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Comparison of hemodynamic response of intravenous lidocaine and esmolol during laryngoscopic intubation under general anesthesia for major abdominal surgery

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ABSTRACT

Background: Many studies have shown the beneficial effect of prophylactic lidocaine or esmolol on hemodynamic response during laryngoscopic intubation. Although many studies observed a better effect of esmolol over lidocaine, some studies have drawn an impression of equal efficacy or even no benefit with the use of either of the drugs. **Aims and Objectives:** The study aimed to compare the heart rate (HR) at 1 min after intubation between the patients receiving lidocaine and esmolol. Other outcome measures were to compare HR at 3 and 5 min post-intubation and to compare the mean arterial pressure at 1, 3, and 5 min after intubation. In addition, the adverse events, if any, were noted. **Materials and Methods:** Fifty patients, 30–45 years, either sex, Mallampati grade 1–2, of the American Society of Anesthesiologists physical status I-II, posted for elective abdominal surgery requiring direct laryngoscopic endotracheal intubation were included. Patients were randomly allocated into two groups to receive esmolol 2 mg/kg (Group E, n = 25) or 2% lidocaine 2 mg/kg (Group L, n = 25), intravenously. HR and mean arterial blood pressure (MAP) were recorded at 1-, 3-, and 5-min interval post-intubation. **Results:** The mean HR at 1-min post-intubation was considerably lower using esmolol in comparison with lidocaine (91.7 ± 9.7 vs. 107.7 ± 5.1, P ≤ 0.0001). The mean HR and MAP at 3-min and 5-min post-intubation were considerably lower with the use of esmolol compared with lidocaine. **Conclusion:** Esmolol is better than lidocaine in attenuating the hemodynamic response of intubation.

Key words: Endotracheal intubation; Esmolol; Hemodynamic response; Lidocaine

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INTRODUCTION

Direct laryngoscopy and endotracheal intubation remain an essential procedure to secure the airway during general anesthesia. It is a powerful stimulus that evokes severe sympathoadrenal stress responses owing to the stimulation of laryngotracheal receptors.[1] Hence, laryngoscopy and intubation can result in a rise in heart rate (HR) and blood pressure that may be detrimental in susceptible patients. Different studies have already evaluated the beneficial effects of intravenous (IV) lidocaine on the hemodynamic response during laryngoscopy and intubation.[2,3] Esmolol is a short-acting cardio-selective β-adrenergic receptor-blocking agent that has been used in preventing hemodynamic response to endotracheal intubation and extubation.[3] Various drugs such as lidocaine, fentanyl, esmolol, metoprolol, and other drugs can suppress the hemodynamic responses to laryngoscopy and intubation.[1,4-8]

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Some studies[5,6,9] have depicted that lidocaine can attenuate the rise in blood pressure with intubation whereas esmolol prevents it maximally. However, other studies[8,10] have observed that both esmolol and lidocaine are effective in attenuating the stress response of laryngoscopic intubation and are not superior to each other. However, Jain and Vats,[11] commented that although both are effective, esmolol could maintain hemodynamic variables with better stability. Kim et al.[12] reported that lidocaine 1.5 mg/kg was ineffective in controlling HR in response to laryngoscopy and intubation. Another study[13] adds to the existing controversy by drawing a mixed impression. They observed that both the drugs with their specified doses are not effective in blunting hemodynamic stress response generated during laryngoscopy and tracheal intubation.[13] However, the same study[13] with the same setting mentions that esmolol can be better than lidocaine in attenuating stress responses.

Thus, it appears that the evidence about the efficacy of these drugs and the supremacy of one over the other is yet to be consolidated. In other words, the quest is still "on." Hence, the present study was designed to compare the effects of IV bolus doses of lidocaine and esmolol in attenuating the hemodynamic responses to laryngoscopic endotracheal intubation during major surgical interventions under general anesthesia.

Aims and objectives

The primary outcome of this study was to compare the HR at 1 min after intubation between the patients receiving lidocaine and esmolol. Other outcome measures were to compare the HRs at 3 and 5 min after intubation and to compare the mean arterial pressure at 1, 3, and 5 min after intubation. In addition, the adverse events, if any, were noted.

MATERIALS AND METHODS

This prospective, randomized, double-blind, experimental study was conducted at Mata Gujri Memorial Medical College (MGMMC), Kishanganj, Bihar, after obtaining the permission from Ethical Clearance Committee and written informed consent from study populations.

