Radioprotective Effect of Cystamine and Heparin in Mice with Different Resistance

B. P. Lukashin and G. A. Sofronov

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The antiradiation effect of the short-acting radioprotector cystamine does not depend on the initial level of radioresistance. The radioprotective action of heparin is the higher the lower the level of the defense and adaptive mechanisms, that is, it depends on genetically determined characteristics of the organism.

Key Words: *cystamine; heparin; irradiation; radioresistance*

Published reports indicate that the effects of immunomodulators and antihypoxants on resistance to infection and hypoxia are governed by genetically determined characteristics of immunity and metabolism [2,7]. In order to disclose such a relationship in the effects of radioprotectors, we compared the antiradiation effects of cystamine and heparin in mice with different levels of radiosensitivity.

MATERIALS AND METHODS

Cystamine (a typical short-acting radioprotector) and heparin as an agent increasing the nonspecific resistance of the organism were used as radioprotectors. In order to determine the optimal times of injecting heparin as a radioprotector, experimental animals (outbred male albino mice and male albino rats) were exposed to short-term γ-radiation with ^{60}Co at a dose of 0.2 Gy/min. Heparin was injected intraperitoneally in single doses of 250 or 500 U/kg at various times before exposure: from 15 min to 30 days. For disclosing the genotypic features in the reaction of the organism to radioprotective agents, experiments were carried out on radioresistant hybrid (CBA×C57Bl/6) F_1 mice, radiosensitive BALB/c mice, and outbred albino mice intermediate in terms of radiosensitivity, all of these weighing 19 to 22 g and kept under standard conditions. In these experiments the animals were irradiated with an RUM-17 device (180 kV, 15 mA, 0.5 mm Cu+1.0 mm Al, 0.65 Gy/min). Cystamine was injected intraperitoneally in a dose of 150 mg/kg 15 min before the exposure, heparin 5 days before. Control animals were injected normal saline at the same times. The efficacy of the agents was assessed from the 30-day survival of irradiated animals. The DRF parameter was used for quantifying the antiradiation activity of the radioprotectors. The results were processed using probit analysis.

Military Medical Academy, St. Petersburg

RESULTS

The efficacy of heparin injected at various times before irradiation was studied in preliminary experiments. With exposure to a dose of 7 Gy, that is, $CD_{75/30}$, preventive injection of heparin improved the survival of animals. The radioprotective effect in such a case developed 1 day after injection of the agent (the survival being 60%) and persisted for a month (Fig. 1). Injection of the agent using the schedule traditional for protectors was ineffective. Doubling the heparin dose to 500 U/kg also failed to lead to a corresponding increase of the survival. This means that the mechanism of the radioprotective effect of heparin is different from that of sulfur-containing radioprotectors.

In order to be certain that the prolonged radioprotective effect of heparin is not specific to a

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TABLE 1. Effects of Cystamine and Heparin on the Survival of Irradiated Mice with Different Levels of Radioresistance

Experimental conditions	Radiation dose, Gy								
	4	5	6	7	8	9	10	11	12
Outbred albino mice									
Control		9/17*	10/20	2/20	2/20	0/10			
Cystamine				18/24	10/24	12/24	4/24	1/12	
Heparin		15/19	13/20	8/20	4/19	4/19	1/10		
BALB/c mice									
Control	14/20	8/20	6/20	2/20	0/11				
Cystamine		18/20	16/20	12/19	8/20	4/20	0/10		
Heparin	18/20	18/20	10/20	4/20	0/10				
Hybrid (CBA×C57Bl/6) F_1 mice									
Control		16/16	16/20	10/20	4/20	0/12			
Cystamine					19/22	16/20	8/20	2/18	0/15
Heparin		15/15	17/20	12/20	8/20	2/20			

Note. Numerator: number of surviving animals; denominator: number of irradiated mice.

certain animal species, experiments on rats were carried out. Animals were exposed to a dose of 7.5 Gy equal to $CD_{80/30}$. The results confirmed the efficacy of heparin as an agent increasing the radioresistance of the organism for a long period (Fig. 1).

In the next series of experiments we compared the antiradiation activity of cystamine and heparin in mice with different levels of radioresistance. The results are presented in Table 1.

Heparin did not affect the survival of radioresistant hybrid mice in our experiments. On the other hand, injection of heparin to radiosensitive BALB/c and outbred albino mice increased the survival of animals in comparison with the control. Cystamine was effective in all groups of animals.

