A bolus dose of esmolol attenuates tachycardia and hypertension after tracheal intubation

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Forty-five patients of ASA physical status I and II undergoing a variety of non-cardiac surgical procedures were studied to determine the effect of bolus administration of esmolol, a new short-acting beta blocking drug, on heart rate and blood pressure responses to induction of anaesthesia and tracheal intubation. Subjects were allocated randomly to receive placebo, 100 mg or 200 mg of esmolol IV as part of an anaesthetic induction technique. The differences in heart rate between the placebo group and both the 100 mg and 200 mg groups were significant prior to intubation (95 ± 7.9 , 82 ± 9.7 , 80 ± 7.3 beats per min respectively), and also at 0.5 min and 1.5 min following intubation for the 200 mg group. In the 200 mg group there was a significant decrease, compared with placebo, in systolic blood pressure at 0.5 min (144 ± 32.1 vs 165 ± 18.7 mmHg) and 1.5 min (154 ± 25.0 vs 170 ± 19.5 mmHg) after intubation. In this study, adequate haemodynamic control was obtained following administration of 200 mg of esmolol.

Quarante-cinq patients ASA classe I et II devant subir une variété de procédures chirurgicales non-cardiaques ont été étudiés afin de déterminer l'effet de l'administration de l'esmolol en bolus sur la fréquence cardiaque et la tension artérielle lors de l'induction de l'anesthésie et l'intubation endotrachéale. Les sujets ont été randomisés afin de recevoir soit du placebo,

soit 100 mg ou 200 mg d'esmolol lors de l'induction. Les différences dans la fréquence cardiaque entre le groupe placebo et les deux groupes de 100 mg et 200 mg étaient significatives avant l'intubation (95 ± 7.9 , 82 ± 9.7 , 80 ± 7.3 batt/minute respectivement), et aussi à 0,5 minutes et 1,5 minutes après l'intubation pour le groupe de 200 mg. Pour le groupe 200 mg, il y avait une diminution significative (comparativement au placebo) dans la pression artérielle systolique à 0,5 minutes ($144 \pm 32,1$ versus $165 \pm 18,7$ mmHg) et à 1,5 minutes ($154 \pm 25,0$ versus $170 \pm 19,5$ mmHg) après intubation. Dans cette étude, un contrôle hémodynamique adéquat était obtenu après administration de 200 mg d'esmolol.

Key words

ANAESTHETIC TECHNIQUES: laryngoscopy;
BLOOD PRESSURE: hypertension;
HEART: tachycardia;
INTUBATION, TRACHEAL: complications;
SYMPATHETIC NERVOUS SYSTEM: beta adrenergic antagonists, esmolol.

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Esmolol is a relatively cardiac-selective beta blocker with a very short half-life (about nine minutes) when administered intravenously.¹ The short duration of action of esmolol has led to its use in a number of situations requiring beta receptor antagonism of limited duration, for example, treatment of supraventricular dysrhythmias,^{2,3} perioperative hypertension,^{4,5} and pheochromocytoma.⁶

An apparent indication for the use of esmolol would appear to be attenuation of the sympathetic response to laryngoscopy and tracheal intubation. Studies have shown that esmolol administered by infusion⁷ can decrease the heart rate and blood pressure response to tracheal intubation. Others have shown that bolus doses of esmolol (approximately $1.5 \text{ mg} \cdot \text{kg}^{-1}$) administered to patients with known or suspected coronary artery disease can effectively control postinduction heart rate.⁸ Use of intravenous or topical lidocaine^{9,10} generally controls blood pressure better than heart rate. Opioids, inhalational agents, and vasodilators have also been used,^{11,12} but may be required in large doses and are not equally effective in control of blood pressure and heart rate. Most beta blockers, such as propranolol, possess prolonged durations of action and may cause increased bronchomotor tone.

This study was designed to determine the effectiveness of 100 and 200 mg pre-induction bolus doses of esmolol in

TABLE I Demographic data

	ASA I	ASA II	Males	Females		Age	Weight kg	Ward HT rate	Ward SBP	Thiopental mg · kg ⁻¹
Esmolol 100 mg <i>n</i> = 15	8	7	5	10	Mean	35.8	71.8	77.7	121.1	5.4
					SD	11.9	14.6	5.1	10.1	0.6
Esmolol 200 mg <i>n</i> = 15	8	7	7	8	Mean	37.6	75.2	76.6	126.9	5.4
					SD	13.6	14.8	4.5	17.1	0.5
Placebo <i>n</i> = 14	6	8	7	7	Mean	38.5	77.2	77.3	124.9	5.3
					SD	13.1	4.8	4.9	11.5	0.7

preventing intubation-induced tachycardia and hypertension in healthy patients.

Methods

Following institutional review and informed written patient consent, 45 patients scheduled for elective non-cardiac surgery were entered into a double-blind, randomized, placebo-controlled study. Exclusion criteria included: heart rate less than 70 beats per minute; systolic blood pressure less than 100 mmHg; presence of first, second or third degree heart block; myocardial infarction in the previous three months; history of bronchospastic disease or asthma; significant hepatic or renal disease; and ingestion of any beta-blocking drug in the past 24 hr. Demographic data including age, sex, weight and ASA physical status were recorded. All patients were premedicated with oral diazepam (0.15 mg · kg⁻¹) 90 min before induction of anaesthesia. Ward heart rate and blood pressure were recorded along with three baseline sets of values prior to the induction sequence.

