Effects of Esmolol on the Prevention of Haemodynamic Responses to Tracheal Extubation after Craniotomy Operations

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Objective: The aim of this study was to evaluate the effects of esmolol infusion on the prevention of haemodynamic responses to tracheal extubation in patients undergoing elective craniotomy.

Methods: With approval from the Medical School Ethics Committee at Marmara University and the patients’ written consent, 30 patients between 20-65 years of age undergoing elective craniotomy were randomly placed in either the Group Esmolol (n=15) or the Group Control (n=15). Anaesthesia was induced with 5-7 mg kg⁻¹ thiopental sodium, 1 µg kg⁻¹ remifentanil, and 0.1 mg kg⁻¹ vecuronium bromide iv, and was maintained with 1 MAC sevoflurane in oxygen-air mixture (50:50) and 0.25 µg kg⁻¹ min⁻¹ remifentanil infusion. At the end of the operation, patients inhaled 100% oxygen after the discontinuation of the anaesthetic agents. For Group Esmolol, 5 min before extubation 2 mg kg⁻¹ esmolol in 50 mL was infused over 10 min (0.2 µg kg⁻¹ min⁻¹), while for Group Control, 50 mL saline was infused over 10 min. The quality of extubation was evaluated with a 5 point scale, recording heart rate, systolic, diastolic, and mean arterial pressures before infusion, 1 min after infusion, during extubation, and at 1, 3, 5, and 10 min after extubation.

Results: In the esmolol group, systolic, diastolic, and mean arterial pressures, as well as heart rate, decreased significantly after esmolol infusion and were significantly lower than in the control group after extubation (p<0.05). The ratio of patients with an extubation score of one was significantly higher in the esmolol group than in the control group (p<0.05).

Conclusion: We concluded that 2 mg kg⁻¹ esmolol infusion before extubation can prevent hypertension and tachycardia caused by extubation in patients undergoing elective craniotomy.

Key Words: Craniotomy, esmolol, extubation

Introduction

Extubation of the trachea should be devoid of significant changes in haemodynamic parameters and adverse events, such as straining at aspiration, coughing, breath holding, or laryngospasm. The receptors, particularly in the larynx, trachea and bronchi, are stimulated by mechanical and chemical factors during extubation as in laryngoscopy and intubation (1, 2). Stimulation of the respiratory tract at the supraglottic and subglottic levels produces respiratory and cardiovascular reflex responses (3, 4). During laryngoscopy, intubation, and extubation, the plasma concentrations of noradrenaline and adrenaline causing a significant increase in blood pressure and heart rate, which may result in severe and even life-threatening complications in patients with coronary heart disease, hypertension, and increased intracranial pressure (5-10). In order to control haemodynamic changes during tracheal intubation and extubation, local anaesthetics, opioids, beta-blocking agents, and calcium channel blockers have been used with varying success rates (11, 12).

Esmolol is a short-acting cardioselective beta-blocker (β1) agent, which is used to prevent or treat hypertension and tachycardia during intraoperative and postoperative periods and has been reported to decrease plasma catecholamine levels (13). It seems to be a proper agent in preventing haemodynamic responses during intubation and extubation. In this study, our goal was to determine the effects of esmolol infusion on haemodynamic responses during endotracheal extubation in patients undergoing craniotomy operations.

Methods

Thirty patients, between 20-65 years of age and of American Society of Anesthesiologists (ASA) physical status class 1-2, scheduled for elective craniotomy were included in this prospective, randomised, and double-blind study after Institutional Ethics Committee approval (No: 09.2011.0033, Date: 03.03.2011) and written consent from the patients. The patients who had significant cardiac, pulmonary, renal, hepatic, and neuropsychiatric disease, chronic alcohol or drug use, a family history of allergy to the drugs used, a heart rate below 50 beats min⁻¹ or over 100 beats min⁻¹, arterial blood pressure below 90/60 mmHg or over 180/100 mmHg, or were using β-blockers, sympathomimetic agents, calcium channel blockers, or monoamine oxidase inhibitors were excluded from the study. Patients were ran-
domly divided into two groups, Group Esmolol (n=15) and Group Control (n=15).

For all patients, heart rate (HR), invasive systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial pressure (MAP), peripheral oxygen saturation (SpO₂), and end-tidal CO₂ pressure (ETCO₂) were monitored. Anaesthesia was induced with 5-7 mg kg⁻¹ thiopental sodium, 1 µg kg⁻¹ remifentanil, and 0.1 mg kg⁻¹ vecuronium bromide iv, and after endotracheal intubation, remifentanil infusion at a rate of 0.25 µg kg⁻¹ min⁻¹. Controlled mechanical ventilation was adjusted to maintain ETCO₂ pressure between 27-30 mmHg.

