EFFECT OF PROLONGED EXPOSURE OF RATS TO HIGH CARBON DIOXIDE CONCENTRATIONS

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The lactate dehydrogenase (LD) isozyme spectrum of heart muscle, the heart rate (HR) and the ECG indices were studied during exposure to high concentrations of carbon dioxide, and the survival rate of rats also was determined in relation to the rate of rise of the carbon dioxide concentration in the atmosphere. Functional changes observed in cardiac activity during exposure to CO_2 in a concentration of 30% for 7.5 h were not accompanied by any disturbance of carbohydrate metabolism of the heart muscle. The most important condition of survival of rats exposed for a long time to an atmosphere with a high (up to 50%) CO_2 concentration is the rate at which the concentration rises.

KEY WORDS: carbon dioxide concentration; lactate dehydrogenase isozymes; ECG; survival rate.

The effects of exposure of animals to high CO_2 concentrations and of differences in the rate of rise of the CO_2 concentration in the atmosphere were studied. Since the cardiovascular system, equally with the respiratory system, is subjected to a considerable load during exposure of the animal to high CO_2 concentrations [1, 3, 6], attention was focused in these experiments on cardiac function. Energy metabolism in the structures of the heart is known to vary depending on the volume of work done; corresponding to the increase in muscular work, the intensity of aerobic conversion of carbohydrates also increases. Under these circumstances the lactate dehydrogenase (LD) isozyme spectrum became increasingly dominated by fractions of H-type, the presence of which is characteristic of the set of myocardial isozymes. The LD isozyme system is very sensitive to changes in the ratio between aerobic and anaerobic conversions of carbohydrates in the tissue [2]. It was therefore decided to compare changes in cardiac function and the isozyme composition of LD in heart muscle during prolonged exposure of animals to an atmosphere with a high CO_2 concentration.

EXPERIMENTAL METHOD

Experiments were carried out on 38 noninbred male rats weighing 160-380 g. The fixed animals were placed in an airtight chamber (from Vötsh), with a capacity of 100 liters, in which an assigned CO_2 concentration was maintained, together with a normal oxygen concentration (21 ± 2°C), temperature 20 ± 2°C, relative humidity 60 ± 10%, and total barometric pressure 760 mm Hg. In the course of the experiment the ECG (lead II) of the animals was recorded continuously. Animals of the control group were kept in the pressure chamber but in an ordinary atmosphere. In the experiments in which ten rats were kept for 7.5 h in an atmosphere with a CO_2 concentration of up to 30% (rising in steps) the LD isozyme composition of the heart muscle was studied. Samples of tissue from the right and left ventricles and the right and left atria were taken for analysis from each of the 10 experimental and 5 control rats. The LD isozyme spectrum was determined by electrophoresis in polyacrylamide gel [7], as described in detail in [5]. In other experiments the survival of the rats was studied as the CO_2 concentration in the atmosphere was increased at different rates from 20 to 50%. The results were subjected to statistical analysis by the t-test and by Van der Waerden's nonparametric X criterion.

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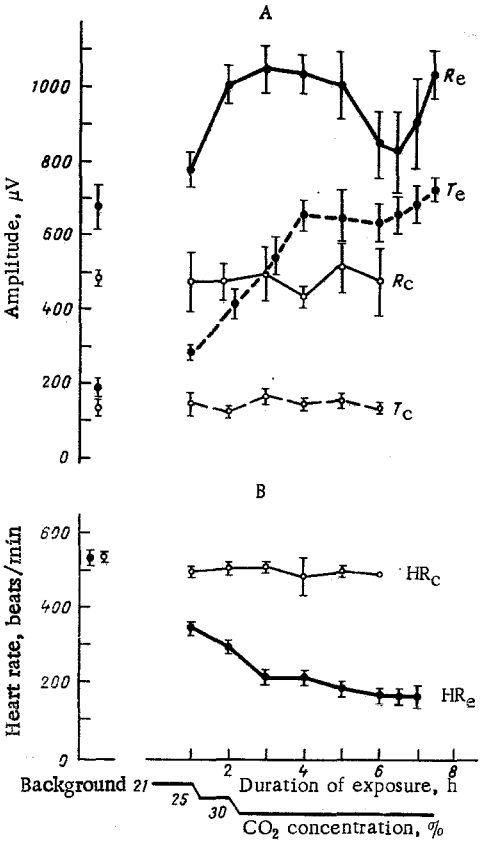

Fig. 1. Changes in HR (B) and amplitude of ECG (A) in rats of experimental (kept in atmosphere of CO_2 in a concentration of 30%) and control groups. R_e, T_e, HR_e) Amplitudes of R and T waves and pulse rate in rats of experimental group; R_c, T_c, HR_c) amplitudes of R and T waves and pulse rate in rats of control group.

