Research Article

Effect of intravenous bolus esmolol on changes in heart rate during laryngoscopy and endotracheal intubation under general anesthesia in patients with mitral stenosis posted for closed mitral commissurotomy

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Abstract

Background: Maintenance of an optimal heart rate during laryngoscopy and endotracheal intubation is a key factor in the management of patients with mitral stenosis undergoing surgery under general anesthesia to minimize mortality. Esmolol is a rapid-onset and short-acting selective β1-blocker.

Objective: To compare the effect of narcotic induction with and without intravenous bolus dose of esmolol on the changes in heart rate in response to laryngoscopy and endotracheal intubation in patients with mitral stenosis posted for closed mitral commissurotomy.

Materials and Methods: Twenty patients of either sex, of age between 18 and 40 years with mitral stenosis posted for closed mitral commissurotomy, and without overt heart failure, other significant valvular disease, significant cerebrovascular disease, bronchial asthma, anticipated difficult airway, in rhythm other than sinus, heart block more than first degree, and already receiving a β-blocker or antihypertensive were allocated randomly to receive either normal saline (Group A, control group) or esmolol (Group B, study group) along with narcotic induction.

Result: The median heart rate in Group B patients was significantly lower just before laryngoscopy, 1 min postintubation, and 2 min postintubation time points in comparison to Group A (Mann–Whitney *U* test). A serial change in the median heart rate was found to be statistically significant $p < 0.05$ (Friedman's analysis of variance) in Group A and nonsignificant in Group B.

Conclusion: Here, esmolol was found to be beneficial to obtund the heart rate response during intubation, especially in patients with mitral stenosis without any untoward responses.

KEY WORDS: Mitral stenosis, laryngoscopy and endotracheal intubation, esmolol, closed mitral commissurotomy

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Introduction

In patients with progressive stenosis at the mitral valve, the left ventricle is chronically volume underloaded whereas the left atrium and structures behind it are subjected to both pressure and volume overloading.[1] The elevated left atrial pressure, in turn, raises pulmonary venous and capillary pressures, resulting in sudden appearance of pulmonary edema.[2] The fixed cardiac output, the altered pulmonary functions,

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and the irritable myocardium all add to the vulnerability of the patients with mitral stenosis to undesirable hemodynamic effects of laryngoscopy and endotracheal intubation. Laryngoscopy and endotracheal intubation is invariably associated with certain hemodynamic changes such as increase in heart rate, arterial blood pressure, and occasional disturbance of cardiac rhythm. These hemodynamic responses arise as a form of sympathoadrenal reflex.[3,4] This adrenergic stress response is extremely harmful in patients with cardiovascular pathology, for example, in case of patients with mitral stenosis, the hemodynamic surge at the time of laryngoscopy and endotracheal intubation may result in increased rate of blood flow across the mitral orifice resulting in further elevation of the left atrial pressure. The pressure gradient through the stenosed valve accordingly increases by the square of the increase in flow rate leading to sudden appearance of pulmonary edema manifested as exertional dyspnea and thereby, increased mortality in such patients.

Transvalvular pressure gradient in severe mitral stenosis is 20 mm Hg, with left atrial pressure of 25 mm Hg, where patients complain of pulmonary edema at rest.[2] Tachycardia raises transvalvular pressure gradient and exaggerates pulmonary back pressure.

Maintenance of an optimal heart rate during anesthetic procedures is a key factor in the management of these patients undergoing surgery under general anesthesia. Esmolol is a rapid-onset and short-acting selective β1-blocker.[5] Many studies have shown satisfactory results in attenuating sympathetic surge during laryngoscopy and endotracheal intubation with esmolol.

Materials and Methods

After obtaining approval from institutional ethics committee, the proposed study was conducted at Institute of Post-Graduate Medical Education and Research/(SSKM) Seth Shukhlal Karnani Memorial Hospital, Kolkata, West Bengal, India. Informed written consent was taken from each patient of either sex, of age between 18 and 40 years with mitral stenosis posted for closed mitral commissurotomy (CMC), and a detailed history, systemic examination, and laboratory findings were checked a day before surgery. Using a random number table for coding syringes of the study drug (esmolol) and placebo (normal saline), all patients were randomly assigned to receive either normal saline (Group A, control group) or esmolol (Group B, study group).

The sample size was estimated from mean and standard deviation variables determined from a previous study by Dutta et al.[6] Assuming a statistical study power of 85% and a 5% probability of a type I error, the minimum sample size was found to be 10 in each group calculated from a mean difference of heart rate of 5 between groups and a within group standard deviation of 3.5. The total sample size was taken as 20, $n = 10$ in each group.

Patients of age less than 18 years and more than 40 years, and with overt heart failure, other significant valvular disease, significant cerebrovascular disease, bronchial asthma, anticipated difficult airway, in rhythm other than sinus, heart block more than first degree, already receiving a β-blocker or antihypertensive, and mitral stenosis with contraindication for CMC were excluded from the study.

