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ACUTE ADRENAL-INDUCED MYOCARDIAL INJURY: PHENOMENON OF PREVENTION BY MECHANICAL LUNG VENTILATION (Experimental Research)

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Abstract

The experiments show that histotoxic doses of catecholamines (CA) significantly decrease myocardial contractility followed by arrhythmia and heart arrest. In addition, pulmonary and myocardial edema, hemorrhages and marked myocardial hemomicrocirculatory disorders, as well as significant alterations of blood pO_2, pCO_2, pH are also recorded.

The mechanical lung ventilation (MLV) prevents myocardial fibrillation and heart arrest, myocardial hyperemia, pulmonary edema and generalized hemorrhages developed after injection of lethal doses of CAs. Moreover, MLV prevents the hypercapnia and acidosis, increases blood oxygenation.

Keywords: catecholamines, cardiotoxic doses, myocardial and lung injury, mechanical lung ventilation, prevention of adrenaline-induced myocardial injury.

Introduction

Many aspects of pathogenetic mechanisms of metabolic (adrenaline-induced) myocardial injury remain unclear, and a number of preventive measures are not completely effective yet [*Gichka S.G., 1985; Gotsura V.V., 1993; Chernov Yu. et al., 1994; Garmash V. et al. 1996*].

According to the Raab's concept, the emotional stress induces release of high amount of CAs into blood, from where the myocardial tissue absorbs adrenaline [*Raab W. et al., 1959*]. CAs increase significantly oxygen consumption by myocardium, while dilation of coronary vessels does not meet myocardial oxygen requirements, and oxygen supply fails to provide its increased consumption by cardiomyocytes leading to hypoxia and necrosis [*Pavlovich L.A. et al., 1980; Hialmarson A., Olsson G., 1991; Frolov V.A., 1994; Sisakyan S.H. et al. 1998*].

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While the small doses of CAs trigger energy metabolism and support normal myocardial function, high doses of CAs manifest cardiotoxic effect [*Sernov L.N., Gatsura V.V., 1991; Meerson F.Z., 1993; Torkunov P.A. et al., 1997*].

The present research is focused on studies of functional activity, hemomicrocirculation of myocardium, partial pressure of blood O_2 (pO_2) and CO_2 (pCO_2), as well as blood pH in rats under the influence of histotoxic doses of CAs, and possible prevention of adrenaline-induced myocardial injury by MLV.

Design and Methods

Experiments were performed in albino male rats (200-250 *g*) that were divided into three groups: Group 1 animals were intact rats (n=6), Group 2 rats (n=10) were anesthetized with Nembuthal and injected *Adrenalini hydrotartrati* 1.8 *mg/kg* i/v (femoral vein). Group 3 animals (n=16) were fixed to MLV apparatus via tracheotomy intubation, and injection of the same dose of adrenaline followed.

Table 1.

Cardiac contractility characteristics in adrenaline injected and MLV exposed rats

Follow-up time after adrenaline injection	Without MLV		With MLV		
	Contraction amplitude on apical lead of ECG, *mm*	HB/min	Contraction amplitude on apical lead of ECG, *mm*	Contraction amplitude on mechanocar-diogram, *mm*	HB/min
baseline	17.3±1.4	284±19	14.3±1.7	19.3±0.5	258±25.1
1-3	6.9±5.7	37±3.2*	7.3±14.1	16.7±3.2	86±34
5-7	lethal outcome		17.2 ±1.6	8.2±0.65*	144±19*
20			11.6±3.8	15.5±4.4	186±32

* - $p<0.05$ – difference of significance between Group 2 and Group 3.

The following studies were realized:

1. ECG recording in standard leads by electrocardiography.

2. Morphometric study of myocardial hemomicrocirculation by Gomori's modified method based on detection of acid phosphatase activity in capillary endothelium [*Sisakyan S.H., 1977*].

