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TITLE: Reduction of Fluorescent Myocardial Ischemia by Lidocaine

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Introduction

Anesthetics exert stabilizing effects on cell membranes and may be important in maintaining cellular integrity during anoxia and reperfusion. To date methylprednisolone, thiopentone and propranolol have been shown to protect anoxic myocardium and reduce loss of intracellular enzymes. Administration of lidocaine has been shown to reduce ultrastructural damage during ischemic arrest normothermic cardiopulmonary bypass.[1] The present study was designed to determine more precisely, and quantitate, the effects of lidocaine on ischemic myocardium, using a real-time in situ NADH-NADPH fluorescent technique.

Methods

Open chested dogs (n=16), anesthetized with thiamylsodium 20 mg/kg, underwent intermittent serial 60 second anterior descending coronary artery ligation, with adequate reperfusion intervals, before and after treatment with lidocaine (2 mg/kg bolus, 0.04 mg/kg/min infusion). A trifurcated fiber-optic probe[2] simultaneously recorded epicardial NADH-NADPH fluorescence (F), reflectance (R) and compensated fluorescence (CF=F-R). Myocardial blood flow was determined in control and ischemic myocardium by radioactive (9 ± 2 μm) microspheres. Heart rate, epicardial ST segment, left ventricular (LV) pressures, LV dp/dt and mean arterial pressure were continuously monitored. Mitochondrial respiratory function was measured in another 16 dogs undergoing 40 minutes cardiopulmonary bypass with normothermic ischemic arrest, with and without lidocaine.

Results

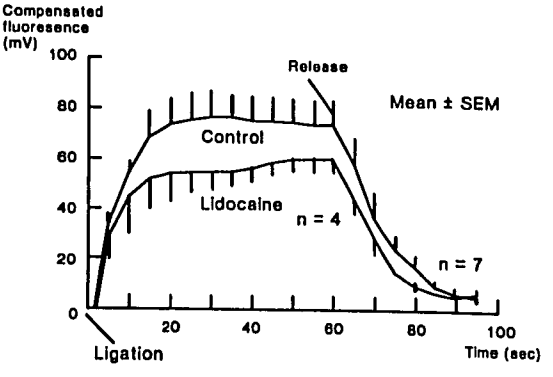
NADH-NADPH fluorescence afforded earliest evidence of onset of myocardial ischemia (1.3 ± 0.2 sec), followed by decreased LV dp/dt max (7.3 ± 1.4 sec), increased LVEDP (9.9 ± 2.4 sec) and ST elevations (12.6 ± 4.9 sec). Lidocaine reduced peak fluorescence by an average 19%, from 94 ± 7 to 76 ± 4 mv ($p < 0.004$), and affected its typical temporal sequence, manifested chiefly as contraction in ischemic duration ($p < 0.002$). Lidocaine increased state 3 respiration by 33% ($p < 0.05$) and RCI by 36% ($p < 0.05$), with both glutamate and succinate-rotenone substrate. These results were independent of changes in blood flow or altered hemodynamics.

Discussion

Advantages of the fluorescent technique include capability of monitoring minute changes in tissue ischemia dynamically, at a molecular and cellular level without tissue destruction. Our findings support previously reported morphologic studies.[1] Fluorometry showed lidocaine delayed onset of ischemic fluorescence, while recovery was more rapid. An effect on myoglobin with facilitation of oxygen diffusion or change in oxygen reserve cannot be excluded. However, a more likely explanation is an effect on mitochondrial electron transport, so that oxidative phosphorylation and oxidation of NADH-NADPH occur during cell anoxia, either primarily or secondary to membrane stabilization with reduced cation fluxes.

References

1. Schaub RG, Stewart G, Strong M, et al: Reduction of ischemic myocardial damage in the dog by lidocaine infusion. Am J Path 87:399-405, 1977
2. Chance B, Mayevsky A, Goodwin C, et al: Factors in oxygen delivery to tissue. Microvasc Res 8:276-282, 1974



The effect of lidocaine infusion on epicardial NADH-NADPH compensated fluorescence in an open chested anesthetized dog. Coronary artery constriction is for 60 seconds. Onset of fluorescence occurs after a 1-2 second delay and rises rapidly with a plateau of 75 mv at 30 seconds. In this dog peak fluorescence is reduced 23% by administration of lidocaine.

	Ischemia 40 Minutes		Ischemia 40 Minutes, Reperfusion 20 Minutes	
	Control	Lidocaine	Control	Lidocaine
ADP:O	2.78±0.12	2.83±0.06	3.04±0.04	2.97±0.04
State 3	61.5±9.8	80.8±9.1	89.9±12.3 *	120.7±11.6
State 4	12.1±1.0	11.6±1.6	8.6±0.6 *	12.4±1.2
RCI†	33.4±7.9 *	63.5±8.2	63.6±4.9 *	86.6±7.6

Indices of mitochondrial respiratory function (glutamate substrate) in ischemic and reperfused dog hearts with and without lidocaine. Mean ± SEM.

* $p < 0.05$, † RCI of ischemic myocardium expressed as a percentage of non-ischemic myocardium.