Title: BEAT-BY-BEAT CARDIOVASCULAR RESPONSES TO RAPID SEQUENCE INDUCTION IN HUMANS: EFFECTS OF LABETALOL

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Introduction. Laryngoscopy and intubation are periods of major stress which impart significant risk of cardiac compromise. In addition, the technique of rapid sequence induction which diminishes the potential for aspiration, increases the cardiovascular stress. Numerous approaches have been taken to blunt the hemodynamic responses to intubation, but one promising approach may be the use of labetalol because of its dual site of action (nonspecific beta and postsynaptic alpha 1 receptor blockade)[1]. In the present study, we examined the effects of labetalol on beat-by-beat cardiovascular responses and catecholamine changes produced by rapid sequence induction.

Methods. These studies were approved by the Institution's Human Research Review Committee. Twenty four age-matched ASA I and II patients (27 to 46 years of age) scheduled for elective surgery were studied after providing informed consent. They were randomized, in double-blinded fashion, into one of three groups: placebo, and two labetalol groups, 0.25 and 0.75 mg/kg (n=8/group). Beat-by-beat heart rate (lead II and V), mean blood pressure (MAP) and stroke volume (SV) were detected with ECG, radial artery cannulation and impedance cardiography, respectively. Cardiac output (CO), total peripheral resistance (TPR) and rate pressure product (RPP) were calculated.

All patients received lorazepam (2 mg) orally 90 minutes prior to the study. Baseline hemodynamics, blood gases and norepinephrine were obtained thirty minutes after instrumentation. Labetalol (or placebo) was given by IV bolus and data collection repeated after five minutes. 100% O_2 (by mask) and vecuronium (0.01 mg/kg) were given and final baseline data collected five minutes later. Thiopental (4 mg/kg), succinylcholine (1.5 mg/kg) and cricoid pressure were administered and laryngoscopy initiated one minute later by a staff anesthesiologist. Hemodynamics were recorded continuously and repeat blood sampling occurred 1.5 and 4 minutes after intubation.

Results. Baseline hemodynamics, blood gases and norepinephrine were similar between groups. Labetalol (0.75 mg/kg) produced a slight but significant reduction in MAP (94±2.2 to 87±2.1) and TPR (1292±102 to 1068±74). Induction (preintubation) produced significant (P<.05) tachycardia and reductions in SV without changing CO, MAP, TPR, or RPP. This response did not differ amongst groups. The duration of laryngoscopy (<30 sec) did not differ between groups. Peak hemodynamic responses occurred 30 seconds after intubation and are shown in the Table.

Table: Delta responses, 30 seconds after intubation.

	Placebo	Labetalol 0.25 mg/kg	Labetalol 0.75 mg/kg
HR, B/min	44±6	33±3*	27±3*
SV, ml	-27±6	-47±6*	-42±6*
CO, L/min	0.2±0.4	-1.1±0.5*	-0.9±0.5*
MAP, mmHg	58±4	38±3*	38±5*
TPR, units	719±143	899±178	743±222
RPP, x 10^3 units	14±2	8±0.4*	7±0.6*

Data are mean±SEM, TPR dyne·sec·cm^{-5}
*= P<0.05 different from placebo, unpaired t-test

Plasma norepinephrine increases and arterial blood gases after induction did not differ between groups. The attenuation of hemodynamic responses did not differ between the two labetalol doses.

Discussion. Cardiovascular parameters during rapid sequence induction, laryngoscopy and intubation were monitored beat-by- beat to detect transient hemodynamic changes. We attenuated hemodynamic responses with a pharmacologic agent with a dual mechanism of action. The cardiac beta blocking effect of labetalol is thought to be more prominent than its postsynaptic alpha receptor blockade. This unequal effect is evident in our data which indicate that labetalol blunts MAP responses primarily by attenuating cardiac function: HR increased less and stroke volume fell more in the labetalol groups after intubation. TPR and norepinephrine increases were not attenuated by labetalol.

References.

1. MacCarthy EP, Bloomfield SS. Labetalol: A review of its pharmacology, pharmacokinetics, clinical uses and adverse effects. Pharmacotherapy 3:193, 1983