LIPID PEROXIDATION IN EXPERIMENTAL MYOCARDIAL INFARCTION: ACTION OF HYPERBARIC OXYGENATION

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Lipid peroxidation (LPO) takes place continuously in the body [2, 3]. The steady-state level of endogenous LPO depends essentially on the partial pressure of oxygen in the tissues and it rises in hyperoxia [4]. It has recently been shown that the development of several pathological processes (stress, ischemia, atherosclerosis, etc.) is accompanied by activation of endogenous LPO [1, 2]. It is to be expected that hyperoxygenation in the cases mentioned above must lead to even greater activation of LPO, possibly nonadditive in character.

Considering that activation of LPO is one of the key stages in the pathogenesis of injuries arising in stress and ischemia, and also the widespread use of the technique of hyperbaric oxygenation (HBO) in clinical cardiology, estimation of the level of endogenous LPO and the state of the antioxidant enzyme systems regulating LPO in the cardiomyocytes of animals in experimental myocardial infarction and under HBO conditions is an extremely important and urgent task.

EXPERIMENTAL METHOD

Male Wistar rats weighing 180-200 g were used. Experimental myocardial infarction was induced by ligation of the descending branch of the left coronary artery by the method in [11]. HBO was carried out in a pressure chamber, containing oxygen with pressures of 0.5 and 2.0 kg/cm^2 for 1 h, 24 h after the operation. The rats were killed immediately after the end of the HBO session. Lipids were isolated by Folch's method [7]. The content of diene conjugates was estimated from the charactristic UV absorption spectrum of a solution of lipids at 232 nm in a mixture of methanol and hexane (5:1), $\varepsilon = 2.1 \times 10^4$ M^{-1} cm^{-1} [6]. The concentration of Schiff's bases was measured from the intensity of fluorescence of chloroform solutions of lipids at 440 nm with maximum of excitation of fluorescence at 360 nm [6] on a Hitachi MPF-4 spectrofluorometer (Japan). Superoxide dismutase (SOD) activity was determined by the method in [8] and catalase activity by the method in [10]. Protein was determined by Lowry's method in the modification in [9].

EXPERIMENTAL RESULTS

As was observed previously [2], the content of LPO products in rats of the control group was higher in the right ventricle than in the left, whereas activity of enzymes regulating LPO activity (superoxide dismutase, catalase), on the other hand, was lower than in the left ventricle (Tables 1 and 2).

HBO under a pressure of 0.5 kg/cm^2 induced a very small increase in the concentration of LPO products in the control animals in both the left and the right ventricle but virtually no change in SOD and catalase activity in the cardiomyocytes. With an increase in the oxygen pressure to 2 kg/cm^2 the LPO activation effect was potentiated in the left and right ventricles, and at the same time activity of antioxidant enzymes was reduced.

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TABLE 1. Concentration of Diene Conjugates and Schiff's Bases in Experimental Infarction and after HBO under Different conditions (M ± m)

Experimental conditions	Number of animals	Diene conjugates**		Schiff's bases, relative units	
		zone	outside zone	zone	outside zone
Control	18	0,39±0,03	0,54±0,06	1,00±0,14	1,37±0,11
Control + HBO (0.5 kg/cm²)	15	0,44±0,06	0,59±0,04	1,21±0,15	1,64±0,15
Control + HBO (2 kg/cm²)	15	0,50±0,07	0,66±0,04	1,38±0,18*	1,86±0,10*
Infarct	15	1,13±0,06*	0,95±0,05*	4,3±0,14*	2,46±0,22*
Infarct + HBO (0.5 kg/cm²)	12	1,60±0,07*	1,27±0,04*	6,49±0,17*	3,52±0,13*
Infarct + HBO (2 kg/cm²)	14	2,97±0,09*	1,94±0,05*	9,55±0,14*	4,64±0,19*

Legend. *P < 0.05 compared with control, **) Concentration of diene conjugates expressed in optical density units per milligram of lipids.

TABLE 2. Activity of Antioxidant Enzymes of Myocardium in Experimental Infarction and after HBO under Different Conditions (M ± m)

Experimental conditions	Number of animals	SOD, relative units		Catalase, nmoles H_2O_2/mg protein	
		zone	outside zone	zone	outside zone
Control	18	30,1±1,6	25,2±1,4	432±26	356±28
Control + HBO (0.5 kg/cm²)	15	28,9±2,0	24,4±1,1	393±23	331±21
Control + HBO (2 kg/cm²)	15	25,3±16	20,9±1,5*	337±16*	281±22*
Infarct	15	18,4±2,1*	21,7±1,0*	219±24*	247±18*
Infarct + HBO (0.5 kg/cm²)	12	16,3±1,9*	20,2±1,8*	186±21*	231±27*
Infarct + HBO (2 kg/cm²)	14	11,7±2,0*	17,1±2,4*	130±11*	182±16*

Legend. *P < 0.05 compared with control.

