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DYNAMICS OF VASCULAR RESPONSE OF THE SMALL INTESTINE IN ANIMALS AT HIGH ALTITUDES

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KEY WORDS: adrenalin; resistive and capacitive vessels of the small intestine; α- and β-adrenoreceptors; adaptation to high altitudes.

Various functional systems are involved in adaptive reactions of man and animals to extremal conditions of life at high altitudes in the mountains, more especially respiration, the circulation, and the blood, which form a single complex responsible for providing the body with oxygen. The main weight of this burden is taken by the cardiovascular system [1, 4, 6, 8, 14]. However, under conditions of natural high-mountain hypoxia only purely hemodynamic changes have been studied [5, 8, 12], and vasomotor reactions at the regional level have been virtually ignored [7].

The aim of this investigation was to study the character and magnitude of responses of resistive and capacitive vessels of the small intestine to regional injection of adrenalin in the course of adaptation to high altitudes.

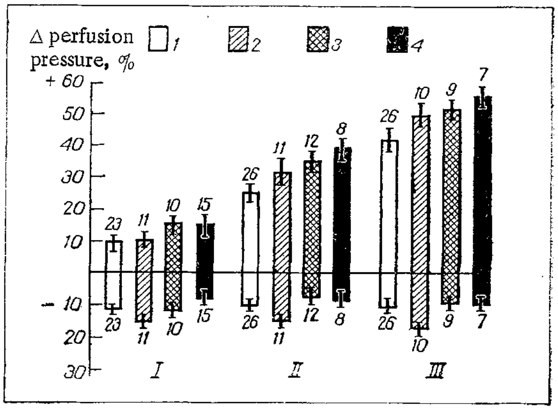

Fig. 1. Changes in responses of resistive vessels of small intestine to intra-arterial injection of adrenalin at different times of adaptation of animals to high-altitude conditions. Ordinate, changes in perfusion pressure (in % of initial level): with + sign, vasoconstrictor, with − sign, vasodilator responses. I) Injection of adrenalin in dose of 0.5 μg, II) 5 μg, III) 10 μg. 1) Control; 2) after adaptation for 3 days, 3) for 15 days, 4) for 30 days. Vertical lines show confidence interval at P = 0.05. Numbers inside triangles denotes number of observations.

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TABLE 1. Magnitude and Character of Responses of Resistive and Capacitive Vessels of Small Intestine to Intra-arterial Injection of Adrenalin into Animals in Frunze (760 m) and at Different Times of Adaptation to High-Altitude Conditions (3200 m above sea level)

