Bolus doses of esmolol for the prevention of perioperative hypertension and tachycardia

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The effectiveness of esmolol, an ultra short-acting cardioselective β blocker, in the prevention and treatment of post-intubation haemodynamic perturbations, was investigated. Forty-eight ASA physical status I and II patients undergoing hysterectomy were randomly assigned to receive a single intravenous bolus of placebo, esmolol 100 mg, or esmolol 200 mg in a double-blind fashion. This was administered over 15 sec, and immediately followed by thiopentone 3–5 mg·kg^{-1}, succinylcholine 1.5 mg·kg^{-1}, and tracheal intubation 90 sec later. The heart rate following induction of anaesthesia was lower in the esmolol 200 mg group ($P < 0.01$); following intubation, the increase in heart rate in the placebo group was greater than in the esmolol groups ($P < 0.05$). The systolic blood pressure post-induction was lower in the esmolol 200 mg group ($P < 0.05$); following intubation, however, no significant differences were seen among groups in systolic, diastolic, or mean blood pressures. Following tracheal intubation, the incidence of ventricular arrythmias was lower in the esmolol groups ($P < 0.05$). In summary, esmolol in 100 mg and 200 mg doses was effective in mitigating the haemodynamic response following tracheal intubation.

L'efficacité de l'esmolol, dans la prévention et le traitement des variations hémodynamiques lors de l'intubation a été investiguée. Quarante-huit patientes ASA I et II devant subir une hystérectomie étaient randomisées afin de recevoir soit un bolus de placebo, soit 100 mg ou 200 mg d'esmolol à double insu. L'administration intraveineuse s'est faite sur 15 secondes immédiatement après du thiopentone 3–5 mg.kg^{-1}, succinylcholine 1,5 mg·kg^{-1} et intubation trachéale 90 sec. plus tard. La fréquence cardiaque après induction de l'anesthésie était plus basse dans le groupe esmolol 200 mg ($P < 0,01$); après l'intubation, l'augmentation de la fréquence cardiaque dans le groupe placebo était plus grande que celle des groupes esmolol ($P < 0,05$). La pression artérielle systolique après l'induction était plus basse dans le groupe esmolol 200 mg ($P < 0,05$); après l'intubation, cependant, il n'y avait aucune différence significative entre le groupe dans la pression artérielle systolique, diastolique ou la pression artérielle moyenne. Après intubation trachéale, l'incidence d'arythmie ventriculaire était plus basse dans les groupes esmolol ($P < 0,05$). En résumé, des doses d'esmolol de 100 mg et 200 mg étaient efficaces pour atténuer la réponse hémodynamique après intubation endotrachéale.

Key words

COMPLICATIONS: hypertension, tachycardia;
INTUBATION, TRACHEAL: cardiovascular responses;
SYMPATHETIC NERVOUS SYSTEM: β adrenergic blockade, esmolol.

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Presented at the Canadian Anaesthetists' Society 46th Annual Meeting, Ottawa, Ontario, June 1989.

Supported by a grant from DuPont Canada, Inc.

Tracheal intubation produces undesirable increases in heart rate and blood pressure.[1–3] These are of particular concern for the patient with coronary artery disease, because of their propensity to cause myocardial ischaemia.[4] Strategies to circumvent these changes have included minimizing the duration of laryngoscopy to less than 15 sec,[5] the use of intravenous narcotics,[6] intravenous lidocaine,[1] vasodilators[7] and long-acting β-blocking agents.[8] Each technique has disadvantages, the most obvious being that the prevention often outlasts the stimulus.

Esmolol is a relatively new β-blocking agent with several desirable properties. It is cardioselective,[9] short-acting (elimination half-life of 9.2 min),[9] and a non-irritating intravenous agent.[10] These characteristics make it ideally suited to use in the operating room. Previous studies have established the effectiveness of esmolol infusions in the prevention of haemodynamic alterations following tracheal intubation;[11–16] few have examined the effectiveness of bolus doses of esmolol in the same setting.

This study was designed to examine the ability of bolus doses of esmolol to prevent post-intubation hypertension and tachycardia, and to evaluate side-effects following its use.

Methods

The study was approved by the hospital ethics committee, and informed consent was obtained from each patent. ASA physical status I and II patients who were at least 18 years of age and undergoing vaginal or abdominal hysterectomy were deemed eligible for the study. Exclusion criteria are listed in Table I. Forty-eight patients were equally randomized by the hospital pharmacist to one of three groups: placebo, esmolol 100 mg and esmolol 200 mg.

