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ORIGINAL ARTICLE

# Effects of the Ultra-Short-Acting Beta-Blocker Esmolol Infusion on Cardiovascular Parameters and Quality of Postoperative Recovery in Patients Scheduled for Elective Plastic Surgery

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## Abstract

**Background/Aim:** Esmolol is an ultra-short-acting, easily titratable β-adrenergic receptor antagonist used for urgent treatment of hypertension and tachycardia in non-surgical and surgical settings. Aim of this clinical study was to investigate its cardiovascular effects and quality of the emergence from anaesthesia in patients scheduled for elective plastic surgery under general balanced anaesthesia.
**Methods:** A total of 30 ASA I/II patients were randomised in two groups of similar demographic characteristics and baseline values of cardiovascular parameters. Esmolol group received esmolol dissolved in glucose 5 % as an intravenous infusion, 0.3 mg/kg/min during the first 5 min and at a rate of 0.1 mg/kg/min thereafter. Control patients received the solvent only, at the same rate and volume. General balanced anaesthesia was induced with thiopentone sodium and fentanyl and maintained with nitrous oxide and oxygen. Neuromuscular relaxation was assured with pancuronium bromide and was antagonised at the end of operation with atropine and neostigmine. Systolic and diastolic blood pressure and heart rate were registered at all critical phases: (1) immediately prior to the induction (baseline value), (2) induction to anaesthesia, (3) tracheal intubation, (4) first skin incision, (5) surgical manipulation with organs, (6) suture of the surgical wound and (7) tracheal extubation. Drug consumption and quality of postoperative recovery were monitored.
**Results:** In most of the critical phases of anaesthesia and operation, patients from the Esmolol group had significantly lower values of cardiovascular parameters than the patients from the Control group. Esmolol-treated patients needed less fentanyl, droperidol and pancuronium and had faster and smoother emergence from anaesthesia than the control patients.
**Conclusion:** Esmolol improved haemodynamics and post-anaesthesia recovery in patients undergoing elective plastic surgery under general balanced anaesthesia.

**Key words:** Esmolol; Beta-blockers; Anaesthesia; Plastic surgery; Cardiovascular parameters.

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## Introduction

Laryngoscopy, tracheal intubation, first incision, manipulations with organs, suture of the surgical wound and tracheal extubation constitute the so-called surgical trauma and represent a source



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of very strong painful stimuli.[1] As a consequence, the activation of the sympatho-adrenal response occurs, resulting in hypertension, tachycardia, arrhythmia, lacrimation, diaphoresis and twitches of skeletal muscles.[2] These phenomena are especially dangerous in patients with serious cardiovascular diseases.[3]

The concept of general balanced anaesthesia was developed in order to suppress painful stimuli and ensure best operating conditions, however avoiding use of large doses of intravenous or high concentrations of inhalation anaesthetics and high doses of opioid analgesics to avoid the depression of cardiovascular system, delayed postoperative recovery and respiratory depression.[4] Adjuvant therapy such as short-acting opioid analgesics, local anaesthetics, $\alpha_2$-adrenergic receptor agonists, regional neural blocks and β-adrenergic receptor antagonists have been tried as supplements to the usual technique of general balanced anaesthesia.[5]

Esmolol is a hydrosoluble, selective $\beta_1$-adrenergic receptor antagonists. It has a unique pharmacokinetics, since it is metabolised by the esterase located in the cytosol of human erythrocytes.[6] It is therefore administered exclusively intravenously (iv), in the form of boluses or infusion, with elimination half-time ($t_{1/2}$) of 10-12 min.[7, 8] This short kinetics is responsible for the titratability of esmolol boluses and infusion when administered to treat episodes of hypertension and tachycardia in various indications, including those arising from perioperative painful stimuli.[9, 10] All these properties make esmolol a logical choice of supplement to the concept of the general balanced anaesthesia.[11-13]

The aim of this clinical trial was to investigate the effect of esmolol on cardiovascular parameters and quality of anaesthesia in patients scheduled for elective plastic surgery.

