POSTER SESSION XVI

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TITLE EFFECTS OF URAPIDIL AND CLONIDINE ON LEFT VENTRICULAR PERFORMANCE: A RADIONUCLIDE ANGIOGRAPHIC STUDY.

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Urapidil, a phenylpiperazine derivative of uracile, belongs to a new class of antihypertensive agents that have selective peripheral α-adrenergic blocking properties and centrally mediated hypotensive effects.[1] Pharmacologic profile and lack of rebound side effects and tachycardia are the rationale for the use of urapidil in anesthesiology. However, its more definite position in the management of perioperative hypertension remains to be established. This study was planned to compare the effects of urapidil (U) and clonidine (C) on left ventricular volumes and function using radionuclide angiography.

Methods: Twenty physical status ASA III patients with chronic coronary artery disease (CCS grade 1-2) and mild, established but untreated essential hypertension, scheduled for major urologic surgery were randomly assigned to two equal groups to receive i.v. U (0.4 mg/kg) or i.v. C (2.5 µg/kg). No patients had congestive heart failure, valvular heart disease, previous myocardial infarction, nor was any patient being treated with ß-blocking agents. Usual anti-anginal medication (nifedipine and isosorbide) were continued up to the time of the procedure. Each patient gave institutionally-approved written informed consent. Heart rate (HR) was measured from lead II of the ECG and blood pressure was monitored with a programmed electro-sphygmomanometer. All patients were studied by radionuclide angiography using first-pass and ECG gated equilibrium blood-pool techniques with *in vivo* 99mTechnetium (TC) labelled red blood cells.[2] Thirty min after stannouspyrophosphate pretreatment, a first-pass study in the 45° left anterior oblique view was done following the i.v. injection of 2 mCi of TC pertechnetate, making possible the measurement of isotopic cardiac output using the Stewart Hamilton principle and the estimation of the attenuation factor (AF). A 20 mCi source was then injected and an equilibrium study was performed: end-diastolic and end-systolic counts, and left ventricular global ejection fraction (LVEF) were calculated for 3 min apiece to be contemporaneous with blood pressure acquisitions; exact numerical values in ml of end-diastolic volume (EDV), end-systolic volume (ESV), stroke volume (SV) and densitometric cardiac output (CO) were obtained by using AF. 6 series of measurements were made (baseline, 3, 6, 9, 12 and 15 min) including the following: HR, mean arterial pressure (MAP), CO, EDV, ESV, SV and LVEF. Systemic vascular resistance (SVR) was calculated using standard formula. Students-t test and one-factor analysis of variance with repeated measurements were used for statistical analysis. Statistical significance was accepted at $P<0.05$.

Results: The two groups were similar with regard to morphologic data, CCS class of coronary artery disease and treatment. There were no significant differences in baseline values among the two groups. The main results, expressed as changes in % from baseline values (mean±SD), are summarized in the table.

		3 MIN	6 MIN	15 MIN	time effect	drug effect
MAP	U	-23.9±12.6	-25.8±11.8	-22.3±11.4	$p<0.001$	NS
	C	-15.6±9.4	-21.6±11.5	-17.5±9.2		
HR	U	+13.3±7.0	+4.8±8.0	+2.7±5.6	$p<0.001$	$p<0.01$
	C	-0.7±6.3	-0.3±5.0	-1.2±5.3	NS	
SVR	U	-27.2±12.7	-26.7±13.9	-23.8±12.5	$p<0.0001$	NS
	C	-17.0±10.8	-23.1±11.7	-19.6±8.3		
SV	U	-6.48±7.9	-2.72±5.7	-0.38±6.2	$p<0.05$	$p<0.05$
	C	+4.49±7.9	+4.26±8.3	+6.45±9.1	NS	
EDV	U	-10.9±11.1	-8.7±10.6	-2.7±10.3	$p<0.001$	$p<0.01$
	C	+4.3±7.5	+3.6±6.5	5.1±5.9	NS	
ESV	U	-18.7±15.0	-17.4±18.7	-5.7±18.0	$p<0.001$	$p<0.01$
	C	+5.0±13.4	+3.6±14.4	+6.0±19.4	NS	
LVEF	U	+5.9±8.3	+7.9±12.5	+3.8±9.4	NS	NS
	C	+0.7±5.1	+0.6±7.9	+1.3±10.4		

