Title: EFFECT OF LABETALOL ON THE HEMODYNAMIC RESPONSE TO INTUBATION; A CONTROLLED RANDOMIZED DOUBLE-BLIND STUDY

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Introduction. Laryngoscopy and endotracheal intubation induce sympathoadrenal responses resulting in hypertension and tachycardia. Many drugs will affect this cardiovascular response including atropine, phentolamine, nitroprusside, halothane, propranolol, esmolol, fentanyl, topical and intravenous lidocaine. This study determined the ability of labetalol, a combined alpha and beta adrenergic blocker to minimize the hypertensive and tachycardic response to intubation in a controlled, randomized, double-blind study.

Methods. Forty adult patients, 21-71 years of age, scheduled for elective surgery were studied after approval by the Human Studies Committee and obtaining informed consent. Each patient was randomized to receive one of four possible drugs intravenously in 2 ml from identical syringes: saline (S), n=10, lidocaine 100 mg. (L) n=10, labetalol 5 mg. (LA5), n=10, or labetalol 10 mg. (LA10), n=10. Patients with CHF, bronchospasm, unstable angina, AV block, and liver disease, were excluded, as were ASA PS-IV patients, or those receiving calcium channel or alpha or beta adrenergic blocking drugs. After obtaining baseline heart rate and blood pressure measurements, each patient was preoxygenated after which the study drug was administered, followed immediately by thiopental 3-6 mg/kg IV. After 60 seconds, succinylcholine 1.5 mg/kg was given. After fasciculation and completing cardiovascular measurements, the patient was intubated and ventilated with 100% oxygen for 2 minutes followed by 50% N_2O/O_2 for an additional two minutes at which point the study concluded and the anesthetic of choice was begun. Heart rate and blood pressure were measured at 1 minute intervals for the 8 minutes of the study.

Results. Labetalol 10 mg IV completely prevented tachycardia in response to endotracheal intubation compared to saline, lidocaine 100 mg, and labetalol 5 mg. ($P<0.05$ by ANOVA) (Fig. 1). (Table 1) Hypertension was not prevented by pretreatment with any of the four drugs. No patient became hypotensive or bradycardic as a result of pretreatment before the stimulus of intubation. The randomization process yielded four extremely well matched groups. Two patients developed minimal wheezing after intubation (1-S, 1-LA10) and 3 patients developed inconsequential arrhythmias (2-S, 1-LA5). The following did not affect the heart rate and blood pressures response to intubation (when data from the S, L, and LA5 groups were combined): 1) Whether or not patients received narcotic premedication. 2) Dose of thiopental: > or < 4 mg/kg, 3) Age: > or < 50 years. 4) Intubation time: > or < 10 seconds.

Discussion. Pretreatment with labetalol 10 mg IV given 2.5-3 minutes before endotracheal intubation blocked tachycardia, but not hypertension associated with laryngoscopy and intubation.

Will larger doses of labetalol block the hypertensive response to intubation? We are concerned that doses larger than 10 mg of labetalol, combined with anesthesia induction drugs might induce hypotension. Furthermore, 0.25 or 0.5 mg/kg labetalol IV before induction of anesthesia, did not attenuate the hypertensive response to endotracheal intubation. (Maharaj RT et al - S. Afr. Med. J. 63: 691, 1983.) Deep general anesthesia may abolish the cardiovascular response to endotracheal intubation, but is not practical in rapid-sequence techniques and would require more than 1.6 MAC (MAC-BAR) since intubation is a more profound stimulus than skin incision. Thus, short lived adrenergic blockade is preferable to profound anesthesia. Our clinical experience indicates that 10 mg of IV labetalol acts within 1 minute and lasts about 15 minutes in most patients, though the pharmacokinetics of the drug are not well described. Compared to esmolol, LA10 is much easier to administer and one-tenth as expensive. Since labetalol 10 mg is unlikely to cause bronchospasm, does not affect platelet function, does not increase cerebral blood flow or ICP, and is easy and inexpensive to administer, it offers a safe, practical means to block the tachycardic response to intubation. The search for drugs which block the hypertensive response to intubation must continue.

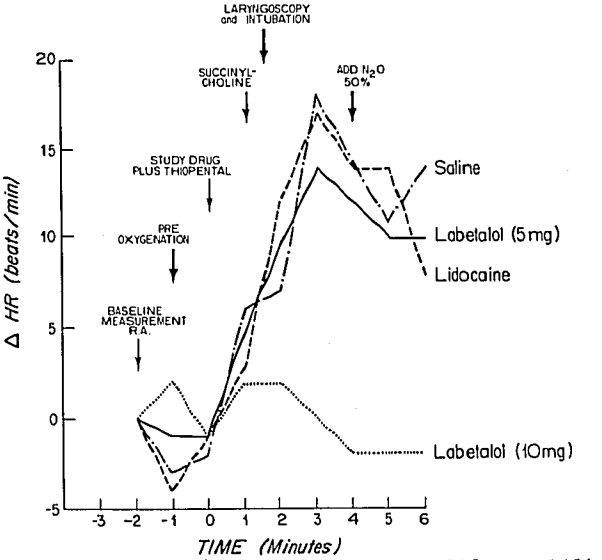

Table n = 10 in each group	S	L	LA5	LA10
Age (years)	49±5	49±5	52±5	53±5
Sex (M/F)	5/5	4/6	5/5	4/6
Weight (Kg)	82±6	74±5	78±8	74±4
Height (Cm)	170±5	170±5	167±3	169±3
ASA - PS I/II/III	3/7/0	2/7/1	2/7/1	2/7/1
Thptl. dose (mg/kg)	3.9±.2	4.5±.2	4.3±.2	4.1±.2
Time to intubate (sec.)	9.5±2	9.3±2	12.7±4	9.9±2
ΔMAP (1-3 min) mm Hg	+44	+35	+40	+35
ΔHR (1-3 min) beats/min	+12	+14	+9	-2*

(mean ± SE) *(P < 0.05 by ANOVA)