Comparison of Two Bolus Doses of Esmolol for Attenuation of Haemodynamic Response to Tracheal Intubation

S Sharma, MD
A A Ghani, FFARCS
N Win, MBBS
M Ahmad, MBBS
Department of Anaesthesiology
Hospital USM, 16150 Kubang Kerian, Kelantan

Summary

This prospective study was designed to compare the effectiveness of esmolol (either 100 mg or 200 mg) with a placebo in blunting the haemodynamic response to laryngoscopy and intubation. Seventy-five patients of ASA I or II scheduled for routine-surgery were selected and entered into a placebo-controlled study. Patients were randomly allocated to receive placebo, 100 mg or 200 mg of esmolol IV as part of an anaesthetic induction technique. There were no significant differences in the demographic distribution of the patients in the study. There was no statistical difference in the baseline heart rate (HR) and systolic blood pressure (SBP) between the three groups. One minute after the administration of the drug (prior to intubation) the differences in HR between the placebo group and both the 100 mg and 200 mg groups were significant ($p < 0.05$), and also at 1 min and 2 min following intubation for the 200 mg group ($p < 0.05$). In the 200 mg group there was a significant decrease, compared with placebo, in SBP at 1 min ($p < 0.05$) and at 2 min ($p < 0.05$) after intubation. In this study, adequate haemodynamic control following was obtained with the administration of 200 mg of esmolol.

Key Words: Tracheal intubation, Haemodynamics, Beta-adrenergic blocker, Esmolol

Introduction

Esmolol is an ultrashort-acting intravenous beta adrenergic blocker. It is relatively beta one selective ("cardioselective"), has no agonist effects (i.e., no "intrinsic sympathomimetic activity") and is broken down by red blood cell esterases giving an elimination half-life of approximately nine minutes.

The potential for life threatening complications associated with laryngoscopy and tracheal intubation in patients with coronary artery disease[1], systemic arterial hypertension, aneurysmal vascular disease and decreased intracranial compliance[2] is well known. The circulatory disturbances consist of elevation in heart rate and systemic[3,4] and pulmonary artery pressures[5], which occasionally lead to myocardial ischaemia[6], heart failure and cardiovascular catastrophies like myocardial infarct, cerebrovascular accident[7]. These changes arise from reflex sympathetic discharge resulting from epipharyngeal and laryngopharyngeal stimulation[8], associated with increased plasma norepinephrine concentrations[9,10] and are marked by increased blood pressure and heart rate. The search for effective

attenuation of these responses has included IV or topical lignocaine[3,11], vasodilators[12], adrenergic blockers[13], narcotics[14] and inhaled anaesthetics[15]. There are pros and cons for using one agent and not using the other. Advocated by some, propanolol's effects outlasted stressful interval by several hours, and not infrequently included increases in bronchomotor tone. Anaesthetist may want to suppress sympathetic nervous system response at one time (e.g., before tracheal intubation), but be able to enhance those responses very soon after. Esmolol[16] is an attractive option because of its short duration of action.

This study was designed to determine the effectiveness of 100 mg and 200 mg pre-induction bolus doses of esmolol in preventing intubation-induced tachycardia and hypertension in healthy patients.

Methods

Following the informed written consent; 75 patients, belonging to ASA I or II, scheduled for elective non-cardiac surgery were entered into a randomized, placebo-controlled study. Exclusion criteria included : pregnant women, AV conduction block greater than first degree, systolic blood pressure less than 100 mmHg, diastolic blood pressure less than 50 mmHg, heart rate less than 70 beats per minute, bronchospasm or bronchial asthma, history of drug allergy or idiosyncracy to beta blockers and patients on beta blockers or calcium channel blockers.

Demographic data including age, sex, weight and ASA physical status were recorded. All patients received diazepam 10 mg in the night and midazolam 7.5 mg 2 hours prior to 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 IV and 100% oxygen by mask. At time zero, the study preparation was administered intravenously (placebo, 100 mg or 200 mg of esmolol) followed by sleep-dose of sodium thiopentone and succinylcholine 1.5 mg/kg IV. Laryngoscopy and tracheal intubation were performed 60 seconds after time zero. Heart rate, oxygen saturation, systolic, mean and diastolic blood pressure were recorded using a Hewlett-Packard monitor "HP

78351A" and "Critikon Dinamap 1846SX". Anaesthesia was maintained with nitrous oxide, 66%, in oxygen and isoflurane 1.5%. Neuromuscular blockade was achieved with vecuronium 0.08 mg/kg IV.

Although no limits were set on the maximum or minimum heart rate and blood pressure, anaesthetists were requested to identify and treat adverse responses according to their usual practice. All drugs administered and changes in anaesthetic concentration were recorded.

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. Two patients were 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 and ward heart rate or systolic blood pressure, or dose of 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 ($p < 0.05$). In the 200 mg the heart rate remained lower well beyond the study period, though not statistically significant (see Table II).

In both the 100 mg and 200 mg groups, there were significant differences in systolic blood pressure (compared to placebo) at three minutes ($p < 0.05$). With the 200 mg dose, the mean and systolic blood pressures were significantly different at two minutes ($p < 0.05$, see Table III. A statistically significant difference between the systolic blood pressure of the 200 mg group compared with 100 mg group occurred at 2 minutes ($p < 0.05$).

