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Title: EVALUATION OF PROPRANOLOL IN MYOCARDIAL ISCHEMIA BY NADH FLUOROMETRY

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Introduction. It is commonly held at present that the beneficial effect of propranolol in angina pectoris and myocardial ischemic injury is due to a more favorable balance between myocardial oxygen supply and demand. This conclusion is mainly based on propranolol's ability to cause a marked reduction in myocardial oxygen consumption. However, there is a lack of direct evidence for improvement of the energy demand-supply balance in the ischemic myocardium under the influence of propranolol. Chance and associates devised a technique for assessing tissue energy demand-supply balance based on the fluorescent characteristics of NAD-NADH system, the initial member of the respiratory chain¹. With insufficient oxygen supply, more NAD is reduced to NADH. NADH fluoresces when excited by ultraviolet light; NAD does not. NADH fluorometry permits the continuous measurement of intracellular redox state from the surface of the heart. This technique was used in the present study to evaluate the effect of propranolol on myocardial energy balance.

Methods. The study was performed on isolated rabbit hearts perfused by a modified Langendorff technique at 37°C with oxygenated Krebs-Henseleit solution. The heart was paced at 200 beats/min. Developed systolic tension was measured with a displacement transducer attached to the ventricular apex. Left ventricular NADH fluorescence was monitored by a fluorometer. Its branched light guide supplied 366 nm excitation light to the surface of the heart through some fibers and transmitted 450 nm fluorescent light through others back to a photomultiplier. Coronary outflow was collected and measured. Graded global ischemia was provided by reducing perfusion pressure from 100 cm H₂O to 0 in 5 equal steps at 5 min intervals. Response to the ischemia in the control hearts (n = 15) were compared to those in the hearts (n = 15) perfused with propranolol (1 mg/L).

Results. Fig. shows that graded decrease in perfusion pressure, and hence in coronary flow, produced increments of increased NADH fluorescence. Propranolol reduced NADH fluorescence responses to moderate ischemia (at 25 cm H₂O, an increment of 14 ± 3% in propranolol group vs 35 ± 5% in control group, p < 0.001). However with severe ischemia, protective effect of propranolol was decreased and the final level of fluorescence at "no flow" stage in propranolol and control hearts was almost equal. Propranolol decreased the developed systolic tension at a perfusion pressure of 100 cm H₂O by 24% (38 ± 3 gm in propranolol group vs 49 ± 3 gm in control group, p < 0.02). Graded decrease in perfusion pressure caused declines in the developed tension in both groups. However, differences between the groups with regard to contraction force gradually decreased and completely disappeared at 12.5 cm H₂O.

Discussion. Our findings show an improvement in energy demand-supply balance in propranolol-treated moderately ischemic myocardium. Since heart rate was controlled, the improvement of the balance may be attributed to the decrease in the force of myocardial contraction. However, it should be noted that at the lowest level of coronary perfusion (12.5 cm H₂O), the difference in the developed systolic tension in control and propranolol groups disappeared. In complete ischemia, we were unable to demonstrate the beneficial effect of propranolol on the final result of changes in myocardial energy balance. This fact is of interest with respect to the problem of myocardial preservation in ischemic arrest.

References.

1. Chance B, Mayevsky A, Goodwin C, et al.: Factors in oxygen delivery to tissue. *Microvasc. Res.* 8:276-282, 1974.

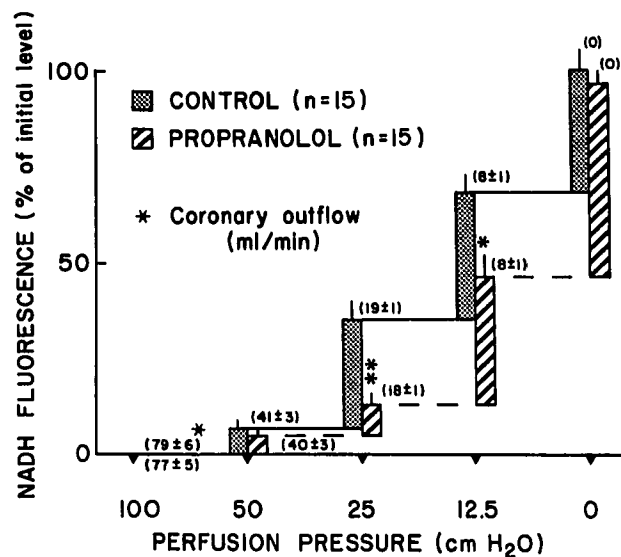


Fig. Effect of propranolol (1 mg/L) on NADH fluorescence responses to graded global ischemia in isolated rabbit hearts. Values are mean ± SE. * - p < 0.01; * - p < 0.001 for differences between control and propranolol. Propranolol reduced NADH fluorescence responses at the coronary perfusion pressure of 25 and 12.5 cm H₂O.