Title : ADMINISTRATION OF LABETALOL TO DOGS ANESTHETIZED WITH ISOFLURANE SEVERELY DEPRESSES LEFT VENTRICULAR CONTRACTILITY

Authors : P. Fyman, M.D., G. Loren, M.D., R. Fine, M.D., K. Lipsitz, M.D., L. Kushins, M.D. C. Fermon, M.D., S.B. Wollman, M.D. and R. Abramowitz, M.D.

Affiliation : Department of Anesthesiology
Long Island Jewish Medical Center
New Hyde Park, New York 11040

Introduction. Labetalol is an antihypertensive agent with alpha and beta blocking properties which is commonly used intraoperatively because of its rapid onset of action. It is frequently assumed that the decrease in blood pressure results from systemic vasodilation (1). While labetalol's cardiovascular effects have been extensively evaluated in the awake patient (2), its interaction with isoflurane has not been studied. This study was undertaken to determine the effects of labetalol, on myocardial contractility in dogs anesthetized with isoflurane.

Methods. This protocol was approved by the Animal Research Committee. Mongrel dogs were anesthetized with thiamylal 3 mg/kg and endotracheally intubated. Anesthesia was maintained with isoflurane 1.4% end tidal in 100% oxygen and the dogs were mechanically ventilated to an end tidal CO_2 of 30-35 mm Hg; gases were measured by an airway gas monitor, which was calibrated prior to each experiment. A catheter was inserted into the femoral artery to measure systemic pressure (BP). A pulmonary artery catheter was threaded through the femoral vein to measure pulmonary artery (PAP), pulmonary capillary wedge (PCWP) and central venous (CVP) pressures and cardiac outputs (CO). Systemic vascular resistance (SVR) was calculated by the standard formula. A micromanometer tipped catheter was inserted retrograde into the left ventricle (LV) via the right carotid artery for direct LV pressure measurements and electronic derivation of LV dP/dt. The maximum LV dP/dt was taken as the peak positive deflection on the LV trace. Heart rate (HR), BP, PAP and LV pressures and LV dP/dt tracings were continuously recorded. When BP, PAP, end tidal CO_2 and isoflurane concentration had stabilized for at least twenty minutes, control measurements (baseline-1) were taken which included HR, systemic, PA and LV pressures, PCWP, CVP and C.O. Labetalol 0.4 mg/kg was then administered intravenously over one minute.

Measurements of the above parameters were then repeated at 1,5,10,15 and twenty minutes. A second dose of labetalol, 0.8 mg/kg was administered immediately after the last value which was used as baseline-2, was obtained. Statistical analysis was done using repeated measured ANOVA and paired t-tests with alpha (2-tailed) set at p 0.05. Values are reported as mean $\pm$ SEM (% change).

Results. Thirteen mongrel dogs weighing 20 $\pm$ 2 kg were studied. Of the parameters measured, significant alterations occurred only with BP, SVR, LV dP/dt max. and HR (see Table). After the first administration of labetalol, the maximum changes always took place within one minute. Values returned toward baseline by twenty minutes but remained significantly lower than baseline-1. The only exception was HR, which decreased steadily throughout the study. The maximum hemodynamic alterations after the first dose of labetalol are as follows: mean BP and SVR decreased 36% ($p<0.01$), LV dP/dt max. was reduced 20% ($p<0.05$) and HR slowed 10% ($p<0.01$). After the second dose of labetalol, maximum changes in mean BP, SVR, LV dP/dt and HR were decreased significantly compared to baselines 1 and 2. Again, peak effects occurred within one minute, except for HR, which continued to decrease. The following are maximum changes compared to baseline 2: mean BP decreased 15% ($p<0.001$), SVR decreased 16% ($p<0.001$), LV dP/dt decreased 16% ($p<0.001$) and HR fell 7% ($p<0.001$). There were no statistically significant changes in CVP, PAP, PCWP or C.O. after either dose.

Discussion. This study demonstrates that administration of labetalol during isoflurane anesthesia results in a marked depression of myocardial contractility as indicated by a decrease in LV dP/dt max. It occurred immediately after each dose was given. Although there was some recovery, depression did persist for twenty minutes. In spite of decreased myocardial contractility, there was no significant change in C.O., PAP or PCWP. This is more likely due to systemic vasolidation permitting the left ventricle to function more efficiently. In conclusion, labetalol administered during isoflurane anesthesia produces a significant decrease in myocardial contractility. This must be considered in patients with pre-existing myocardial depression or patients who may have a predisposition to this, such as someone who has just undergone cardiopulmonary bypass.

References.

(1) Scott DB, et. al.: BRJ Clin. Pharmac. Suppl: 817-21, 1976.

(2) Vlachakis, ND, et. al.: Clin. Pharmacol 38: 503-8, 1985.

Table

Dose - 0.4 mg/kg

	Baseline-1	Maximum change from Baseline	
Mean BP	76 (4)	49 (5)	(-36%)
SVR	1831 (142)	1059 (114)	(-36%)
LV DP/DT	2003 (160)	1839 (167)	(-20%)
Heart Rate	119 (5)	107 (4)	(-10%)

Dose - 0.8 mg/kg

	Baseline-1	Max. Change	Change from Baseline-1	Change from Baseline-2
Mean BP	60 (2)	51 (2)	-32%	-15%
SVR	1451 (81)	1204 (74)	-31%	-16%
LV DP/DT	2003 (160)	1667 (129)	-26%	-16%
Heart Rate	107 (4)	99 (3)	-16%	-7%

All data - Mean (± SEM)