Effects noted by the attending anaesthetist included tachycardia (heart rate greater than 120 beats/min)

Table I
Demographic data

	ASA I	ASA II	Males	Females	Age	Weight (kgs)	Ward HR	Ward SBP	Thio (mg/kg)
Esmolol 100 mg n=25	13	12	14	11	37.6 ±10.8	65.6 ±10.8	73.4 ±5.2	124.3 ±11.2	5.1 ±0.4
Esmolol 200 mg n=24	11	13	13	11	35.8 ±13.2	63.7 ±9.6	75.6 ±4.3	126.3 ±16.2	4.9 ±0.5
Placebo n=24	13	11	12	12	39.3 ±13.3	61.8 ±8.3	77.4 ±4.6	123.7 ±11.3	4.8 ±0.4

HR = heart rate
SBP = systolic blood pressure

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

	Baseline	0 minute	1 minute	2 minute	3 minute	4 minute	5 minute
Esmolol 100 mg	77 ± 9.8	83 ± 9.2	81 ±10.6*	98 ± 11.2	92 ± 8.6	91 ± 9.8	88 ±10.5
Esmolol 200 mg	76 ± 10.6	86 ±10.8	79 ± 8.2*	84 ± 12.9*	85 ± 10.7*	84 ± 9.6	83 ±12.9
Placebo	74 ± 11.6	89 ±15.2	98 ± 9.2	103 ± 9.7	98 ± 11.2	96 ± 9.8	92 ± 7.8

* 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 minute	1 minute	2 minute	3 minute	4 minute	5 minute
Esmolol 100 mg	135 ± 15.8	128 ± 13.8	121 ± 16.7	166 ± 14.7	152 ± 16.5*	144 ±21.8	135 ±17.8
Esmolol 200 mg	139 ± 18.9	122 ± 18.6	110 ± 15.8	142 ± 26.9*	150 ± 28.2*	146 ±25.2	138 ±21.6
Placebo	136 ± 19.8	134 ± 12.8	128 ± 16.4	170 ± 20.8	175 ± 18.2	150 ±22.3	140 ±20.8

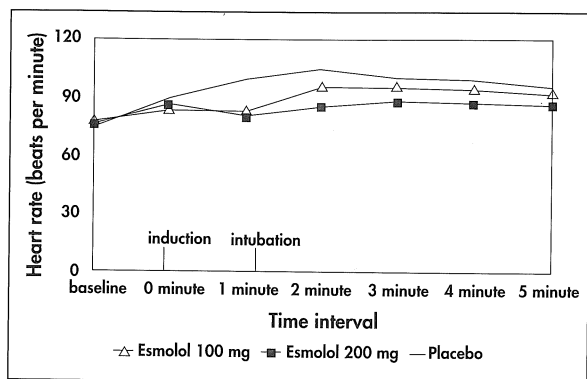* Statistically significant compared with placebo : $p < 0.05$

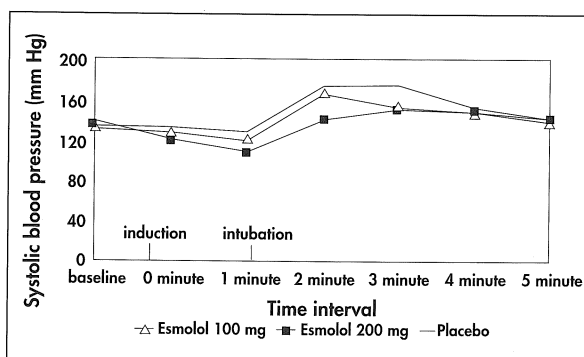Fig. 1: Changes in heart rate in patients given esmolol 100 or 200 mg or placebo

Fig. 2: Changes in SBP in patients given esmolol 100 or 200 mg or placebo

requiring treatment (two in 100 mg group and one in 200 mg group). Hypertension (systolic blood pressure greater than 200 mmHg) requiring treatment was noted in twelve patients (ten were from placebo group and one each in 100 and 200 mg groups). Clinically evident increases in bronchomotor tone, ECG changes like greater than 1 mm. ST segment change, or a noticeable increase in PR interval did not occur in any patient.

Discussion

Esmolol hydrochloride is an ultrashort acting, beta-one selective blocker with a distribution half-life of two minutes[17]. Esmolol appears quite suitable for use during a short-lived stress such as tracheal intubation, organ manipulation like handling adrenal and thyroid gland and extubation. Administration of esmolol by

bolus and infusion has been found to be effective in blunting the haemodynamic effects of laryngoscopy and intubation[18] as well as intra-operative[19] and post-operative[20] stresses. However, the dosing regimen and time required for preparation of an infusion may be cumbersome and unnecessary for treatment of perioperative cardiovascular responses that, although important, are often transient in nature. Esmolol can effectively be administered as a set dose rather than adjusting for patient weight[17]. However if one desires, a mg/kg dose can also be administered. Proper bolus timing and dosage in relation to the stimulus is important. The esmolol bolus should be given within two minutes of the expected stimulus[21] since a bolus dose given three to four minutes before the stimulus may be too early[22].

Recent studies have investigated the use of bolus doses of esmolol for the prevention of post intubation tachycardia and hypertension. Miller *et al.* demonstrated 1.5 mg/kg of esmolol is optimal for blunting haemodynamic responses to intubation. However in this study, a higher dose of esmolol (200 mg or 3 mg/kg) 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 side effects.

Although the haemodynamic response to tracheal intubation can be effectively blocked by opioid administration, for short surgical procedures with little post-operative 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 disease[23] 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 beneficial in light of apparent safety of the drug in terms of short half life, no significant interaction with various anaesthetic agents[24-29] and the ability to titrate and control the magnitude and the duration of beta blockade[30].

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