Fifty patients aged 30–45 years, of either sex, conforming to the American Society of Anesthesiologists physical status I and II, having Mallampati grade 1 and 2, posted for elective major abdominal surgery under general anesthesia and requiring direct laryngoscopic endotracheal intubation were included in this study. Unwilling patients, known hypersensitivity to study drugs, morbid obesity, hemodynamic unstable, heart block, ischemic heart disease, raised intracranial pressure, bronchial asthma, diabetic autonomic neuropathy, and duration of laryngoscopy >15 s were excluded from this study.

Sample size calculation

The sample size was calculated using the formula and methods described by Das et al.[14]

$$n = \frac{2SD^2(Za/2 + Z_b)^2}{d^2}$$

In a previous study,[11] the HR at 1 min after intubation in patients receiving lidocaine and esmolol was 90.57±5.41 and 85.37±5.51, respectively. The average standard deviation of the population was 5.5 approximately. It was assumed that detecting at least 5 beats/min of HR at 1 min after intubation between the two groups would be the minimum clinically important difference. Thus, the effect size (d) was 5. Considering 1:1 group allocation and setting the power of the study at 90% and at 95% confidence level (allowing an alpha error of 5%), the sample size was calculated as 25 in each group. Hence, the present study recruited a total of 50 patients.

A detailed pre-anesthetic check-up and necessary investigations were done on each patient. Preoperatively patients were kept on fasting as per guideline and all the patients received alprazolam 0.5 mg tablet in the night before surgery and tablet pantoprazole 40 mg in the morning of surgery. After arrival at the operation theater, an IV cannula (18G) was inserted and injection Ringer's lactate was started. Patients were connected to a multichannel cardiocap II monitor (ECG, SpO_2, non-invasive blood pressure, and $EtCO_2$). Baseline HR and mean arterial pressure (MAP) were recorded. Patients were randomly allocated into two groups to receive injection esmolol 2 mg/kg IV (Group E, n=25) or 2% preservative-free injection lidocaine 2 mg/kg IV (Group L, n=25).

Randomization was done using computer-generated random numbers and allocation concealment was done by the serially numbered opaque sealed envelope method. The study participants and investigators were kept blind. A nurse who was not involved with the study prepared the study drugs in 10 mL syringes. According to the group allocation, she handed over the drug-filled syringe to the investigator without revealing the drug name.

Patients were pre-oxygenated with 100% oxygen for 5 min and subsequently were induced with IV thiopentone sodium 5 mg/kg (2.5%) till the eyelash reflex disappeared. It was followed by administration of IV vecuronium bromide 0.1 mg/kg and ventilated for 4 min to get adequate time for a better intubating condition. The intervention

drugs (lidocaine or esmolol) were administered 90 s before laryngoscopy. HR and MAP were recorded at 1-, 3-, and 5-min intervals following endotracheal intubation. Pethidine was administered 5 min after intubation, i.e., when the study period was over, in doses of 1 mg/kg. Anesthesia was maintained with 33% oxygen in nitrous oxide and repeated doses of vecuronium 0.02 mg/kg along with 0.5 to 1% isoflurane as required. At the end of surgery, reversal of neuromuscular blockade was done with IV neostigmine 0.05 mg/kg and atropine 0.02 mg/kg and extubated when extubation criteria were fulfilled.

For the purpose of observing the adverse event, intraoperative bradycardia was defined as HR <50 beats/min (bpm), and rescue treatment with IV 0.5 mg of atropine was set. Hypotension (defined as a 20% decrease in the MAP from the baseline) was supposed to receive treatment with an aliquot of 250 mL of normal saline and increments of 3 mg ephedrine IV.

The collected data were entered into MS Excel spreadsheets; missing data were managed after cross-checking with the original documents to ensure consistency, reliability, and accuracy. Statistical comparison of HR and mean arterial pressure was done between the groups using an unpaired t-test. Intragroup comparison of these parameters (HR and MAP) was done using a paired t-test. Categorical data were compared using the Chi-square test. Data were analyzed with Epi-Info 2018 version 7.2 and SPSS version 16.0. The P≤0.05 was considered statistically significant.

Compliance with ethical standards

Study approved by Institute Ethical Committee (MGM/IEC-43/2021). The Declaration of Helsinki has been followed as per recommendations.

RESULTS

The study spanned over 22 months (from March 2021 to December 2022). Data from all 50 participants were available for analysis.

The demographic parameters were comparable between the two groups (Table 1).

The mean HR at 1 min, 3 min, and 5 min after intubation was considerably lower with the use of esmolol in comparison with the use of lidocaine (Table 2).

