



Use of an Ultrashort-Acting Selective β_1 -Adrenergic Receptor Antagonist Esmolol in Ear, Nose and Throat Surgery

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Abstract

Background / Aim: The concept of general balanced anaesthesia was devised in order to assure cardiovascular stability and fast post-anaesthesia recovery. This clinical trial was organised in order to investigate the parameters of cardiovascular function and emergence from anaesthesia in elective ear, nose and throat (ENT) surgery patients.

Methods: A total of 40 ASA I and II patients of both sexes scheduled for elective ENT surgery were randomly divided into two equal groups. Both groups received a continuous iv infusion of glucose 5 % solution and in the esmolol group this infusion also contained esmolol. Esmolol infusion rate was 0.3 mg/kg/min during the first 5 min and thereafter 0.1 mg/kg/min. In critical phases of anaesthesia and operation (induction, intubation, first incision, surgical manipulations, wound suture, extubation), systolic and diastolic blood pressure were monitored. Recovery after anaesthesia was assessed based on times of eye opening on command, spontaneous eye opening and regaining of full orientation. Increases in cardiovascular parameters by 20 % of the baseline values or more were treated with iv boluses of fentanyl, alone or with droperidol and, if necessary, by adding isoflurane 0.5 % to the inhalational mixture. Consumption of drugs was recorded.

Results: Esmolol assured stable values of cardiovascular parameters that were in most critical phases of anaesthesia and operation lower than in the control group. The duration of anaesthesia did not differ between the groups. In the esmolol group, lower consumption of fentanyl, droperidol and sevoflurane was registered. Patients in the esmolol group emerged from anaesthesia faster than patients in the control group.

Conclusion: Continuous iv infusion of esmolol assures better cardiovascular stability, necessitates lower consumption of analgesics and anaesthetics and results in faster emergence from general anaesthesia in elective ENT surgery.

Key words: Beta-adrenergic receptor antagonists; Esmolol; General anaesthesia; Hypertension; Tachycardia.

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Introduction

Hypertension and tachycardia occur during surgical procedures as a consequence of complex reflex mechanism activated by surgical trauma that include activation of sympathetic nervous system

resulting in increased secretion of catecholamines from adrenal medulla and at the nerve endings of the postganglionic sympathetic fibres.¹ In order to alleviate these potentially harmful phenomena,

combinations of various drugs are employed. For these purposes, a concept of balanced anaesthesia was introduced, including benzodiazepines for pre-anaesthetic medication, suxamethonium for tracheal intubation, thiopentone or similar drugs for rapid induction of anaesthesia, inhalation anaesthetic for maintenance of anaesthesia, opioid analgesics for counteracting the especially painful stimuli, competitive neuromuscular antagonists for maintenance of the neuromuscular blockade and atropine and neostigmine for the reversal of this blockade.²

A new addition to the concept of balanced anaesthesia was formed: instead of counteracting the increases in blood pressure and heart rate in the critical phases of operation by adding additional doses of analgesics and/or by adding more potent inhalation anaesthetics, they should be treated with esmolol, an easy titratable and rapid-acting and selective antagonist of β_1 -adrenergic receptors.³ Esmolol was first used to manage the episodes of hypertension and tachycardia in cardiac surgery^{4,5} and later in all other types of surgery.^{6,7,8}

Critical phases of anaesthesia and operation, such as induction to anaesthesia, tracheal intubation, first incision, surgical manipulation with organs, suture of the surgical wound and tracheal extubation require additional cardiovascular control. In ear, nose and throat (ENT) surgery sometimes a controlled hypotension is needed, like in functional endoscopic sinus surgery and in tympanoplasty.^{9,10} The rationale for that is the prevention of unnecessary blood loss and the improvement of the quality of the visibility of the surgical field in these types of operations.¹¹

The goal of this research was to study the cardiovascular effects and parameters of emergence from anaesthesia of the continuous esmolol infusion in patients scheduled for elective ENT surgery.