Variables to be monitored were heart rate, systolic, diastolic and mean blood pressures, and ECG morphology. Heart rate and systemic pressures were obtained at one-minute intervals using an automated sphygmomamometer with strip chart recording capability (Critikon Canada Inc., Markham, Ontario). Leads II and V_5 of the ECG were followed continuously with a Holter monitor (Delmar Avionics, Irvine, California) from the baseline period to at least 30 min after the last dose of esmolol, and subsequently analyzed for ST segment changes and arrythmias. This was done by a cardiologist who was blinded to the patient's group.

Patients were premedicated with diazepam 5–10 mg PO, one hour before surgery. Upon arrival in the operating room, and with the monitors in place, three baseline readings were obtained. Pancuronium, 1 mg, was then given for defasiculation. Three minutes later, under double-blind conditions, patients were injected over 15 sec with 20 ml of solution containing esmolol 100 mg, esmolol 200 mg, or saline (placebo). Anaesthesia was then induced with thiopentone 3–5 $mg \cdot kg^{-1}$ and succinylcholine 1.5 $mg \cdot kg^{-1}$. The tracheas were intubated 90 sec after the administration of the study drug. Anaesthesia was maintained with 50 per cent nitrous oxide, and enflurane 1–3 per cent. Vecuronium 0.07 $mg \cdot kg^{-1}$ was given for muscular relaxation, and supplemented with doses of 0.025 $mg \cdot kg^{-1}$. Surgical incision occurred at least five minutes after induction of anaesthesia. Monitoring of haemodynamic variables continued for at least 15 min after the administration of the study drug.

Changes in heart rate, and systolic, diastolic, and mean arterial blood pressure were analyzed by analysis of covariance, with the baseline variables as the covariants. Means presented were the least squares adjusted means. Baseline demographics were compared by a one-way analysis of variance. Fisher's exact test was used to evaluate differences in side-effects among the three groups. A P value of less than 0.05 was taken to indicate statistical significance. Data are presented as means ± SD.

TABLE I Exclusion criteria

Treatment with β blockers or calcium channel blockers within the previous 24 hrs.
Ward or baseline heart rate <70 bpm.
Ward or baseline systolic blood pressure <100 mmHg.
P-R interval >0.24 sec, 2nd degree, or 3rd degree heart block.
Sick Sinus Syndrome.
Right ventricular or left ventricular failure.
Treatment with adrenergic augmenting or depleting drugs.
Myocardial infarction within past three months.
Reactive airways disease.
Treatment with other experimental drugs within 14 days.

Results

Sixteen patients were included in each of the three groups. There were no significant differences in age, weight, baseline haemodynamic variables, or dose of thiopentone between the esmolol 100 mg, esmolol 200 mg and placebo groups (Table II). No difficulties were encountered during tracheal intubation, and the duration of laryngoscopy never exceeded 15 sec.

Following induction of anaesthesia, the heart rate in the esmolol 200 mg group was significantly lower when compared with placebo ($P < 0.01$). Following intubation, the heart rates in the two esmolol study groups were significantly lower than placebo ($P < 0.01$ at 0.5 min, $P < 0.05$ at 1.5 min and 2.5 min); at 2.5 min following intubation, no further significant differences among the three groups were seen (Figure 1).

The systolic blood pressure was similarly decreased

TABLE II Demographic data

	esm 100	*esm 200*	*Placebo*
Age (yr)	43.9 ± 13.8	42.1 ± 10.0	41.9 ± 11.0
Weight (kg)	71.5 ± 16.3	63.5 ± 13.5	72.2 ± 16.2
Heart rate (bpm)	79.3 ± 5.0	77.1 ± 10.0	75.9 ± 5.4
Systolic BP (mmHg)	117.2 ± 9.8	118.9 ± 10.1	123.3 ± 22.4
Diastolic BP (mmHg)	74.5 ± 8.6	73.8 ± 8.4	72.2 ± 8.2
Dose thiopentone ($mg \cdot kg^{-1}$)	4.54 ± 0.8	4.92 ± 1.0	4.32 ± 1.0

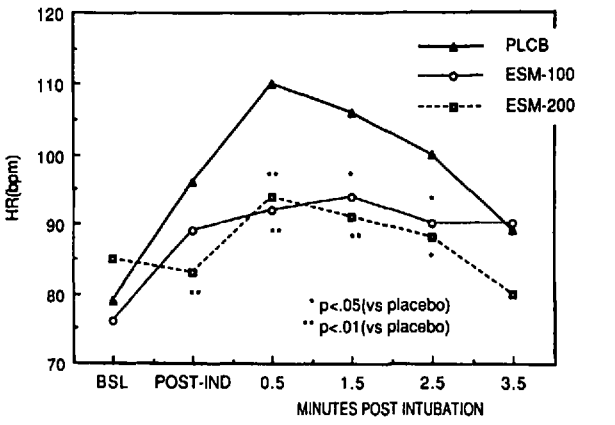

FIGURE 1 Change in heart rate.

