TITLE: **A COMPARISON OF THE PDE INHIBITOR ENOXIMONE WITH DOBUTAMINE FOLLOWING MITRAL VALVE REPLACEMENT.**

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INTRODUCTION: Mitral valve surgery may be complicated by a post-operative low cardiac output state requiring pharmacological support. Such patients may have pre-existing high pulmonary artery pressures, pulmonary vascular resistance (**PVR**) and be at particular risk of developing right heart failure. Dobutamine (**D**) has been advocated as the inotrope of choice in these patients because it is claimed there is no increase in **PVR** associated with its use. Enoximone (**E**) has both inotropic and vasodilator properties, it acts by specific phosphodiesterase (PDE) inhibition and has been shown to be effective in low output states following cardiac surgery.

This study was designed to compare the hemodynamic properties of dobutamine with enoximone from the time of weaning from cardiopulmonary bypass (CPB) in a group of patients undergoing mitral valve replacement (MVR) for non-ischemic valvular disease.

METHODS: Following ethical committee approval and informed consent, 24 patients undergoing MVR were studied. Patients were randomly allocated to receive either **D** at $7\mu g.kg^{-1}.min^{-1}$. commenced 5 minutes before weaning from CPB, or **E** administered as a bolus of $0.5mg.kg^{-1}$. over 10 minutes followed by a continuous infusion of $5\mu g.kg^{-1}.min^{-1}$. also commenced 5 minutes before the end of CPB (Time 0). Hemodynamic parameters, including cardiac output (mean of 3 values) were determined prior to commencing CPB (Control,C) and at 5,10,15,30,45,60,90, 120,180 and 240 minutes after the end of CPB. Mean values ±SD are given. Statistical analysis was by ANOVA and $p<0.05$ considered significant.

RESULTS: 24 patients were investigated, 13 received **D** and 11 **E**. All patients were weaned from CPB at the first attempt. There were no significant differences between the two groups with respect to age, total CPB and aortic cross-clamp times.Heart rate (**HR**) significantly increased with D from 92±20 $beats.min^{-1}$.(C) to between 102±25 and 107±12 $beats.min^{-1}$ post-operatively, this was also significantly higher than the rate observed with **E** which was unchanged during the study (C 82±16) with a range 81±17 to 94±18 $beats.min^{-1}$. Mean arterial pressure (**MAP**) showed no difference either within or between the two treatment groups. **D** showed a range of values 67±11 to 89±16mmHg while for **E** this was 67±13 to 85±18mmHg. Cardiac index (**CI**) was significantly increased above C in both groups, by 40% to 61% (C 1.92±.64$L.min^{-1}.m^{-2}$.) for **D** and by 44% to 84% (C 1.81±.46$L.min^{-1}.m^{-2}$.) for **E**. Systemic vascular resistance (**SVR**) was significantly reduced in both groups, but with no difference between **D** and **E**. Pulmonary vascular resistance (**PVR**) was unchanged from C in both groups with no value was above C. The overall ranges were 220±138 to 313±142$dynes.s.cm^{-5}$ for **D** and 189±162 to 285±140$dynes.s.cm^{-5}$ for **E**.

CONCLUSIONS: Both **D** and **E** in the doses described produce similar increases in **CI** with a fall in **SVR** and unchanged **MAP** and **PVR**. However D achieves this at the expense of a significantly higher **HR**. While with **E** there is no change in **HR** during the study period.

A122

TITLE : HEMODYNAMIC EFFECTS OF INTRAVENOUS DILEVALOL IN PATIENTS WITH CORONARY ARTERY DISEASE

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Dilevalol is a new antihypertensive agent which combines both nonselective beta-blockade with selective peripheral beta-2-vasodilation. The aim of this study was to evaluate the hemodynamic effects of the intravenous administration of dilevalol in anesthetized patients with coronary artery disease.

With informed consent and ethical committee approval, 8 patients with a history of angina and hypertension controlled with medication without beta-blockers and scheduled to undergo elective CABG were admitted to the study.

After premedication with lorazepam, induction of anesthesia was performed with etomidate (0,3 mg/kg), sufentanil and pancuronium (0,1 mg/kg). Anesthesia was maintained with sufentanil up to a dose of 15 ug/kg before sternotomy.

Dilevalol was administered IV by a continuous infusion at a dose of 0,04 mg/kg over a 30 min period, immediately prior to CPB. In addition to ECG, HR, MAP, PAP, PCWP, CVP and CO using thermodilution technique were recorded. Using standard formulae CI, SVI, LVSWI and SVR were calculated. A Millar tip-manometer was placed for left ventricular pressure (LVSP) monitoring and LVdP/dt measurements.

Hemodynamic data were obtained before (baseline) and at 5 min intervals during a 30 min infusion period.

Mean values (± SD) and statistically significant differences are summarized in table I.

Dilevalol administration was associated with a significant decrease in LVSP (-19,9 %), MAP (-18 %), +LVdP/dt (-18,8 %) and HR (-8,9 %). CI and LVSWI remained uncharged and an increase in SVI was found, related to a significant decrease in SVR (-24,2 %).

Dilevalol, given by a continuous IV infusion of 1,2 mg/kg over a 30 min period was shown to be effective in maintaining CI, SVI and LVSWI while reducing blood pressure to a safe extent. Arteriolar dilatation cause by Dilevalol might give this drug a potential advantage over other beta-blockers in hypertensive patients with coronary artery disease.

MEASURE POINTS

Time	Baseline	+ 5 min	+10min	+15min	+20min	+25min	+30min
HR	72±6	66±5	67±4	67±5	66±5	66±6	65±6*
LVSP	124±16	117±20	109±20*	109±20*	106±18*	102±17*	101±16*
MAP	69±10	63±12	73±12*	77±11*	76±12*	72±10*	72±9*
PCWP	8±1	7±1	7±2	7±2	7±1	7±1	7±1
CI	2.6±0.6	2.7±0.7	2.7±0.7	2.8±0.6	2.8±0.5	2.7±0.6	2.8±0.6
SVI	37.5±10.2	39.3±10.3	41.0±10.7	41.6±10.2	41.5±9.1	42.1±9.4	42.9±12.6*
LVSWI	45.3±14.5	45.1±15	44.5±15	44.0±13.5	43.6±13	42.0±13.4	43.0±16.3
+LVdP/dt	1538±366	1394±441	1322±392	1314±418	1281±435*	1268±455*	1264±453*
SVR	1540±352	1401±258	1298±265	1243±236*	1196±160*	1202±237*	1167±240*