Methods

This randomised clinical trial was organised by enrolling 40 American Society of Anesthesiologists (ASA) I or II category patients aged 18 or more that were scheduled for elective ear, nose and throat (ENT) operations. The study had pre-

viously been approved by the local ethics committee and each participant signed an informed consent. The block randomisation was used to randomise the enrolled patients into two groups – control and esmolol.

Each patient was subjected to the standardised premedication and anaesthetic technique. Each of them was premedicated with diazepam 10 mg intramuscularly (im) 30-45 min before the induction into anaesthesia with thiopentone 3-5 mg/kg iv and fentanyl 1.5 mcg/kg. Suxamethonium 1-2 mg/kg iv was injected in order to facilitate the tracheal intubation. Pancuronium bromide 0.07 mg/kg was administered as an iv bolus to induce a neuromuscular blockade. If needed, additional iv boluses of pancuronium bromide 0.01 mg/kg were added. General inhalational anaesthesia was maintained with a mixture of nitrous oxide and oxygen (2:1). At the end of the operation, atropine 0.5 mg iv and neostigmine 1.5 mg iv were injected, in order to neutralise the competitive pancuronium-induced neuromuscular blockade.

The values of cardiovascular parameters – systolic and diastolic blood pressure and heart rate – were recorded before the induction of anaesthesia (baseline) and at all critical points during anaesthesia and operation: induction of anaesthesia, tracheal intubation, first incision, surgical manipulation in the operation field, wound suture and extubation of trachea. In case that any of these parameters was increased by 20 % of the baseline values, fentanyl 1.5 mcg/kg was administered.

The patients from both groups received an iv infusion of glucose 5 % solution, during the first 5 min at a speed of 0.03 mL/kg/min and 0.01 mg/kg afterwards. The only difference was the addition of esmolol to this infusion in the patients belonging to the esmolol group. A total of 5 g of esmolol were dissolved in the half-litre infusion bottle containing glucose 5 % to reach the final esmolol concentration of 10 mg/mL. During the maintenance phase, esmolol was therefore delivered at a rate of 0.1 mg/kg/min. This infusion rate was chosen because it was found that hypotension practically does not occur at infusion rates below 0.15 mg/kg/min¹² and because the values of cardiovascular parameters do not change by more than 10 % when esmolol is infused at a rate of 0.118 mg/kg/min.¹³

Parametric data were statistically analysed by

Student t test and ANOVA, while the non-parametric data were analysed by Chi-square test. Statistical Package for Social Sciences (SPSS) version 18.0 was used for these analyses.

Results

The control and esmolol groups of patients consisted of 20 patients each. There were no significant differences among them when comparing their demographic data and values of their mean pre-induction (baseline) values of cardiovascular parameters (Table 1).

Table 1: Demographic data and pre-induction values of the cardiovascular parameters in control patients and patients infused with esmolol during the operation under the general balanced anaesthesia

Parameter (unit)	Control (mean ± SE)	Esmolol (mean ± SE)	Statistical significance
Age (years)	30.33 ± 3.71	31.33 ± 4.84	ns
Body weight (kg)	70.67 ± 7.54	70.33 ± 5.04	ns
Gender: Male/Female	12 vs 8	11 vs 9	ns
Systolic BP (mm Hg)	125.00 ± 10.41	123.33 ± 6.67	ns
Diastolic BP (mm Hg)	78.33 ± 6.01	83.33 ± 3.33	ns
Heart rate (bpm)	81.00 ± 1.16	84.00 ± 3.06	ns

ns - not significant; BP - blood pressure; bpm - beats per minute

The obtained values of cardiovascular parameters in critical phases of anaesthesia and operation are shown in Figures 1, 2 and 3, respectively.

Values of systolic blood pressure are shown in Figure 1. During the intubation phase, systolic blood pressure was significantly lower in esmolol than in the control group of patients remaining at the baseline level. In the last two critical phases of operation and anaesthesia – operative wound suture and extubation of trachea - the values of systolic blood pressure were significantly higher in the esmolol group than in the patients from the control group, remaining close to the pre-induction values.

