TITLE: AMRINONE, REGIONAL MYOCARDIAL METABO-

LISM, AND HYPOPERFUSION IN DOGS

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Amrinone, a phosphodiesterase-inhibiting, non-adrenergic, nonglycoside agent with combined inotropic and vasodilator properties, may affect myocardial supply and demand for O_2 . We studied whether amrinone affects regional metabolism in ischemic myocardium during coronary hypoperfusion in dogs.

In 18 dogs anesthetized (barbiturate) and ventilated, the pulmonary artery (PA), aorta (Ao), left ventricle (LV), left anterior descending artery (LADa) and vein, and circumflex vein were cannulated. A micrometer was used to constrict the LADa to decrease flow by 50%, 75%, and 100% of resting flow for 15 min with 1 h of normal flow between each. In 9 dogs, amrinone, 0.75 mg/kg followed by 10 ug/kg/min, was given before each constriction. Heart rate (HR), electrocardiogram, LADa flow, LV first time derivative (LV dP/dt), and Ao, PA, LADa, and LV pressures were measured continuously. Before and during constrictions, CO by thermodilution and regional myocardial blood flow (RMBF) by microspheres were measured and blood was sampled for measurement of blood gas values, lactate, sodium, and potassium.

Before and during constriction, mean PA, systolic LV, and LV end-diastolic (LVEDP) pressures were lower with amrinone (table). An pressure, HR, CO, stroke volume index (SVI), LV dP/dt, and RMBF in ischemic and nonischemic areas were similarly affected

A548

TITLE: ESMO

ESMOLOL ABLATES THE ADRENAL

MEDULLARY RESPONSE TO HYPOTENSION

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Introduction: In response to hemorrhagic hypotension or electrical stimulation of the splanchnic nerve, catecholamines released by the adrenal medullary chromaffin cells stimulate beta receptors located on the adrenal medullary vasculature resulting in vasodilatation and increased adrenal medullary blood flow (MQ). Our purpose was to determine whether the adrenal response pattern to hypotension induced by blood loss differs from that induced by beta adrenergic blockade; and whether the attenuation of the MQ response significantly alters systemic norepinephrine and epinephrine concentrations.

Protocol: Sixteen pentobarbital anesthetized, intubated, mechanically ventilated mongrel dogs were randomly allocated to one of four groups. Animals in Group1 and Group2 (n=4) were given two separate hypotensive stimuli to a mean arterial blood pressure (MAP) of 60mmHg for 15 minutes. The first stimulus was effected by blood loss into a pressurized bottle system, while the second hypotensive stimulus was effected by either repeat hemorrhage (Group1) or esmolol infusion (Group2). Adrenal cortical blood flow and MQ were measured (radiolabelled microsphere technique) prior to and after ten minutes of hypotension. Animals in Group3 and Group4 (n=4) were subjected to unilateral exteriorization of adrenal effluent and given a hypotensive stimulus for 60 minutes by either esmolol infusion or hemorrhage. Adrenal blood flow, adrenal venous norepinephrine and epinephrine, arterial norepinephrine and epinephrine were measured at 0, 5, 10, 15, 30, 45 and 60 minutes.

in the 2 groups before and during constrictions. The SVI/LVEDP ratio was higher with amrinone. During constriction in the ischemic zone, electrolytes, glucose, lactate extraction, and arteriovenous (a-v) 02 content difference, regional 02 delivery and consumption, and lactate flux ([a-v] lactate x RMBF), consumption ([a-v] lactate x flow), and extraction (a-v/a) were similar in the 2 groups.

Regional metabolism in ischemic myocardium during ischemia in dogs was not affected by amrinone, even though pressure in the left and right chambers was eased, which improved LV performance.

TABLE. Effects of Amrinone During LADa Constriction in 18 Dags

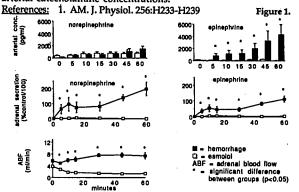
	Base-	During Constriction		
Group	line	50%	75%	100%
	Mean	Pulmonary A	rtery Pressure	(mm Hg)
Control	20 <u>+</u> 3	21 <u>+</u> 2	22 + 2	21 + 2
Amrinone	19 <u>+</u> 1	16 <u>+</u> 1*	16 <u>+</u> 2*	16 <u>+</u> 1*
		Systolic L	/ Pressure (mm	Hg)
Control	144 <u>+</u> 7	147 <u>+</u> 9	131 + 11	128 + 12
Amrinone	129 ± 5	121 <u>+</u> 6*	110 <u>+</u> 9 .	88 <u>+</u> 6*†
		SVI/LVEDP	Ratio (ml/mm	Hg)
Control	4.0 ± 0.5	2.9 + 0.4	1.8 + 0.2†	1.0 + 0.1†
Amrinone	6.0 ± 1.0	4.4 <u>+</u> 0.6*	4.0 ± 0.7*	4.1 ± 0.6*
	Lactate	Extraction	Ischemic Area	(% change)
Control	19 <u>+</u> 6	-47 <u>+</u> 15†	-140 ± 21†	-181 + 38†
Amrinone	15 <u>+</u> 6	-62 <u>+</u> 49†	140 ± 28†	-127 <u>+</u> 29†

Values: means + SEM; abbreviations are defined in the the text.

Statistical significance (p<0.05) was determined by two way analysis of variance procedure for repeated measures.

Results: In response to hemorrhagic hypotension, MQ increased three-fold and is comparable on repeated stimuli (Group1). Esmolol induced hypotension (Group2) ablated the adrenal medullary blood flow response to hypotension. The data from Group3 and Group4 are presented in figure 1. Esmolol attenuates the adrenal secretory response to hypotension. In addition, the rise in arterial epinephrine concentration normally observed during hypotension was ablated by esmolol, while the rise in arterial norepinephrine was maintained.

<u>Conclusions</u>: The present study demonstrates that esmolol ablates medullary vasodilatation and thereby significantly attenuates the adrenal secretion of catecholamines. Thus, the data suggest that locally induced changes in adrenal medullary blood flow alter arterial catecholamine concentrations.



^{*}P < 0.05 compared with control at same time.

 $t\underline{P}$ < 0.05 compared with baseline in same group.