TITLE: HYPOXEMIA DOES NOT INHIBIT CARDIAC MITOCHONDRIAL ENZYMES

AUTHORS: P. Rothstein, M.D., W.F. Cao, M.D.

AFFILIATION: Departments of Anesthesiology and Pediatrics, College of Physicians and Surgeons, New York, NY 10032

INTRODUCTION: The effect of oxygen deprivation on mitochondrial function has long been the subject of investigation. The interaction of hypoxemia and tissue blood flow makes the problem a complex one. It has been reported that mitochondrial enzyme activities are depressed when cells are exposed to an hypoxic environment (1). To investigate this problem we studied the activity of cardiac mitochondrial enzymes in normal and chronically hypoxic rats.

METHODS: Female Sprague-Dawley rats, 249 ±7 g were placed in a chamber in which the ambient $PatmO_2$=59±2mmHg, for a period of two weeks. This resulted in a PaO_2=30±2mmHg. After two weeks, animals were sacrificed. Pooled mitochondria from the left ventricle (7-8 rats/experiment) were isolated. Enzymes from the electron transport chain and citric acid cycle were studied. Control animals consisted of rats breathing room air. Values are reported as mean±S.D. Enzyme activities, reported as units of activity, were compared between the two states using an unpaired t-test.

RESULTS:

Enzyme	Control (N=11)	Hypoxia (N=5)
Cytochrome oxidase	12.88±1.47	12.36±2.14
Citrate synthase	2.86±0.27	2.89±0.23
NADH-dehydrogenase	5.29±0.83	5.14±0.73
Succ dehydrogenase	0.181±.018	0.193±.025

Enzyme activities for each enzyme under hypoxic conditions were not significantly different from the control state.

DISCUSSION: Severe hypoxemia, produced in the absence of confounding factors (e.g. respiratory failure, myocardial ischemia, cardiac failure) induced no changes in mitochondrial enzyme activities. In our animals, it is likely that coronary blood flow was increased to compensate for the decreased PaO_2, thus maintaining O_2 delivery. At the degree of hypoxemia studied, in intact animals, postulated mechanisms of mitochondrial depression do not appear to be operative.

REFERENCES: 1. Science, 1984; 223: 707-709.

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TITLE: HALOTHANE DECREASES IONIC FLUXES DUE TO METABOLIC INHIBITION, HYPOTHERMIA OR ISCHEMIA IN ATRIAL MUSCLE STRIPS.

AUTHOR: R.G. Eckenhoff, M.D.

AFFILIATION: Dept. of Anes. and Institute for Environ. Med., Univ. of Penn. Med. Ctr., Phila., PA 19104-6068.

Halothane has been reported to alter membrane permeability and transport properties to ions, notably Ca[1,2]. Although little attention has been given to other ions, there is suggestive evidence for an effect on Na and K as well[3]. In order to further understand the effects of halothane on cellular ionic composition under both normal and stressful conditions, electron probe microanalysis (EPMA) was used to examine cytoplasmic (cyto) and mitochondrial (mito) Na, K and Ca conc. in atrial myocytes in situ. Rat atrial strips were rapidly isolated, tied under slight tension to ends of clean wooden applicator sticks, and incubated in Kreb's buffer at 30°C. The media was equilibrated with 95% O_2/5%CO_2 with 0, 1.5 or 4.7% halothane, and, after 60 minutes, the strips were rapidly frozen in Freon-22 at -160°C. Other conditions: addition of 1.0 uM FCCP, switching equilibration gas to 95%N_2/5%CO_2, or decreasing the media temp. to 2°C. Only 0 and 1.5% halothane were used for the latter conditions. Cryosections (150 nm) were cut from the frozen atrial strips, cryotransferred into an electron microscope, freeze-dried at -100°C and examined for morphology/ionic composition with EPMA. Cyto and mito were examined in at least 10 myocytes from 2 preparations for each condition. Under normal conditions at 30°C, there was no change in cyto or mito Na, K or Ca in tissue exposed to halothane (ANOVA [halothane] vs [Na,K or Ca], P=NSx6). FCCP-treated and ischemic tissue showed significant increases in Na and Ca, and reductions in K conc. in both intracellular compartments when compared to control tissue. 2°C conditions produced significant elevations in Na and reductions in K conc. in both compartments, but no significant change in Ca in either compartment. Most of the above changes also occurred in the presence of halothane (1.5%), but the magnitude was reduced in all instances (P<.001). In conclusion, clinical conc. of halothane reduce the alterations in intracellular ionic composition produced by stressful conditions.

References. (1) Rusy BF, Komai H. Anesthesiology 1987;67:745-766. (2) Lynch C. Anes Anal 1988;67: 1036. (3) Gallagher JD, et.al. Anesthesiology 1989;71:695.

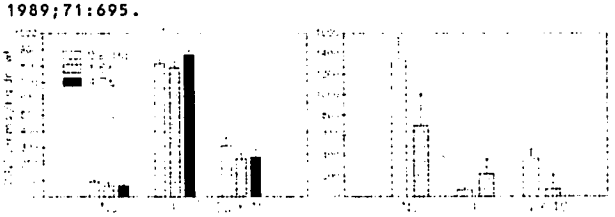

Fig. 1. Cytoplasmic Na, K and Ca (x10 or x100) in normal 30°C Kreb's (left) or in Kreb's with 1.0 uM FCCP (right). (* = P<.001).