Title: PROTECTIVE EFFECT OF HALOTHANE AGAINST HYPOXIC INJURY IN THE ISOLATED GUINEA PIG HEART.

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Introduction. Global hypoxia of the myocardium is associated with compromised cardiac function and ventricular dysrhythmias. Although the mechanisms underlying myocardial injury under these conditions are not fully understood, calcium accumulation appears to be one of the primary events leading to cell necrosis and interventions limiting calcium overload appear to reduce the extent of injury. Besides its beneficial effects, due to indirect hemodynamic influences,[1] halothane (H) might also decrease postischemic calcium accumulation.[2] The present study examines the direct effects of H on functional recovery of the myocardium following global hypoxia in the isolated guinea pig heart.

Methods. Twenty-three guinea pigs (350-500 g) were decapitated after I.P. administration of ketamine (20 mg) and heparin (1000 units). The hearts were quickly excised and perfused at constant pressure (55 mmHg) by the Langendorff technique with modified Krebs-Ringer solution equilibrated with 97% O_2 and 3% CO_2 (pH 7.38, PO_2 535 mmHg) at 36.5°C. Heart rate (HR) and atrioventricular (AV) conduction time were recorded with bipolar electrodes placed in the right atrium and right ventricle. Left ventricular (LV) systolic and diastolic pressure were measured with a transducer connected to a thin latex balloon inserted into the left ventricle through the mitral valve. Balloon volume was initially adjusted to zero diastolic pressure. H at 1% was delivered by a vaporizer and measured at the aorta by gas chromatography (0.40 ± 0.01 mM). After a 30 min equilibration period, all hearts were perfused for 30 min with a solution equilibrated with 97% N_2 and 3% CO_2 (PO_2 90 mmHg) followed by 40 min of reoxygenation. In the H group, H was present for 10 min prior, during and for 10 min after hypoxic period. Measurements were made at initial control, after 10 min H, at 5, 15 and 30 min of hypoxia and at 10 and 40 min of reoxygenation. Statistical differences were determined by using Chi-square test and Students t-test.

Results. 1% H decreased HR by 13.8 ± 2.1% and increased AV time from 61.7 ± 1.4 to 81 ± 2.9 ms. Effects of H and hypoxia on LV systolic and diastolic pressures are shown in Fig. 1. Although H decreased systolic pressure by 48 ± 3%, after only 5 min of hypoxia the differences in systolic pressures between the control and H group disappeared. Hypoxia increased diastolic pressure in the control group only. During reoxygenation HR and AV conduction recovered completely to initial control levels in both groups. Although systolic pressure was decreased in both groups, it was significantly lower in Group C. Diastolic pressure continued to rise during reoxygenation in C group while it returned back to control level in H group. The incidence of ventricular fibrillation (VF) for H and C groups are shown in table 1. VF was preceeded by AV dissociation with PVC's or ventricular tachycardia. H reduced the incidence of VF as compared to C group.

Discussion. The negative inotropic action of H is often used to advantage in limiting myocardial oxygen demand and the occurrence of ischemic episodes in patients undergoing myocardial revascularization.[3] Beside peripheral hemodynamic effects, direct cardiac effects of H include depression of intracellular calcium[4] and lower calcium accumulation following myocardial ischemia.[2] This study indicates that the presence of H significantly improves functional recovery of isolated hearts from a hypoxic episode as assessed by: (1) decreased incidence of VF; (2) lower diastolic pressure and (3) improved myocardial contractility. Although the therapy of intraoperative myocardial hypoxia needs to be individualized, it seems plausible that H may reduce the extent of myocardial damage during ischemia and improve functional recovery on reperfusion.

Figure 1.

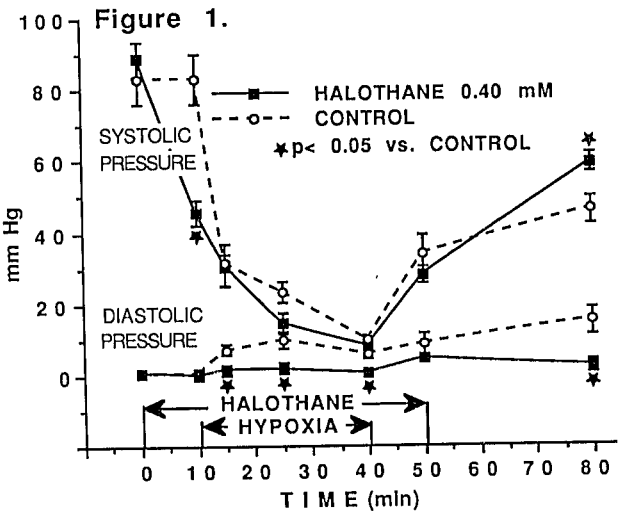

Table 1. Incidence of ventricular fibrillation

Group	15' Hypoxia	30' Hypoxia	30' REOX
Control (N=11)	2	6 *	9 *
H (1%) (N=12)	0	2	3 +

* p<0.05 vs. initial C, + p<0.05 vs. C group
REOX = Reoxygenation

References
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