Title : EFFECT OF DILTIAZEM ON REGIONAL LEFT VENTRICULAR FUNCTION IN THE PRESENCE OF GRADUAL CORONARY CONSTRICTION IN THE DOG

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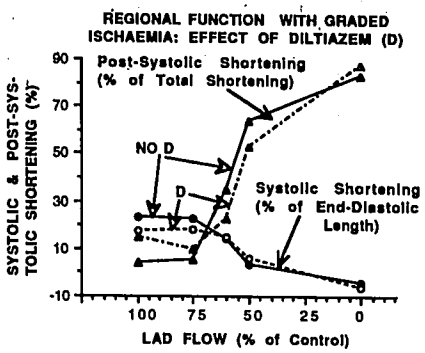
Diltiazem (D) has been shown to cause selective depression and dysfunction of myocardium with critically compromised blood supply (1). This study was designed to determine whether the adverse effects of D would be exaggerated in the presence of severe myocardial ischaemia.

Ten dogs were acutely instrumented under halothane anaesthesia to measure aortic and left ventricular pressure, aortic and left anterior descending coronary artery (LAD) blood flow, and segmental shortening (sonomicrometry) in the near apical region (LAD supply territory) of the left ventricle. After completion of surgery, halothane was replaced by propofol (bolus dose of 5 mg/kg iv, followed by a continuous infusion of 200 mcg/kg/min). Prior to and after administration of D (0.2 mg/kg iv), the effects of reducing coronary blood flow by tightening a micrometer controlled snare were recorded. The gradual reductions in flow were similar before and after D, averaging 25%, 40%, 50% and 100%.

D significantly depressed arterial pressure, LV dP/dt max, stroke volume, and cardiac output*. These were of similar magnitude irrespective of the degree of coronary flow reduction. With normal coronary flow, systolic shortening (SS) decreased (-23.7*) in the near apical region after D. However, D did not alter the magnitude of reduction in shortening brought about by coronary constriction. With normal coronary flow, a small amount of post-systolic shortening (PSS) was noted after administration of D, but this did not reach statistical significance. However, at 40% and 50% flow reduction, PSS was significantly less after than before D (-35.5%* and -16.6%*, respectively).

While D may worsen regional function when administered in the presence of critical coronary constriction, it neither protects nor worsens SS in the face of gradual coronary constriction. The significant decrease of PSS at 40% and 50% flow reduction may indicate a small degree of protection.

However, as PSS is considered an active process (2), its reduction may simply be an expression of the global depression of cardiac performance due to D. The clinical implication of this study is that D causes global depression of the left ventricle irrespective of the degree of regional ischaemia and does not appear to provide significant protection to the ischaemic myocardium. *p<0.05



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TITLE: THE DEPRESSIVE EFFECT OF ISOFLURANE ON MYOCARDIAL BETA-ADRENERGIC RESPONSIVENESS IS NOT RELATED TO AN ALTERATION OF BETA-RECEPTOR DENSITY

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Isoflurane has been reported to exert a depressive effect on positive sino-atrial chronotropic response to beta-agonists (1). To delineate the possible effect of isoflurane on myocardial beta-adrenoceptors, we have used positron emission tomography (PET) to visualize and quantify myocardial beta-adrenoceptors.

Beagle dogs (n = 5) were anesthetized with thiopental (C) and one week later, with thiopental plus isoflurane (3 %, end tidal). Cardiac output (measured by thermodilution) was adjusted, during isoflurane anesthesia, at the same value than that measured during control anesthesia, by fluid loading. Chronotropic response to incremental doses of isoproterenol was assessed. The slope of the relationship between dose of isoproterenol and heart rate response was used as an index of adrenergic responsiveness.[1] Myocardial beta-adrenoceptor density (Bmax) was determined by computerized modelling of PET scan data, recorded following the IV administration of ^{11}C-CGP 12177.[2] The regions of interest selected for PET scan were interventricular septum and free wall of the left ventricule (LV).

During isoflurane anesthesia, a significantly greater dose of isoproterenol was required to obtain the same heart rate response when compared to control anesthesia. Bmax was not significantly altered by isoflurane anesthesia.

	Control	Isoflurane (3%)	Paired t test
Slope (bts/min/mcg of isoproterenol)	28±2	15±2	p<0.001
Bmax (pmol/ml of LV)	30±3	32±5	NS

This study confirmed previous data, obtained in guinea pig, indicating that isoflurane induced a beta-adrenergic hyporesponsiveness. Our study showed that this effect is not related to a significant decrease in myocardial beta-adrenoceptor density. Post-receptor mechanisms are likely involved in the alteration of beta-adrenergic function induced by isoflurane.

References

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