CHANGES IN THE MICROCIRCULATORY BED AND TISSUE METABOLISM IN CHRONIC REGIONAL ARTERIAL HYPOTENSION

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It has been shown [5] that a fall of pressure in vessels of the hind limb in rats significantly reduces the hydraulic resistance and leads to a fall in mean capillary pressure. These changes, it has also been shown, cannot be explained by an increase in the number of concomitantly functioning vessels (recruiting of an extra number of reserve vessels into the circulation) [2]. It has therefore been postulated that the decrease in hydraulic resistance in the region of hypotension is due to dilatation of resistive vessels that are already acting.

The aim of this investigation was to test the above hypothesis. Certain parameters characterizing the state of tissue metabolism, which is known to have a significant effect on the microcirculatory bed, also were studied.

EXPERIMENTAL METHOD

Experiments were carried out on nine control and 35 experimental male albino rats initially weighing 180-210 g, and kept under normal animal house conditions, with normal daylight schedule and on an ordinary diet. Arterial hypotension in vessels of the hind part of the body was induced by constricting the abdominal aorta distally to the origin of the renal arteries by a nichrome coil [4], reducing the pressure in the femoral artery by 30-50%. The animals took part in acute experiments, under pentobarbital anesthesia (5 mg/100 g) at different times after constriction of the aorta.

The state of the microcirculatory bed was studied in m. extensor hallucis longus [6] with the MBI-6 microscope, equipped with constant-temperature stage and a system for irrigating the muscle with heated physiological saline. Depending on the diameter of the vessel, a total magnification of 250, 164, or 10 (ocular 6.3; objectives 40, 26, or 19 respectively) was used. To measure the diameter of the vessels, the image splitting method was used [1]. The results were recorded on a "San-ei 142-8" polygraph (Japan). Arterial blood for determination of the acid-base balance (ABB) was taken from the central end of the femoral artery, venous blood through a catheter inserted into the lateral branch of the femoral vein.

Parameters of ABB were determined by the micro-Astrup method on a BMS-2 apparatus connected to a PHM-71 unit. The true pH of the blood was measured directly by two electrodes: a glass G-298A and a calomel K-171 electrode. The remaining parameters of ABB of the blood were calculated by means of a Siggaard-Andersen nomogram, by equilibrating the blood with a gas mixture containing 3.92 and 7.91% of CO_2 in oxygen. The partial pressure of the gases in the blood was determined by means of an E-5046 electrode with PHA-930 (PO_2) and E-5036 electrode with PHA-931 unit (pCO_2). The significance of differences was estimated by Student's test.

EXPERIMENTAL RESULTS

Immediately after constriction of the aorta the pressure in the femoral artery fell to 20-25 mm Hg, but later it gradually rose and stabilized at the level of 50-70 mm Hg. Similar results were obtained by other workers [7, 8]. The fall of arterial pressure (BP) in vessels located distally to the site of constriction of the aorta was accompanied by a sharp decrease

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TABLE 1. Parameters of ABB and Gas Composition of Blood in Control Rats and Rats with Regional Arterial Hypotension

Parameter	Control	Duration of arterial hypotension			
		1 h	1 day	2 days	5 days
pH_a	7,38±0,008	7,15±0,12	7,36±0,03	7,34±0,04	7,38±0,01
pH_v	7,33±0,02	—	7,27±0,02	7,29±0,04	7,32±0,02
BBS_a	—5,3±11,05	—21,8±4,6	—5,95±1,6	—7,5±1,3	—5,1±0,07
TB_a	18,8±1,03	6,4±1,5	16,70±0,53	16,7±0,7	18,3±0,6
p_aO_2	97,4±2,4	114,5±7,6	98,7±3,5	94,3±0,96	95,2±2,4
p_vO_2	60,0±4,6	—	58,0±3,9	61,7±4,6	53,0±1,7
p_aCO_2	31,2±1,13	19,0±1,0	32,7±2,5	32,0±1,5	31,5±1,04
p_BCO_2	36,6±2,48	—	43,5±1,9	37,0±2,1	38,0±1,8

Legend. pH_a and pH_v denote pH of arterial and venous blood respectively, BBS_a and TB_a denote buffer base shift and true bicarbonate of arterial blood respectively; P_aO_2 and p_vO_2 partial pressure of oxygen in arterial and venous blood.

TABLE 2. Kernohan's Index for Microvessels of Skeletal Muscle in Control Rats and Rats with Regional Arterial Hypotension

Experimental conditions	Diameter of vessels, μ		
	Under 15	15—25	Over 25
Control	1:(3,87±0,28)	1:(3,36±0,14)	1:(4,58±0,38)
Duration of hypotension, days			
3	1:(4,39±0,24)	1:(4,67±0,23)*	1:(5,43±0,40)
7	1:(6,46±0,50)**	1:(7,42±0,50)**	1:(5,95±0,40)*
14	1:(4,47±0,24)	1:(4,94±0,35)**	1:(5,50±0,30)
30	1:(4,49±0,26)	1:(4,87±0,29)**	1:(5,87±0,30)*
90	1:(4,12±0,19)	1:(4,38±0,25)*	1:(4,86±0,30)*

Legend. *P <0.05; **P <0.01.

