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Attenuation of cardiovascular responses to laryngoscopy and intubation –A comparative study between IV esmolol hydrochloride and lignocaine hydrochloride

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ABSTRACT

Background: Laryngoscopy and tracheal intubation are frequently associated with sympathetic stress response. Lignocaine and esmolol are useful to decrease the sympathetic response to laryngoscopy and intubation. **Aims and Objectives:** The aim of the study was to study the effectiveness of lignocaine and esmolol administered intravenously before laryngoscopy and intubation in attenuating the sympathetic response. **Materials and Methods:** The prospective, randomized, and controlled study was conducted in Maharajah's Institute of Medical Sciences Hospital for a period of 18 months from January 2016 to June 2017. A clinical comparative study of attenuation of sympathetic response to laryngoscopy and intubation was done in 90 patients posted for elective surgeries. The sample size estimation is calculated based on findings from the previous study done by Singh et al., (2013).Group I was control group. In this group, no drug was administered. Group II was lignocaine group. Here, patients received 1.5mg/kg lignocaine i.v. bolus. Group III was esmolol group. All patients in this group received 2mg/kg i.v. bolus. **Statistical Analysis:** Descriptive data presented as Mean ± SD and in percentage. Pair-wise comparison between the groups was done by "Z" test. For all tests, "Z" value of >1.96 was considered significant and "P' <0.05" was considered significant. **Results:** Esmolol at a bolus dose of 2mg/kg i.v. administered 3 min before laryngoscopy and intubation is more efficient than lignocaine given at a dose of 1.5mg/kg. **Conclusions:** Esmolol at bolus dose of 2mg/kg i.v. administered can be recommended to attenuate sympathetic responses due to laryngoscopy and intubation.

Key words: Esmolol; General anaesthesia; Lignocaine

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INTRODUCTION

Endotracheal intubation has become an integral part of anesthetic management. Even though elevation in blood pressure and heart rate due to laryngoscopy and intubation is brief, they may have detrimental effects in high-risk patients such as patients with myocardial infarction, cardiac failure, and intracranial hemorrhage.[1] Circulating catecholamine's include norepinephrine, epinephrine and dopamine levels rise, but rise in norepinephrine levels is consistently associated with elevation of blood pressure and heart rate.[2-5]

The main objective of the study is to observe the variations in sympathetic response inpatients administered with lignocaine 1.5mg/kg i.v. and esmolol 2mg/kg i.v. before laryngoscopy and intubation.

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Aims and objectives

The aim of the study was to study the drug efficacy of lignocaine and esmolol in attenuating the intubation response to laryngoscopy before intubation.

MATERIALS AND METHODS

A clinical comparative study of attenuation of sympathetic response to laryngoscopy and intubation was done in 90 patients posted for elective surgeries. The study was conducted in Maharajah's Institute of Medical Sciences Hospital for a period of 18months from January 2016 to June 2017.

Sample size was calculated based on findings from the previous study. According to the study done by Singh et al.,(2013) percentage change in hemodynamic variables in control, lignocaine, and esmolol groups at 1 min is as follows: HR=30.45, 26.00, and 1.5% and MAP=20.80, 15.89, and 10.20%, respectively. Patients in control group had more increase in HR and MAP. The other parameters considered for sample size calculation include 95% confidence interval, allowable error 1, and standard deviation of 4.80, the required sample size was 30 patients in each group.

$$n = \frac{Z^2\sigma^2}{e^2}$$

n = sample size
Z = 1.96 (95% confidence limits)
σ = standard deviation
e = allowable error

Patients undergoing various orthopedic, ENT, gynecological, general surgical, and laparoscopic procedures were selected.

Following criteria were adopted for selecting patients.

Inclusion criteria

The following criteria were included in the study:

- Patient scheduled for elective surgeries
- Age between 20 and 50 years of both the sexes.
- Patients with ASA Grade I or II.
- Mallampati airway assessment of Grade I and II.

Exclusion criteria

The following criteria were excluded from the study:

- Unwilling patients
- Emergency surgeries
- Anticipated difficult intubation
- Patients with ASA Grade III or higher
- Patients with cardiovascular diseases
- Patients on beta blockers or calcium channel blockers
- Patients in whom laryngoscopy and intubation proved to be prolonged or difficult.