Dose of adrenalin, μg	Time of adaptation, days	Number of animals	Initial systemic arterial pressure, mm Hg	Perfusion pressure				Venous outflow		
				initial	number of animals	magnitude of change, % of initial	area of response, % of control	number of animals	magnitude of change, ml/100 g tissue	magnitude of change, % of initial blood volume
0,5	Control	23	137±5,6	147±4,3	23	—11,6±0,8	100	8	—2,44±0,47	36,2±7,0
						+9,8±0,6	100	15	+2,40±0,29	35,7±4,3
	3	13	146±8,1	156±7,2	11	—15,4±1,6*	323*	10	—2,73±0,44	50,9±8,2
						+10,5±1,3	298*	3	+3,37±0,33*	62,9±6,1*
					2	—19,4	811			
			110±6,2*	120±6,5*	10	—11,8±1,4	95	9	—1,92±0,68	23,5±8,3
	15	16				+15,5±1,4*	370*	6	+1,70±0,40	20,9±4,9*
					6	—13,5±1,7	150	1	0	0
	30	17	114±4,3*	125±4,5*	15	—7,9±1,0*	79*	10	—1,59±0,32	18,7±3,8*
						+14,7±2,1*	317*	6	+1,23±0,20*	14,5±2,3*
					2	—10,2	337	1	0	0
5	Control	26	127±4,7	137±4,4	26	—10,6±0,9	100	10	—321±0,43	47,7±6,4
						+25,1±1,5	100	16	+2,56±0,37	38,0±5,5
	3	12	140±10,2	150±10,7	11	—15,3±1,0*	317*	9	—4,04±0,61	75,4±11,4*
						+32,1±3,6	188			
					1	—15,0	504	3	+3,01±0,71	56,1±13,2
			100±5,7*	112±4,9*		—7,4±1,5	93	9	—2,03±0,95	24,9±11,6
	15	16			12	+35,1±2,3*	135*	6	+2,57±0,49	31,5±6,0
					4	+32,3±4,3	123	1	0	0
			94±2,9*	107±2,9*		—9,3±1,1	97	10	—3,22±0,66	37,9±7,8
	30	17			8	+38,9±2,6*	144*	7	+1,54±0,35*	18,1±4,1*
					9	+39,2±4,1	154			
10	Control		112±4,1	122±4,5	26	—10,9±1,3	100	12	—3,26±0,34	48,4±5,0
		26				41,6±3,0	100	14	+3,18±0,53	47,2±7,9
			121±5,6	133±7,0	10	—17,8±1,5*	302*	9	—3,86±0,48	72±8,9*
	3	12				+49,3±3,1	123	3	+3,96±0,80	73,9±14,9
					2	—21,7	882			3
	15		93±5,6*	102±5,6*		—9,4±1,5	123	9	—2,15±0,49*	26,3±6,0*
		16			9	+50,7±2,6*	131*	7	+3,37±0,71	41,3±8,7
					7	+58,3±6,4	140			3
			86±5,8*	97±5,4*		—9,7±1,0	132	10	—3,63±0,72	42,7±8,5
	30	17			7	+54,8±4,0*	125*	6	+1,50±0,17*	17,6±2,0*
					10	+59,6±7,2	130	1	0	0

Legend. +) Increase, and −) decrease in perfusion pressure or outflow of venous blood from small intestine; 0) no response; *) differences from control are significant (P < 0.05).

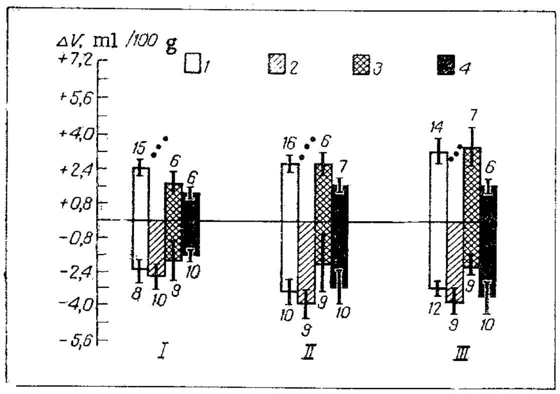

Fig. 2. Changes in responses of capacitive vessels of small intestine to intra-arterial injection of adrenalin at different times of adaptation of animals to high-altitude conditions. Ordinate, changes in outflow of venous blood from small intestine (in ml/100 g tissue). Points denote single observations. Remainder of legend as in Fig. 1.

EXPERIMENTAL METHOD

Experiments were carried out on 72 cats anesthetized with urethane (1.3 g/kg, intravenously). The locations of the experiments were the City of Frunze (760 m above sea level, control) and the Tuya-Ashu Mountain base (altitude 3200 m) on the 3rd, 15th, and 30th days of adaptation. Responses of resistive and capacitive vessels of the small intestine were studied under conditions of humoral and nervous isolation by methods of resistography and the extracorporeal venous reservoir [9]. Responses of resistive vessels were assessed from changes in the perfusion pressure, as a percentage of its initial level, and responses of capacitive vessels by measuring the quantity of blood flowing from the intestine and expressing the result in ml/100 g body weight. In some experiments, to compare the change in capacity of the vessels with the initial blood volume, the absolute quantity of blood in the test organ was measured by washing it out [2, 11]. The intensity of the responses of the resistive vessels was determined by calculating the area of the triangle on each curve. The height of the triangle was the peak value of the rise or fall of perfusion pressure and the base of the triangle the reaction time. The "areas" of the responses were calculated as percentages of the control values. Adrenalin, in doses of 0.5, 5, and 10 μg in 1 ml physiological saline, was injected as a single dose into the arterial system of the intestine after division of the splanchnic nerve. A single injection of the same dose of the drug was given to each animal.