In rats with experimental myocardial infarction 24 h after the operation a decrease in activity of the antioxidant enzymes (SOD by 39%, catalase by 49%) and an increase in the concentration of LPO products (diene conjugates) and Schiff's bases by 2.9 and 4.3 times respectively) was observed in the zone of ischemia. After HBO, and with oxygen under a pressure of 0.5 kg/cm², additional inhibition of enzyme activity was observed in the animals with infarction (SOD by 11%, catalase by 15%), and the concentration of diene conjugates and Schiff's bases was increased, by 41 and 51% respectively.

With oxygen under a pressure of 2 kg/cm² the additional decrease in SOD and catalase activity was 36 and 41% respectively for the zone of ischemia, and the accumulation of diene conjugates and Schiff's bases amounted to 162 and 122% compared with levels in the zone of ischemia without the use of HBO.

Outside the zone of ischemia, after the formation of an experimental infarct, the decrease in enzyme activity was 14% for SOD and 31% for catalase, whereas the levels of diene conjugates and Schiff's bases increased by 81 and 80% respectively. HBO with oxygen under a pressure of 0.5 kg/cm² caused an additional decrease in SOD activity by 7% and catalase activity by 6%, whereas the level of diene conjugates and Schiff's bases increased compared with the same zone without HBO by 34 and 43% respectively.

With oxygen under a pressure of 2 kg/cm² an additional fall in SOD and catalase activity took place, by 21 and 26% respectively, but the levels of LPO products were approximately twice as high as in the nonischemic zone without the use of HBO.

With a combination of ischemic damage and treatment with HBO, it is thus not simple summation of their activating effects on LPO which arises (the level of LPO was bound to rise in this case — for example, for Schiff's bases outside the zone of necrosis and with oxygen under a pressure of 2 kg/cm² the increase would be only 116%, much less than the figure of 239% recorded experimentally), but the superadditive effect of accumulation of endogenous LPO products both inside the zone of infarction and also outside it. The intensity of this effect increases along with an increase in the oxygen pressure in HBO. Considering that LPO products can injure membrane structures of cardiomyocytes [2], the need for strict control over the use of HBO in myocardial infarction must be recognized, for the action of hyperoxygenation therapy is not limited to eradication of the oxygen debt of the affected tissue, but it also causes changes in antioxidant status and in the level of endogenous LPO in the cells composing it.

It will be evident that the combined use of HBO and of antioxidant preparations preventing the development of LPO would allow the beneficial action of HBO to be manifested to the full.

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INHIBITION OF SUPEROXIDE DISMUTASE AS A FACTOR PROMOTING MYOCARDIAL DYSFUNCTION IN OXYGEN LOADING

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Diethyldithiocarbamate (DEDTC) is an inhibitor of superoxide dismutase (SOD), an enzyme controlling the intracellular level of superoxide radicals (O_2^-) in aerobic organisms [8]. If DEDTC is administered to animals, the SOD activity of their heart is reduced [5, 6].

The writers showed previously that injection of DEDTC into rabbits with hypertrophy of the heart not only inhibits SOD activity but also seriously impairs the contractility and pumping function of the heart in the presence of an excess of O_2^- caused by sessions of hyperbaric oxygenation (HBO) [3]. Meanwhile in experimental myocarditis induced by injection of adrenalin, an SOD preparation had a protective action on cardiac function and prevented the disturbance of contractility due to more intensive oxidation [4].

Beneficial effects of other substances with antioxidant action on cardiac function during stimulation of free-radical injury to the heart have been described [7]. These observations indicate that one condition for manifestation of the toxic action of oxygen on the heart is inadequate capacity of its antioxidant defensive systems. To confirm this hypothesis directly it was decided to study the effect of DEDTC on myocardial contractile function under conditions stimulating O_2^- formation.

EXPERIMENTAL METHOD

Experiments were carried out on Chinchilla rabbits weighing 2.5-3.3 kg. DEDTC was injected intraperitioneally twice a day into intact animals in a dose of 0.5 g/kg, and into animals with adrenalin-induced cardiac damage (AICD) in a dose of 0.25 g/kg daily for 3 days. AICD was produced by slow intravenous injection of 1% caffeine solution (20 mg/kg) and 0.1%

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