Title: FLUNARIZINE PRETREATMENT PREVENTS MYOCARDIAL STUNNING

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Flunarizine (Flu) is a new calcium entry blocker (CEB) which has been shown to be of benefit in the protection against postischemic brain damage. The cardioprotective effect has also been shown in cardomyocites. The aim of this study was to examine the effect of Flu pretreatment on postischemic myocardium in terms of recovery of function and preservation of high energy phosphates (HEP).

Twenty-one isolated working rabbit hearts were perfused at 37°C with heated and oxygenated Krebs Henseleit Buffer. The hearts underwent 20 min of Langendorff perfusion (LD), followed by 15 min of working heart. During the experiments, hemodynamic parameters, including heart rate (HR), aortic pressure (AP), aortic flow (AF), coronary flow (CF), and left ventricular pressure (LVP), and its first derivative (dP/dt+ and -) were monitored. For the next 30 min period the hearts were at random allocated to 4 groups. Group one (n=6) received solvent. Groups two through four (n=5 each) received 0.16, 0.32, 0.64mg/L of Flu respectively. A period of 20 min normothermic global ischemia was induced. Reperfusion was then initiated: 5 min LD mode, followed by 20 min in the WH mode. During the reperfusion period drugs were not present in the perfusate. At the end of the exp. left ventricular biopsies were taken to assess HEP.

Results: Flu produced a decrease in both cardiac output and heart rate but not significant (p> 0.05). There was also a decrease in left ventricular filling pressure and dP/dt + and - in all doses used, but not statistically significant. Coronary flow was increased in all doses (p>0.05).

Twenty min of global normothermic ischemia in solvent treated hearts resulted in severe myocardial damage, in which 50% of the hearts developed ventricular fibrillation. 20% had partial recovery of AF, and HR (see fig. 1). At 0.16mg/L Flu did not significantly influence recovery parameters: AF recovered only to 26.7% of control. At doses of 0.32 and 0.64mg/L, Flu prevented ventricular fibrillation after reperfusion and all hearts kept on beating (p<0.02). Furthermore, all hearts in both groups did develop a high LVP resulting in the production of aortic flow.

After 20 min reperfusion, the HEP contents were as follows: in the solvent group the ATP was 6.7±3.9 uMol/g and the 0.16 mg/L group had a mean ATP of 8.8±3.3 uMol/g (p>0.05). In Groups three and four, the HEP were significantly better preserved: 12.5±1.6 and 11.6±2.0 uMol/g respectively (p<0.01), see fig. 2.

We conclude that pretreatment with Flu in doses higher than 0.16 mg/L has a cardioprotective effect in terms of hemodynamic recovery and preservation of HEP.

Fig. 1

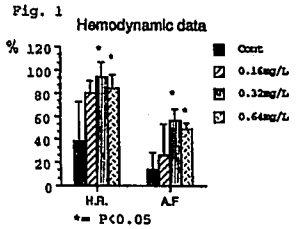
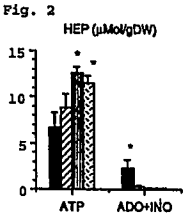


Fig. 2



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2. Amer J of Emergency Medicine Vol. 8, P 1-6

Title: EFFECT OF THE VOLATILE ANESTHETICS ON THE HYPOTHERMIC MYOCARDIUM

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Hypothermia is likely to influence not only excitation-contraction (EC) coupling per se but also the potency of drugs, such as Halothane and Isoflurane which interfere with various steps of EC coupling. In this study we investigated the effect of Halothane (H) and Isoflurane (I) on the hypothermic myocardium.

The model used is an isolated Langendorff rabbit heart. Via the left atrium a fluid-filled balloon is placed in the left ventricle (LV) to obtain isovolumetric contraction. The hearts were perfused with oxygenated and heated Krebs Henseleit buffer. LV systolic (LVSP) and end diastolic (LVEDP) pressure, LV dp/dt + and - were measured continuously with a pressure tipmanometer in the ventricle. The hearts were paced on the right ventricle at a constant rate of 150 beats per minute.

Sixteen rabbit hearts were randomized. After a 30 minute equilibration period at 37°C the hearts were gradually cooled to 30°C. The control group (n=8) received no volatile anesthetics. During cooling, Group II (n=4) and Group III (n=4) were exposed to H, 1.5% and I, 2.3% respectively. Heart rate and ventricular volume were kept constant throughout the protocol.

During cooling the contractility (LVdp/dt+) decreased significantly (P<0.05): from 1506±108 at 37° to 606±105mmHg/sec at 30°C. Also, relaxation was impaired significantly: LVdp/dt- decreased from 1100±93 at 37°C to 381±78 at 30°C (Fig. 2). A significant increase in the LVEDP was noted from 32° to 30° from 12 ± 1.5mmHg to 32 ± 6mmHg. Simultaneously there was a decrease in LVSP: (Fig. 1).

There was a further depression of systolic function (peak LVP and LVdp/dt+) with the induction of inhalation anesthetics (see Figs.). H depressed systolic function more than I (p<0.05). Diastolic properties of the heart (compliance i.e. LVEDP and relaxation i.e. LVdp/dt -, (see Figs.) were also depressed by the volatiles but to the same extend with H and I (p>0.05).

Although the solubility of the inhalation anesthetics is greater at lower temperature,[1] the function is not depressed further with the higher concentration.

Contrary to previous reports on papillary muscles,[2] in the intact heart, hypothermia at constant rate and LV volume, exerts a profound negative inotropic effect. The volatile anesthetics have an additive depressive effect that is significantly greater for H than for I.

Fig. 1

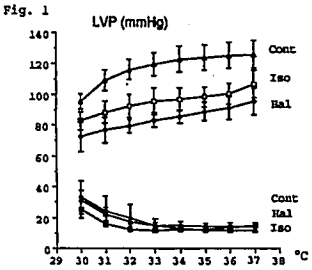
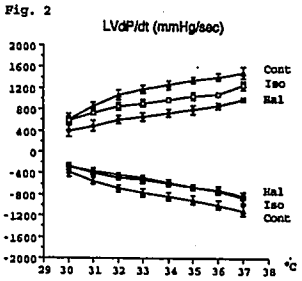


Fig. 2



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