 0,5	139 ±12	14,5 ± 1,8	3,7 ± 0,5	5,1± 0,4	11,3 ± 1,7	6,3 ± 0,7
Irradiated 5 Gy							
1 days	10,1 ± 0,8	171 ± 16	2,1 ± 0,3	1,1 ±0,2	1,7± 0,2	5,8 ± 0,7	2,1 ± 0,3
4 days	8,4 ± 0,7	139 ±15	2,3 ± 0,4	1,5± 0,2	1,9 ± 0,1	6,0 ± 0,6	2,3 ± 0,4
8 days	6,5 ± 0,4	102 ± 9	3,4 ± 0,3	1,7± 0,3	1,8± 0,3	5,9± 0,4	2,8 ± 0,3
16 days	7,7 ± 0,8	125±13	5,9 ± 0,5	2,4 ±0,4	1,7± 0,3	6,5 ± 0,8	4,4 ± 0,6
30 days	9,6 ± 1,1	145 ± 14	9,8 ± 1,1	3.5 ± 0,3	2,2 ± 0,4	7,1 ± 0,7	6,3 ± 0,8
Irradiated 5 Gy + VS-1							
1 day	9,0 ± 0,7	142 ± 15	8,3 ± 0,9*	2,4 ± 0,3*	3,9 ± 0,6*	11,5 ± 1,2*	4,8 ± 0,5*
4 days	8,4 ± 0,9	143 ± 16	7,9 ± 0,8*	2,7 ± 0,4*	4,2 ± 0,4*	10,9± 1,2*	5,3 ±0,7*
8 days	7,6 ± 0,8	125 ± 11*	7,6 ±0,8*	3,2 ± 0,3*	4,8 ±0,5*	12,3 ± 1,4*	4,9 ± 0,6*
16 days	8,0 ± 0,9	132 ± 14	11,9 ±1,3*	3,5 ± 0,5*	5,3 ± 0,7*	12,8 ± 1,3*	5,7 ± 0,8
30 days	8,7 ± 1,0	138 ± 13	12,5 ± 1,4*	3,8 ± 0,5	5,5 ± 0,6*	13,4± 1,1*	6,6 ± 0,9

Table 3. Changes in the cellular composition of peripheral blood and mitotic activity of bone marrow cells of rats irradiated with X-rays at a dose of 6 Gy and also irradiated after the action of the VS-1 preparation.

Experience conditions. Time after irradiation, days	Erythrocytes, 10^{12} /l.	Hemoglobin, g/l	Leukocytes, 10^9 /l	Neutrophils, 10^9 /l	Monocytes, 10^9 /l	Lymphocyte, 10^9 /l	Mitotic index, %
Control	8,4 ±0,5	139 ± 12	14,5 ± 1,8	3,7 ±0,5	5,1 ±0,4	11,3± 1,7	6,3 ±0,7
Irradiated 6 Gy							
1 days	10,4 ± 1,3	176 ± 16	1,9 ±0,2	0,9 ±0,1	1,3 ±0,4	5,0 ± 0,7	1,7± 0,2
4 days	8,2 ±0,9	133 ±13	2,0 ± 0,3	1,2 ±0,3	1,6 ±0,1	5,3 ± 0,6	2,0 ± 0,3
8 days	6,3 ±0,7	91 ±10	2,3 ± 0,3	1,6 ±0,2	1,5 ±0,2	5,6 ± 0,7	3,7 ±0,5
16 days	7,5 ±0,8	120 ± 13	4,1 ±0,6	1,9 ±0,3	1,8 ±0,3	5,9 ± 0,7	4,1 ±0,6
30 days	8,7 ± 0,8	142 ± 15	7,0 ± 0,9	2,2 ±0,4	1,9 ±0,3	6,3 ± 0,9	4,8 ±0,5
Irradiated 6 Gy + VS-1							
1 day	10,1 ± 1,2	169 ± 18	2,3 ± 0,4	1,1 ±0,3	1,5 ±0,3	5,3 ± 0,6	1,9 ±0,3
4 days	8,4 ±0,9	131±15	2,1 ±0,3	1,2 ±0,2	1,4 ±0,2	5,1 ±0,8	1,6± 0,2
8 days	6,6 ±0,7	98 ± 11	2,6 ±0,5	1,5 ±0,4	1,7 ±0,3	6,2 ±0,9	3,8 ±0,5
16 days	7,6 ±0,8	119± 12	4,5 ±0,7	2,0 ± 0,3	2,0 ± 0,4	6,0 ±0,5	4,0 ±0,4
30 days	8,9 ± 1,0	140 ± 16	7,4 ± 1,0	2,1 ±0,4	1,8 ±0,2	5,9 ± 0,7	4,7 ±0,6