At the end of surgery, all anaesthetic agents were discontinued and the patients were ventilated with 100% oxygen. Neuromuscular block was antagonised with iv 0.03 mg kg⁻¹ neostigmine and 0.01 mg kg⁻¹ atropine sulphate. As previously determined, the patients received either esmolol (Brevibloc premixed, 10 mg mL⁻¹, Baxter Healthcare Corporation, USA) or saline infusions. The solutions were prepared and administered in a double-blind manner. For the patients in Group Esmolol, 5 min before extubation, 2 mg kg⁻¹ esmolol diluted in 50 mL was infused over 10 min (0.2 µg kg⁻¹ min⁻¹), and for those in Group Control, 50 mL 0.9% saline infused over 10 min. When spontaneous breathing began, the patients were extubated after aspiration of oropharyngeal secretions. The quality of extubation was assessed with a 5-point rating scale, where 1: no cough and normal breathing, 2: mild cough, 3: moderate cough, 4: severe cough and difficulty in breathing, 5: laryngospasm with severe cough and forced breathing (14). After extubation, the patients inhaled 100% oxygen with an oxygen mask for 5 min. Heart rate, SAP, DAP, and MAP were recorded 1 min before infusion, at first min of infusion, during extubation, and at 1, 3, 5, and 10 min after extubation.

The following treatments were provided: 0.5 mg atropine sulphate was administered for bradycardia (HR <50 beat min⁻¹), 5 mg ephedrine was administered for hypotension (systolic arterial pressure <100 mmHg), and 0.02 mg nitroglycerine iv was given for hypertension (systolic arterial pressure >180 mmHg).

Statistical analysis
Statistical analysis of the data was performed using Predictive Analytics SoftWare/Statistical Package for the Social Sciences (PASW/SPSS) 19.0 program package. The categorical measurements were summarised as the number and percentage, continuous measurements as the mean and standard deviation (if necessary as the median of the minimum-maximum). The distribution of the data was analysed by the Kolmogorov-Smirnov test. The T-test was used for the analysis of discrete data, and two-way ANOVA for the analysis of repeated measures. The chi-square and Fisher tests were used for proportional analysis. A p value <0.05 was considered statistically significant.

Results
No statistically significant differences were found between the control and esmolol groups in demographic data, duration of anaesthesia, and surgery (Table 1).

The SAP was significantly lower in the esmolol group as compared to the control group during extubation and at 1, 3, and 5 min after extubation (Figure 1).

The DAP was significantly lower in the esmolol group when compared to the control group at extubation, and 3 and 5 min after extubation (Figure 2).

The MAP in the esmolol group was found to be significantly lower than those of the control group during extubation and at 3 and 5 min after extubation (Figure 3).

The HR in the esmolol group was significantly lower than in the control group at extubation and 1, 3, 5, and 10 min after extubation (Figure 4).

The ratio of patients with an extubation score 1 was significantly higher in the esmolol group than in the control group (Figure 5).

The incidence of hypertension and hypotension did not differ between the groups. No significant difference was noted between the groups with respect to the need for atropine.

Discussion
Tracheal intubation and extubation are associated with marked elevations in heart rate and arterial pressure. Tachycardia and hypertension occurring during tracheal extubation may result in complications such as cardiac failure, pulmonary oedema, and cerebrovascular haemorrhage (15, 16). Although the mechanism of changes occurring in the cardiovascular system during extubation remains to be elucidated, it is associated with increased release of catecholamines as a result of the stress response (5).

<table>
<thead>
<tr>
<th>Table 1. Demographic data, duration of anaesthesia and surgery.</th>
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<tr>
<td>Control Group</td>
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<tr>
<td>Age (years)</td>
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<td>Sex (F/M)</td>
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<td>Anaesthesia duration (min)</td>
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<td>Duration of surgery (min)</td>
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<td>Values are expressed as mean±SD, F/M: female/male</td>
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Figure 1. Systolic arterial blood pressure (mmHg)
T1: Preoperative, T2: Before medication, T3: 1 min after medication, T4: During extubation, T5: 1 min after extubation, T6: 3 min after extubation, T7: 5 min after extubation, T8: 10 min after extubation. *: p<0.05 Group I:Esmolol Group, Group II: Control Group.
Our goal was to investigate the effect of 2 mg kg⁻¹ 10 min⁻¹ esmolol infusion on the control of the haemodynamic response due to extubation. Different pharmacological agents were used in several studies to control haemodynamic changes during tracheal intubation and extubation. In a study involving hypertensive patients, it was reported that 1 mg kg⁻¹ lidocaine and 0.2 mg kg⁻¹ diltiazem did not prevent the increase in heart rate and mean arterial pressure at extubation (17).

