EFFECT OF ATROPINIZATION ON DEVELOPMENT OF AN EXPERIMENTAL MODEL OF HIGH ALTITUDE ACUTE PULMONARY EDEMA

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The mechanisms of development of high altitude acute pulmonary edema (HAAPE) are largely determined by the state of the nervous structures controlling activity of the functional systems which prevent or promote its development. This paper gives the results of experiments aimed at studying the action of pharmacological blocking of parasympathetic influences on the development of HAAPE.

EXPERIMENTAL METHOD

Experiments were carried out on 12 male chinchilla rabbits weighing 2.5-4 kg, which received an injection of the peripheral muscarinic cholinolytic atropine (1.5 mg/kg), after which the animals were transferred to a climatic pressure chamber where meteorological factors corresponding to an "altitude" of 6000 m were created. Under these conditions, the various parameters for study were determined on the rabbits every hour

TABLE 1. Parameters of Respiratory Function and Hemodynamics in Atropinized Animals before and after Ascent to an Altitude of 6000 m

Parameter	Initial data	Exposure, min					
		60	120	180	240	300	360
Respiration rate, min^{-1}	136±15	165±22	167±25	169±25	166±26	161±21	166±21
Respiration volume, ml	5,70±0,72	6,33±0,9	5,88±0,81	5,72±1,0	5,72±0,8	5,61±0,56	5,46±0,6
RMV, ml/min	777±128	1042±197	981±201	964±214	949±208	989±117	902±128
O_2 in expired air, vol. %	17,05±0,17	16,93±0,27	16,94±0,21	16,90±0,15	17,41±0,22	17,59±0,25	17,64±0,21
O_2 in alveolar air, vol. %	15,8±0,42	15,74±0,28	15,93±0,27	15,75±0,17	14,9±0,17	14,69±0,35	14,35±0,28*
CO_2 in expired air, vol. %	3,94±0,19	4,03±0,18	3,82±0,28	3,90±0,43	3,5±0,35	3,38±0,30	3,21±0,23*
CO_2 in alveolar air, vol. %	5,59±0,42	5,56±0,39	5,52±0,38	5,38±0,33	6,05±0,31	6,32±0,31	6,39±0,31
O_2 saturation of arterial blood, %	92,3±2,16	56,6±6,5†	56,3±7,6†	56,0±9,6†	64,2±10,3†	62,2±8,4†	56,7±9,4†
Physiological dead space, ml	1,67±0,45	1,70±0,31	1,56±0,33	1,68±0,76	2,42±0,62	2,68±0,38	2,72±0,39
Ratio of alveolar to pulmonary ventilation	0,76±0,03	0,77±0,07	0,8±0,05	0,78±0,06	0,58±003†	0,54±0,05†	0,50±0,04†
A-V difference for O_2, vol.%	3,03±0,6	0,7±0,09†	0,64±0,06†	0,66±0,2†	0,62±0,14†	0,56±0,1†	0,58±0,1†
Heart rate, beats/min	250,1±34,4	268,2±50,2	285,7±48,9	281,6±41,0	272,3±37,1	268,7±41,4	267,8±42,4
Minute volume of heart, ml/min	754±123	955,5±142,6	963,5±169,1	960±165	879,5±185	858±123	824±139
Systolic pressure, mm Hg	111,9±6,8	117,6±9,8	117,3±10,7	115,4±7,9	108,4±8,77	98,7±5,2	100,8±5,1
Diastolic pressure, mm Hg	66,7±8,68	76,5±11,1	73,3±10,8	72,3±13,0	76,2±9,2	76,9±9,03	77,9±7,9
Total peripheral resistance, dynes-sec-cm^{-5}	9634±1401	8299±1110	8085±1479	8805±2007	8809±2491	8255±766	8839±1357

*P < 0.05.

†P < 0.02.

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TABLE 2. Parameters of Respiratory Function and Hemodynamics before and after Ascent to an Altitude of 6000 m by Animals Not Receiving Atropine

Parameter	Initial data	Exposure, min					
		60	120	180	240	300	360
Respiration rate, min^{-1}	119.4±19,4	141,1±17,8	147,7±18,5	148,3±22,0	151,2±21.9	151,1±18.2	152,2±17,9
Respiratory volume, ml	5,56±0,98	5,62±0,96	5,66±0,94	5,72±1,14	5,38±1,1	5,0±0,8	4,8±0,8
RMV, ml/min	652,5±93,68	795,5±99	820,7±93,4	826,0±104	791,2±120	752,±104	729±104
O_2 in expired air, vol.%	17,09±0,27	16,84±0,29	16,89±0,28	17,05±0,37	17,34±0,30	17,82±0,33	18,92±0,37*
O_2 in alveolar air, vol.%	15,61±0,39	15,54±0,40	15,48±0,37	15,30±0,46	15,27±0,56	15.79±0,61	16,43±0,50
CO_2 in alveolar air, vol.%	5,63±0,35	5,28±0,25	5,12±0,34	5,12±0,45	6,50±0,55	5,23±0,35	5,14±0,33
CO_2 in expired air, vol.%	3,42±0,32	3,66±0,29	3,68±0,30	3,41±0,35	3,09±0,31	2,74±0,20	2,46±0,14*
O_2 saturation of arterial blood, %	95,6±1,75	69,15±3,48 †	65,7±6,02*	66,6±5,8 †	61,6±5,8 †	49,8±4,45 †	39,9±3,04*
Physiological dead space, ml	1,51±0,45	1,31±0,47	1,43±0,49	1,77±0,69	1,93±0,68	1,94±0,46	1,97±0,42
Ratio of alveolar to pulmonary ventilation	0,72±0,06	0,76±0,08	0,74±0.08	0,69±0,08	0,64±0,08	0,61±0,07	0,59±0,05
A-V difference for O_2, vol.%	2,69±0,34	0,65±0,07 †	0,66±0,06 †	0,64±0,07 †	0,57±0,08 †	0,51±0,08 †	0,45±0,08 †
Heart rate, beats/min	203±22	232±28	232,0±26,8	230,9±26,5	231,0±23,8	227,8±20,5	226,0±17,9
Minute volume of heart, ml/min	677,7±97,3	778,0±114,3	789,7±111,6	778,5±103,7	771,0±104,3	716,2±110,0	677,5±114,0
Systolic pressure, mm Hg	102,5±4,4	111,2±3,7	113,8±5,25	110,4±7,7	104,6±9,33	99,2±4,82	96,2±4,4
Diastolic pressure, mm Hg	65,0±5,82	65,5±5,13	63,3±5,82	69,0±7,24	70,7±7,11	71,8±4,63	73,7±5,45
Total peripheral resistance, dynes·sec·cm^{-5}	10044±1494	9238±1325	9106±1265	9322±1115	9215±1272	9750±1594	10251±1677