There were no significant differences between the values of the diastolic pressure between the control and esmolol group of patients, with the exception of the phase of tracheal intubation, where significantly lower values were registered in the esmolol than in the control group (Figure 2).

In all the critical phases of anaesthesia and operation values of heart rate were significantly lower

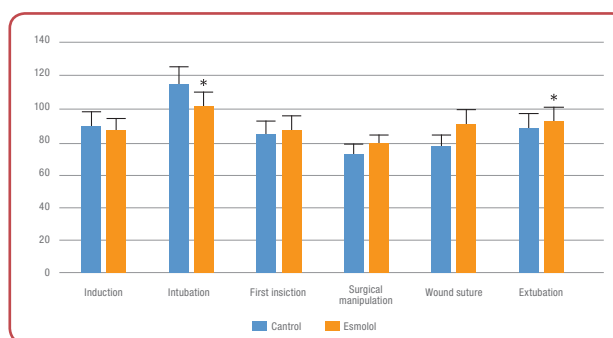


Figure 1: Systolic blood pressure in various phases of anaesthesia and operation in control patients (n = 20) and patients infused with esmolol (n = 20) during the ear, nose and throat (ENT) operations under the general balanced anaesthesia. Values are expressed as percentages of pre-induction values.

* - statistical significance in comparison with the baseline value (p < 0.05);

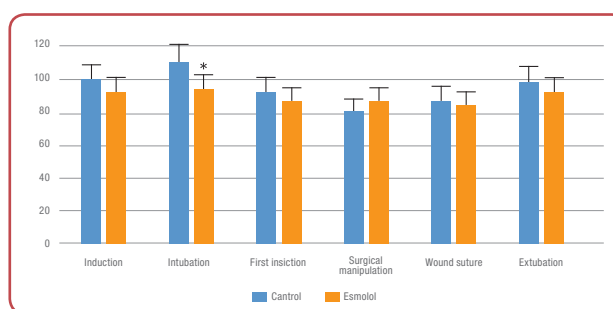


Figure 2: Diastolic blood pressure in various phases of anaesthesia and operation in control patients (n = 20) and patients infused with esmolol (n = 20) during the ear, nose and throat (ENT) operations under the general balanced anaesthesia. Values are expressed as percentages of pre-induction values.

* - statistical significance in comparison with the baseline value (p < 0.05);

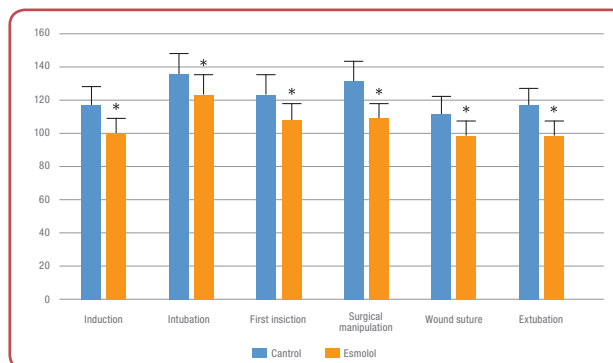


Figure 3: Heart rate in various phases of anaesthesia and operation in control patients (n = 20) and patients infused with esmolol (n = 20) during the ear, nose and throat (ENT) operations under the general balanced anaesthesia. Values are expressed as percentages of pre-induction values.

* - statistical significance in comparison with the baseline value (p < 0.05);

in the esmolol group, however remaining within the relatively narrow and physiological range of 98 – 122 % of the pre-induction values (Figure 3).

The parameters of post-anaesthesia recovery were significantly shorter in the esmolol group of patients, in comparison with the control group, with the exception of the consumption of atropine, where no difference could be found (Table 2).