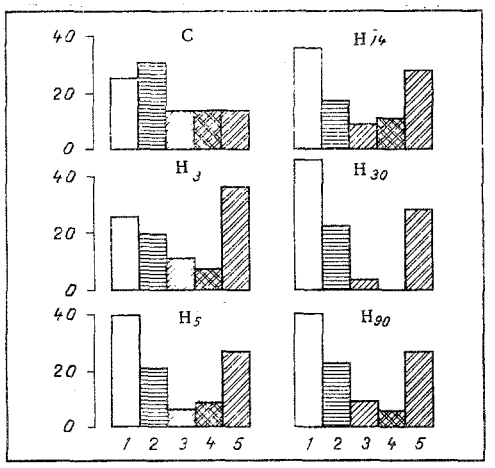

Fig. 1. Histogram of distribution of microvessels by external diameter (in % of total number of vessels measured) in skeletal muscle of control rats (C) and rats with arterial hypotension lasting 3, 5, 14, 30, and 90 days (H_3, H_5, H_{14}, H_{30}, and H_{90} respectively). 1-5) Vessels with diameter of under 15, 15-19.9, 20-24.9, 25-29.9 μ, and over 30 μ respectively.

in the blood flow in the region of hypotension and, judging by the marked changes in the parameters of ABB and the blood gases, by considerable disturbances of tissue metabolism (Table 1). Disturbances of metabolism in the limb tissues in the early stages after constriction of the aorta were probably so severe that signs of metabolic acidosis were observed even when the arterial blood was analyzed. However, by 24 h after constriction of the aorta the normal ABB and gas composition of the blood were virtually completely restored, although signs of acidosis were still observed in the venous blood.

It will be clear from Table 1 that 2 days after lowering of BP all parameters of ABB and the blood gas composition were restored to normal. This indicates virtually complete satisfaction of the metabolic demands of the tissues. One of the leading causes of the rapid normalization of the parameters characterizing the state of metabolism, despite the persistent fall of BP, is an increase in blood supply to the tissues, due to reduction of the hydraulic resistance of the vessels as a result of their dilation.

It follows from the data in Fig. 1 that after a fall of BP the fraction of blood vessels over 30 μ in diameter actually showed a definite increase. Most probably the formation of this population of vessels was induced by marked dilatation of the smaller arterioles, as a result of which the vessels of intermediate caliber switched into the population of larger vessels.

The validity of this hypothesis was confirmed by an analysis of the dynamics of Kernohan's index, which is the ratio of the thickness of the vessel wall to the width of its lumen (internal diameter). A decrease in Kernohan's index is evidence of a relative increase in the lumen of the vessel, i.e., its dilatation.

Analysis of the data in Table 2 shows that after a fall of BP and throughout the period of observation the lumen of the vessels with an external diameter of under 15 μ showed little change (disregarding a temporary increase in this parameter on the 7th day of the experiment, when considerable dilatation of vessels of all calibers was observed). For example, the increase in the lumen of vessels with a diameter of 15-25 μ was particularly considerable, it appeared soonest of all, and persisted throughout the period of observation.

The results described above show that a fall of BP causes adjustments to the microcirculatory bed in the region of hypotension, the most characteristic feature of which is dilatation of the resistive vessels, leading to a decrease in their hydrauliic resistance, and thus contributing to the maintenance of the normal blood supply and metabolism of the tissues, despite a considerable fall of perfusion pressure.

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EFFECT OF PRELIMINARY ADAPTATION TO SHORT-TERM STRESS ON RESISTANCE OF MYOCARDIAL CONTRACTILITY TO HYDROGEN PEROXIDE

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Adaptation of animals to short-term stress has no significant effect on myocardial contractility but, at the same time, it prevents any marked disturbance of contractility such as usually arises under the influence of long-term stress [6, 7]. When the mechanism of this prophylactic effect is studied it must be recalled that during long-term stress in animals [5] and man [8] lipid peroxidation (LPO) is activated, and this activation is particularly marked in the heart muscle. Activation of LPO plays a key role in injury to cardiomyocyte membranes and the development of stress-induced disturbances of cardiac function [2]; such disturbances are therefore prevented by administration of antioxidants [3, 4]. This suggested that the heart muscle of animals adapted to short-term stress ought to have increased resistance to factors inducing LPO. One such factor is hydrogen peroxide (H_2O_2), which induces LPO in the isolated working heart and disturbs its contractility [9, 10].

The aim of this investigation was to study the effect of preliminary adaptation to short-term stress on resistance of contractility of the isolated right atrium (IRA) of animals to H_2O_2.

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