## Methods

This clinical trial was performed at the Military Medical Academy and approved by the local Ethics Committee. A total of 30 American Society of Anesthesiologists (ASA) class I or II patients aged 18 or above, scheduled for elective plastic surgery were randomly divided into two equal groups – Control and Esmolol. Patients from the Esmolol group received esmolol solution in glucose 5 %, as an iv infusion. Its rate was 0.3 mg/kg/min during the first 5 min and 0.1 mg/kg/min thereafter. This maintenance dose was chosen based on the finding that esmolol, when infused at rates up to 0.15 mg/kg/min, was practically hypotension-free.[14] Patients from the Control group received the same volume and rate of the plain glucose 5 % solution iv.

All patients received anaesthesia according to the same protocol. They were premedicated 30-45 min before anaesthesia with diazepam 10 mg intramuscularly (im). Induction to anaesthesia was performed by injecting thiopental sodium 3-5 mg/kg iv and fentanyl 1.5 μg/kg iv. Neuromuscular blockade was assured by injecting an iv bolus of pancuronium bromide 0.07 mg/kg. The desired level of neuromuscular blockade was maintained by incremental boluses of 0.01 mg/kg. Mixture of oxygen and nitrous oxide ($O_2/N_2O$ 2 : 1) was used for maintenance of general anaesthesia.

According to the study protocol, every episode of increase of systolic and diastolic blood pressure or heart rate by more than 20 % of its pre-induction (baseline) value was treated with fentanyl 1.5 μg/kg alone or in combination with droperidol 1:50 (Thalamonal®). After the end of operation, atropine 0.5 mg iv bolus was injected and neostigmine 1.5 mg iv was used for decurarisation. Atropine 0.5 mg iv was used during the operation to treat episodes of bradycardia. It was defined as a decrease of heart rate below 60 beats/min or by more than 20 % of the baseline values.[15]

Systolic and diastolic blood pressure and heart rate were registered in the following phases of anaesthesia and operation: (1) immediately prior to the induction (baseline value), (2) induction to anaesthesia, (3) tracheal intubation, (4) first skin incision, (5) surgical manipulation with organs, (6) suture of the surgical wound and (7) tracheal extubation. In addition to it, total consumption of fentanyl, droperidol, atropine and pancuronium was registered. Quality of the post-anaesthesia recovery was evaluated based on the registration of times needed to regain ability to open eyes on command, to open eyes spontaneously and to regain full orientation. Overall assessment of the quality of anaesthesia was performed by the experienced anaesthesiologist, with the scale: 1 – poor, 2 – good and 3 – excellent.

Statistical analysis was performed by using parametric or non/parametric tests, depending on the nature of the parameters observed and the normality of their distribution. Software IBM SPSS 18.0 was used for these analyses.

## Results

There were no significant differences between the Control and Esmolol groups of patients regarding their age, weight, gender ratio and the baseline values of the cardiovascular parameters (Table 1).

*Table 1: Demographic data and preinduction (baseline) values of cardiovascular parameters in patients undergoing elective plastic surgery under general balanced anaesthesia*

| Parameter (unit) | Control (mean ± SEM) | Esmolol (mean ± SEM) | Statistical significance |
|---|---|---|---|
| Age (years) | 41.33 ± 5.33 | 37.33 ± 7.57 | n.s. |
| Body weight (kg) | 75.67 ± 8.29 | 74.00 ± 6.66 | n.s. |
| Gender (male/female) | 8/7 | 6/9 | n.s. |
| Systolic blood pressure | 125.00 ± 10.41 | 131.67 ± 6.01 | n.s. |
| Diastolic blood pressure | 81.67 ± 4.41 | 88.33 ± 13.02 | n.s. |
| Heart rate (beats per min) | 76.76 ± 10.14 | 80.00 ± 11.55 | n.s. |

*SEM – standard error on the mean; n.s. – not significant*

Figure 1 contains data on the values of systolic blood pressure in the critical phases of anaesthesia and operation, expressed as percentages of their baseline values. In both Control and Esmolol group induction to anaesthesia resulted in decrease in systolic blood pressure, which continued well into the operation. When comparing the values in the two groups in all the critical phases of anaesthesia and operation, it was evident that they tended to be lower in the Esmolol group and this difference reached statistical significance at intubation, first skin incision, suture of the surgical wound and extubation.