Patients received the following medications intravenously as per the sequence mentioned below:

- Fentanyl 2 μg/kg to all patients
- Midazolam 0.1 mg/kg to all patients
- Supplemental dose of thiopentone (25–50 mg), if required to induce sleep to patients not induced by fentanyl and midazolam
- Group A patients(control group) and Group B patients (study group)
- Group B (study) patients received 0.5 mg/kg body weight of esmolol hydrochloride (made up to 5 mL with normal saline), intravenously over 60 s
- Injection vecuronium bromide (0.1 mg/kg) to all patients

Mask ventilation was started with 100% O_2 as spontaneous ventilation got depressed. Laryngoscopy was performed after 4 min of injecting vecuronium. Endotracheal intubation was followed under direct laryngoscopic vision. The time taken from introduction of laryngoscope to cuff inflation of endotracheal tube was measured. No manipulation such as painting and draping the area of operation was allowed till 5min after endotracheal intubation, that is, during the study period. Any other anesthetic and narcotic drug for maintenance was introduced only after the study period.

The instantaneous heart rate from the ECG monitor was recorded at the following points of time:

- HRp: 10 min before induction, that is, preinduction/baseline value
- HRL: Just before laryngoscopy
- HR1: 1 min after completion of intubation
- HR2: 2 min after completion of intubation
- HR5: 5 min after completion of intubation

Data Analysis

For statistical analysis, raw data were entered into a Microsoft Excel spreadsheet and analyzed by appropriate statistical tests.

Normally distributed numerical variables were compared between groups by the unpaired "*t*" test. Nonparametric variables (e.g., change in heart rate after laryngoscopy and endotracheal intubation) were compared between groups by applying the Mann–Whitney *U* test. Within a group, serial changes in nonparametric variables were analyzed by Friedman's analysis of variance followed by Wilcoxon's matched pair signed rank test as post hoc test for comparison between any two reference points. Categorical variables (e.g., gender distribution, frequency of adverse effects) were compared between groups by the Fisher's exact test as appropriate. All analyses were two-tailed. A *p*-value of <0.05 was considered statistically significant.

Result

Group A and Group B were comparable in terms of demographic data, that is, age, sex, and body weight.

Table 1 shows the descriptive statistics for the heart rates per minute in patients belonging to Group A and B at various unequal time points.

The median heart rate in Group B patients was significantly lower just before laryngoscopy (HRL), 1 min postintubation (HR1), and 2 min postintubation (HR2) time points in comparison with Group A (Mann–Whitney *U* test).

Table 2 shows that Group A serial changes in median heart rate were found to be statistically significant, $p < 0.05$ (Friedman's analysis of variance).

Table 3 shows that Group B serial changes in median heart rate were found to be statistically nonsignificant (Friedman's analysis of variance).

At the time points just before laryngoscopy (HRL), 1 min (HR1), and 2 min (HR2), postintubation mean heart rate in Group B was lower than Group A. This difference between the two groups was statistically significant ($p < 0.05$).

No adverse effects were noted in both the groups during this study.

Discussion

Tachycardia is especially not desirable in patients with mitral stenosis. It shortens diastole relatively more than systole and thus, reduces the time for transmitral valve flow.[2] This may not only reduce the diastolic filling and cardiac output but may also suddenly increase transmitral pressure gradient, which elevates the left atrial pressure and precipitates an attack of pulmonary edema in previously asymptomatic patients with mitral stenosis.

In this study, 20 patients of either sex, of age between 18 to 40 years with mitral stenosis posted for CMC were allocated into two groups.

Group A served as control (they were given 15 mL of normal saline, intravenously over 60 s just before induction).

Group B served as study group (they were given 0.5 mg/kg body weight of esmolol hydrochloride made up to 15 mL with normal saline intravenously over 60 s just before induction).

Change in heart rate in both the control and esmolol groups was as follows:

- There was no significant difference in the value of mean preinduction heart rate between groups. In both the groups, the basal heart rate increased at just before laryngoscopy and at 1-, 2-, and 5-min postintubation, which was maximal at 1 min after intubation, thereafter, heart rate started declining in both the groups. At 5 min after intubation in Group A (control group), the heart rate was still higher than basal value as compared with Group B (esmolol group).
- The increase in heart rate at different time intervals was highly significant ($p < 0.001$) in Group A (control group), whereas it was insignificant ($p > 0.05$) in Group B (esmolol group) as compared with basal value. There was a highly significant ($p < 0.001$) decrease in heart rate in Group B (esmolol group) as compared with Group A (control group) after 1 and 2 min of intubation.

Our study could not detect any type of untoward effects at any time point, at and after intubation in both the groups.

Similar findings as in our study were seen in the study by Dutta et al. in 1999.[6] The study was conducted on 30 patients with mitral stenosis scheduled for CMC, receiving either saline or nitroglycerine or esmolol hydrochloride 4 min before intubation and extubation. The heart rate and mean arterial pressure response were noted. They concluded that esmolol significantly decreases the heart rate changes compared with saline and nitroglycerine.

Esmolol being a selective β1-blocker was effective in counteracting the increase in heart rate. The magnitude of changes in heart rate was less marked in patients receiving esmolol. Therefore, the use of esmolol during intubation may provide protection from the increases in heart rate. Side effects such as bradycardia and hypotension were not encountered in any of the patients. It is necessary to obtund the heart rate response during intubation, especially in patients with mitral stenosis for life-threatening complications, and esmolol was found to be beneficial in our study without any untoward responses.