EXPERIMENTAL RESULTS

Intra-arterial injection of adrenalin in the control series of experiments caused biphasic dilator-constrictor responses of the resistive vessels (Table 1). On the first days of the stay in the mountains, in most experiments the animals continued to show the biphasic character of responses of the resistive vessels to adrenalin (Fig. 1). However, a dose of 0.5 μg, in 12-38% of experiments (depending on the times of adaptation), evoked prolonged dilatation of these vessels (Table 1). On the 15th day of adaptation, in response to injection of 5 and 10 μg adrenalin, in 25-44% of cases constrictor responses were seen without preliminary dilatation. By the 30th day an increase in the number of constrictor responses was observed (53-60% of experiments). In the course of adaptation of the animals to high altitudes quantitative changes also were found. For instance, on the 3rd day the amount of dilatation and its "area" were increased, but on the 15th day these indices had fallen to the control level. The degree of constriction and the "area" of the constrictor responses to injection of either of the doses of adrenalin increased to the 15th day of adaptation and then remained high until the end of the observations (Fig. 1).

In Frunze in 54-65% of cases (depending on the dose of adrenalin) constrictor responses of the capacitive vessels were observed, and in the rest vasodilator responses (Fig. 2). During adaptation to high altitudes the character of the responses changed substantially: Initially in 75-77% of cases dilatation of the capacitive vessels took place, but by the 15th day an increase in the number of constrictor responses was observed. However, predominance of the dilator responses persisted until the 30th day of adaptation. The degree of constriction of the capacitive vessels in the control animals increased with an increase in the dose of adrenalin and was significantly higher than the mean values of the responses observed during adaptation for 30 days to high-altitude conditions (Fig. 2). The magnitude of the dilator responses increased during the first days after the cats had been taken into the mountains, but by the end of the period of investigations it had fallen to the control levels.

The experimental results indicate a considerable change in the character and magnitude of the vascular responses of the small intestine to injection of adrenalin at high altitudes. Since the experiments were performed on the denervated intestine, these changes may have been due to changes in reactivity of the adrenoreceptors of the vessels studied. The blood vessels of the intestine are known to contain α- and β-adrenoreceptors [13, 15]. The results suggest that as adaptation to high-altitude hypoxia takes place the sensitivity of the α-adrenoreceptors of the intestinal resistive vessels increases whereas that of the capacitive vessels decreases. The reactivity of the β-adrenoreceptors falls in the resistive and rises in the capacitive part. This hypothesis regarding the possible change in reactivity of the α- and β-adrenoreceptors of the blood vessels of the small intestine in animals adapted to high-altitude conditions is confirmed by the results of experiments [10] with α- and β-adrenoblockers (dihydroergotoxin and propranolol). Changes in the properties of the adrenorecptors during adaptation to high altitudes is only one of the possible causes of the changes observed in the vascular responses of the small intestine. It has been shown that vascular effects under the influence of vasoactive substances depend on the initial vascular tone [3]. The increase in the degree of dilatation of the resistive vessels during the first few days of the animals' stay in the mountains may therefore be due to some increase in the initial level of the perfusion pressure. On the 15th and 30th days of adaptation the significant decrease in the initial vascular resistance may perhaps have caused weakening of the vasodilatation and potentiation of vasoconstriction in response to adrenalin. The effect of phasic fluctuations in the absolute volume of blood in the blood vessels of the small intestine on the magnitude of the responses of the capacitive portion cannot be ruled out. On the 3rd day of adaptation a significant decrease in the blood volume ($P < 0.05$) was observed, with some increase by the 30th day.

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