EXPERIMENTAL RESULTS AND DISCUSSION

In the rats kept for 1 h in an atmosphere containing 21% CO_2 the heart rate (HR) fell distinctly from 530 ± 19.8 to 342 ± 9.6 beats/min ($P < 0.05$; Fig. 1). For another hour in an atmosphere containing 25% CO_2, followed by exposure to an atmosphere containing 30% CO_2, the heart rate decreased still further – to 295 ± 14.6 and 208 ± 17.9 beats/min respectively ($P < 0.05$). During the next 4 h in an atmosphere with 30% CO_2 HR fell gradually to reach 148 ± 9.6 beats/min after 7 h. In the animals of the control group changes in HR at the different times of the experiments and, probably, connected with the experimental conditions, were not significant (by contrast with those in the experimental group). Throughout the period of their stay in the pressure chamber in an ordinary atmosphere, there was no significant change in HR of the rats of the control group ($P > 0.05$). Characteristic findings in the ECG of the experimental rats were changes in the amplitudes of the R and T waves: in all 10 rats these amplitudes increased, that of the R wave during the first 3 h of exposure to the high CO_2 concentration, whereas the amplitude of the T wave increased almost throughout the experiment. It is also interesting to note that after exposure for 5 h the amplitude of the T wave of two rats, unlike in the rest of the animals, reached the same level as the amplitude of the R wave. During the next 1.5-2 h of exposure the amplitude of the R wave of the experimental animals fell sharply, whereas the amplitude of the T wave remained high. In the rats of the control group no characteristic changes were observed in the R and T waves ($P > 0.05$; Fig. 1). In all ten rats of the experimental group the P-Q interval was increased almost continuously for the duration of the experiment. The duration of the P-Q interval was increased by 3.4 times after exposure for 6.5 h.

An increase in the amplitude of the T-wave on the ECG during prolonged hypercapnia is known to accompany accumulation of potassium in the myocardium and a disturbance of blood aeration [5]. Lengthening

TABLE 1. LD Isozyme Composition (in %) Determined by Electrophoresis in Polyacrylamide Gel in Heart Muscle of Rats of Experimental (n=10; atmosphere containing 30% CO_2) and Control (n=5) Groups

Isozyme	Left ventricle			Left atrium			Right ventricle			Right atrium		
	control	expt.	x	control	expt.	x	control	expt.	x	control	expt.	x
LD_1	28,2	28,4	0,06	24,3	28,0	—1,65	29,5	27,6	0,91	15,7	13,8	1,14
LD_2	40,3	37,2	1,65	34,6	35,1	0,19	39,0	37,5	1,09	32,7	31,4	0,05
LD_3	19,9	21,5	2,14	21,0	20,7	0,38	18,6	22,0	—2,53	29,4	28,8	—0,45
LD_4	6,5	7,5	—0,91	12,4	10,1	1,08	8,3	8,8	—0,20	18,4	21,7	—0,66
LD_5	5,1	5,4	—0,35	7,7	6,1	0,76	4,6	4,1	1,16	3,8	4,3	—0,68
	X_0 2,72											

of the P-Q interval indicates disturbance of atrioventricular conduction [4]. These results suggest that the ECG changes observed in the rats are evidence of a progressive disturbance of metabolism and of atrioventricular conduction in the heart muscle. However, on analysis of the LD isozyme spectrum of the myocardium, no significant changes were found in the carbohydrate metabolism of the heart of the rats of the experimental group (Table 1). In other words, during exposure for 7.5 h to an atmosphere with a CO_2 concentration of up to 30%, despite various functional changes in cardiac activity, no disturbance of anaerobic carbohydrate metabolism took place in the heart muscles.

To determine the effect of prolonged exposure to a high concentration (up to 50%) of CO_2 with different rates of increase of its concentration, a series of experiments was carried out in which the assigned CO_2 concentration was reached in times which varied from 3 to 21 min.

When the CO_2 concentration was increased to 25% in 21 min, 11 rats tolerated a stay in this atmosphere for 10 h well. During a more rapid rise (in 12 min) in the CO_2 concentration to 30%, 2 of 5 rats died 20 min after the beginning of the experiment. The CO_2 concentration was then gradually reduced (in 1.5 h) to 20% and maintained at that level for 3 h 20 min. During the next 53 min the CO_2 concentration was increased stepwise to 35%; not until 45 min after that did one of the remaining 3 rats die. The last two rats were kept in an atmosphere with CO_2 in a concentration of 35% for another 20 min, after which they were returned to an atmosphere of ordinary air.

These results show that during an increase in the CO_2 concentration to 30% the life of the rats is threatened, mainly, perhaps, on account of the sharpness of its rise. In this connection it was interesting to discover how a gradual rise in the CO_2 concentration in the atmosphere to 30% or higher would affect the survival of the rats. During a stepwise increase (up to 30%) in the CO_2 concentration from 20%, only 1 of the 10 rats died 4 h after the beginning of exposure; the remaining rats tolerated a stay of 7.5 h in this atmosphere. In another experiment the CO_2 concentration was increased by 5% every hour, starting from 20%. In this case after exposure for 5 h all the 7 rats in the chamber were still alive, even though the CO_2 concentration by that time had reached 45%. Only during the next 37 min, when the CO_2 concentration was 50%, did the first four rats die. The remaining 3 rats lived for a further 30 min in this high concentration of CO_2.

Physiological changes in the cardiac activity of rats kept for 7.5 h in an atmosphere containing CO_2 in concentrations of up to 30% were thus characterized by changes in the amplitudes of the R and T waves and in the duration of the P-Q interval (probably indicating disturbances of metabolism and atrioventricular conduction) and were not accompanied by any disturbance of anaerobic carbohydrate metabolism in the heart muscle. One of the most important conditions affecting the rate of survival of rats kept for a long time in an atmosphere of high concentrations (up to 50%) of CO_2 is the rate of rise of its concentration.

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