Similar results were registered with diastolic blood pressure (Figure 2). Esmolol values of diastolic blood pressure were significantly lower in all critical phases of anaesthesia and operation, except during the first incision.

Results for heart rate values are contained in Figure 3. While the values of the systolic in diastolic blood pressure in the Control group were during most phases of anaesthesia and operation below their baseline values, the Control group values of heart rate were constantly above the baseline ones. At the same time, in the Esmolol group sig-

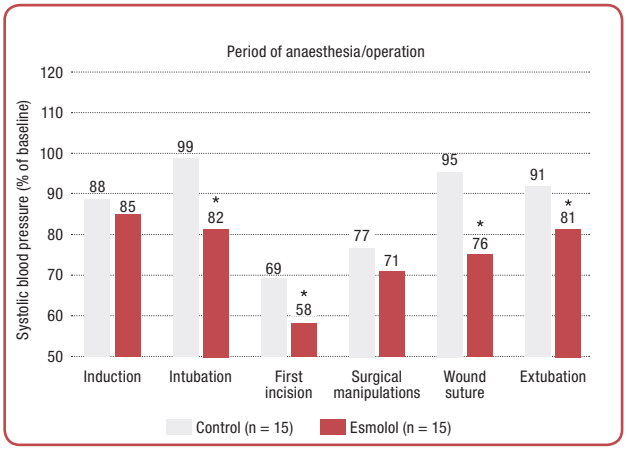


*Figure 1: Effect of esmolol on systolic blood pressure in patients undergoing elective plastic surgery under general balanced anaesthesia*
**p < 0.05 versus Control*

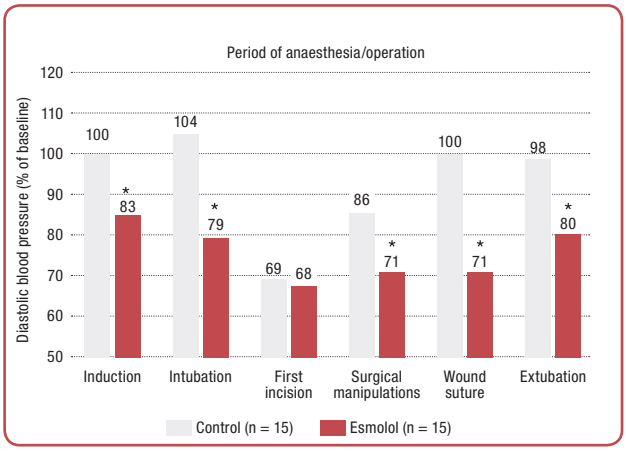


*Figure 2: Effect of esmolol on diastolic blood pressure in patients undergoing elective plastic surgery under general balanced anaesthesia*
**p < 0.05 versus Control*

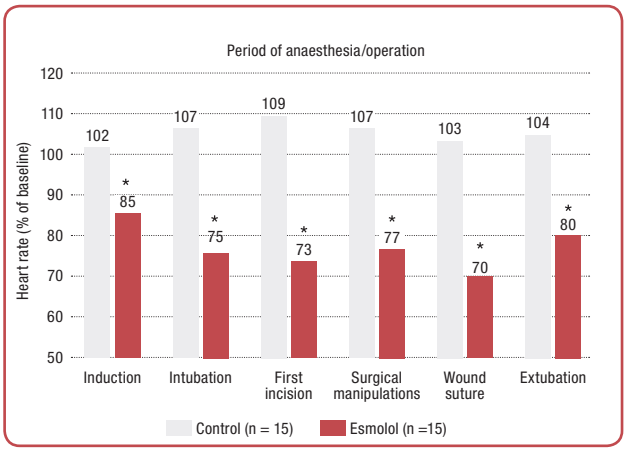


*Figure 3: Effect of esmolol on heart rate in patients undergoing plastic surgery under general balanced anaesthesia*
**p < 0.05 versus Control*

nificantly lower heart rate values, ranging 70-85 % of baseline, were registered.

Table 2 contains data on the total drug consumption. Only atropine was used in a similar dosage in both groups, while in the Esmolol group a significantly lower consumption of fentanyl, droperidol and pancuronium was registered.

