9. R. Egdahl and J. Richards, Am. J. Physiol., 185, 239 (1956).
10. H. Nelson, K. Egdahl, and D. Hume, Endocrinology, 58, 309 (1956).
11. C. A. Nugent and D. M. Mayes, J. Clin. Endocrinol., 26, 1116 (1966).

EFFECT OF PERIOD OF ADAPTATION ON THE COURSE OF EXPERIMENTAL HEART FAILURE AT HIGH ALTITUDES IN THE MOUNTAINS

A. Kadyraliev

UDC 616.12-008.46-092.9:613.12(23.03)

Data on the state of compensatory hyperfunction of the circulation and respiration in animals with varied degrees of mitral incompetence are given in relation to the periods of adaptation to high-altitude hypoxia in the mountains. In unadapted animals with mitral incompetence more severe disturbances of the hemodynamics and gas exchange were found, accompanied by congestion in the pulmonary and systemic circulatory systems. During the first day after formation of the lesion 52.9% of the animals died. In animals adapted to high-altitude hypoxia the disturbances of the circulation and respiration were milder and only 28.6% of the animals died.

KEY WORDS: adaptation; mitral incompetence; compensatory hyperfunction.

Despite many clinical and experimental studies of circulatory failure, few such investigations have been undertaken under high mountain conditions. Most of these observations have been made in cases of combined, decompensated cardiac defects [5, 7, 9, 11]. Under the climatic conditions of the Tyan'-Shan' Mountains valvular disease of the heart accounts for a high proportion of diseases of the cardiovascular system [1, 6]. According to the statistics [2], about 70% of all valvular lesions of the heart affect the mitral valve.

Hence the urgency of the study of the functions of the cardiovascular and respiratory systems in animals with mitral incompetence under extremal mountain conditions.

The object of this investigation was to study the degree of compensatory hyperfunction of the heart developing after measured resection of the mitral valve in animals depending on the periods of stay in the mountains and to determine any special features of the course of heart failure under the conditions of high-altitude hypoxia.

EXPERIMENTAL METHOD

Experiments were carried out on mongrel dogs of both sexes weighing 17-30 kg. In the experiments of series I (17 dogs) mitral incompetence was produced by surgical operation on the 2nd-4th day after the ascent from the city of Frunze (760 m above sea level) to the Tuya-Ashu Pass (3200 m above sea level). In series II (14 dogs) mitral incompetence was produced after preliminary adaptation for 60 days to an altitude of 3200 m above sea level. Measured mitral incompetence (10-15% of the total area) was produced by the method suggested by Chechulin and Bobkov [10]. Function tests were carried out on the animals before and for 30-60 days after the operation. The gas exchange was determined by the open method, hemodynamic indices by the dye method in the writer's modification for chronic experiments [4], and the venous pressure in the lesser saphenous vein in the leg was measured by Waldman's apparatus. Phase analysis of left ventricular systole was carried out by acceleration kinetocardiography [8], with synchronous recording of the ECG by the Élkar apparatus. The calculations and statistical analysis of the results were carried out by the Iskra-112 and Mir-1 computers.

Department of Pathological Physiology, Kirghiz Medical Institute, Frunze. (Presented by Academician of the Academy of Medical Sciences of the USSR P. D. Gorizontov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 85, No. 3, pp. 274-277, March, 1978. Original article submitted April 4, 1977.

TABLE 1. Indices of Gas Exchange and Hemodynamics in Animals with Mitral Incompetence Unadapted and Adapted to High-Altitude Hypoxia