The Institutional Human Ethics Committee reviewed and approved the proposed title "Attenuation of cardiovascular responses to laryngoscopy and intubation – A comparative study between IV esmolol hydrochloride and lignocaine hydrochloride." Informed written consent was obtained from all the study participants. The risks and benefits involved in the study and voluntary nature of participation was explained to participants before obtaining consent.

Computer generated randomization was done.

Group I was control group. In this group, no drug was administered for attenuating sympathetic response to laryngoscopy and intubation.

Group II was lignocaine group. Here, patients received 1.5 mg/kg lignocaine i.v. 3 min before laryngoscopy and intubation.

Group III was esmolol group. All the patients in this group received 2 mg/kg i.v. bolus 3 min before laryngoscopy and intubation.

All the patients were visited the day before surgery and pre anesthetic counseling was done. All patients received alprazolam 0.25 mg orally at night on the day before surgery.

On the day of surgery, intravenous line was secured with 18G cannula ringers lactate infusion started and injection midazolam 0.04 mg/kg i.v. was given 45 min before induction.

Patients were monitored by pulse oximeter.

On entering the OT pulse oximeter, non-invasive blood pressure and ECG monitors were connected. A pre-induction heart rate, systolic, and diastolic blood pressures were recorded. The i.v. infusion of DNS solution was started. All patients were pre medicated with i.v. ondansetron 0.08 mg/kg and glycopyrolate 0.004 mg/kg 10 min before induction.

All the patients were pre oxygenated with 100% oxygen for 3 min before induction. Induction was achieved with inj. thiopentone sodium 5 mg/kg i.v. given in 2.5% solution. After induction of anesthesia (loss of eyelash reflex), heart rate, systolic, and diastolic blood pressure were recorded.

Succinylcholine was administered at a dose of 2 mg/kg i.v. Laryngoscopy was done using rigid laryngoscope with

standard Macintosh blade. Intubation was done with appropriate sized, disposable, and high volume low pressure cuffed endotracheal tube. Oral intubation was done for all surgical procedures. Laryngoscopy and intubation was done within 15–20 s.

Heart rate, systolic, and diastolic blood pressure were recorded before induction and immediately post-induction and at 1,3,5,7, and 10 min intervals from the onset of laryngoscopy.

Patients were connected to bains circuit and anesthesia was maintained with oxygen (33%), N_2O(66%), and sevoflurane 1% in 6L of fresh gas flow using IPPV. Bolus i.v. dose of 0.08 mg/kg followed by intermittent dose of 0.02 mg/kg non-depolarizing muscle relaxant vecuronium bromide was used for muscle relaxation.

Adequacy of ventilation was monitored clinically and SpO_2 was maintained at 99–100%.

Positioning, epinephrine infiltration, throat packing, and surgery were with held till the completion of recording. Injection fentanyl 2mcg/kg i.v. was given before surgery.

At the end of the surgery, reversal was done with inj.neostigmine 0.05mg/kg and inj.glycopyrrolate 0.08mg/kg i.v.

An observation was made related to adverse effects of drugs and anesthesia-related problems and was attended to appropriately.

Statistical analysis

Descriptive data presented as Mean±SD and in percentage. Pair-wise comparison between the groups was done by "Z" test. For all tests, "Z >1.96" was considered significant and "P<0.05" was considered significant. Data were analyzed using SPSS software version 20.

RESULTS

The Table 1 shows the age distribution in control and the two study groups. The age range was 20–50 years for control and study groups. The mean values of age with standard deviations are 36.36±9.56, 34.53±9.28, and 36.33±8.99 for control, lignocaine, and esmolol groups, respectively. There was no significant difference between the three groups (P>0.05).

Table 2 in the control group shows 6.7% of the patients were males and 53.3% of the patients were females. In lignocaine group, 43.3% of the patients were male and 56.7% female.

In esmolol group, 50% of the patients were male and 50% of the patients were females.

No significant difference was observed in sex-wise distribution of the cases between the three groups(P>0.05).

