Title: LABETALOL FOR THE CONTROL OF ELEVATED BLOOD PRESSURE FOLLOWING CORONARY BYPASS GRAFTING

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Acute blood pressure elevation is common following coronary artery bypass graft surgery (CABG), and increases risk of ischemia, bleeding and cardiac failure. Treatment with direct vasodilators may cause reflex tachycardia and hypercontractility, while beta-blockers may cause excessive myocardial depression and reflex vasoconstriction. We studied the effects of labetalol (LAB), a combined beta- and alpha-adrenergic blocker (1), to evaluate its safety, efficacy and hemodynamic effects in patients with elevated blood pressure after CABG.
Methods: Following human subjects committee approval, written informed consent was obtained from 48 patients undergoing elective, simple CABG. Patients with ejection fraction <40%, bradycardia, bronchospasm or postoperative hypovolemia were excluded. After surgery, if systolic blood pressure (SBP) was >140 mmHg for >5 min, LAB was injected I.V. every 10 min as follows: 5 mg, 10 mg, 20 mg, 40 mg. Titration continued until SBP was decreased by >10%, or a total of 75 mg LAB was given. Responders entered a 6 hr maintenance period and received LAB 10-40 mg I.V. as needed to control SBP. Non-responders were removed from the study and alternative therapy was given. The following data were recorded at baseline, every 10 min after LAB during titration, and at 6 hrs: heart rate (HR), SBP, diastolic pressure (DBP), pulmonary artery diastolic (PAD), central venous pressure (CVP), cardiac index (CI), core temperature (TEMP). Pulse pressure (PP) and systemic vascular resistance index (SVRI) were calculated. Data were compared using ANOVA and an independent t-test with p<0.05 considered significant.
Results: LAB was effective in decreasing SBP by >10% in 36 of 48 patients (75%). 19 patients responded after 5 mg LAB; an additional 16 responded after 35 mg. The figure and table illustrate the mean values +SEM for hemodynamic data and TEMP for patients who responded to LAB. SBP, DBP and PP and CI were significantly decreased, but HR, PAD and CVP did not change. Data at 6 hr reflected rewarming vasodilation. Patients with initial CI <2.5 l/m/m/m² had SVRI which was significantly higher than those with CI >2.5 l/m/m² and was not reduced by LAB. Three of these patients were removed from the study because further decreases in CI. One of these developed hypotension during titration. Two other patients developed hypotension associated

with hypovolemia during rewarming. One other patient died of perioperative myocardial infarction; relationship to LAB therapy is unknown.
Discussion: LAB effectively lowers elevated blood pressure after CABG. This is accomplished primarily by a reduction in cardiac output with little net change in vascular resistance. Pressure reduction is accomplished smoothly with decreased PP and no reflex tachycardia, which favors myocardial oxygen balance. Based on these effects of LAB in our experience, LAB appears to be most effective in patients with good left ventricular function and elevated blood pressure following CABG, but should be avoided or used cautiously in patients with low CI (<2.5 l/m/m²) and elevated SVRI.

References:
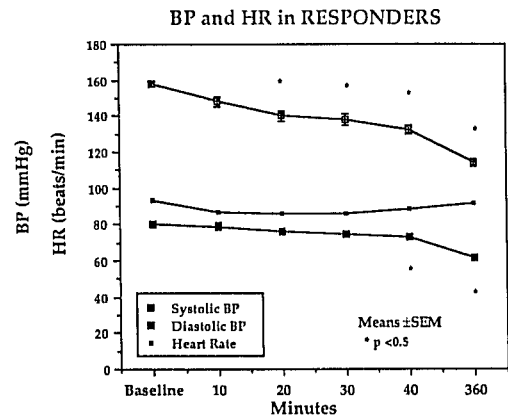1. Richards DA. Pharmacological effects of labetalol in Man. Br J Clin Pharmacol. 1976; 3: 721-3.

BP and HR in RESPONDERS

Table. Hemodynamic data in LAB responders.

	BS	10 m	20 m	30 m	40 m	6 hr
CI	2.9 ±0.1	2.6* ±0.1	2.5* ±0.1	2.4* ±0.1	2.4* ±0.1	2.9 ±0.1
SVRI	2776 ±172	3042 ±188	2995 ±142	2905 ±168	2699 ±160	1968* ±135
PAD	15.2 ±0.8	15.4 ±0.7	15.5 ±0.6	15.3 ±0.7	15.5 ±0.9	16.2 ±0.8
CVP	9.4 ±0.7	10.3 ±0.6	10.3 ±0.7	10.9* ±0.8	10.5 ±0.9	9.7 ±0.8
Temp	36.1 ±0.2	36.1 ±0.2	36.1 ±0.2	36.1 ±0.2	36.4* ±0.2	37.5* ±0.2

Means ±SEM
CI in l/m/m²; SVRI in dyne.cm.sec⁻⁵/m²; PAD, CVP in mmHg; Temp in °C.
*different from baseline, p<0.05