Times of investigation	Number of animals	Series	Indices of gas exchange			Hemodynamic indices			
			MRV, g/liter	O_2 uptake, ml/min	COU	pulse rate (beats/min)	mean circulation time, sec	cardiac index, liters/m^2	venous pressure, mm water
Initial data (Frunze)	17	I	5,4±0,5	100,0±10 4	18,5±1,4	150,0±7,5	22,0±2,4	3,3±0,3	105,0±0,09
	14	II	4,0±0,8	106,4±17,9	26,6±2,4	140,0±11,4	28,7±1,4	3,3±0,58	114,7±4.0
2nd-4th day of stay at altitude of 3200 m	17	I	4,9±0,4	161,3±16,9**	32,9±2,4**	171,4±10,4	20,0±1,12	3,4±0,15	99,6±1,1
	14	II	4,9±0,6	143,7±13,2*	29,3±1,4	146,0±1,0	23,3±0,7	3,7±0,2	131,0±10,9
30th day at altitude of 3200 m	14	II	4,6±0,6	151,9±14,2*	33,0±2,1**	162,0±7,4	23,6±1,4*	3,2±0,4	131,1±11,2
60th day at altitude of 3200 m	14	II	5,2±0,5*	174,0±16,7**	33,5±2,6**	176,5±8,9	22,1±1,5*	3,3±0,2	111,4±23,5
60 min after resection of mitral valve	14	I	4,6±0,6	71,6±9,7**	15,6±3,0**	133,0±11,5	24,3±4,6	2,7±0,3*	146,6±30,2**
	14	II	4,2±0,5	81,1±11,4**	19,3±1,9**	171,0±7,7	36,9±2,6**	2,5±0,3*	113,3±18,1
5th-10th day after operation	10	I	5,5±0,6	135,1±21,8	24,6±2,9	171,4±8,1	29,8±3.3**	3,1±0,4	94,9±29,8
	12	II	3,9±0,4*	125,0±16,5	32,1±2,2	158,0±6,1	30,6±2,6**	3,9±0,6*	104,4±5,9
30th day after formation of mitral incompetence	9	I	5,3±0,6	153,6±14,1*	28,9±2,0	182,0±17,0*	22,1±2,4	3,4±0,5*	81,3±22,4
	10	II	3,4±0,3*	136,5±19,9*	39,9±3,1	162,0±6.0*	22,3±1,9	3,9±0,6*	113,3±9,4

Legend: 1. MRV – minute respiratory volume; COU – coefficient of oxygen utilization. 2. Values for which $P < 0.05$ and $P < 0.01$ respectively marked by one and two asterisks (compared with initial data).

TABLE 2. Phase Analysis of Left Ventricular Systole in Animals with Mitral Incompetence Unadapted and Adapted to High-Altitude Hypoxia (M ± m)

Times of investigation	Number of animals	Series	Period of contraction		Period of expulsion		Mechanical systole, sec	Total systole, sec	ISI, %	Blumberger's coefficient
			asynchronous contraction	isometric contraction	maximal expulsion	reduced expulsion				
Initial data (Frunze)	17	I	0,05±0,003	0,03±0,004	0,05±0,003	0,07±0,01	0,150±0,01	0,200	80,0	1,5
	14	II	0,051±0,003	0,026±0,003	0,053±0,009	0,086±0,006	0,165±0,02	0,216	84,2	1,8
2nd-4th day of stay at altitude of 3200 m	17	I	0,06±0,001	0,03±0,003	0,04±0,006*	0,07±0,007	0,140±0,009*	0,200	78,6	1,2
	14	II	0,046±0,009	0,036±0,01*	0,063±0,007*	0,086±0,01	0,185±0,013*	0,231	80,5	1,8
30th day at altitude of 3200 m	14	II	0,053±0,003	0,024±0,002*	0,048±0,003	0,08±0,006	0,159±0,005	0,212	84,9	1,8
60th day at altitude of 3200 m	14	II	0,053±0,004	0,025±0,002	0,045±0,003*	0,075±0,007*	0,145±0,009*	0,198	82,8	1,5
60 min after resection of mitral valve	14	I	0,055±0,005	0,03±0,006	0,05±0,005	0,08±0,008	0,160±0,01*	0,215	81,3	1,5
	14	II	0,053±0,003	0,028±0,004	0,04±0,006	0,082±0,007	0,157±0,012*	0,210	82,2	1,6
5th-10th day after operation	10	I	0,055±0,003	0,030±0,002	0,048±0,005	0,063±0,013	0,141±0,011	0,196	78,7	1,3
	12	II	0,056±0,005	0,028±0,01*	0,051±0,006	0,071±0,008*	0,150±0,007	0,206	81,3	1,5
30th day after formation of mitral incompetence	9	I	0,05±0,01	0,02±0,007*	0,04±0,004	0,071±0,008	0,131±0,006*	0,181	84,7	1,6
	10	II	0,047±0,003*	0,027±0,004*	0,047±0,003*	0,088±0,007	0,162±0,006*	0,209	83,3	1,8

Legend: 1. ISI – intrasystolic index (comparison with initial data). 2. Values for which $P < 0.05$ marked by asterisk.