Table 2: Consumption of medicines in control patients ($n = 20$) and patients infused with esmolol ($n = 20$) during the ear, nose and throat (ENT) operations under the general balanced anaesthesia

Drug (unit)	Control (mean \pm SE)	Esmolol (mean \pm SE)	Statistical significance
Fentanyl (mg)	0.38 \pm 0.03	0.17 \pm 0.03	$p < 0.05$
Droperidol (mg)	14.17 \pm 2.20	5.83 \pm 0.83	$p < 0.05$
Atropine (mg)	0.83 \pm 0.17	0.70 \pm 0.15	ns
Pancuronium (mg)	8.00 \pm 1.67	4.67 \pm 0.88	$p < 0.05$
Isoflurane (% of patients)	100.00	8.33	$p < 0.05$

ns - not significant

The parameters of the post-anaesthesia recovery were significantly shorter in the esmolol than in the control group (Table 3).

Table 3: Effect of esmolol on speed and quality of postoperative recovery in control patients ($n = 20$) and patients infused with esmolol ($n = 20$) during the ear, nose and throat (ENT) operations under the general balanced anaesthesia

Parameter (unit)	Control (mean \pm SE)	Esmolol (mean \pm SE)	Statistical significance
Duration of anaesthesia (min)	174.17 \pm 16.62	170.00 \pm 18.64	ns
Opening of eyes on command (min)	16.33 \pm 1.94	4.40 \pm 1.21	$p < 0.01$
Spontaneous opening of eyes (min)	25.20 \pm 3.09	10.70 \pm 2.70	$p < 0.01$
Full orientation (min)	29.83 \pm 3.34	16.00 \pm 3.85	$p < 0.05$
Extubation possible (% of patients)	50.00	90.00	$p < 0.05$
Evaluation of quality of anaesthesia	1.50 \pm 0.15	2.17 \pm 0.17	$p < 0.01$

ns - not significant

It should be also pointed out that there were no differences between the two groups regarding the duration of anaesthesia.

Discussion

Overall results of this clinical trial demonstrate the favourable effect of esmolol on cardiovascular parameters during anaesthesia and operation in elective ENT surgery, its analgesic- and anaesthetic-saving effect and consequential better recovery of patients after anaesthesia.

The results obtained are in accordance with other clinical studies. Indeed, injection and/or iv infusion of esmolol alleviated increases in blood pressure and heart rate induced by tracheal intubation and extubation.¹⁴⁻¹⁶ The nociceptive sympathetic nervous system reflexes can be causally

blocked with opioid analgesics, but also symptomatically with a beta-adrenergic antagonist like esmolol, however without need for additional doses of opioids. A significant opioid-sparing effect of esmolol showed in the present study is corroborated by similar findings of other clinical trials.¹⁷⁻²¹ In some clinical studies esmolol even reduced the need for the administration of intravenous and inhalation anaesthetics.^{22, 23} Similar result was obtained, where a significantly lower number of patients in the esmolol group required isoflurane addition in comparison with the control group of patients.

In the present study esmolol had a stronger effect on heart rate than on blood pressure, which is supported by Ornstein et al. These researchers found that the half-time for a 14 %-decrease in heart rate of only 1.2 min, which was much shorter than the esmolol half time of 17.8 min for a 25 %-decrease in mean arterial blood pressure.²⁴

Some other agents were tried with the same goal to counteract a reflex sympathomimetic reaction resulting from laryngoscopy and intubation²⁵ or from tracheal extubation.²⁶ It seems that esmolol should be preferred over nitroglycerin^{9, 27} or lidocaine,²⁸ while dexmedetomidine^{10, 27} or nicardipine²⁸ could be more efficient than esmolol. In clinical trials on induction of controlled hypotension for endoscopic sinus surgery, esmolol seemed to be equally safe and efficient as magnesium sulphate²⁹ or labetalol.³⁰

Conclusion

Ultrashort-acting beta-adrenergic receptor antagonist esmolol, administered as a continuous iv infusion, assures better cardiovascular stability and smoother emergence from the balanced inhalation general anaesthesia than the control glucose infusion in elective neurosurgical patients.

Acknowledgements

None.

Conflict of interest

None.

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