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Esmolol: A Unique Beta-Blocker in Maintaining Cardiovascular Stability Following Neurosurgical Procedures

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ABSTRACT

Purpose: Patients with increased intracranial pressure (ICP) are prone to severe cardiac and or cerebral complications following emergence from general anesthesia and especially post-extubation phase. Administering beta blockers including esmolol is believed to be helpful in providing a stable hemodynamic at the end of the surgery and recovery stages and reducing recovery phase length. ***Methods:*** In a double-blind prospective randomized clinical trial, 60 adult patients with ASA (American Society of Anesthesiologist) class of I-II scheduled to undergo elective neurosurgery operations were randomly divided into two groups receiving esmolol (n=30) and placebo (n=30) as IV infusion within four minutes prior to extubation continued by an IV infusion for 10 minutes after extubation. ***Results:*** There was a significant difference between two groups regarding the changes of systolic blood pressure and heart rate at all studied stages after extubation ($P \leq 0.05$). However, no significant difference existed between esmolol and control groups regarding recovery and extubation times emphasizing the fact that esmolol is of excellent early recovery and extubation profiles. ***Conclusion:*** Esmolol is advised to be used in preventing hyperdynamic status throughout extubation phase without extending recovery phase length.

Introduction

Patients with increased intracranial pressure (ICP) are prone to severe cardiac and or cerebral complications following emergence from general anesthesia and especially post-extubation phase which may lead to increase in oxygen consumption, and catecholamine release. This phase lasting 15 to 5 minutes could frequently be accompanied by tachycardia and hypertension.[1] This temporary encountered situation could however be endured appropriately by most patients.[2] Patients with preoperative hypertension and cardiovascular and cerebrovascular diseases and patients with increased ICP could be prone to severe cardiac and or cerebral complications.[3] Therefore, preventing postoperative and post-intubation sympathetic excitations in high-risk patients to maintain stability in the dynamic status is of great importance which may reduce the mortality and morbidity rates in these patients.[1] Esmolol, a selective beta-adrenergic receptor antagonist, is water-soluble, short acting (9 minutes) and of a rapid effect commencement. Administering esmolol throughout anesthesia reduces hyperdynamic cardiovascular responses however very few studies have been carried out to prove its efficacy at extubation and post-extubation stages. Considering the fact that pain is one of the major factors contributing to sympathetic excitement at the end of the surgery and recovery stages, we aimed to evaluate the efficacy of pre-extubation administration of esmolol on maintaining the hemodynamic stability at the end of the surgery and recovery stages and its effects on recovery phase length.

Materials and Methods

This study is a double-blind prospective placebo-control randomized clinical trial which was carried out after obtaining approval of the ethics committee of Tabriz University of Medical Sciences and informed written consents from the patients. Sixty adult patients with ASA (American Society of Anesthesiologist) class of I-II which were scheduled to undergo elective neurosurgery operations were randomly divided into two groups of 30 people. Exclusion criteria from the study included pregnant females, patients with heart rate (HR) less than 60, systolic blood pressure less than 100 mmHg, considerable hepatic, renal or

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cardiovascular complications, atrioventricular block, sick sinus syndrome, history of intolerance to beta-blockers, bronchospasm and asthma, and chronic obstructive pulmonary disease. All patients were premedicated with fentanyl (2 µg/kg IV) and lidocaine (1.5 mg/kg IV) and intubated using Sodium Thiopental (7-5 mg/kg) and Cis-atracurium (0.15 mg/kg). Anesthesia was maintained using Isoflurane (1-1.5%) and a mixture of O_2 (50%) and N_2O (50%).[4] Mechanical ventilation was maintained with a tidal volume of 10 mL/kg and at a rate to keep End-tidal CO_2 at the range of 35-30 mmHg. Repeated doses of Cis-atracurium (0.05 mg/kg) were used to provide intraoperative muscle relaxation.[5] Administration of anesthetics was terminated when suturing the skin and muscle relaxation was antagonized with neostigmine (0.05 mg/kg) and atropine (0.02 mg/kg) after reestablishment of spontaneous breathing.[6]

Esmolol group (n=30): in this group IV infusion of Esmolol (0.5 mg/kg) was administered within four minutes prior to extubation continued by an IV infusion of Esmolol at the rate of 0.15 mg/kg/min for 10 minutes after extubation.

Control group (n=30): in this group IV infusion of normal saline (0.5 ml/kg) was administered within four minutes prior to extubation continued by an IV infusion of normal saline at the rate of 0.15 ml/kg/min for 10 minutes after extubation.

Medications were prepared and coded previously by a colleague so that the coworker performing the records was unaware of the contents of the syringes. All patients were given IV lidocaine (1.5 mg/kg) 90 seconds prior to extubation. Systolic and diastolic blood pressure, mean arterial pressure and HR were recorded before and after medication administration and extubation. Vital signs were recorded every five minutes at recovery phase until the patient was discharged from the recovery unit. Time required for performing eye opening to verbal commands, spontaneous eye opening and a recognition of the location and people at the recovery unit were recorded for both groups.

All studied data were analyzed using statistical software SPSS16. To evaluate the statistics, descriptive statistical approaches (frequency, percentage, mean and standard deviation) were used. To compare qualitative variables, chi-square statistical test and to compare quantitative variables in paired groups, independent t-test was used. The changes in quantitative findings throughout the study in groups were evaluated using repeated measure of ANOVA. P <0.05 was considered significant in this study.

Results

Table 1 presents the demographic findings between two groups. As it can be seen, demographic findings are equal in two groups and no statistically significant difference is observed.

