TITLE: THE HEMODYNAMIC INTERACTION OF EPINEPHRINE WITH THE SPECIFIC BRADYCARDIC AGENT UL-FS 49

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UL-FS 49 (U) is a specific bradycardic agent which acts by a mechanism different from beta or calcium channel blocking agents. Previous studies in dogs have suggested that U has little effect on the hemodynamic response to isoproterenol. This investigation characterized the hemodynamic interaction between U and epinephrine (E) in the canine model.

Femoral and thermodilution pulmonary arterial lines were inserted to measure mean arterial blood pressure (MAP) and cardiac output (CO) in 8 dogs anesthetized with sodium pentobarbital. After median sternotomy, a Millar catheter was introduced into the left ventricle via the left atrium and mitral valve to measure left ventricular dP/dT. Renal artery blood flow (RBF) was measured using an electromagnetic flow probe placed on the left renal artery via a midline abdominal incision. Group-A dogs received E, 0.1 - 0.8 UG/KG/MIN IV for 15 - 30 MIN followed by U, 1.0 MG/KG IV bolus. Group-B dogs received U, 1.0 MG/KG IV bolus followed by E, 0.1 - 0.8 UG/KG/MIN IV infusion 30 minutes later. Measurements were continued for 1 to 2 hours after drug administration. dP/dT data were corrected for changes in HR. Results reported as mean ± SD were compared with either analysis of variance, the Wilcoxon, or the Friedman test. $P < 0.05$ was considered significant.

GROUP-A (n = 5)

	BASELINE	EPINEPHRINE	UL-FS 49
HR	140±16 (NS)	149±22 (p<.001)	84±13
MAP	117±34 (NS)	119±30 (NS)	108±25
CO	3.8±0.6 (p=.05)	6.3±1.0 (NS)	4.9±1.6
dP/dT	1181±673 (p<.06)	2072±1180 (NS)	1300±498
RBF	768±350 (NS)	664±316 (NS)	656±236

GROUP-B (n = 3)

	BASELINE	UL-FS 49	EPINEPHRINE
HR	132±31 (p<.05)	84±16 (NS)	93±17
MAP	122±32	106±35 (NS)	121±27
CO	4.2±0.3	4.3±1.5 (p<.06)	6.2±1.5
dP/dT	800	813±255(p<.05)	1781±462

The most striking effect of UL-FS 49 is its ability to selectively decrease HR without altering contractility, CO, MAP, or RBF. The possibility of combining the negative chronotropic effects of U with the positive inotropic effects of E may potentially benefit patients with severe heart failure.

TITLE: EFFECT OF AORTIC OCCLUSION ON CANINE STUNNED MYOCARDIUM

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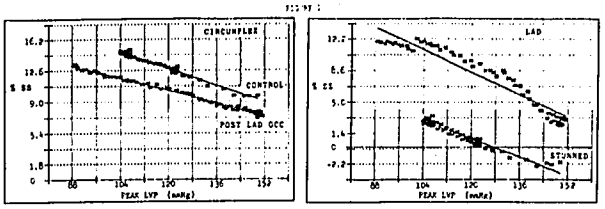
INTRODUCTION: Transient myocardial ischemia followed by reperfusion produces prolonged reversible ventricular dysfunction (stunned myocardium). We studied the effect of increased afterload, as occurs clinically during aortic cross clamping, on regional function of both stunned and normal canine myocardium.

METHODS: Ten pentobarbital and fentanyl anesthetized dogs underwent 15 minutes of left anterior (LAD) coronary artery occlusion and reperfusion. Regional function was measured with pairs of sonomicrometry crystals in the LAD and circumflex (CX) myocardium. The effect of increased afterload was determined by a gradual (30 sec) occlusion of the descending aorta prior to (PRE) LAD occlusion and 15 minutes after (POST) reperfusion. For each aortic occlusion the % systolic shortening (%SS) at maximum and minimum peak left ventricular systolic pressure (LVP) was calculated. Also, the relationship of peak LVP to %SS for each occlusion was derived from the slope and x intercept (LVP at 0 %SS) of the regression lines plotted as in Figure 1. Data was analyzed by ANOVA.

RESULTS: Aortic occlusion significantly increased peak LVP and decreased function of LAD and CX myocardium both before and after LAD stunning. The slopes of the LVP-%SS plots were unchanged, but the intercept (LVP at 0 %SS) was significantly decreased in the stunned LAD myocardium. In 5 dogs, POST LAD %SS changed from positive to negative (ie to bulging or dyskinesia) during aortic occlusion, despite increased LAD blood flow and no ST change in 4.

TABLE	CX %systolic shortening at min LVP	at max LVP	LAD %systolic shortening at min LVP	at max LVP
PRE LAD Occ	12.9±2.1	9.3±2.0 *	13.9±4.4	7.8±5.2 *
POST repfn	12.3±3.4	8.8±3.5 *	5.2±4.0 !α	0.5±2.7 *!α
	CX slope	x intercept	LAD slope	x intercept
PRE LAD Occ	-.10±.04	274±48	-.12±.05	280±103
POST repfn	-.13±.04	249±47	-.13±.05	161±36 !α

*-p<0.05 vs. min LVP value. !-p<0.05 vs. Pre LAD Occ Mean±SD
α-p<0.05 vs. CX at same time period. Occ=occlusion, repfn=reperfusion



DISCUSSION: Increased afterload produced by aortic occlusion reduces systolic function of both normal and stunned myocardium. However, dyskinesis occurs more readily in stunned myocardium. Whether this is due to mechanical properties rather than ischemia has important implications for the detection of ischemia using regional wall motion abnormalities.

REFERENCE: Circulation 66:1146, 1982.