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Title: REDUCTION OF THE CATECHOLAMINE RESPONSE TO CABG SURGERY BY CLONIDINE
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Introduction: The use of clonidine (C) in CABG patients was found by Flacke to result in lower catecholamine (CAT) levels prebypass. The absence of a double blinded protocol decreased the conclusiveness of these findings as the investigators could have influenced hemodynamic interventions. We are conducting a placebo controlled double-blinded, randomized trial of clonidine (C) in order to conclusively confirm the promising results of Flacke, et al.
Methods: Institutional Human Subjects Review Committee approval was obtained to study relatively good risk patients. After informed consent, twenty-four patients who were all undergoing elective CABG surgery were studied. Exclusionary criteria were: high-grade left main coronary artery stenosis, congestive heart failure with LVEF <40%, use of C, alpha-methyl-dopa, or guanibenz within the past week, AV block greater than first degree, renal or hepatic failure or any gastrointestinal disturbance which would hinder enteric absorption of oral medication. Ninety minutes prior to induction, all patients received 40 mcg/kg lorazepam orally, and randomly received C 5 mcg/kg or a placebo (P) by staff not involved in the anesthetic management of the patient. Induction of anesthesia was with an initial 50 mcg of sufentanil (S) and 5 mg of vecuronium. The S was then further titrated to loss of consciousness. A CNS EEG monitor was used to further evaluate S's effect. Muscle relaxation was enhanced with vecuronium or pancuronium as needed. A standard 0.05 mcg/kg/min infusion of S was utilized for maintenance of anesthesia. Thirty minutes prior to cardiopulmonary bypass, a second dose of C at 5 mcg/kg or P was given as a dilute slurry dissolved in 20cc normal saline via the nasogastric tube. An additional 20 mcg/kg of lorazepam was administered during CPB. Arterial blood was drawn at baseline, post-intubation, and after sternotomy and EPI, NE, and DOPA levels analyzed.
Results: The anesthesia team caring for the patients were successfully blinded from the administration of C or P to the patients. Patient demographics were essentially equivalent and representative of our CABG patient population. The reduction in anesthetic requirement and hemodynamic response were reasonably correlated to the difference in CAT levels between P and C patients. Both baseline and 5 minutes after intubation NE and EPI responses were nearly half in the C patients compared to the P patients (Table 1). The C patients had recovery times (102 ± 48 min) that were less than half of the recovery times than the placebo patients (283 ± 198 min).
Conclusion: The decrease in anesthetic requirement, stable hemodynamics, early awakening, and lower CAT response confirm that C can be a useful and positive contribution to the reduction of stress in CABG surgery patients.

Table 1

	Placebo Mean ± SD	Clonidine Mean ± SD
Baseline		
NE	294 ± 34	160 ± 60 ^a
EPI	123 ± 84	46 ± 37 ^a
DOPA	21 ± 19	41 ± 18
5 min After Intubation		
NE	245 ± 146	147 ± 38 ^a
EPI	97 ± 124	58 ± 33 ^a
DOPA	20 ± 15	33 ± 15
5 min After Sternotomy		
NE	218 ± 102	208 ± 77
EPI	76 ± 84	54 ± 29
DOPA	24 ± 27	33 ± 15

Note: NE is norepinephrine, EPI is epinephrine, DOPA is dopamine, and SD is standard deviation. (a) is a significant p < 0.05 difference between study groups.

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Title: EFFECT OF MIDAZOLAM ON CARDIAC PUMP PERFORMANCE AND CONTRACTILITY
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Introduction: Transesophageal echocardiography (TEE) allows analysis of left ventricular (LV) contractility by measurement of LV systolic function as described by % fractional shortening (%FS) and % area change (%AC) of the LV cavity, with end-systolic wall stress (ESS) and end diastolic wall stress (EDS) as measures of afterload and preload.^{1,2}

Methods: Forty patients (with informed consent) undergoing coronary artery bypass graft surgery were studied. Anesthesia was induced with 20 mcg/kg of fentanyl and 2 mg/kg of thiopental. Succinylcholine, 1.5 mg/kg, was given to permit tracheal intubation. Pulmonary artery catheter data were used for derived hemodynamic values. Recordings of LV (short axis view at the papillary muscle level) were made before administration of midazolam and 5 minutes after giving midazolam, 0.1 mg/kg. This was done prior to skin incision.

TEE measurements were made by 2 independent readers, at end-diastole (d) and end-systole (s). Cross-sectional cavity area (CA), myocardial area (MA) and internal diameter of the LV cavity (LVID) were measured from endocardial and epicardial tracings. Least squares linear regression analysis was used to relate % fractional shortening and % area change to end-systolic stress and end-diastolic stress for load independent measures of LV function, where ESS = SBP x CAs/MAs, EDS=(PCWP x CA_d)/MA_d, %FS = (LVID_d-LVID_s)/LVID_d and %AC = (CA_d-CA_s)/CA_d.

Results: After midazolam significant balanced reductions of cardiac afterload (systemic and pulmonary arterial pressure, resistance and ESS) and preload (pulmonary capillary wedge pressure, central venous pressure and EDS) were noted (p < 0.05 by paired t-test). No change in pump performance (stroke volume or cardiac index) occurred.

Patients were subdivided into normal and depressed LV function groups, based on preoperative catheterization data. With regard to pump performance and contractility, there was no significant difference between the normal and depressed group response to midazolam.

Conclusion: Midazolam reduced preload and afterload without a reduction in cardiac output or contractility. Thus midazolam did not have an important depressant effect on cardiac function.

References

1. Am J Cardiol 64:1338-1343, 1989.
2. Circulation 65:988-997, 1982.