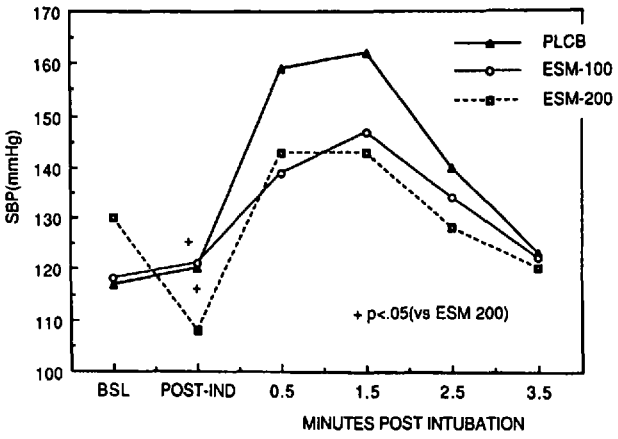

FIGURE 2 Change in systolic BP.

after induction of anaesthesia, being significantly lower in the esmolol 200 mg group than in the esmolol 100 mg and placebo groups ($P < 0.05$). However, no significant differences were seen among the three groups at any time following intubation (Figure 2). No significant differences were seen in diastolic and mean arterial blood pressures at any time during the study.

The incidence of pain on injection, hypotension, and bradycardia, was not significantly different among the three groups. Ventricular premature beats (including couplets and bigeminy) were detected in three patients in each of the esmolol groups, and in eight patients in the placebo group. When the esmolol groups were combined and compared with placebo, this difference was significant ($P < 0.05$). No episodes of myocardial ischaemia were detected during the study.

Discussion

Several strategies have evolved to blunt the haemodynamic response to tracheal intubation. These have included the use of narcotics, lidocaine, vasodilators, and β blockers. Each of the techniques has disadvantages. Large doses of narcotics may lead to postoperative respiratory depression, and fentanyl, lidocaine and vasodilators may produce hypotension, resulting in coronary hypoperfusion.[17] The use of traditionally available β blockers may lead to haemodynamic depression that far outlasts the duration of the noxious stimulus.

Numerous studies[11-16] have confirmed esmolol's efficacy when given as an infusion, in the amelioration of the hypertensive and tachycardic response following intubation. Other haemodynamic variables such as cardiac output and stroke volume are decreased in a dose-dependant manner.[10,18] We chose to evaluate esmolol initially in healthy subjects, to appreciate fully the cardiovascular effects, before testing in a more haemodynamically labile patient population.

The effectiveness of esmolol was studied in 100 mg and 200 mg doses, in the prevention of the haemodynamic response to intubation. The rise in heart rate was blunted for 2.5 min following intubation. It then became indistinguishable from placebo; this probably reflects cessation of the stimulus of intubation, and the establishment of an adequate depth of anaesthesia. The rise in blood pressure, however, was not mitigated by either dose of esmolol when compared with placebo. This descrepancy with other published reports may be related to the higher doses of esmolol used in the majority of infusion studies, and in some, the concomitant use of fentanyl as part of anaesthetic induction. Bernstein[20] used similar doses of esmolol in bolus fashion, and found that hypertension and tachycardia were both prevented following rapid-sequence induction. This may reflect a more sedating premedication or a slightly larger dose of thiopentone (5 $mg \cdot kg^{-1}$ vs 4.6 $mg \cdot kg^{-1}$) given in closer proximity to the time of laryngoscopy and intubation. There were no significant side effects attributable to esmolol. Analysis of the Holter monitor tracings revealed a significantly lower incidence of post-intubation ventricular arrythmias in the esmolol groups.

In summary, bolus doses of 100 mg and 200 mg of esmolol were used to ameliorate the tachycardic response to tracheal intubation. Both doses were equally effective. Esmolol also decreased the incidence of post-intubation ventricular arrythmias. Neither dose of esmolol prevented the hypertensive response to intubation. No side-effects attributable to esmolol were seen. Further studies are needed to delineate the role of esmolol in combination with short-acting narcotics, in preventing the haemodynamic response to intubation and other surgical stimuli.

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