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Title : VERAPAMIL-HALOTHANE: EPINEPHRINE ARRHYTHMIAS AND CARDIOVASCULAR FUNCTION

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Introduction. Verapamil (V) inhibits slow calcium currents across excitable membranes and thereby relaxes vascular smooth muscle, inhibits myocardial contractility, and has depressant effects on the sinus node and atrioventricular conduction. V is particularly effective against reentrant cardiac arrhythmias. Empirically successful treatment of arrhythmias during "light" halothane (H) anesthesia has been reported, though associated with blood pressure decreases and PR interval prolongation.[1] We have therefore evaluated in a controlled manner the effect of V on epinephrine (E) arrhythmias during H anesthesia as well as the effects of V on cardiovascular dynamics and AV conduction.

Methods. Mongrel dogs were induced with i.v. thiopental 17.6±0.5 mg/kg (mean ± S.E.M.) and ventilated to maintain a pH of 7.37±0.01 and pCO_2 of 39.5±0.7 torr. H in O_2 was given to maintain a serum level of 1% (1.2 MAC) as measured by gas chromatography. Lead II of the EKG was continuously monitored as was heart rate (HR), mean arterial pressure (MAP), and central venous (CVP) and pulmonary artery (PA) pressures through a balloon tipped, flow directed catheter. Cardiac outputs (CO) were obtained by thermodilution.

Group I: In 6 dogs after at least 75 minutes of stabilization on H the epinephrine arrhythmogenic dose (EAD) was determined by the method of Pace et al.[2] Standardized, logarithmically increasing infusions of E were given for 3 minutes each at 10 minute intervals until 4 or more premature ventricular contractions within 15 seconds occurred on duplicate trials. Three doses of V, 0.2 mg/kg, were then given and the EAD determined after each.

Group II: Five dogs were anesthetized, instrumented, and monitored as described with the addition of left ventricular (LV) pressure from a manometer tipped catheter (Millar) introduced through the left carotid artery. Unperturbed by infusions of E the dogs received V in the same sequence and at similar intervals, except that the drug was given over 30 seconds instead of 10 minutes. Statistical comparison was by the Student t-test.

Results. EAD results are shown in Table 1. V significantly and cumulatively raised the arrhythmogenic dose of E. In 8 attempts in 5 dogs V also terminated ongoing E-arrhythmias and converted ventricular tachycardia to sinus rhythm despite continuing E infusion. In Group II hemodynamic data and PR interval was examined during control, immediately after injection, and at 10 minute intervals thereafter. Data from all 3 doses were combined since analysis of variance revealed no difference at the $p < .05$ level. Results are summarized in Table 2. The post V values represent the maximal changes seen. Except for HR there were pronounced changes in all functions ($p < .001$). MAP decreased by 37%, LV dp/dt by 24%, and SVR (systemic vascular resistance) by 51%. SVR recovered ($p > .05$) by 10 minutes. Others values remained below control for up to 70 minutes. LVEDP rose by 27%, CVP by 44%, and CO by 16%. In 9/13 cases, CO fell subsequently by 20% below control for up to 50 minutes. PR interval was prolonged by 40% and returned to control 90 minutes after V. In 5 cases 2^0 heart block resulted from V doses of 0.4-1.6 mg/kg and lasted for 10 to 76 minutes. One dog had sinus arrest after a total dose of 1.2 mg/kg V.

Discussion. V can be used to terminate E induced arrhythmias during H anesthesia and to raise the threshold dose of E. However, rapid injection of V caused myocardial depression and fall in SVR although initially CO was increased transiently. The stable HR probably resulted from reflex tachycardia plus direct depression of the sinus node. Clinical observations must determine if careful administration of V can abolish E arrhythmias with acceptable hemodynamic depression. In patients on chronic oral V for supraventricular arrhythmias or angina pectoris, hemodynamic changes similar to those resulting from other cardiac depressants may be expected during anesthesia.

References.

1. Brichard G, Zimmerman PE: Verapamil in cardiac dysrhythmias during anesthesia. Br J Anaesth 42: 1005-1012, 1970.

2. Pace NL, Ohmura A, Wong KC: Epinephrine-induced arrhythmias: effect of exogenous prostaglandins and prostaglandin synthesis inhibition during halothane-O_2 anesthesia in the dog. Anesth Analg (Cleve) 58:401-404, 1979.

Table 1. Epinephrine Arrhythmia Threshold

	E dose* (ug/kg/min)	vs. control	vs. dose 1	vs. dose 2
control	2.58±0.77			
V,0.2mg/kg				
dose 1	5.17±1.27	p<.02		
dose 2	8.07±1.85	p<.005	p<.01	
dose 3	12.03±2.76	p<.001	p<.001	p<.01

*mean S.E.M.

Table 2. Effect of Verapamil During Halothane Anesthesia.

n=14	HR (bpm)	MAP (torr)	CVP (torr)	LV dP/dt (torr/sec)	LVEDP (torr)	CO (l/min)	SVR (dy·s·cm^{-5})	PR (msec)
Control+	125±5	97±3	7±1	2324±316	14±2	2.8±0.2	2840±232	114±4
Post V+	127±5*	62±3	9±1	1759±277	17±2	3.3±0.2	1394±116	160±8

*NS; all other changes significant at the 0.1% level
+ mean ± S.E.M.