Table 3 shows weight range in control group is 42–65kg, mean value is 53.83 with standard deviation of 5.46.

In lignocaine group, weights ranged from 47 to 66 kg with a mean of 54.96 and a standard deviation of 4.70.

In esmolol group, the range of weights were between 45 and 67 kg with a mean value of57.03 and standard deviation of 5.46.

No significant differences were observed weight-wise between the three groups (P>0.05).

Heart rate increased by a maximum of 34.93% in the Table 4 when compared to pre-induction value in the control group (Z>1.96, P<0.01). Similar increases in lignocaine were 25.33% and in esmolol group by 10.66%. Both lignocaine and esmolol attenuated the heart rate significantly (Z>1.96 and P<0.001). It reaches a level which is clinically less significant by the end of 7 min in control group and by the end of 5 min in lignocaine and esmolol group. Attenuation of maximum rise in the heart rate by esmolol is evident and statistically highly significant when compared with lignocaine (Z > 1.96 and P < 0.001).

Table 2: Sex distribution

Sex	No. of Cases	Percentage
Control Group		
Males	14	46.7
Females	16	53.3
Lignocaine Group		
Males	13	43.3
Females	17	56.7
Esmolol Group		
Males	15	50.0
Females	15	50.0

Table 1: Age distribution

	Control	Lignocaine	Esmolol
Minimum	20.00	21.00	20.00
Maximum	50.00	49.00	47.00
Mean	36.36	34.53	36.33
Std. deviation	9.56	9.28	8.99

Table 3: Weight distribution

	Control	Lignocaine	Esmolol
Minimum	42.00	47.00	45.00
Maximum	65.00	66.00	67.00
Mean	53.83	54.96	57.03
Std.deviation	5.46	4.70	5.46

Table 4: Comparision of heart rates

	Heart Rate						Z-Test					
	Control		Lignocaine		Esmolol		I–II		I–III		I–III	
	Mean±SD	Mean Diff	Mean±SD	Mean Diff	Mean±SD	Mean Diff	Z-Value	P-Value	Z-Value	P-Value	Z-Value	P-Value
Pre-induction	82.86±7.53	-	80.10±7.26	-	78.50±6.02	-	1.44	0.142	0.92	0.356	2.47	0.012
Post-induction	90.83±10.47	7.96	82.80±6.75	2.7	83.26±5.47	4.76	3.60	**0.31***	0.29	0.762	3.08	**0.002**
1 Min	117.80±10.51	34.93	105.43±7.30	25.33	88.76±5.76	10.26	23.23	**0.00001***	9.80	**0.00001***	33.46	**0.00001***
3 Min	117.03±13.53	34.16	102.76±9.89	22.66	89.16±5.40	10.66	4.66	**0.00001***	6.60	**0.00001***	10.47	**0.00001***
5 Min	106.70±13.70	23.83	91.40±7.22	11.30	86.40±4.32	7.90	7.17	**0.00001***	3.25	**0.0011***	7.73	**0.00001***
7 Min	92.93±9.39	10.06	86.70±6.62	6.60	80.86±3.21	2.36	2.97	**0.00297***	4.34	**0.00001***	6.65	**0.00001***
10 Min	84.63±6.02	1.76	82.36±6.05	2.26	78.73±2.92	0.23	1.45	0.146	2.95	**0.00317***	4.82	**0.00001***

*P value <0.05 statistically significant

In control group, Table 5 shows systolic blood pressure increased maximally after 1 min from the onset of laryngoscopy and intubation. It gradually decreased to pre-induction values over 10 min. With lignocaine group, the maximum rise in systolic blood pressure was 20.63% above pre-induction values and with esmolol; it was only 5.0% above pre-induction values by the end of 1 min. Both drugs compared with control showed significant attenuation (P>1.96 and P<0.05). Among the two drugs studied, esmolol showed a better attenuation over lignocaine upto 5 min post laryngoscopy (Z>1.96 and P<0.001).

