Title: ATTENUATION OF HEART RATE RESPONSE TO INTUBATION BY A NEW BETA-ADRENERGIC BLOCKING DRUG, ESMOLOL

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Introduction: Esmolol is a water soluble beta-1 adrenergic blocking agent with rapid onset and ultrashort duration of action.[1,2] Potentially, it is an excellent drug to prevent or treat undesirable increases in heart rate (HR) and contractility which may occur during general anesthesia and surgery in response to increased adrenergic activity. These increases are most likely to occur during such stimuli as tracheal intubation, incision and surgical manipulations. By attenuating the positive inotropic and chronotropic effects of increased adrenergic activity, beta blockade minimizes increases in HR and blood pressure (BP) and may thus be desirable in patients with ischemic heart disease. The present investigation was designed to determine the dosage of esmolol that is safe and effective in reducing the cardiovascular response to laryngoscopy and tracheal intubation during general anesthesia in man.

Methods: Informed consent was obtained in 40 patients electively scheduled for myocardial revascularization surgery. Patients were divided into four groups of 10 patients each: a control (untreated) group and three groups given different dosages of esmolol infusion. Premedication consisted of diazepam (0.15 mg/kg p.o.), morphine sulfate (0.1 mg/kg i.m.), and scopolamine (0.3 to 0.4 mg i.m.), 60 to 90 min before anesthesia induction. Anesthesia was induced with diazepam (0.5 mg/kg i.v.) and pancuronium (0.1 mg/kg i.v.) while breathing N_2O/O_2 (50:50). Esmolol infusion began 3 min after induction. All patients in the treatment groups received 500 mcg/kg/min of esmolol for the first min. Thereafter, esmolol infusion varied: group 1 received 100 mcg/kg/min for an additional 6 min; group 2 received 500 mcg/kg/min for an additional min followed by 200 mcg/kg/min for 5 min; and group 3 received 500 mcg/kg/min for an additional 2 min followed by 300 mcg/kg/min for 4 min. Laryngoscopy occurred 6 min after anesthesia induction in all groups. EKG, HR, systolic and diastolic BP were continuously monitored. Data were collected and analyzed at six stages (table).

Results: Esmolol attenuated the HR response to induction and intubation (table). HR (72 ± 2.6, Group 3) was significantly lower than 84 ± 3.3. (control) 3 min into the esmolol infusion (Stage III). In all three esmolol treated groups, HR was significantly lower than the control group at 1 and 4 min post-intubation (Stages IV and V); however, 5 min post-esmolol infusion (Stage VI) all groups were similar. MAP was significantly lower than control in all esmolol treated groups immediately before intubation and in Groups 2 and 3 one min after intubation; all groups were similar at Stage VI. RPP was significantly lower in esmolol treated groups at Stages III, IV and V and were similar at Stage VI. There were no adverse effects attributed to esmolol infusion.

Discussion: Esmolol is ideally suited to attenuate or abolish transient tachycardia because it has a prompt onset and short duration of action. The present data demonstrate that, compared to untreated patients, esmolol produced lower HR (all groups) and BP (groups 2 and 3) after intubation. Cessation of infusion is rapidly (5 min) followed by a return of HR and BP to those of the control group. O_2 consumption was not measured in these patients, but the RPP is a good correlate of MVO_2 and esmolol significantly attenuated the rise in RPP in all treated groups. Furthermore, the rise in RPP that occurred in esmolol treated groups was, compared with the control group, much more a result of an increase in blood pressure rather than HR, a state more compatible with equalizing oxygen supply and demand rather than having greater increases in HR. In summary, esmolol is a safe, beta-adrenergic blocking drug which effectively attenuates the HR response to intubation.

HEMODYNAMIC DATA

	HR	MAP	RPP
Control (n = 10)			
Stage I	71 ± 4.3	99.7 ± 3.7	10792 ± 884
Stage II	82 ± 4.3	98 ± 4.6	11833 ± 717
Stage III	84 ± 3.3	98 ± 4.9	12087 ± 705
Stage IV	102 ± 3.9	133 ± 5.6	19355 ± 856
Stage V	96 ± 4.3	110 ± 4.8	15397 ± 839
Stage VI	86 ± 7.4	100 ± 4.7	12460 ± 1284
Group 1 (n = 10)			
Stage I	69 ± 2.8	91.2 ± 3.3	9931 ± 811
Stage II	82 ± 4.6	89 ± 4.6	10563 ± 1064
Stage III	76 ± 3.3	82 ± 4.9*	9204 ± 953+
Stage IV	86 ± 3.8++	117 ± 7.0	14562 ± 1115++
Stage V	83 ± 3.1+	109 ± 3.8	12836 ± 817*
Stage VI	82 ± 2.6	96 ± 3.1	11411 ± 545
Group 2 (n = 10)			
Stage I	70 ± 4.0	92 ± 3.6	10060 ± 705
Stage II	81 ± 5.3	87 ± 3.6	10374 ± 797
Stage III	75 ± 3.6	74 ± 3.8++	8235 ± 628++
Stage IV	85 ± 2.5++	109 ± 6.5+	13208 ± 987++
Stage V	82 ± 2.3+	92 ± 5.1*	11056 ± 745++
Stage VI	82 ± 3.3	89 ± 3.0	10690 ± 613
Group 3 (n = 10)			
Stage I	68 ± 4.0	86 ± 3.4+	8978 ± 858
Stage II	77 ± 3.6	85 ± 5.1*	9637 ± 938
Stage III	72 ± 2.6+	73 ± 4.5++	7655 ± 634++
Stage IV	83 ± 2.5++	109 ± 6.2+	12614 ± 926++
Stage V	81 ± 2.5+	102 ± 6.7	11786 ± 1077+
Stage VI	80 ± 2.1	97 ± 5.3	11059 ± 798

All values ± SEM. Where HR = heart rate, MAP = mean arterial pressure, RPP = rate pressure product. Stage I = baseline, Stage II = 3 min after induction - pre-esmolol, Stage III = min 3 of esmolol infusion - pre-intubation, Stage IV = 1 min post-intubation, Stage V = 4 min post-intubation - esmolol off, Stage VI = 9 min post-intubation and 5 min post-infusion. * = $p < 0.05$ vs control group, + = $p < 0.01$ vs control group, ++ = $p < 0.005$ vs control group.

References:

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