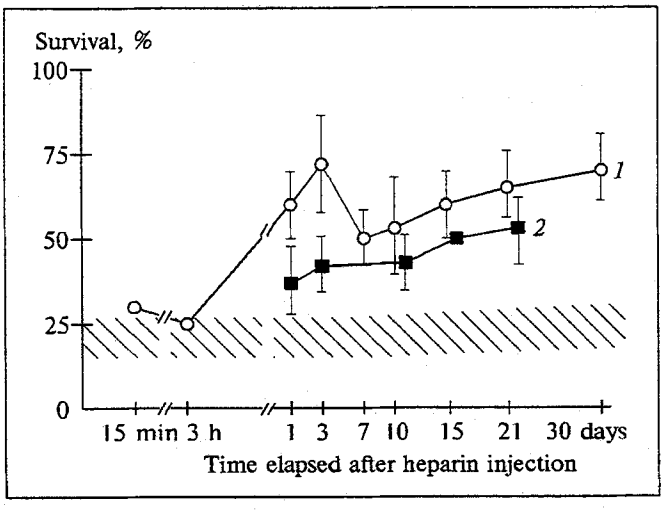

Fig. 1. Effect of heparin on the survival of irradiated white mice (*1*) and rats (*2*). Cross-hatched area: survival of animals in the control.

TABLE 2. Antiradiation Activity of Cystamine and Heparin in Experiments on Mice with Different Levels of Radioresistance

Animals	$CD_{50/30}$, Gy	DRF	
		cystamine	heparin
Outbred albino mice	5.8	1.47	1.16
BALB/c mice	5.0	1.50	1.20
(CBA×C57Bl/6) F_1 mice	6.9	1.48	1.06

Probit analysis allowed us to estimate the $CD_{50/30}$ and DRF values of the agents (Table 2). The results indicate that the antiradiation activity of cystamine virtually does not depend on the level of radioresistance of the organism. Contrary to this, the magnitude of the radioprotective effect of heparin is directly governed by genetically determined characteristics of the organism.

The results confirm that the resistance of the organism to radiation under conditions of chemical protection (cystamine) is due not so much to the labilization of the endogenous defense resources, as to suppression of the systems actively contributing to the development of the primary postirradiation processes [1,5,6,10]. This evidently explains the similar DRF value of cystamine for mice of different strains.

Heparin as a biological protector evidently activates the genetically determined potential of the organism [3,4,8,9]. Its radioprotective effect is the higher the lower the initial level of the organism's defense and adaptive mechanisms.

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Detection of *Chlamydia trachomatis, Mycoplasma hominis,* and *Ureaplasma urealyticum* by Polymerase Chain Reaction in Men and Women with Genital Diseases

A. V. Zhdanov, E. V. Malinina, O. V. Burmenskaya, L. Z. Faizullin, V. I. Kulakov, G. T. Sukhikh, M. Yu. Brodskii,* V. M. Govorun,* and E. M. Khalilov

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Polymerase chain reaction was clinically used to diagnose chlamydial and mycoplasma infection in the cervix and male urethra. Examinations of 2260 patients with disorders of reproductive function detected *C. trachomatis, M. hominis,* and *U. urealyticum* in 32.9, 9.7, and 25.7% of cases, respectively. A high incidence of mixed nongonococcal urogenital infections was observed, particularly in women. Seasonal fluctuations were shown in the detection rates of chlamydial and ureaplasmic infections.

Key Words: *polymerase chain reaction; C. trachomatis; M. hominis; U. urealyticum; mixed urogenital infections*

Independent clinical studies carried out in different countries have shown that in 50 to 90% of cases disorders of reproductive function are caused by mixed infections of the urogenital tract, the most common of which are nongonococcal infections, specifically, chlamydial and mycoplasmic [1,2,7-9,11]. The prolonged asymptomatic course and multiple clinical manifestations greatly impede the symptomatic diagnosis of these diseases. Traditional immunological methods of analysis are not always effective either, as these infections are usually latent. Isolation of the agent in a cell culture is expensive and laborious, making such a procedure difficult for routine laboratory diagnosis.

Advances in biotechnology have led to the development of highly sensitive and specific methods for the diagnosis of infections, based on unique properties of their agent's genome, one of these methods being polymerase chain reaction (PCR). PCR has been shown to be not inferior to the classical cell culture method in its basic parameters and

Research Center of Obstetrics, Gynecology, and Perinatology, Russian Academy of Medical Sciences; Research Institute of Physicochemical Medicine, Ministry of Health and the Medical Industry of Russia, Moscow

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