In the Table 6, maximal rise in diastolic blood pressure was 12.93% when compared to pre-induction values in the control group (Z>1.96 and P<0.001). In lignocaine group, the maximal increase was 10.90% and in esmolol group, it was 5.36%. Attenuation of diastolic blood pressure is very significant in the two group as compared to control group until the end of 5 min (Z>1.96 and P<0.001). Among the two study groups, esmolol showed a better attenuation of diastolic blood pressure compared to lignocaine.

Similarly, Table 7 shows mean arterial pressure was increased by 16.88% in control group while it increased by 12.27% in lignocaine group and only by 5.28% in esmolol group compared to pre-induction values by 1 min post laryngoscopy. Attenuation of mean arterial pressure is significant in esmolol group as compared to both lignocaine and control group (Z>1.96 and P<0.05).

The HR, SBP,DBP and MAP of both control group, lignocaine and esmolol group are shown in Graphs 1-4, respectively. Figures indicate better attenuation of pressor response to esmolol group than lignocaine and control group from time of induction to post intubation.

DISCUSSION

In our study, we included 90 normotensive ASA GradeI and II patients scheduled for various elective surgical procedures under general anesthesia with endotracheal intubation.

In the control group, heart rate, systolic, diastolic, and mean arterial blood pressures showed wide fluctuation, maximal increase at 1 min post laryngoscopy and returned gradually to basal values over 10 min.

In lignocaine group, a significant suppression of sympathetic response as compared to control group was observed. Heart rate and blood pressures remained little over baseline by the end of 10 min.

Table 5: Comparison of systolic blood pressure

	Systolic bloodPressure						Z–Test					
	Control		Lignocaine		Esmolol		I–II		II–III		I–III	
	Mean±SD	Mean Diff	Mean±SD	Mean Diff	Mean±SD	Mean Diff	Z-Value	P-Value	Z-Value	P-Value	Z-Value	P-Value
Pre-induction	130.80±9.68	-	131.00±11.63	-	128.86±11.49	-	−0.07	0.942	0.70	0.476	0.69	0.484
Post-induction	127.30±9.23	3.50	129.83±11.35	1.16	124.73±11.12	4.13	−0.94	0.346	1.75	0.074	0.97	0.332
1 Min	155.56±9.28	24.76	151.63±12.07	20.63	133.86±10.33	5.00	1.41	0.152	6.12	**0.00001***	8.55	**0.00001***
3 Min	153.96±10.89	23.16	148.90±14.31	17.90	133.73±9.57	4.86	2.54	**0.024***	4.82	**0.00001***	7.64	**0.00001***
5 Min	143.33±12.40	12.53	137.96±10.82	6.96	132.06±9.22	3.20	2.78	**0.032***	2.27	**0.024***	3.99	**0.00006***
7 Min	135.30±10.15	4.50	131.43±11.05	0.43	129.96±8.87	1.10	1.41	0.154	0.56	0.575	2.16	**0.034***
10 Min	130.40±8.95	0.40	128.63±11.46	2.36	128.53±8.73	0.33	0.66	0.502	0.03	0.962	0.81	0.412

*p value <0.05 statistically significant

Table 6: Comparison of diastolic blood pressure

	Diastolicbloodpressure						Z-Test					
	Control		Lignocaine		Esmolol		I–II		II–III		I–III	
	Mean±SD	Mean Diff	Mean±SD	Mean Diff	Mean±SD	Mean Diff	Z-Value	P-Value	Z-Value	P-Value	Z-Value	P-Value
Pre-induction	77.00±6.03	-	77.10±5.79	-	76.63±5.51	-	−0.06	0.942	0.31	0.742	0.24	0.802
Post-induction	73.93±6.02	3.06	75.90±5.64	1.20	74.00±4.51	2.63	26.00	**0.00001***	1.43	0.151	28.39	**0.00001***
1 Min	89.93±4.84	12.93	88.00±4.45	10.90	81.80±4.79	5.16	1.60	0.101	5.18	**0.00001***	6.53	**0.00001***
3 Min	89.40±4.81	12.40	86.56±4.56	9.46	82.00±4.22	5.36	2.34	**0.010***	4.02	**0.00005***	6.32	**0.00001***
5 Min	85.13±5.87	8.13	81.13±3.43	4.03	80.50±4.50	3.86	3.21	**0.001***	0.61	0.534	3.42	**0.00062***
7 Min	80.30±5.27	3.30	77.36±4.18	0.26	79.46±4.49	2.83	2.38	**0.017***	1.87	0.062	0.65	0.504
10 Min	77.96±5.31	0.96	75.80±4.65	1.30	78.03±3.98	1.40	1.67	0.094	1.99	**0.042***	0.05	0.952