The mean of MAP at 1-min post-intubation was comparable between the two groups. However, the mean of MAP at 3 min and 5 min after intubation was considerably lower with the use of esmolol compared with lidocaine (Table 3).

Table 1: Demographic characteristics

Parameters	Groups		P-value
	Group L (n=25)	Group E (n=25)	
Age (years)	37.4±4.4	36.8±4.2	0.624
Body weight (kg)	50.8±5.2	51.7±4.6	0.520
Male/female	14/11	15/10	0.774 (Chi-square value 0.0821)

Parameters are analyzed using Student's unpaired t-test except marked with * which is categorical data and analyzed using Chi-square test. P<0.05 indicates that the difference is statistically significant

Table 2: Comparison of heart rate at different time points

Parameters	Groups		P-value
	Group L (n=25)	Group E (n=25)	
Baseline	88.2±5.3	89.7±5.2	0.318
1-min post-intubation	107.7±5.1	91.7±9.7	<0.0001
3-min post-intubation	109.5±5.7	90.5±4.5	<0.0001
5-min post-intubation	106.2±5.1	88.7±5.1	<0.0001

Intergroup analysis, Student's unpaired t-test, P<0.05 indicates that the difference is statistically significant. Group L, patients receiving IV lignocaine, Group E, patients receiving IV esmolol

Table 3: Comparison of MAP at different time points

Parameters	Groups		P-value
	Group L (n=25)	Group E (n=25)	
Baseline	92.9±1.9	92.7±2.5	0.752
1-min post-intubation	96.9±6.5	94.2±6.9	0.161
3-min post-intubation	103.9±2.0	93.2±1.8	<0.0001
5-min post-intubation	102.8±6.4	89.7±2.6	<0.0001

Intergroup analysis, Student's unpaired t-test, P<0.05 indicates that the difference is statistically significant. Group L, patients receiving IV lignocaine, Group E, patients receiving IV esmolol. MAP: Mean arterial pressure

The difference of HRs at different time points (at 1-min, 3-min, and 5-min post-intubation) from their respective baselines was considerable in lidocaine group while the difference was not significant in esmolol group. In other words, the rise in HR was considerable at all three observed time points with the use of lidocaine while the rise was minimal during the use of esmolol. This translates into a greater effect of HR control with the use of esmolol compared with lidocaine (Table 4).

The difference of MAP at different time points (at 1-min, 3-min, and 5-min post-intubation) from their respective baselines was considerable in the lidocaine group whereas the difference was reduced to non-significant level at 3-min post-intubation and even the value was reduced below the baseline at 5-min post-intubation time point in esmolol group. This translates into a better effect of MAP control with the use of esmolol compared with lidocaine. The

effect is considerable at 3-min post-intubation and was maximum at 5-min post-intubation time point during the use of esmolol (Table 5).

DISCUSSION

The present study observed that patients receiving esmolol had lower HR at 1 min after intubation compared with those receiving lidocaine. The difference between mean HRs achieved was about 16 beats/min. The HRs at other time points were comparable with the baseline in the esmolol group whereas the HRs showed considerable difference with the baseline in lidocaine group. This signifies more strict control of the HR was achieved with the use of esmolol. There was at least 10 mmHg less MAP at 3 and 5 min post-intubation time points with the use of esmolol compared with lidocaine. HR and mean arterial pressures at other time points of observation were also lower with the use of esmolol compared with lidocaine.

Singh et al.[15] observed better control of HR and blood pressure levels (mean, systolic, and diastolic) with the use of esmolol immediately after the intubation and up to 5- min post-intubation. In attenuating stress response due to laryngoscopy and intubation, esmolol was found to be better than lidocaine in other studies.[6,9,11]

In a recent study, Khobragade et al.[8] reported that esmolol and lidocaine were equally effective in attenuation of stress response to laryngoscopy and intubation. However, another study,[13] has depicted a negative impression in the fact that both esmolol (50 mg bolus) and lidocaine (2 mg/kg) were found to be not effective in attenuating the hemodynamic responses to laryngoscopy and tracheal intubation. Although, in the same study,[13] the authors observed that esmolol was superior to lidocaine in blunting the stress response.

Muralidharan et al.[16] compared the use of lidocaine and esmolol, both used at a dose of 2 mg/kg 2 min before intubation. They observed a considerable increase in mean HR during laryngoscopy and intubation with the use of lidocaine and the parameter did not come back to baseline level even after 5 min. They also observed that there was a considerable attenuation of HR during intubation and 1-, 3-, and 5-min post-intubation with the use of esmolol. The use of esmolol also led to better attenuation of MAP when compared with lidocaine.[16] In a recent study, Mendonça et al.[17] have observed that esmolol can be a safe and more effective drug than lidocaine to reduce the incidence of tachycardia and control of HR immediately post-intubation.