3. Assessment of blood pO_2, pCO_2 and pH by Astroop micromethod on BMS 3Mk 2 "Blood microsystem" (Radiometer, Copenhagen, Denmark).

Statistical analysis was conducted by Student's *t*-test in Excel 2002.

Table 2.

Blood pH, partial pressure of CO_2, and O_2 in adrenaline-injected and hyperventilated rats

Parameters	**pH**	**pCO_2** *mm* HG	**pO_2** *mm* Hg
Group 1	7.3 ± 0.02	35 ± 3.4	62 ± 3.5
Group 2	6.95 ± 0.03*	119 ± 7.2*	13.3 ± 2.1*
Group 3	7.19 ± 0.02**	42.0 ± 4.1**	99.15±5.7**

*- $p<0.01$ – significance of differences between Group 1 and Group 2, ** - $p<0.001$ – significance of differences between Group 3 and Group 2

Results

ECG records showed that adrenaline injection to Group 2 animals caused significant suppression of heart rate (by 87%), decrease of contraction amplitude up to 60 % in 1-3 *min.* follow-up. Further cardiotoxic effect was accompanied with arrhythmias of polytopic origin such as tachysystoly and extrasystoles leading to fibrillation and cardiac arrest in 5-7 *min.* follow-up (Table 1).

Macroscopic examination of the cardiopulmonary complex of dissected animals showed expressed edema and hemorrhages of myocardial and lung tissues (Figure 1).

Studies of microscopic specimens of the myocardium revealed microcirculatory alterations manifested in inhomogenous capillary staining and blood stasis (Figure 2; Table 3).

Injection of lethal doses of adrenaline following prior appliance of MLV to Group 3 animals caused only short-term depression of cardiac activity and mild arrhythmias. However, in contrast to rats treated with adrenaline only, no fibrillation and cardiac arrest developed. No microscopic disorders were observed on micropreparations of the myocardium. Macroscopic observations showed no expressed myocardial hyperemia and absence of pulmonary edema and hemorrhages.

Results of studies on blood pO_2, pCO_2 and pH showed that cardiotoxic doses of adrenaline lead to hypercapnia (pCO_2 = 119 mm Hg vs. 35 *mm*

