Title: HEMODYNAMIC INTERACTION OF NIFEDIPINE AND HALOTHANE IN DOGS

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INTRODUCTION: Nifedipine is a calcium (Ca^{++}) channel blocker used for treatment and prevention of coronary artery spasm associated with ischemic heart disease. Coronary spasm can occur during anesthesia. We have examined in the dog the hemodynamic effects of acute administration of nifedipine and the interaction of halothane, since it is likely that this drug combination may be encountered clinically.

METHODS: Sixteen mongrel dogs were anesthetized with thiopental 20 mg/kg and maintained at normothermia, ventilated to keep arterial blood gases normal and divided into 2 groups of 8 animals each. Anesthesia was maintained with 1% halothane given nifedipine 10 µg/kg i.v. (Group I), 2% halothane with nifedipine 10 µg/kg i.v. (Group II). Nifedipine was administered over 2 minutes. Central aortic systolic (SBP), diastolic (DBP) and mean blood pressures (MAP), right and left atrial pressure (LAP), heart rate (HR), left ventricular dP/dt, peak left ventricular pressure (PLV), and left anterior coronary artery blood flow (QLAD) with a Statham flow probe were continuously monitored and recorded on a grass polygraph. A 7 fr. thermodilution thermister tipped pulmonary artery catheter was placed for intermittent determination of cardiac output (duplicate thermodilution measurements). Systemic vascular resistance (SVR) was calculated. Measurements were recorded at the following times: 30 min of stable (± 10%) hemodynamic variables (C); 2 min after the end of infusion of nifedipine (D1); 15 min after nifedipine (D2). Data were analyzed using a split-plot in time analysis to determine drug effects and drug interaction effects with time.

RESULTS: The administration of nifedipine produces a more significant decrease in MAP in Group II (-23%) than in Group I (-14%), $p < .02$ (Table). SVR decreased in both groups. Of interest is the significant ($p = .02$) drug interaction effect on PLV (Fig.); nifedipine (Group II) tends to depress the PLV not seen with 1% halothane (Group I). This interaction was not found with dP/dt. All parameters returned to control values at D2.

DISCUSSION: Nifedipine and halothane both alter intracellular calcium kinetics in cardiac and smooth muscle. The Ca^{++} changes wrought by these drugs explain their respective negative inotropic and vasodilation effects. Nifedipine produces a significant, transient decrease in BP which is more pronounced in Group II. In contrast, indices of myocardial contractility (dP/dt and PLV) are less affected, reflecting 1) the known predominant effect of nifedipine on smooth muscle and 2) perhaps baroreflex activity that preserves contractility. Of note is the tendency for the higher halothane dosage (2%) to inhibit probable compensatory reflex changes to nifedipine: 1) the tachycardia is prevented and 2) the PLV is depressed.

The conclusion is that acute administration of nifedipine during halothane anesthesia produces important decreases in blood pressure. Increased halothane has a significant effect on the blood pressure response, and halothane in higher doses tends to ameliorate the compensatory response in contractility and probably in SVR. If nifedipine is to be administered to anesthetized patients, the major hemodynamic response will be decreased SVR and BP. Nifedipine should be administered with caution in deeply anesthetized patients.

GROUP I	C	D1	P
HR	132 ± 7.8	169 ± 25.5*	.07
MAP	94 ± 7.8	81 ± 8.0	.04
LAP	7.0 ± 1.24	7.8 ± 1.30	NS
PLV	124 ± 4.9	124 ± 6.3	NS
CO	3.6± 0.32	4.9 ± 1.2	NS
QLAD	37.4 ± 7.85	41.3 ± 8.42	NS
dP/dt	2312 ± 168.7	2228 ± 142.6	NS
SVR	2100 ± 224.8	1855 ± 473.5	.05
GROUP II	**C**	**D1**	**P**
HR	128 ± 6.9	134 ± 9.0	NS
MAP	71 ± 4.3#	54 ± 3.6+	.003
LAP	8.1 ± 1.19	8.0 ± 0.92	NS
PLV	108 ± 7.1	95 ± 7.5+	NS
CO	2.9 ± 0.53	4.2 ± 0.79	NS
QLAD	28.3 ± 4.07	24.7 ± 4.19	NS
dP/dt	2144 ± 164.6	1948 ± 203.9	NS
SVR	1986 ± 401.9	885 ± 117.8	NS

* $p = .02$ change greater in Group I than Group II
\+ $p = .02$ change greater in Group II than Group I
\# $p = .02$ lower in Group II than in Group I