ARTERIOLAR REACTIVITY OF RAT SKELETAL MUSCLE TO NORADRENALIN AFTER WHOLE-BODY GAMMA-IRRADIATION IN A DOSE OF 1 Gy

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UDC 615.849.114.065:616.74-008.94-092.9-07

KEY WORDS: ionizing radiation; noradrenalin; arterial blood pressure; skeletal muscular arterioles; spontaneous vasomotor reactions.

The clinical study of vascular effects of radiation lesions indicates the appearance of phenomena of an astheno-neurotic character in irradiated persons, with a tendency toward fluctuations of blood pressure [2]. We know that if allowable levels of irradiation are exceeded and signs of radiation sickness appear, lasting symptoms of neurocirculatory dystonia may develop, sometimes accompanied by peripheral circulatory failure [3, 5, 6]. Marked and rapidly developing changes in the cerebral circulation have been found in rats receiving irradiation in doses of 10 Gy [11]. The circulation of the intestinal wall of rats responds just as rapidly to full-body irradiation in a dose of 5-10 Gy [8]. Responses of the peripheral vessels to small doses of irradiation, below the level causing the bone marrow syndrome of radiation sickness, have not been adequately studied.

The aim of this investigation was to study reactions of the peripheral circulation of rats receiving whole-body irradiation in a dose of 1 Gy, which does not lead to the appearance of signs of radiation sickness [1].

EXPERIMENTAL METHOD

Male Wistar rats weighing 200-315 g were irradiated on the ROKUS-M gamma-therapy apparatus, with a dose rate of 0.96 Gy/min. The animals were kept in individual plastic constraining containers. Whole-body irradiation was given consecutively in opposite (cranial and caudal) directions. The absorbed dose was 1 Gy. Measurements made with a type 27-012 dosimeter with No. 2018 spherical chamber in similar containers, filled with water dummies, showed that nonhomogeneity for absorbed dose in the irradiated volume does not exceed 3%. Vessels of the skeletal muscles possess developed mechanisms of nervous and myogenic regulation [4, 9], and for that reason, the vascular bed of the extensor hallucis muscle of the hind limb was chosen for investigation. Experiments were carried out on control (six rats) and irradiated (10 rats – on the 1st day, seven rats – on the 3rd day, nine rats – on the 5th-6th days after irradiation) animals. In acute experiments under ether anesthesia the caudal vein, the femoral vein of the right hind limb, and the carotid artery were isolated and catheterized. The extensor hallucis muscle was isolated in the left hind limb and its tendon divided and the muscle freed from fascia. At the end of the surgical procedure the animal was anesthetized by intravenous injection of a 20% solution of urethane ("Serva") in physiological saline into the

Institute of Physicotechnical Problems, Moscow. Moscow Roentgeno-Radiologic Research Institute. (Presented by Academician of the Russian Academy of Medical Sciences A. D. Ado.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 114, No. 10, pp. 355-357, October, 1992. Original article submitted April 23, 1992.

 0007-4888/92/0010-1416$12.50

TABLE 1. Blood Pressure, Diameter of Arterioles, Linear Velocity of Blood Flow, and Frequency of Spontaneous Vasomotor Reactions in Control Experiments and at Various Times after Irradiation (M ± m)

Parameter	Control	Time after irradiation, days		
		1	3	5—6
BP, mm Hg	108.6±2.67 (n=6)	95.2±2.91 (n=14)	99.3±4.93 (n=7)	101.3±2.67 (n=9)
Diameter, μm	20±2.1 (n=6)	26.8±4.8 (n=8)	25.5±3.3 (n=7)	17.8±1.5 (n=6)
Linear velocity, mm/sec	5.36±1.14 (n=6)	6.55±1.51 (n=8)	6.76±1.67 (n=8)	5.77±1.03 (n=6)
Frequency of spontaneous vasomotor reactions, min^{-1}	37.8±1.24 (n=6)	25±2.02** (n=8)	29±1.98* (n=6)	24.4±2.2** (n=7)

Legend. *$p < 0.01$, **$p < 0.001$.

caudal vein, and placed on a special thermostated table. The dissected muscle was placed on the illuminator of the thermostated table, and to prevent it from drying, it was covered with a histologic coverslip. The thermostated table was perfused with water from a type U-8 ultrathermostat (East Germany), keeping the dissected muscle at a temperature of +36°C. The animal's body temperature was measured by means of a TPÉM-1 electrothermometer. The thermostated table with the animal was placed on the stage of an ML-2 microscope, adapted for intravital work. For microscopic study of the vessels a 25× objective with long working distance and 12.5× ocular ("Leitz," West Germany) were used. A television image was obtained by means of an MK-2532 television camera ("Proxitronic," West Germany), fixed to the photomicrographic attachment of the MFN-10 microscope. The blood pressure in the carotid artery was recorded by a P23Db electromanometer ("Gould," USA), the linear velocity of the blood flow in the arterioles was measured by means of a model 102B velocity tracker correlator with photo-diode pick-up, and the internal diameter of the arteriole by means of a model 303H video dimension analyzer or model 907 image shearing monitor ("IPM," USA); the television image was observed on a "Conrac" monitor (USA). The frequency of spontaneous vasomotor reactions was counted visually on the television image. The parameters for investigation were recorded on a type R-50 recorder ("Rikadenki," Japan). The experiments began 30-50 min after the end of the surgical procedure and choice of the part of the muscle for investigation. At the end of the period of stabilization of the state of the preparation, noradrenalin ("Fluka") was injected into the animal's femoral vein in doses of 0.1, 0.3, 1.0, and 3.0 μg/kg body weight. To compare the initial values of blood pressure, diameter of the arterioles, and linear velocity of the blood flow in them in the different groups of animals, data obtained at the end of the stabilization period were used. The significance of differences was determined by Student's statistical t test.

