Effect of Acute Hypoxia on the Concentrations of Potassium and Phosphorus in the Cardiomyocyte of a Pregnant Animal during Early Organogenesis

A. G. Pogorelov

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 145, No. 5, pp. 542-543, May, 2008
Original article submitted March 11, 2008

The concentrations of potassium and phosphorus in the cardiomyocyte cytoplasm of the Wistar rat were measured by means of electron probe microanalysis. Pregnancy was accompanied by a decrease in cytoplasmic phosphorus concentration and an increase in cytoplasmic potassium concentration. Acute hypoxia modified the concentrations of these elements in the cytoplasm.

Key Words: *hypoxia; early organogenesis; Wistar rat; cardiomyocyte; cytoplasmic potassium and phosphorus; electron probe microanalysis*

According to basic cardiology, the phenomena of stunning [4] and preconditioning [11] are related to a short-term effect of hypoxia. One of the immediate responses of the cardiomyocyte to hypoxia is cell deenergization, which results in cytoplasmic potassium deficiency [1-2] and phosphate release [3,7]. These changes occur during early organogenesis, which is accompanied by episodes of acute hypoxia [5]. It should be emphasized that variations in the concentration of the main cytoplasmic ion K^+ are followed by key molecular and genetic transformations [6,8,12].

Here we studied the effect of acute hypoxia on the concentrations of potassium and phosphorus in cardiomyocytes of a pregnant animal.

MATERIALS AND METHODS

Experiments were performed on the hearts from female Wistar rats (250-300 g). The animals were maintained at 20±2°C under standard conditions and received food (PK-121-2, INFORMKORM) and water *ad libitum*. The rats were deprived of food, but had free access to water over 12 h before the study. The day of sperm detection in vaginal smears was considered as day 1 of pregnancy. The animals were exposed to acute hypoxia on day 10 of pregnancy. Acute hypoxia was modeled in an altitude chamber by decreasing the pressure to 145 mm Hg over 1 min. The reference group consisted of females (11 days of pregnancy), which were not exposed to acute hypobaric hypoxia (AHH).

Tissue samples of the right atrium were isolated on the next day after AHH. The samples were treated as described previously [10]. Tissue samples were cryofixed in liquid nitrogen (-188°C) and dehydrated at -100°C under vacuum conditions. Lyophilized tissue samples were embedded into the medium of Epon 812. Epoxide resin was subjected to thermal polymerization. The blocks were used to obtain semithin sections. These sections were mounted on copper grids for electron microscopy. The sections (2 μ) were examined under a JSM-U3 electron microscope (JEOL) to measure the intracellular concentrations of potassium and phosphorus by the method of electron probe microanalysis. The measurements were performed under the following conditions: accelerating potential, 25 kV; measuring

Institute of Theoretical and Experimental Biophysics, Russian Academy of Sciences, Pushchino, Russia. ***Address for correspondence:*** agpogorelov@rambler.ru. A. G. Pogorelov