*P < 0.05.
†P < 0.02.

for 6 h. The initial data were recorded beforehand. To assess the state of function of the cardiovascular system the ECG was recorded in standard lead II on the 6NÉK-410 apparatus and the left and right sides of the heart, pulmonary artery, and aorta were catheterized to record the pressure curves by means of electromanometers on a Mingograph-81 recorder (Elema, Sweden). The concentrations of gases in samples of expired and alveolar air were determined by a Haldane gas analyzer. The control group consisted of ten rabbits not receiving atropine. Pulmonary edema was diagnosed by determining the pulmonary coefficient, based on the dry residue of lung tissue [5], and also by histological methods. The animals were killed by decapitation.

EXPERIMENTAL RESULTS AND DISCUSSION

As Table 1 shows, immediately after transfer of the atropinized animals to the pressure chamber their respiration rate rose appreciably, causing a distinct rise in the respiratory minute volume. This parameter, it will be noted increased not only as the result of an increase in the number of respiratory movements, but also because of their deepening. This was shown both by an increase in respiratory volume during the first 180 min and also by decrease in the physiological respiratory dead space. Because of the increased ventilation of the lungs, excretion of carbon dioxide with the expired air was intensified and the oxygen concentration in the alveolar air rose. All these shifts enabled a sufficiently high degree of oxygen saturation of the arterial blood to be maintained, compared with values obtained in the group of animals not receiving atropine (Table 2). The changes described confirm data in the literature [3] showing that atropinization, while not causing significant changes in the surfactant system, leads to an increase in the respiratory volume and compliance of the lungs. Calculation of the ratio of the alveolar ventilation to pulmonary ventilation also showed an increase in this parameter during the first few hours of exposure to a "high altitude."

An increase in the heart rate was observed in the experimental animals and it remained above its initial value throughout the period of exposure. This was accompanied by a small increase in the minute volume of the heart. The systolic volume increased during the first few hours but later showed a tendency to decrease. Calculation of the peripheral vascular resistance revealed a greater decrease in the atropinized animals than in the control group. It can be concluded from phase analysis of cardiac activity that the left heart was not significantly overloaded. The work of the right heart increased as exposure continued, but determination of the

phases of the cardiac cycle revealed nothing more than a decrease in its functional capacity. The circulation time from the right heart to the ear was increased (by 120%), indicating the development of congestive manifestations, although this value was much less than in the group of animals with HAAPE (an increase of 240-270%). Morphological analysis of lung tissue after sacrifice of the animals showed that the frequency of development of HAAPE was sharply reduced in the atropinized animals (one cause of mild HAAPE) compared with the group of control animals (four cases).

The results do not agree with those of some workers [6] who state that an increase in the flow of afferent impulses along the vagus nerve may prevent the development of pulmonary edema (admittedly, not of the high altitude type), whereas blocking them contributes to its development. One of the factors preventing HAAPE is evidently an adequate degree of oxygen saturation of the arterial blood. This is achieved through maintenance of adequate ventilation of the lungs, as a result of which the oxygen concentration in the alveolar air does not fall to the critical values which were observed in the animals with HAAPE. The effectiveness of the gas exchange in the atropinized animals was probably attributable to the improvement of bronchial patency, enabling an increase in the volume and improvement of the composition of the alveolar gases [1, 4]. Comparison of the oxygen saturation of the blood in the two groups of animals described above and also the results of previous investigations [2] show that the shift of this parameter toward a decrease (under 50%) is one of the factors which provokes HAAPE. A marked fall in the O_2 saturation of the blood causes a sharp increase in the central blood volume, a rise of pressure in the pulmonary vessels, and an increase in the load of the right heart. If the liberation of various metabolites increasing vascular permeability during hypoxia of this kind is also taken into account, the increase in the frequency of occurrence of HAAPE in animals with low blood arterialization will be easily understood. Conversely, maintenance of arterial blood saturation at above the critical level in atropinized animals evidently prevented the activation of pathological shifts of the regulatory systems that frequently lead to the development of HAAPE.

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