The present study has evaluated the effect of a single dose of either of the drugs at a dose of 2 mg/kg administered 1½ min before intubation. Different authors have examined both drugs at different dose schedules. Some researchers have used both drugs at a single dose of 1.5 mg/kg[10] or at a dose of 2 mg/kg.[16] Administered 2 min before laryngoscopy and intubation. Khobragade et al.[8] used both drugs at 2 mg/kg administered 3 min before laryngoscopy and intubation. Singh et al.[15] evaluated lidocaine 1.5 mg/kg and esmolol 2 mg/kg both administered 2 min before

Table 4: Comparison of mean difference in heart rate between baseline and various time points

Intragroup comparison	Deviation of HR from baseline			
	Group L (n=25)		Group E (n=25)	
	Mean difference±SE	P-value	Mean difference±SE	P-value
A versus B	−16.8±1.94	<0.001	−3.02±1.71	>0.05
A versus C	−20.14±1.88	<0.001	−1.62±1.28	>0.05
A versus D	−17.08±1.88	<0.001	1.02±1.48	>0.05

Intragroup analysis, paired t-test, between the baseline parameter and heart rates at different time points. A=baseline, B=at 1-min post-intubation, C=at 3-min post-intubation, D=at 5-min post-intubation, SE=Standard error. When the values of B, C, and D are bigger than A, the difference carry negative sign. Group L, patients receiving IV lignocaine, Group E, patients receiving IV esmolol

Table 5: Comparison of mean difference in mean arterial pressure between baseline and various time points

Intragroup comparison	Deviation of MAP from baseline			
	Group L (n=25)		Group E (n=25)	
	Mean difference±SE	P-value	Mean difference±SE	P-value
A versus B	−2.8±1.85	<0.05	−1.08±1.29	<0.05
A versus C	−7.66±0.93	<0.001	−0.34±0.65	>0.05
A versus D	−6.56±0.87	<0.001	3.06±0.83	<0.01

Intragroup analysis, paired t-test, between the baseline parameter and mean arterial pressures at different time points. A=baseline, B=at 1-min post-intubation, C=at 3-min post-intubation, D=at 5-min post-intubation. When the values of B, C, and D are bigger than A, the difference carries negative sign. Group L, patients receiving IV lignocaine, Group E, patients receiving IV esmolol. MAP: Mean arterial pressure

intubation. Koju et al.[6] evaluated lidocaine 1.5 mg/kg versus esmolol 1.4 mg/kg although the authors did not mention the time of administration of the study drugs. Rajbhandari et al.[13] evaluated esmolol (50 mg bolus) and lidocaine (2 mg/kg) administered 2 min before induction in preventing hemodynamic response to intubation. In another recent study,[17] the effect of 1.5 mg/kg esmolol bolus followed by 0.1 mg/kg/min esmolol infusion was compared with 1.5 mg/kg lidocaine bolus followed by 1.5 mg/kg/min lidocaine infusion. In a dose-finding study,[18] lidocaine at a dose of 2 mg/kg appeared more effective than its lower doses for the attenuation of pressor response of tracheal intubation.

Limitations of the study

The invasive arterial line monitoring can yield benefits in terms of real-time beat-to-beat monitoring of blood pressure. In the present study, it was not possible owing to resource constraints. Further study with a larger sample using different doses of both drugs can reveal important observations.

CONCLUSION

From the observed data, it can be said that esmolol has a greater effect than lidocaine in attenuating the rise of HR and mean arterial pressure at every time points of post-intubation phase. The study concludes that esmolol is better than lidocaine in attenuating the hemodynamic response of intubation.

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MS- Conception and design, questionnaires development, collection and assembly of data, statistical expertise, analysis and interpretation of data, drafting of the article, and final approval of the article; **MB-** Analysis and interpretation of data, drafting of the article, and final approval of the article; **AG-** Provision of study materials, analysis and interpretation of data, drafting of the article, and final approval of the article; **RP-** Provision of study materials, analysis and interpretation of data, critical revision of the article for important intellectual content, drafting of the article, and final approval of the article; **MM-** Conception and design, questionnaires development, collection and assembly of data, statistical expertise, analysis and interpretation of data, drafting of the article, and final approval of the article.

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