0007-4888/08/1455-0604

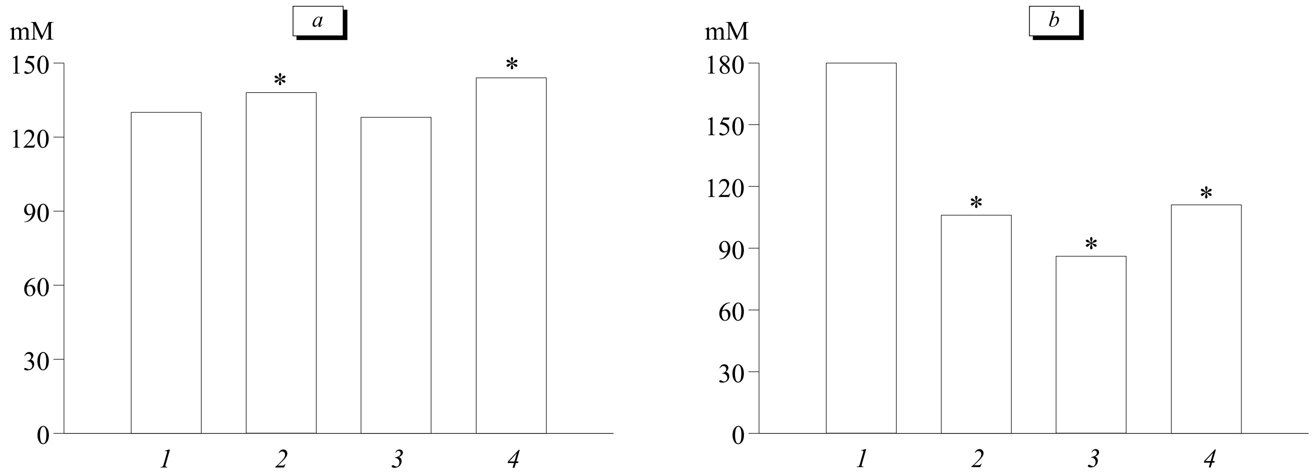

Fig. 1. Concentrations of K (*a*) and P (*b*) in the right atrial cardiomyocyte of Wistar rats (n=6). Control (nonpregnant animals, *1*); pregnant animals not exposed to AHH (*2*); group 1 pregnant animals exposed to AHH (*3*); and group 2 pregnant animals exposed to AHH (*4*). *p<0.05 compared to the control.

current, 5 nA; recording time, 20 sec; and probe diameter, 0.1 μ. The characteristic roentgen radiation (Kα-line) of elements was recorded on a diffraction spectrometer (PET crystal). Morphological characteristics of the section were evaluated in transmitted electrons (STEM regimen). The significance of differences was estimated by nonparametric Mann—Whitney test (*T* test).

RESULTS

Potassium concentration in the cardiomyocyte increased during early organogenesis (Fig. 1). This reaction corresponds to the cascade response of cardiomyocytes to prolonged hypoxia [1-2,9]. Na^+/H^+ exchange compensates for cellular acidosis, which is accompanied by Na^+ accumulation in the cytoplasm. Activation of Na^+/K^+-ATPase is directed toward the maintenance of sodium concentration. Deenergization is accompanied by potassium accumulation, which results in decomposition of macroergic substrates, washing out of phosphate, and decrease in intracellular phosphorus concentration (Fig. 1).

Two pools of cardiomyocytes were revealed on day 1 after AHH. Group 1 was characterized by a decrease in the concentrations of potassium and phosphorus (Fig. 1), which coincides with the effect of global hypoxic deenergization of cells. No significant changes were found in group 2. Our experiments revealed 2 groups of animals, which differed in the response to AHH.

The resistance of animals to AHH is probably associated with impaired transport of exogenous and/or endogenous substrates that provide energy for the cell. The role of indirect mechanisms cannot be excluded (*e.g.*, decrease in anaerobic glycolysis, transport of metabolites through the membrane, release of metabolites from the intercellular space, or oxygen transport rate). Even short-term hypoxia causes a potassium imbalance in the cardiomyocyte of female animals, which can affect the course of pregnancy and state of the offspring.

I am grateful to L. K. Trofimova (postgraduate student, Department of Human and Animal Physiology of the M. V. Lomonosov Moscow State University) for her help in the preparation of samples in experiments with AHH.

REFERENCES

1. A. G. Pogorelov, V. N. Pogorelova, M. I. Dubrovkin, *et al.*, *Biofizika*, **47**, 744-752 (2002).
2. A. G. Pogorelov, V. N. Pogorelova, E. V. Khrenova, *et al.*, *Zh. Evolyuts. Biokhim. Fiziol.*, **40**, 353-358 (2004).
3. D. G. Allen and C. H. Orchard, *Circ. Res.*, **60**, No. 2, 153-168 (1987).
4. R. Bolli, *Circulation*, **82**, No. 3, 723-738 (1990).
5. E. Casanueva and F. E. Viteri, *J. Nutr.*, **133**, 1700-1708 (2003).
6. W. H. Goldmann, *Cell Biol. Int.*, **27**, 391-394 (2003).
7. A. S. Lader, Y.-F.U. Xiao, C. R. O'Riordan, *et al.*, *Am. J. Physiol.*, **279**, 173-187 (2000).
8. G. N. Parkinson, M. P. Lee, and S. Neidle, *Nature*, **417**, 876-880 (2002).
9. G. N. Pierce and M. P. Czubryt, *J. Mol. Cell. Cardiol.*, **27**, 53-63 (1995).
10. A. Pogorelov, B. Allachverdov, I. Burovina, *et al.*, *J. Microscopy*, **12**, 24-38 (1991).
11. R. Schultz, J. Rose, H. Post, and G. Heusch, *Pflugers Archiv*, **430**, 273-282 (1995).
12. S. Taurin, V. Seyrantepe, S. N. Orlov, *et al.*, *Circ. Res.*, **91**, No. 10, 915-922 (2002).