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Study of NOS-inhibitors effectiveness in therapy of combined radiation injuries

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In case that the ionizing radiation is an inherent part of human life, there is the risk of radiation accidents, accompanied by explosions, fires and radionuclide emissions. This is dangerous not only due to radiation exposure, but also thermal burns, mechanical and chemical influences. Each of these component significantly burdens manifestations of acute radiation sickness, and increases the likelihood of fatalities. Our medical research center, A. Tsyb MRRC, has extensive experience research in the province of searching tools therapy of combined radiation-thermal injuries (CRTI). Recently, we have obtained our own data about the high efficiency of NOS-inhibitors from the class of N, S-of substituted derivatives of isothiourea, both as radioprotectors, and as radiomitigators, that suggests its high perspective in the treatment of combined radiation, in particular radiation-thermal injuries.

The investigations have been done in male mice F1 [CBA×C57BL6j], 12 animals per group. Mice exposed to lethal doses of 6 Gy and 10 Gy γ -radiation of 60Co at a dose rate of 0.4 - 0.8 Gy/min. Combined injury included total body γ - irradiation at a dose of 7 Gy and III B degree thermal burn of 10 % body surface with the aid of powerful flash light. Mice of experimental groups were injected with NOS inhibitors at dose of 1/8 LD16. The effectiveness of NOS inhibitors were studied using 30-day survival test and survival of endogenous colony-forming cells in the bone marrow.

Research results of radioprotective properties of NOS inhibitors have shown its high efficiency (60-75% survival) in relatively low doses (1/8 LD16). Moreover, the use of NOS inhibitors before the radiative forcing 3-3,5 times increased the survival of hematopoietic colony-forming cells in the bone marrow.

On the model of combined radiation-thermal injuries we demonstrate that the use of NOS inhibitors after 5 minutes and 4 hours after the combined injury increased the survival of animals to 90-100%, whereas in the control group the survival rate was only 20%.

These studies have shown high promise NOS inhibitors as radioprotective tools and treatments of combined radiation-thermal injuries.

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