Conclusion: In patients with ischemic heart disease and untreated hypertension, and with normal LVEF and normal filling pressures, U and C induced a similar decrease in MAP associated with a reduction in SVR. Contrary to C, U induced an early and shortly increase in HR, and a decreased SV. The decreased EDV after U injection suggested a decreased venous return. In both groups, left ventricular performance, as assessed by LVEF, remained unchanged.

1-Am J Cardiol, 64: 1D-6D, 1989; 2-Anesth Analg 67: 949-955, 1988.

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TITLE: HYDRALAZINE VS. TRIMETHAPHAN ON ISOLATED RABBIT MYOCARDIUM

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Different vasodilators may have various effects on myocardial contractility. Hydralazine (HLZ), a phthalazine derivative, reduces blood pressure and peripheral resistance as a result of a direct vasodilatory effect, more on arterioles than on veins. Trimethphan (TMP) causes similar effect through ganglionic blockade. They also increase heart rate, cardiac output and stroke volume, probably secondary to a reflex response to afterload reduction. Nevertheless, their direct effects on myocardial contractility have not been clearly characterized. The purpose of this study was to investigate and compare the direct effects of HLZ and TMP on myocardial contractility in isolated rabbit myocardium.

Nine New Zealand white rabbits, weighing 2-3 kg, were anesthetized with 45 mg/kg i.v. pentobarbital. The heart was immediately removed. The first septal perforator of the left coronary artery was cannulated with a small polyethylene tube (PE-50) and perfused with warmed (37°C) oxygenated modified Kreb Ringer bicarbonate buffer (KRB) solution at 1 mg/gm/min. The septum was then dissected out and suspended from a Grass FT03 tension transducer. The other two corners were fixed with tension by opposing clamps through which a 5-voltz/5 msec electrical stimulation was given from a Grass stimulator at 1.5Hz. The peak developed tension (PDT) and the maximal acceleration (dT/dt) were recorded. After reaching fully stabilized contractions for at least 30 min., alternating perfusions with HLZ and TMP diluted in KRB were then started at doses of 1, 10, 100, and 50 mcg/ml each for 10 min. The plain oxygenated KRB solution was perfused in between as the control. The PDT and dT/dt were calculated as % of control values. The results were analyzed with paired t-test and summarized in Fig. 1 and 2.

TMP used to be the drug of choice for dissecting aortic aneurysm because it does not increase shearing force. On the other hand, HLZ has been perceived to have little effect on nonvascular smooth muscle, even though animal studies indicate that it may decrease uterine contractions and blood flow in toxemia of pregnancy. However, in isolated rabbit myocardium, our studies showed that HLZ had dose-dependent, rapidly reversible depressant effect, while TMP demonstrated slightly increased dT/dt and inotropic activity.

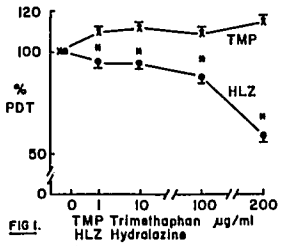

FIG 1.

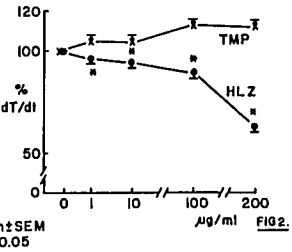

FIG 2.

References:
1. Anesthesiology 46:40-48, 1977
2. Am Heart J 95:1-31, 1978