DOSE RELATED HAEMODYNAMIC EFFECTS OF INTRAVENOUS ENCAINIDE.

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The acute haemodynamic and metabolic effects of intravenous Encainide (E) in cumulative doses of 1.0 and 2.0 mg/Kg infused over 15 minute periods were measured in 14 patients with obstructive coronary artery disease. Baseline right and left heart pressures, left ventricular (LV) dp/dt and thermodilution cardiac output and coronary sinus blood flow, myocardial lactate and oxygen extraction were recorded. Measurements were repeated after completion of the 1.0 and 2.0 mg/Kg infusions of E and 30 minutes later.
On completion of the 1.0 and 2.0 mg/Kg cumulative infusions of E significant dose related falls occurred in cardiac index (2.7 to 2.3 to 2.2 L/min/m^2 $p< 0.02$), LVdp/dt max. (1595 to 1405 to 1276 mmHg/sec. $p< 0.01$) with a rise in peripheral resistance (21 to 25 to 26.5 Wood units $p< 0.02$) and coronary sinus blood flow (113 to 126 to 133 mls/min. $p< 0.005$). Coronary vascular resistance fell (0.90 to 0.79 to 0.76 units $p< 0.05$). The fall in LVdp/dt max. persisted for 30 minutes after E 2.0 mg/Kg (1595 to 1381 mmHg/sec. $p< 0.05$).
Minor and insignificant changes only occurred in heart rate, left ventricular end-diastolic pressure and myocardial lactate and oxygen extraction. Plasma E levels were in the therapeutic anti-arrhythmic range.
The dose related cardiac depressant effects observed with intravenous E indicate the need for caution when doses above 1.0 mg/Kg are used particularly in the presence of LV dysfunction.

ELECTROPHYSIOLOGIC EFFECTS OF PROPAFENONE ON CANINE ISCHEMIC CARDIAC CELLS

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Electrophysiologic effects of the new antiarrhythmic drug propafenone (P), (2-(3-propylamino)-2-(hydroxy)-propoxy-3-phyenylpropiophenone HCl) were studied by conventional microelectrode technique in two types of preparations from 24-hour-old myocardial infarction in dog: 1)epicardial strips containing myocardial cells (M) from ischemic and normal zones, 2) endocardial strips containing ischemic Purkinje fibers (PF). Of the concentrations tested, (0.1 mg/L - 25mg/L), the most effective dose range was 2-4mg/L. P resulted in a concentration-dependant increase in threshold of stimulation, slowing of conduction and reduction of amplitude, overshoot and V max of action potentials of M and PF but had no effect on resting membrane potential. These effects were more marked on depressed ischemic M and PF. We have recently shown that abnormal automaticity seen 24 hours following MI in dogs is due to triggered automaticity (TA), (Circulation, In press). In endocardial preparations from 24-hours-old MI, TA (rate 60-120/min) arising from delayed after depolarization (DAD) was consistently induced in depolarized ischemic PF by a critical cycle length during regular pacing or premature stimulation and only when DAD attained threshold. P depressed the amplitude of DAD, slowed and inhibited TA. We conclude: 1) P has a membrane anesthetic effect with depressed ischemic cells being more sensitive, 2) P also depresses ionic currents responsible for TA in depolarized PF. 3) Actions of P could result in an antiarrhythmic effect in vivo on both reentrant activation and abnormal automaticity.

THURSDAY, MARCH 19, 1981
AM
NUCLEAR CARDIOLOGY—CLINICAL APPLICATION OF THALLIUM 201 MYOCARDIAL IMAGING
8:30-10:00

THE ADVERSE PROGNOSTIC SIGNIFICANCE OF AN ABNORMAL THALLIUM MYOCARDIAL PERFUSION SCINTIGRAM.

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No data are available which describe the prognostic significance of abnormal exercise thallium myocardial scintigrams (Tl scans). We therefore analyzed the natural history of 192 patients (pts) (mean age 55.9 yrs) followed over a mean interval of 35.5 months in whom Tl scans were performed. Of the 192 pts, 12 suffered cardiac deaths and two had noncardiac deaths. All scans were interpreted with attention to the location, size and severity of any defect and the number of standard views in which it was seen. Left ventricular dilation (LV dil) was also noted if the chamber appeared larger than 1.5 x the thickness of the posterolateral wall. Scan abnormalities were scored as a product of the percent circumference and percent loss of activity involved in the defect and expressed as the sum of defects in all three standard views. Among 31 pts with LV dil there were eight deaths compared with four of 159 pts without LV dil ($p<0.001$). Death occurred an average of 20.7 months following scanning. Of the 88 pts with exercise scans having defect scores of 30 or more eight died while none of the 84 with scores less than 30 died ($p<0.01$). While only four pts had myocardial infarction (MI) following scanning, none of 55 pts with an exercise defect score of <10 died or had a MI compared to 12 such events among 116 who had scores >10 ($p<0.025$). This study demonstrates a significantly higher mortality among pts found to have LV dil or large perfusion defects as scored by exercise Tl scan while showing no serious cardiac events following exercise scans with no or small defects.

UTILITY OF SERIAL THALLIUM IMAGING FOLLOWING DIPYRIDAMOLE

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Dipyridamole provides an alternative approach to exercise for detection of coronary artery disease (CAD) using Thallium-201 (Tl). Therefore, the presence and significance of Tl redistribution after dipyridamole was studied in 50 patients having coronary angiography, 30 with CAD and 20 normals. After 0.56 ml/kg/4 min intravenous infusion of dipyridamole, Tl was given and images in 3 views were obtained initially and after 2-3 hrs. Segmental Tl activity (3/view) was scored by 3 independent observers from 0 (no activity) to 2 (normal) using 0.5 grade steps. Using previously defined criteria for initially abnormal segments, the sensitivity was 93% (28/30) and specificity was 85% (17/20). There were 117 (43%) abnormal segments in the 30 CAD patients and 4 (2%) in the 20 normals. These 121 abnormal segments were then divided into 3 groups based on the completeness of Tl redistribution and compared to segmental wall motion as assessed by contrast ventriculography. In 34 segments with a persistent defect (no redistribution), 79% were akinetic and 97% showed either akinesis or hypokinesis; while in 58 segments with complete redistribution, only 9% demonstrated akinesis ($p<.01$).

These data suggest that serial Tl imaging after dipyridamole can detect CAD and assess myocardial viability in a manner similar to exercise Tl imaging.