

Title : DOBUTAMINE RESPONSE IN PATIENTS TAKING PROPRANOLOL

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**Introduction:** Dobutamine may be a useful  $\beta_1$ -agonist in patients undergoing coronary artery bypass grafting (CABG). Prior studies indicate that dobutamine has fewer undesirable side effects than many other catecholamines and raise the question of the effectiveness of dobutamine in the presence of propranolol, which is often part of the treatment of angina prior to CABG. The purpose of this study is to determine the response to dobutamine before and after cardiopulmonary bypass (CPB) in patients on chronic propranolol therapy up to the day of CABG.

**Methods:** Ten patients with normal ventricular function undergoing elective CABG gave informed consent for this study, approved by the Human Investigations Committee. All patients were taking propranolol in doses over 80mg/day with the last dose 10 hours prior to the study. Anesthesia consisted of morphine, diazepam, pancuronium, 50% N<sub>2</sub>O and O<sub>2</sub>. Monitoring consisted of radial and thermidilation pulmonary artery catheters, ECG leads II and V<sub>5</sub>, esophageal phonocardiogram, and arterial blood gases. After cannulation of the aorta and vena cava, but prior to CPB, control measurements were made of mean arterial pressure (AP), heart rate (HR), central venous pressure (CVP), pulmonary artery pressure (PAP), pulmonary capillary wedge pressure (PCWP), ECG, duplicate cardiac outputs, and systolic time intervals. Dobutamine was then administered at 5, 10 and 15  $\mu$ g/kg/min for 5 min each and the above measurements repeated after each dose. After CPB, measurements were again made with the same doses of dobutamine. Derived parameters included cardiac index (CI), pulmonary (PVR) and systemic (SVR) resistances, stroke work (SW), PEP/LVET, 1/PEP<sup>2</sup>, rate pressure product (RPP), and endocardial viability ratio (EVR). The ECG was analyzed for ST-segment depression and dysrhythmias. Blood was drawn immediately prior to and after CPB for determination of plasma propranolol concentrations.<sup>1</sup> Paired t tests were used to compare measurements to control values.

**Results:** Prebypass, with propranolol levels of  $19 \pm 2$  ng/ml, dobutamine produced significant dose-related increases in HR, RPP, CI and 1/PEP<sup>2</sup> (Fig). No consistent changes were found in AP, PAP, PCWP, CVP, PVR and SVR. Postbypass, with propranolol levels of  $16 \pm 1$  ng/ml, dobutamine produced significant elevations in HR, RPP, AP, 1/PEP<sup>2</sup> and SVR but not in CI. There were no ST-segment changes noted during the study. Occasional premature ventricular contractions (PVC) were noted in 3 patients at the 15  $\mu$ g/kg/min dose of dobutamine.

**Discussion:** Dobutamine is effective in the face of maintenance doses of propranolol,

producing significant increases in HR and contractility. These findings are consistent with results obtained using isoproterenol in CABG patients with similar propranolol levels.<sup>1</sup> Dobutamine increased HR, RPP and 1/PEP<sup>2</sup> after CPB when it is most often used. In addition, AP and SVR were increased but without an increase in CI which may be related to lower SVR and higher CI control values after CPB. Myocardial oxygen supply/demand balance did not appear adversely affected, since no ST-segment depression or changes in EVR occurred. As noted in prior studies, dobutamine produced few dysrhythmias, with PVCs observed only at the highest dose used.<sup>2</sup> We conclude that dobutamine is an effective  $\beta_1$ -agonist during CABG even when patients are maintained on propranolol therapy until the day of surgery.

**References:**

1. Hug CC, Kaplan JA, Rigel EP: The effect of cardiopulmonary bypass on plasma propranolol concentrations and the response to isoproterenol. ASA abstract, October, 1977.
2. Sakamoto T, Yamada T: Hemodynamic effects of dobutamine in patients following open heart surgery. Circ 55:535-533, 1977.