*Table 2: Consumption of drugs in patients undergoing elective plastic surgery under general balanced anaesthesia*

| Parameter (unit) | Control (mean ± SEM) | Esmolol (mean ± SEM) | Statistical significance |
|---|---|---|---|
| Fentanyl (mg) | 0.38 ± 0.04 | 0.13 ± 0.03 | $p < 0.05$ |
| Droperidol (mg) | 6.67 ± 1.67 | 0.83 ± 0.83 | $p < 0.05$ |
| Atropine (mg) | 1.00 ± 0.29 | 1.03 ± 0.09 | n.s. |
| Pancuronium (mg) | 14.00 ± 3.06 | 3.67 ± 0.88 | $p < 0.05$ |

*SEM – tandard error on the mean; n.s. – not significant*

*Table 3: Speed and quality of postoperative recovery in patients undergoing elective plastic surgery under general balanced anaesthesia*

| Parameter (unit) | Control (mean ± SEM) | Esmolol (mean ± SEM) | Statistical significance |
|---|---|---|---|
| Duration of anaesthesia (min) | 131.67 ± 15.90 | 123.00 ± 33.21 | n.s. |
| Opening of eyes on command (min) | 11.67 ± 1.67 | 2.67 ± 1.20 | $p < 0.05$ |
| Spontaneous opening of eyes (min) | 16.67 ± 4.41 | 4.50 ± 1.61 | n.s. |
| Regaining of full orientation (min) | 25.00 ± 2.89 | 7.33 ± 1.76 | $p < 0.01$ |
| Extubation possible (% of patients) | 100 | 100 | n.s. |
| Evaluation of quality of anaesthesia* | 2.00 ± 0.00 | 2.67 ± 0.33 | n.s. |

*SEM – tandard error on the mean; n.s. – not significant;*
*Quality of anaesthesia: 1 - poor, 2 - good, 3 - excellent;*

Although the duration of anaesthesia and operation were similar in both groups, all the times registered – time until regaining ability to open eyes on command, time until regaining ability to open eyes spontaneously and time until regaining full orientation – were significantly shorter in the Esmolol group.

## Discussion

The obtained results are generally in accordance with some other reports. Esmolol proved to be very efficacious in antagonising haemodynamic changes that accompany laryngoscopy and tracheal intubation.[10, 16-19] Like in the present study, esmolol prevented increases in blood pressure and heart rate during the phase of tracheal extubation.[20-22] Esmolol also assured a more stable haemodynamics during the non-cardiac[23-25] and cardiac surgery.[26, 27]

Esmolol-induced continuous β-adrenergic receptor blockade leads to a more sparing use of opioid analgesics, which was demonstrated in the present study and other clinical trials alike.[28-30] In the current study, a very significant sparing of fentanyl and droperidol were registered.

As a consequence, the patients infused with esmolol had much faster and smoother emergence from anaesthesia than those ones in whom the increases in blood pressure and heart rate were treated with incremental doses of opioid analgesics.[31, 32] The quality of this recovery includes the postoperative nausea and vomiting – a very frequent consequences of opioid administration.[32] Rarely, opposite results were published – in patients undergoing gynaecologic laparoscopic surgery esmolol did not assure better recovery from anaesthesia, as compared with the saline infusion.[33] When compared with lidocaine bolus and infusion, esmolol nevertheless also assured better recovery from anaesthesia.[34]

There are some reports that esmolol, similarly like local anaesthetic lidocaine, decreases pain and withdrawal movements after the administration of non-depolarising neuromuscular relaxant rocuronium, via yet unclear mechanisms.[35, 36] It is possible that such mechanisms are responsible for the decreased consumption of pancuronium noted in the present study.

## Conclusion

Esmolol acts as a useful supplement to the other components of the general balanced anaesthesia technique. It blunted the cardiovascular responses to nociceptive stimuli during the critical phases of anaesthesia and operation in patients undergoing elective plastic surgery, assured less consumption of fentanyl, droperidol and pancuronium, leading to faster and smoother emergence from anaesthesia.

## Acknowledgements

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## Conflict of interest

None.

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