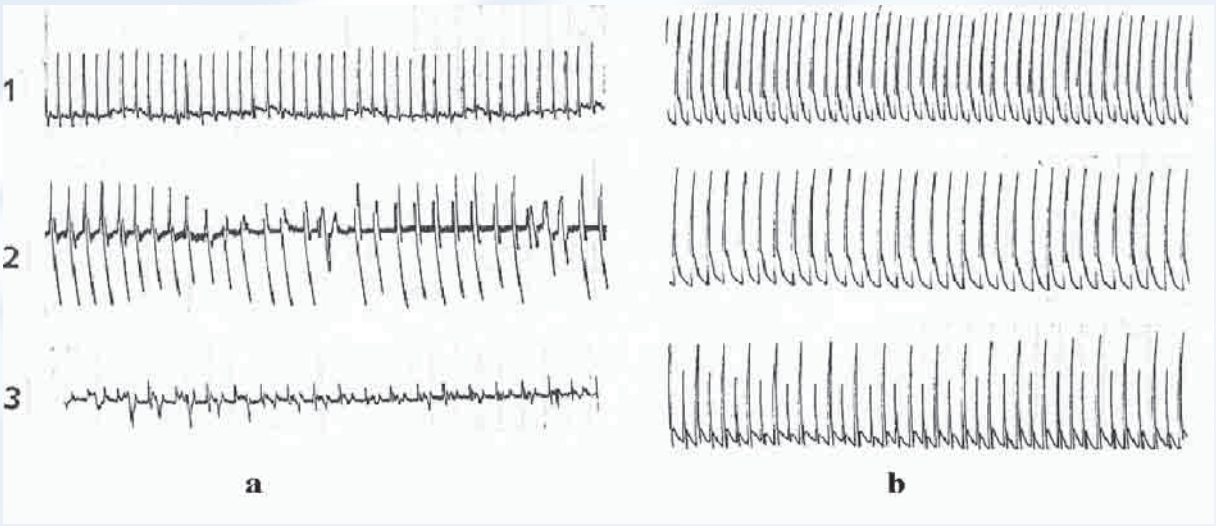

Figure 1. *ECG records:*
a) *1. ECG in intact animal (252 beats/min); 2. after injection of adrenaline – (192 beats/min); 3. heart fibrillation and death in 6min follow-up;*
b) *1. ECG in hyperventilated rat (264 beats/min); 2. after injection of adrenaline in mechanically ventilated animals – (194 beats/min); 3. in 16 min follow-up – sinus rhythm (246 beats/min)*

Hg in Control Group 1; $p<0.01$). Acidosis developed along to hypercapnia (blood pH = 6.95 vs. 7.3 in intact rats, $p < 0.01$). In hyperventilated Group 3 rats pCO_2 increased for only 20%, and blood pH decreased insignificantly (Table 2).

Discussion

Whether the cardyomyocyte hypoxia is the primary reason to cause non-coronarogenic myocardial injury, or whether cardiac damage is secondary result to CA-induced injury of pulmonary tissue remains uncertain. The studies of G. Engstrom and co-authors suggest that moderately reduced lung function is associated with an increased occurrence of ventricular arrhythmias, and that lung function should be considered when assessing the prognostic significance of arrhythmias [*Engstrom G. et al., 2001*]. Our investigation, to our knowledge, is the first study to propose improvement of alveolar gas exchange for prevention of adrenaline-induced myocardial injury and suggests new pathophysiological mechanisms for development of myocardial damage.

The present study revealed that adrenaline caused macroscopically detected lung injury expressed in microcirculatory and pulmonary

Table 3.

Morphofunctional characteristics of myocardial left ventricle capillary system in adrenaline-induced myocardial injury

Microcirculation parameters	Group 1	Group 2	
		30 min follow-up	2-hour follow-up
Total length of capillaries (L), *mm*	2035±85	1701±71*	747.24±45.02
Capillary diameter (d), *mcm*	6.52±0.16	6.83±0.12	5.30±0.24
Capillary metabolic surface (CMS), mm^2	41.40±1	36.47±1.33**	29.07±0.55*
Capillary bed capacity (CBC), mm^3	0.065±0.04	0.064±0.0022*	0.037±0.002*
Diffusion distance, *mcm*	13.28±0.68	14.34±0.25*	14.22±0.37*

* - $p<0.01$, ** - $p<0.05$ – significance of differences between Group 1 and Group 2.

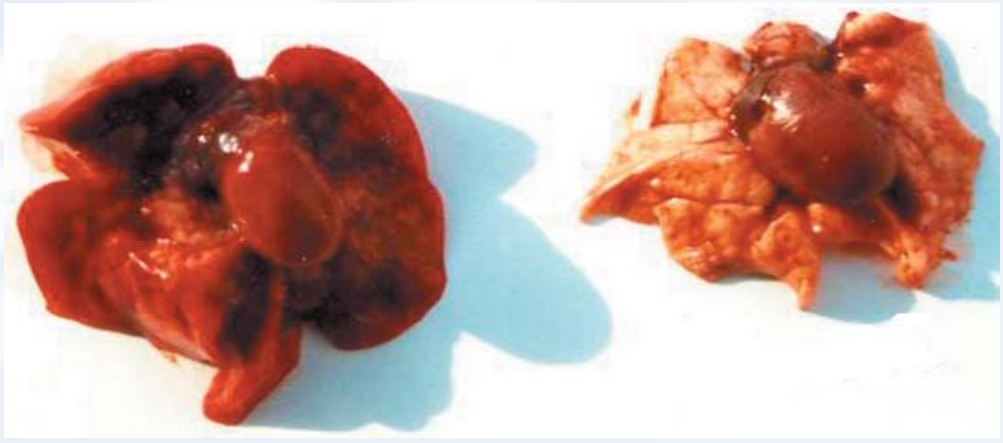

Figure 2. *Cardiopulmonary complex of dissected rats after injection of histotoxic dose of adrenaline and following MLV*