Used together, PGE1 (0.1 µg kg⁻¹ min⁻¹) and lidocaine (1 mg kg⁻¹) were reported to be more effective for treatment of increased blood pressure as compared to when used individually (18). Although increased heart rate could be controlled in the lidocaine group and in the PGE1-lidocaine group, it could not be achieved in the group using PGE1 alone. In a study comparing lidocaine to verapamil, it was concluded that lidocaine infusion during intubation suppressed tachycardia and hypertension, but it was insufficient to suppress the overall sympathetic response and to eliminate the effects of increased plasma catecholamine concentrations at extubation (19).

Keskin et al. (20) found that both esmolol and lidocaine suppressed haemodynamic responses at intubation, but not during extubation. Wang et al. (21) studied five groups of patients to determine the effects of different doses of esmolol on the haemodynamic response due to extubation. They reported that, when compared to values before premedication, 1.5 mg kg⁻¹ and 2.0 mg kg⁻¹ doses of esmolol decreased the heart rate and systolic blood pressure after extubation.

Esmolol 1.0 mg kg⁻¹, 1.5 mg kg⁻¹, and 2.0 mg kg⁻¹ were also used in patients before extubation in a study by Dyson et al. (22), which showed that the increase in systolic blood pressure could be prevented with 1.5 mg kg⁻¹ and 2.0 mg kg⁻¹ esmolol, but 1 mg kg⁻¹ esmolol was found to be ineffective. Since distinct hypotension was observed with 2.0 mg kg⁻¹ esmolol, 1.5 mg kg⁻¹ esmolol was reported as the optimal dose for the prevention of haemodynamic response due to tracheal extubation. Fuhrtman et al. (23) compared the effects of esmolol with alfentanil on heart rate and systolic blood pressure after extubation. The heart rate and systolic blood pressure during extubation did not change significantly in the esmolol group. However, extubation time in this group was significantly prolonged. Therefore, they recommended esmolol to control the haemodynamic responses associated with extubation. We compared 2 mg kg⁻¹ esmolol to the saline group, without the use of any other drug, and found that the activity could be suppressed by using esmolol.

Lim et al. (24) sought to find the optimal prophylactic esmolol dose for controlling hemodynamic responses in patients undergoing intracranial surgery. Systolic blood pressure and heart rate increased in all groups after extubation. There was no statistically significant difference between infusion doses and, although 0.2 mg kg⁻¹ min⁻¹
was observed to be more effective, 100 mg kg\(^{-1}\) min\(^{-1}\) was considered to be safe. In our study, 2 mg kg\(^{-1}\) 10 min\(^{-1}\) esmolol attenuated the heart rate and blood pressure responses during extubation.

The above mentioned and other similar studies had some differences, such as the type of the selected pharmaceutical agent, the doses, and administration times for esmolol. At the planning stage of this study, we assumed that it would be convenient to block sympathetic stimulation using esmolol, a \(\beta\)-blocker agent, in order to prevent exaggerated haemodynamic stimulation during extubation. In previous studies comparing the effectiveness of esmolol with other agents, it was concluded that the prolonged sedative effect of an opioid agent, even if short-acting, may cause delayed extubation (23, 24). Also, as the intracranial pathology and trauma caused by the operation may affect central nervous system functions, we did not want to use an opioid agent to prevent the haemodynamic response at extubation after craniotomy. The reason we did not prefer the method of infusion used in various studies or did not use bolus esmolol after the extubation, was that we wanted to ensure the overlap of the onset of action of esmolol with the time of extubation. We started esmolol infusion 5 min before the predicted extubation time and continued it for 10 min, including the period during, before, and after extubation. Thus, we concluded that the effect of esmolol was achieved when sympathetic impulses were at their highest level. For this reason, no patient had bradycardia or hypotension requiring treatment.

**Conclusion**

Our findings suggest that, in patients undergoing craniotomy, 2 mg kg\(^{-1}\) 10 min\(^{-1}\) esmolol infusion beginning 5 min before extubation provides haemodynamic stability by preventing hypertension and tachycardia without any serious side effects during and after extubation.

**Ethics Committee Approval:** Ethics committee approval was received for this study from the ethics committee of Marmara University School of Medicine (03-03-2011, 09-2011.0033).

**Informed Consent:** Written informed consent was obtained from patients who participated in this study.

**Peer-review:** Externally peer-reviewed.


**Conflict of Interest:** No conflict of interest was declared by the authors.

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**References**