Three minutes before induction of anaesthesia, patients received d-tubocurarine 0.04 mg · kg⁻¹ IV and 100 per cent oxygen by mask. At time zero, the study preparation was administered intravenously (placebo, 100 mg or 200 mg of esmolol) followed by sodium thiopentone 3–5 mg · kg⁻¹ and succinylcholine 1.5 mg · kg⁻¹ IV. Laryngoscopy and tracheal intubation were performed 90 sec after time zero. Heart rate, systolic, mean, and diastolic blood pressures were recorded using a Hewlett Packard (#78354A) monitor incorporating a non-invasive blood pressure cuff. Anaesthesia was maintained with nitrous oxide, 50 per cent, in oxygen and isoflurane 1.5 per cent.

Neuromuscular blockade was achieved with vecuronium 0.08 mg · kg⁻¹ IV.

While no limits were set on the maximum or minimum heart rate and blood pressure, anaesthetists were instructed to identify and treat adverse responses according to their usual practice. All drugs administered and changes in anaesthetic concentration were recorded. At the end of the anaesthetic, the anaesthetist was asked to rate the anaesthetic induction compared with his or her usual induction technique.

The haemodynamic data were tabulated and analysis of covariance was applied to detect differences among the three groups. A significance level of $P < 0.05$ was chosen. The study code was broken only after 45 patients had been entered. One patient was withdrawn from the study because of a baseline heart rate of less than 70 beats per minute.

Results

There were no significant differences between the three groups in ASA physical status, sex, age, weight, ward heart rate or systolic blood pressure, or dose of sodium thiopentone administered (see Table I).

The differences in heart rate between the placebo and both the 100 mg and 200 mg groups were significant at one minute (prior to intubation). There were significant differences in heart rate between the placebo group and 200 mg group at both two and three minutes. The heart rate remained lower in the 200 mg group for up to eight minutes, but the later data were not statistically significant (see Table II).

In both the 100 and 200 mg groups, there were

TABLE II Changes in heart rate in patients given esmolol 100 or 200 mg or placebo

		Baseline	0 Min	1 Min	2 Min	3 Min	4 Min	5 Min
Esmolol 100 mg	Mean	77	81	82*	91	91	90	89
	SD	10.2	8.5	9.7	9.3	7.5	9.0	10.7
Esmolol 200 mg	Mean	79	84	80*	86*	85*	83	83
	SD	11.9	13.5	7.3	11.9	11.7	9.0	13.1
Placebo	Mean	71	87	95	99	94	95	93
	SD	9.2	17.8	7.9	9.7	10.2	10.1	6.7

*Statistically significant compared with placebo: $P < 0.05$.

TABLE III Changes in systolic blood pressure in patients given esmolol 100 or 200 mg or placebo

		Baseline	0 Min	1 Min	2 Min	3 Min	4 Min	5 Min
Esmolol 100 mg	Mean	132	126	122	152	150*	142	132
	SD	16.0	14.9	17.1	15.6	18.8	22.5	20.9
Esmolol 200 mg	Mean	140	119	112	144*	154*	147	139
	SD	21.5	21.0	17.3	32.1	25.0	28.5	22.9
Placebo	Mean	133	133	123	165	170	143	136
	SD	10.6	13.5	17.4	18.7	19.5	21.1	21.7

*Statistically significant compared with placebo: $P < 0.05$.

significant differences in systolic blood pressures (compared to placebo) at three minutes. With the 200 mg dose, the mean and systolic blood pressures were significantly different at two minutes (see Table III). A statistically significant difference between the systolic blood pressure of the 200 mg group compared with the 100 mg group occurred 30 sec following intubation.

Adverse effects noted by the attending anaesthetist included: pain on injection (one each from the placebo and 100 mg group), and tachycardia requiring treatment (one from each group). Hypertension requiring treatment was noted in nine patients (six patients were from the placebo group). There was no evidence of bronchospasm or wheezing in any patient.

Discussion

The administration of esmolol by infusion has been described in a number of applications.²⁻⁶ While infusions are easy to set up, they require additional equipment and time. Bolus doses of esmolol may circumvent these problems. Recent studies have investigated the use of bolus doses of esmolol for the prevention of post-intubation tachycardia and hypertension in patients with coronary artery disease. Withington *et al.*⁵ have shown that in these patients, esmolol delivered in a bolus of approximately $1.5 \text{ mg} \cdot \text{kg}^{-1}$ appeared to prevent hypertension and tachycardia. In the present study, a larger dose of esmolol (approximately $3 \text{ mg} \cdot \text{kg}^{-1}$) was required to control effectively post-intubation heart rate and blood pressure. This may reflect the absence of opioids in the premedication, generally healthier patients (ASA physical status I and II), and absence of any preoperative beta-blockade. The larger dose of esmolol produced minimal adverse effects.

While esmolol has been used clinically to provide haemodynamic control in patients at risk from coronary artery disease, it may also prove useful in clinically

healthy patients. Although the haemodynamic response to tracheal intubation can be effectively blocked by opioid administration, for short surgical procedures with little postoperative pain, esmolol may provide an alternative. In addition, recent information about the prevalence of silent myocardial ischaemia reveals that many totally asymptomatic patients have advanced coronary artery disease¹³ and thus may be at risk from hypertension and tachycardia associated with laryngoscopy and tracheal intubation. The use of esmolol for short periods of stress provoked by anaesthesia and surgery seems particularly attractive in light of the apparent safety of the drug.

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