TITLE: INOTROPIC EFFECT OF KETAMINE ON CARDIAC PAPILLARY MUSCLE IN NORMAL AND CARDIOMYOPATHIC HAMSTERS

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Recent studies (1,2) have demonstrated that ketamine (KET) has a direct positive inotropic effect on normal rat heart muscle. The question to be answered is whether KET is a positive inotropic agent on diseased myocardium. We studied the mechanical effects of KET on intrinsic contractility of cardiac papillary muscles in normal (NO) and cardiomyopathic (CM) hamsters.

Left ventricular papillary muscles were excised from NO (n=10) and CM (n=10) (Strain BIO 82-62) hamsters (6-month old). They were suspended in a Kreibs-Henseleit solution bubbled with 95% O2-5% CO2 (pH 7.40, 29°C, Ca++ 2.5 mM), field stimulated (3/min), and exposed to 2 concentrations of KET (10-5 then 10-4 M) which correspond to the concentrations reached during maintenance and induction of anesthesia respectively (3). The following parameters of inotropy were determined from various afterloaded twitches : the maximum unloaded shortening velocity (Vmax), and the active isometric force normalized per cross-sectional area (AF/s). The Hill's equation was determined from the force-velocity curve to calculate peak power output (Emax). A two-way analysis of variance and Student's t test with Bonferroni correction were used. Data are mean ± SD.

A positive inotropic effect was observed in NO hamsters as shown by the increase in Vmax, AF/s, and Emax. In CM hamsters, the slight increase in inotropic parameters was not significant (Table).

It was concluded that: 1) KET was a direct positive inotropic agent in NO hamsters; this positive inotropic effect was consistant with previous studies on isolated rat myocardium (1, 2); 2) KET did not induce any significant inotropic effect in CM hamsters.

References
1. Br J Pharmacol 76 : 85-93, 1982
2. Anesthesiology 71 : 116-125, 1989
3. Br J Anaesth 51 : 1167-73, 1979

Table: Inotropic effect of ketamine.

	NORMAL (n=10)		CARDIOMYOPATHIC (n=10)		P value
KET (M)	10-5	10-4	10-5	10-4	
Vmax	119* ±11	134* ±17	107 ±18	107 ±13	0.025
AF/s	131* ±26	157* ±36	114 ±27	113 ±23	0.001
Emax	140* ±25	180* ±51	109 ±17	113 ±24	0.001

Mean percent of control values ± SD. * : p < 0.05 compared to control values. P value concerns the difference between the 2 groups.

A556

THE EFFECTS OF PROPOFOL ON CEREBRAL BLOOD FLOW IN CORRELATION TO CEREBRAL BLOOD FLOW VELOCITIES IN DOGS

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This study investigates the effects of propofol on cerebral hemodynamics and intracranial pressure (ICP) in dogs and correlates cerebral blood flow (CBF) using microspheres with cerebral blood flow velocities using transcranial Doppler sonography (TCD).

Methods: Following approval of the Institutional Animal Care Committee, 6 mongrel dogs were anesthetized with isoflurane and catheters were inserted into both femoral arteries, veins and the lateral ventricle for blood pressure measurement, blood sampling and ICP determination. Temperature, arterial blood gases and pH were maintained constant. Radioactive microspheres were injected using a left atrial catheter for measurement of cortical CBF. A pulsed TCD-probe (8 MHz, TC2-64 B™, EME) was placed on the dura via a temporal bone window to obtain mean flow velocity (Vmean) and pulsatility index (PI = (Vsyst-Vdiast)/Vmean) as an indicator of peripheral cerebral vascular resistance in the middle cerebral artery. EEG was recorded from temporo-parietal recording sites vs. a frontal reference. At completion of surgery all animals were equilibrated at 0.5 MAC isoflurane in 50% N_2O/O_2 for 30 min. Following recordings of baseline data, propofol (0.8mg/kg/min) was infused and a second series of measurements was performed at induction of burst suppression. Propofol infusion was then discontinued and a third series of measurements was done following recovery of EEG to baseline levels. Propofol infusion (0.8mg/kg/min) was repeated and the last measurements were obtained after induction of burst suppression.

Results: Arterial blood pressure did not change over time. Data for CBF, Vmean, PI and ICP are given in table 1. Propofol significantly reduced CBF and Vmean from baseline values and cerebral hemodynamics remained reduced following recovery (recovery time: 50-80 min). A second infusion of propofol produced cerebral hemodynamic depression similar to the first burst suppression period. Changes in CBF and Vmean were closely correlated (r = 0.86). PI increased significantly in response to propofol. The reduction in CBF and Vmean was associated with decreases in ICP at each respective propofol treatment.

Discussion: The close correlation between decreases in CBF and Vmean indicates that TCD continuously measures changes in CBF following administration of propofol. Changes in PI suggest increased cerebral vascular resistance. The significant decline in ICP indicates that propofol-induced decreases in CBF are associated with reductions of cerebral blood volume.

time	CBF (ml/100g/min)	Vmean (cm/s)	PI	ICP (mmHg)
baseline	156±69	37±15	0.61±0.22	15±6
propofol 1	48±14*	15±4*	0.91±0.18*	11±2*
recovery	73±27*	25±7*	0.77±0.19*	16±4
propofol 2	44±8*	16±4*	0.88±0.14*	13±3

Table 1: Cerebral hemodynamic data (mean±SD) during baseline, propofol treatments and recovery (* = p < 0.05 compared to baseline).