Various methods have been used to attenuate the cardiovascular responses to laryngoscopy and endotracheal intubation. These methods include deepening of the plane of anesthesia,[4,7] topical anesthesia of laryngopharynx and epiglottis,[8–10] and use of fentanyl and alfentanil before intubation, which produce significant attenuation of cardiovascular response during intubation.[11,12] The effect of esmolol, an ultrashort-acting β-blocker introduced in the late eighties, with an elimination half-life of about 9 min was found to be much satisfactory as far as attenuation of cardiovascular responses to laryngoscopy and intubation is concerned.[13] A dose of 0.5 mg/kg body weight was administered intravenously at about 5 min before endotracheal intubation in the present series.

Intravenous lignocaine 1.5 mg/kg administered 90 s before laryngoscopy and viscous lidocaine 25 mL (4%) administered as mouth wash 10 min before laryngoscopy were found to be equally protective but former seemed to be a more logical choice.[9] But viscous or intravenous lignocaine was of no or little value when laryngoscopy was of very short duration (less than 15 s).[11]

Tanaka and Nishikawa[14] studied the effect of oral clonidine premedication in attenuating hypertensive response to ketamine. Taittonen et al.[15] studied the effects of clonidine and dexmedetomidine premedication on perioperative oxygen consumption and hemodynamic states.

For attenuating hypertensive and tachycardia response during endotracheal intubation, various other agents have been used such as metoprolol, labetalol, magnesium sulfate,

Table 1: Comparison of pre- and postintubation heart rates in patients of Groups A and B at various time points

Group	*N*	Mean	Median	Minimum	Maximum	Standard deviation	Standard error
HRp							
A	10	77.50	74.50	72	97	7.487	2.368
B	10	82.40	81.50	69	90	6.222	1.968
HRL							
A	10	87.90	87.50	77	105	7.505	2.373
B	10	68.70	69.50*	45	83	11.945	3.777
HR1							
A	10	97.20	96.00	86	119	8.638	2.732
B	10	82.90	79.50*	61	115	14.918	4.717
HR2							
A	10	95.40	95.00	84	114	7.777	2.459
B	10	80.50	80.50*	61	92	9.336	2.952
HR5							
A	10	81.80	80.00	76	98	6.697	2.118
B	10	78.80	80.00	64	91	9.953	3.147

HRp, heart rate preinduction; HRL, heart rate before laryngoscopy; HR1, heart rate 1 min after intubation; HR2, heart rate 2 min after intubation; HR5, heart rate 5 min after intubation.
*p-Value < 0.05 considered statistically significant.

Table 2: Comparison of median heart rates within Group A at different time points

Group	HRp	HRL	HR1	HR2	HR5
A	74.50	87.50**,***,*	96.00**	95***	80*

HRp, heart rate preinduction; HRL, heart rate before laryngoscopy; HR1, heart rate 1 min after intubation; HR2, heart rate 2 min after intubation; HR5, heart rate 5 min after intubation.
, *, *$p < 0.05$ (Wilcoxon's matched pair signed-rank test) considered statistically significant.

Table 3: Comparison of median heart rates within Group B at different time points

Group	HRp	HRL	HR1	HR2	HR5
B	81.50	69.50	79.50	80.50	80

HRL, heart rate before laryngoscopy; HRp, heart rate preinduction; HR1, heart rate 1 min after intubation; HR2, heart rate 2 min after intubation; HR5, heart rate 5 min after intubation.

and captopril. However, none of these approaches entirely block the pressure response and tachycardia. The methods may themselves carry some additional risk and the drug used may be long acting or have undesirable side effects.

Esmolol has been used to attenuate the hemodynamic responses to laryngoscopy and endotracheal intubation in varied dose range from 20 to 200 mg bolus (0.2 to 3 mg/kg body weight) as observed by Jacque et al.,[16] Sheppard et al.,[17] Helfman et al.,[18] and Miller et al.[19]

However, there are limited studies regarding the effects of esmolol on attenuating hemodynamic response to laryngoscopy and endotracheal intubation, in patients with mitral stenosis posted for CMC under general anesthesia, where it plays a crucial role in decreasing mortality.

Patients with mitral stenosis may present in rhythm other than sinus and may be already receiving a β-blocker or antihypertensive, so these types of patients should be studied regarding the effects of esmolol on attenuating hemodynamic response to laryngoscopy and endotracheal intubation to comment on the benefits and as well as occurrence of untoward effects if any, to come to a conclusion. These are the limitations of our study.

Conclusion

Laryngoscopy and endotracheal intubation often evokes cardiovascular responses characterized by an increase in the arterial pressure and heart rate and the disturbance of cardiac rhythm. Usually these transient changes have no deleterious effects on healthy patients, but in patients with altered tone in cardiovascular system, these changes may provoke life-threatening consequences. Esmolol was effective in attenuating the

increase in heart rate response after laryngoscopy and endotracheal intubation without any significant complications in patients with mitral stenosis.

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