EXPERIMENTAL RESULTS

The picture of the vascular network of the extensor hallucis muscle of rats exposed to ionizing radiation, observed through the microscope and on the screen of the monitor, did not differ from that found in the control animals. In arterioles of the second and third orders (if the central artery of the muscle is considered to be a vessel of the first order), which are usually studied in irradiated and control rats, well marked spontaneous vasomotor reactions were observed. The results (Table 1) indicate that the diameters of the arterioles studied and the linear velocity of the blood flow in them do not differ statistically significantly in the control and irradiated rats. It can accordingly be concluded that, first, the experiments were conducted on comparable groups of microvessels and, second, no marked degree of dilatation or constriction of the arterioles or disturbances of the circulation of the

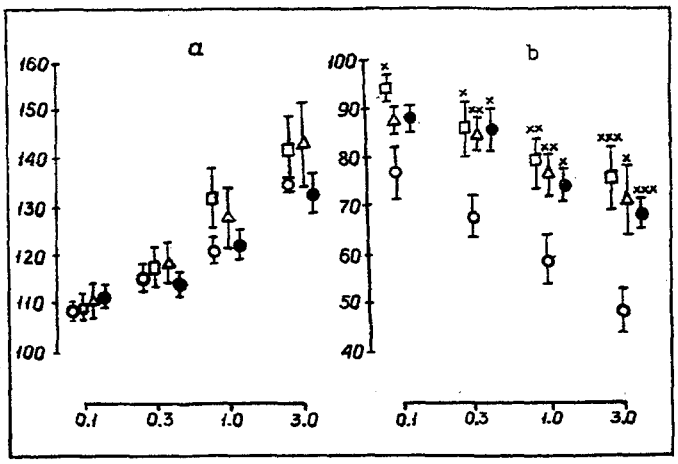

Fig. 1. Pressor reactions of blood pressure (A) and constriction of skeletal muscular arterioles (B) of control and irradiated rats in response to intravenous injection of various doses of noradrenalin. Abscissa, doses of noradrenalin (in μg/kg body weight); ordinate: a) blood pressure (in percent of initial value); b) diameter of arterioles (in percentage of initial value). Empty circle – control experiments (n = 6), square – 1 day (n = 8), triangle – 3 days (n = 8), filled circle – 5-6 days (n = 6) after irradiation. Data shown in the form M ± m, *p < 0.05, **p < 0.02, ***p < 0.01 compared with corresponding control values.

skeletal muscle took place in the irradiated animals while at rest. Meanwhile a significant fall of blood pressure was observed in the animals 1 day after irradiation, as well as a marked decrease in the frequency of spontaneous vasomotor reactions at all times after irradiation.

The results of determination of the reactivity of the circulatory system of the control and irradiated rats to intravenously injected noradrenalin are given in Fig. 1. The amplitudes of the pressor reactions of the blood pressure and constrictor reactions of the arterioles in the control experiments, expressed as percentages of initial values, do not differ significantly from those found by other investigators over the whole dose range of noradrenalin [7, 10], indicating that the state of the animals' vascular system and of the skeletal muscle preparation used in the experiments is sufficiently good. Pressor reactions in all groups of irradiated rats do not differ from those in the control animals, whatever the dose of noradrenalin given. Constrictor reactions of skeletal muscular arterioles of the irradiated animals were statistically significantly lower at all times after irradiation, and with all doses of noradrenalin used, compared with the corresponding responses of vessels of the control rats. Changes in linear velocity of the blood flow in the arterioles were observed in the control and irradiated animals, with virtually all doses of noradrenalin given. These reactions were complex, often biphasic in character, and they varied greatly in different animals. The complex character of changes in linear velocity may probably reflect not only the reaction of the vessel at the place of measurement, but also the state above and below the arranged arterioles. Interpretation of the results of measurements of the linear velocity of the erythrocytes in the arterioles is difficult, and for that reason these data are not given here.

Whole-body gamma-irradiation of rats in a dose of 1 Gy thus causes hypotension 1 day after irradiation, but probably does not lead to any significant change in regulation of the systemic blood pressure. Meanwhile a marked and persistent decrease in the efficacy of the local mechanisms of regulation of the peripheral circulation is observed.

REFERENCES

1. R. A. Besyadovskii et al., A Guide for Radiobiologists [in Russian], Moscow (1978).
2. E. I. Vorob'ev and R. P. Stepanov, Ionizing Radiations and Blood Vessels [in Russian], Moscow (1985).
3. A. K. Gus'kova and G. D. Baisoglob, Radiation Sickness in Man [in Russian], Moscow (1971).
4. P. Johnson, The Peripheral Circulation [Russian translation], Moscow (1982).
5. E. M. Kachanova et al., Med. Radiol., **26**, No. 7, 72 (1981).
6. A. V. Kozlova and M. A. Merkova, Med. Radiol., **15**, No. 2, 7 (1970).
7. V. A. Levtov, Chemical Regulation of the Local Circulation [in Russian], Leningrad (1967).
8. V. S. Nesterenko et al., Radiobiologiya, **19**, No. 3, 433 (1979).
9. B. Folkow and E. Neil, The Circulation [Russian translation], Moscow (1976).
10. L. M. L. Le Noble et al., Pflügers Arch., **410**, No. 3, 250 (1987).
11. S. P. Stearner and E. J. Christian, Radiat. Res., **62**, No. 3, 608 (1975).