Esmolol group was associated with significantly lower levels of systolic blood pressure (SBP) compared with the control group at all studied stages after extubation (All P<0.05) (Table 2).

Table 1. Demographic findings between two groups

	Control group	Esmolol group	P value
Age (Year)	49±17	46±16	0.42
Sex (M/F)	9.21	15.15	0.14
Weight (Kg)	71±12	73±10	0.49
Operation duration (Minutes)	186±62	184±42	0.76
ASA (II/I)	16.14	15.15	0.39

The study of the changes in diastolic blood pressure (DBP) in both groups revealed a statistically significant difference after extubation and 10 minutes after extubation (P< 0.05) (Table 2).

A significant difference was observed comparing the changes in HR in both groups at all HR values after extubation (P< 0.001 in all cases) indicating the fact that esmolol is of unique characteristic of blunting cardiovascular responses caused by catecholamine release following extubation (Table 2).

The mean of recovery phase and extubation duration for both groups have been presented in Table 3. As surprisingly observed, no significant difference regarding extubation phase length or recovery phase exists between esmolol and control groups.

Discussion

Patients with hypertension and cardiovascular or cerebrovascular diseases and patients with increased ICP could accompany severe cardiac and or cerebral complications at extubation phase.[3,7] Therefore, managing hemodynamic responses such as HR and blood pressure while disconnecting from mechanical ventilation would be of great importance.

Numerous strategies have been introduced to prevent hemodynamic responses caused by emergence from anesthesia including extubation under deep anesthesia, administration of local anesthetics, vasodilators and short acting opioids.[8]

Administering vasodilators such as sodium nitropruside, nitroglycerine and hydralazine could be associated with complications like reflexive tachycardia and increase in the plasma rennin activity.[2]

Beta-adrenergic blockers are also frequently used to suppress adrenergic activity caused by extubation especially throughout neurosurgery operations.[9,10] In the present study, esmolol, a selective short-acting beta-blocker, was administered and its preventive characteristics against cardiovascular responses caused by extubation in the surgeries involving cerebral masses were evaluated. The results obtained from the present study revealed that esmolol could be administered to prevent hemodynamic instability caused by extubation. It has previously been proven

that hyperdynamic cardiovascular status caused by sympathetic excitation followed by extubation could endure for 5 to 10 minutes.[1] Considering the fact that esmolol is of very short half-life, in addition to administration of a bolus does before extubation, we used IV infusion of esmolol within 10 minutes after extubation which was associated with desirable results. In the study of Unal et al., it was stated that esmolol had the characteristic of preventing hyperdynamic status which was in line with the findings of our study.[2]

Table 2. Changes in Vital signs [Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and Heart Rate (HR)] between two groups at different stages (prior to extubation until 15 minutes post-extubation)

	Stage	Control group	Esmolol group	P value
SBP	Before extubation	115 ± 14	109±17	0.16
	After extubation (immediate)	137 ± 21	115±17	<0.001
	After extubation (5 minutes)	134 ± 21	116±16	0.001
	After extubation (10 minutes)	132 ± 24	112±17	0.001
	After extubation (15 minutes)	125± 17	113±17	0.01
DBP	Before extubation	71± 13	69 ± 13	0.53
	After extubation (immediate)	85± 15	76 ± 14	0.02
	After extubation (5 minutes)	85 ± 18	77 ± 13	0.06
	After extubation (10 minutes)	84± 23	72± 14	0.01
	After extubation (15 minutes)	76± 12	74 ± 13	0.58
HR	Before extubation	77±12	73±13	0.28
	After extubation (immediate)	91±12	75±12	<0.001
	After extubation (5 minutes)	89±15	73±10	<0.001
	After extubation (10 minutes)	83±12	73±11	0.001
	After extubation (15 minutes)	81±10	71±9	<0.001

Table 3. The mean of extubation and recovery phase length (tested using three different criteria) between two groups (minutes)

	Control group	Esmolol group	P value
Extubation	4±1	4±1	0.16
Eye opening with verbal commands	12±3	11±3	0.93
Spontaneous eye opening	16±4	15±4	0.50
Orientation	21±6	20±6	0.73

Similar to our study, in the study of Dyson et al., hemodynamic changes were also less in esmolol group compared with the control group.[11] Wang et al. reported that esmolol, especially in higher doses, can reduce BP and HR increase followed by extubation which is in accordance with the results obtained from our study especially the post-extubation stage of their study.[12]

An appropriate anesthetic for neurosurgery should provide the possibility of early evaluation of the neurologic status of the patients and early diagnosis of the potential postoperative complications (for instance; hematoma and major cerebral edema) by a rapid and short recovery phase.[13] In the present study, there was no significant difference between studied groups regarding the time of eye opening (to verbal commands and spontaneous) and the recovery phase length. However in the study of Unal et al., the time of eye opening (to verbal commands and spontaneous) was recorded to be shorter in esmolol group compared with the control group.[2]

Conclusion

Sympathetic excitation followed by extubation would lead to increase in blood pressure and heart rate and therefore the patients at risk of cardiovascular and cerebral complications should be prevented from these excitations. Esmolol could safely be used in preventing hyperdynamic status throughout extubation phase without extending recovery phase length. Based on the results obtained from the present study, it could be advised to administer esmolol as one of the effective medication in cases in which control of hemodynamic status is required in high-risk patients undergoing intracranial surgeries. However, further studies with larger sample sizes to achieve more accurate results are required.

Conflict of interest

The authors report no conflicts of interest in this work.

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