EXPERIMENTAL RESULTS

The data in Tables 1 and 2 indicate that during adaptation in healthy animals the cardiac index increases, the velocity of the blood flow rises, and signs of tachycardia develop. The results agreed with data in the literature [12-15]. The oxygen uptake increased simultaneously with an increase in the efficiency of utilization of the tidal air ($P < 0.05$). During analysis of left ventricular systole a positive inotropic effect was observed. The expulsion period was shortened and Blumberger's mechanical coefficient and the intrasystolic index (ISI) both fell. Mitral incompetence was accompanied by overloading of the left heart, with a consequent disorganization of circulatory function. In these cases the animals' blood flow was slowed, the cardiac index fell, and the rate of the cardiac contractions was slightly reduced.

In animals with mitral incompetence, adapted to high altitudes, the results of analysis of left ventricular systole showed a very small increase in mechanical systole and shortening of the phase of maximal expulsion of blood, reflecting compensatory hyperfunction of the heart and evidence of a high level of contractile power of the myocardium.

In animals not adapted to the conditions of high-altitude hypoxia the contractile power of the myocardium was reduced. During ventricular systole the phase of maximal expulsion of blood was increased, with an increase in ISI. The commencing embarrassment of the work of the heart led to the development of stasis in the pulmonary and later in the systemic circulation. The venous pressure rose ($P < 0.001$). The oxygen uptake fell almost equally, it will be noted, in the animals in both series of experiments 1 h after the development of mitral incompetence ($P < 0.001$).

The severer disturbances of the hemodynamics in the unadapted animals with mitral incompetence affected the duration of their survival. For instance, 52.9% of the animals in this series of experiments died from acute heart failure (mainly during the first few days after formation of the defect). The mortality among the animals adapted to altitudes was reduced by almost half to 28.6%.

The greater resistance of the animals as their stay under high altitude conditions increased in length was evidently due to the development of adaptive reactions in them. The possibility cannot be ruled out that these adaptive processes are consolidated at the cellular level [3]. Whatever the case, during a long stay in the mountains the vital activity of the whole organism is preserved, even in such complicated situations as a combination of circulatory and high-altitude hypoxia.

The results indicate that keeping animals at an altitude of 3200 m above sea level for 2 months is sufficient to ensure a definite degree of adaptation to hypoxia. Experimental mitral incompetence, accompanied by phenomena of circulatory hypoxia runs a milder course in animals previously adapted in the mountains, with less marked circulatory disturbances.

It can tentatively be suggested that adaptive mechanisms aimed at the "fight for oxygen" are activated in the mountains, and consequently pathological processes in whose pathogenesis an important role is played by oxygen deficiency follow a milder course.

LITERATURE CITED

1. K. D. Abdullin, "Cardiovascular pathology under high mountain conditions in Kirghizia," Candidate's Dissertation, Frunze (1965).
2. Yu. I. Bobkov, "Cardiac failure after graded injury to the mitral valve," Candidate's Dissertation, Moscow (1971).
3. Z. I. Barbashova, in: Oxygen Therapy and Oxygen Deficiency [in Russian], Kiev (1952), p. 85.
4. A. K. Kadyraliev, Nauch. Trud. Kirgiz. Med. Inst., 102, 35 (1974).
5. Z. M. Kudaiberdiev, "Some special features of the contractile function of the myocardium in healthy persons and patients with mitral heart disease living at high altitudes in the Tyan'-Shan' and Pamir," Author's Abstract of Candidate's Dissertation, Frunze (1970).
6. M. M. Mirrakhimov and E. A. Goloma, Sov. Zdravookhr. Kirgizii, No. 3, 42 (1962).
7. O. N. Narbekov, "Hemodynamic indices in healthy subjects and patients with rheumatic heart disease living at high altitudes in the Tyan'-Shan' and Pamir," Author's Abstract of Candidate's Dissertation, Frunze (1970).
8. I. E. Oranskii, Acceleration Kinetocardiography [in Russian], Moscow (1973).
9. A. D. Dzhailobaev, A. Yu. Tilis, and M. M. Mirrakhimov, Proceedings of the 2nd Scientific Conference of the Institute of Therapy, Academy of Medical Sciences of the USSR, on Problems in Climatopathology of Cardiovascular Diseases [in Russian], Leningrad (1965), p. 238.