tissue alterations. CA-induced lung injury was noted also by B. Rassler who explained histologically shown pulmonary edema and inflammation through primarily hemodynamic effects of norepinephrine [*Rassler B. et al., 2003*]. Adrenaline increases capillary permeability resulting in swelling and hemorrhages of lungs [*Meier M. et al., 1998; Liu H.P. et al., 1999*; *Rassler B. et al., 2003*].

Conclusion

The results obtained allow concluding that MLV assistance prevents heart fibrillation and arrest, as well as development of hypercapnia, acidosis and improves blood oxygenation in conditions of injection of cardiotoxic doses of adrenaline.

Dissection of animals treated with adrenaline following the MLV assistance does not show any expressed cardiac affection, pulmonary edema and disseminated hemorrhages common for adrenaline-induced injuries.

In conclusion, stress-induced CA hypersecretion, that is one of the major causes of sudden cardiac death and myocardial infarction in humans, leads also to disruption of alveolar respiration, myocardial hypoxia, and finally results in arrhythmias and cardiac arrest. These CA-induced alterations can be prevented by improvement of alveolar gas exchange.

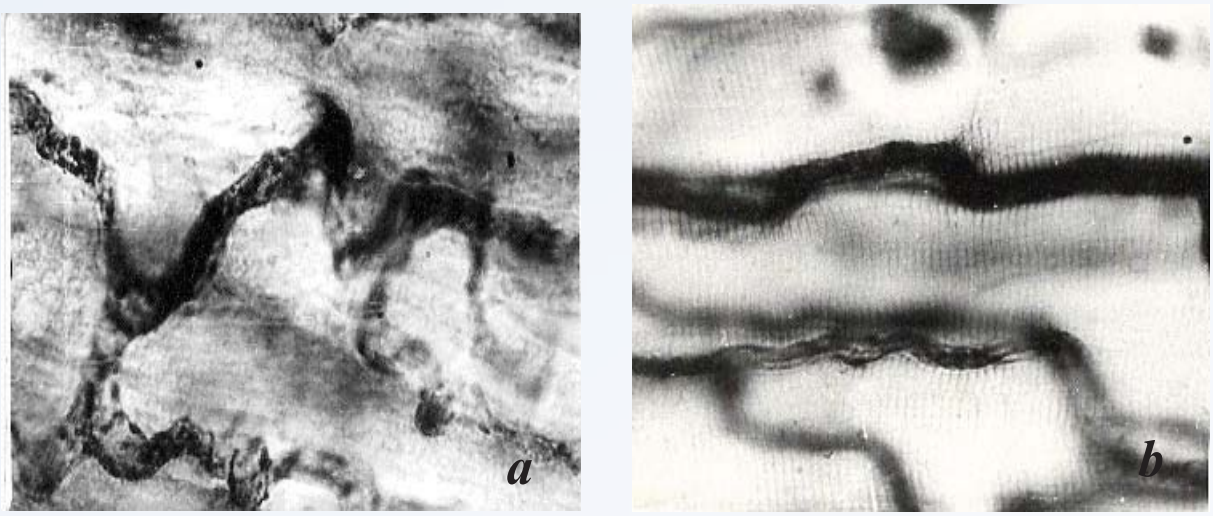

Figure 3. *Capillary network of rat myocardium. 40x15;*
a) *tortuous course of inhomogeneously stained capillaries in adrenaline-injected animals' myocardium.*
b) *parallel course of myocardial capillaries in MLV-treated rats prior to adrenaline injection.*

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