Table 4. Changes in the cellular composition of peripheral blood and mitotic activity of bone marrow cells of rats irradiated with X-rays at a dose of 7 Gy and also irradiated after the action of the BC-1 preparation.

Experience conditions. Time after irradiation, days	Erythrocytes, 10^{12} /l.	Hemoglobin, g/l	Leukocytes, 10^9 /l	Neutrophils, 10^9 /l	Monocytes, 10^9 /l	Lymphocyte, 10^9 /l	Mitotic index, %
Control	8,4 ±0,5	139 ±12	14,5 ± 1,8	3,7 ± 0,5	5,1 ± 0,4	11,3 ± 1,7	6,3 ± 0,7
Irradiated 7 Gy 1 days	10,6 ± 1,7	185 ± 16	1,7 ± 0,2	0,7 ± 0,1	1,0 ± 0,2	4,7 ± 0,6	1,4 ±0,2
4 days	7,8 ±0,9	127 ± 14	1,9± 0,3	0,9 ± 0,1	1,1 ±0,2	5,1 ± 0,7	1,8 ±0,3
8 days	6,2 ±0,7	86 ± 13	2,0 ± 0,3	1,2 ±0,2	1,3 ±0,3	4,9 ±0,7	2,5 ±0,3
16 days	7,3 ± 0,9	113± 15	2,5 ± 0,4	1,5 ±0,3	1,2 ±0,3	5,2 ± 0,8	2,9 ± 0,4
30 days	7,8 ±1,1	125 ±12	4,2 ±0,6	1,3 ±0,3	1,6 ±0,2	5,8 ±0,9	3,0 ±0,5
Irradiated 6 Gy + VS-1							
1 day	10,7 ±1,4	188 ±21	1,6 ±0,3	0,8 ±0,1	0,9 ±0,2	4,6 ±0,7	1,2 ±0,1
4 days	7,6 ±0,9	129 ± 15	2,1 ±0,4	0,9 ±0,2	1,2 ±0,3	4,9 ± 0,5	1,9 ±0,3
8 days	6,3 ±0,7	87 ± 11	2,3 ± 0,3	1,3 ±0,2	1,0± 0,2	5,2 ± 0,7	2,7 ± 0,5
16 days	7,2 ±0,8	116 ± 15	2,8 ±0,5	1,4 ±0,3	1,5± 0,3	5,1 ± 0,6	3,1 ± 0,6
30 days	7,9 ± 0,6	122 ± 11	4,2 ± 0,4	1,6 ±0,4	1,7± 0,3	5,7 ±0,8	2,8 ± 0,4

Conclusions:

1. The VS-1 preparation exhibits radioprotective properties in terms of the cellular composition of peripheral blood and the mitotic activity of bone marrow cells of irradiated animals in the range of absorbed radiation doses up to 5 Gy.
2. Irradiation of animals at a dose of 6 Gy (LD 50/30) against the background of the action of the BC-1 preparation only leads to a tendency to normalize the studied parameters, which at the same time is insignificant, which indicates the absence of a sufficiently acceptable radioprotective efficacy.
3. At an irradiation dose of 7 Gy (LD 80/30), VS-1 is ineffective.
4. The dynamics and nature of hematopoiesis recovery (according to the studied indicators) in the early critical post-radiation periods for the body indicates the promising use of the BC-1 preparation as a radioprotector in the range of radiation doses up to LD 50/30.

Literature.

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