10. Yu. S. Chechulin and Yu. I. Bobkov, in: Problems of the Use of Models in Cardiology [in Russian], Moscow (1968), pp. 53-60.
11. N. Ya. Yusupova, "Clinical and functional characteristics of decompensated mitral heart disease (with predominance of stenosis) in patients living at different altitudes and some special features of the action of strophanthin," Author's Abstract of Doctoral Dissertation, Frunze (1975).
12. A. Grolman, Am. J. Physiol., 93, 19 (1930).
13. K. Jensen, W. Kratz, and W. Schoedel, Luftfahrtmedizin, 5, 40 (1940).
14. A. Loewy and E. Wittkower, The Pathology of High Altitude, London (1937), p. 212.

DYNAMICS OF INSULIN SECRETION IN DOGS WITH ALLOXAN DIABETES

L. N. Dagaeva, F. S. Belikova, O. I. Podotykina, and A. V. Makarova

UDC 616.379-008.64-092.9-07: 616.379-008.6-072.7

Hypoinsulinemia in the superior pancreatico-duodenal vein and depression of the first phase of insulin secretion by the pancreas, characteristic of alloxan diabetes of different degrees of severity, are not observed in the femoral vein. The results of an investigation of the dynamics of the insulin and glucose concentrations in the superior pancreatico-duodenal vein emphasize the dominant role of the pancreatic factor in the pathogenesis of alloxan diabetes in dogs. Data obtained by the study of these indices in the peripheral femoral vein do not reflect this state of affairs adequately.

KEY WORDS: insulin secretion; alloxan diabetes.

There is no general agreement in the literature on the character of the insulin insufficiency in diabetes mellitus. It has been suggested that the cause of the diabetes is not an absolute but a relative insulin deficiency [1] caused by depression of the "acute" liberation of insulin [9, 10]. The insulin response to glucose in patients with diabetes mellitus has been shown [12] to be weaker, and that the first phase of insulin secretion is depressed particularly sharply in this case. The study of the concentration of immunoreactive insulin (IRI) has also revealed a reduction in the "acute" liberation of insulin after intravenous injection of glucose in patients with diabetes mellitus, which is more marked in the portal vein than in the peripheral vessels [2]. The weakening of the insulin response, it is considered, may be the principal pathogenetic component common to all types of diabetes, including prediabetes [3-7]. Unlike the insulin level in blood from the portal vein, the peripheral insulin level has been shown not to reflect insulin secretion adequately [8].

The object of this investigation was to study the dynamics of insulin secretion in dogs with alloxan diabetes of different degrees of severity.

EXPERIMENTAL METHOD

Alloxan diabetes was induced in 9 dogs weighing 18-25 kg by intravenous injection of alloxan in a dose of 60-65 mg/kg body weight. A glucose tolerance test (GTT) was carried out 16-18 days later on these and 5 control animals. The superior pancreatico-duodenal and femoral veins were catheterized under anesthesia, after which 100 ml physiological saline was injected subcutaneously by the drip method during the next 90 min. The first blood samples were taken from the catheters from fasting dogs, and 40% glucose solution was injected over a period of 10 min into the opposite femoral vein to the one catheterized, in a dose of 1 g/kg body weight. Blood samples were taken immediately after the end of the glucose infusion and at definite times during the

Laboratory of Pathological Physiology, Institute of Experimental Endocrinology and Hormone Chemistry, Academy of Medical Sciences of the USSR, Moscow. Department of Normal Physiology, North-Ossetian Medical Institute, Ordzhonikidze. (Presented by Academician of the Academy of Medical Sciences of the USSR N. A. Fedorov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 85, No. 3, pp. 278-281, March, 1978. Original article submitted April 14, 1977.

0007-4888/78/8503-0289$07.50