*p value<0.05 statistically significant

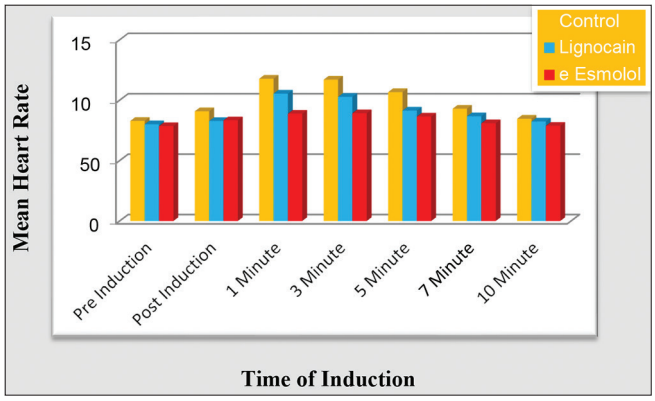
Table 7: Comparison of mean arterial pressure

	Meanarterialpressure						Z–Test					
	Control		Lignocaine		Esmolol		I–II		II–III		I–III	
	Mean±SD	Mean Diff	Mean±SD	Mean Diff	Mean±SD	Mean Diff	Z-Value	P-Value	Z-Value	P-Value	Z-Value	P-Value
Pre-induction	94.93±6.49	-	95.06±6.42	-	93.92±5.79	-	0.08	0.936	0.72	0.464	0.63	0.524
Post-induction	91.72±5.91	3.21	93.88±6.15	1.18	90.79±5.15	3.13	1.38	0.164	2.10	**0.031***	0.64	0.512
1 Min	111.81±5.13	16.88	105.91±18.70	10.84	99.12±5.36	5.20	1.66	0.092	1.91	0.056	9.35	**0.00001***
3 Min	110.92±5.82	15.99	107.34±6.84	12.27	99.21±4.68	5.28	2.18	**0.024***	5.37	**0.0001***	8.58	**0.00001***
5 Min	104.53±6.47	9.60	100.07±4.23	5.01	97.65±4.71	3.72	3.15	**0.001***	2.10	**0.034***	4.70	**0.00001***
7 Min	98.62±5.84	3.69	95.38±4.93	0.32	96.29±4.69	2.36	2.32	0.518	0.72	0.464	1.70	0.087
10 Min	95.44±5.47	0.51	93.41±5.71	1.65	94.96±4.49	1.04	1.40	0.159	1.17	0.241	0.36	0.712

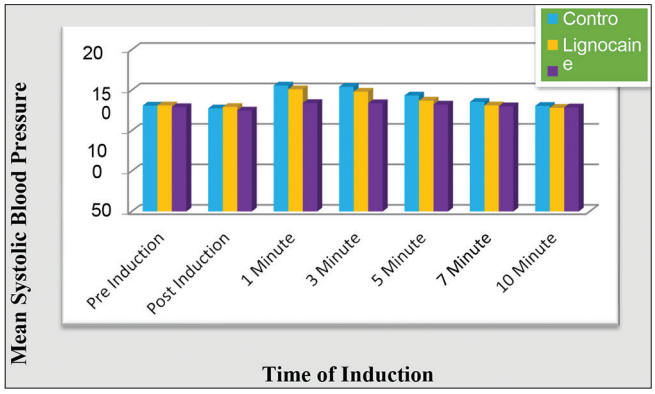
*p value <0.05 statistically significant

In esmolol group, very highly significant and consistent attenuation of sympathetic responses as compared to control group was noted. Heart rate and blood pressures rose steadily over 1 and 3 min with a gradual return to near basal level of heart rate and below basal levels of blood pressure. Among the two study groups, superiority of esmolol over lignocaine in attenuating the sympathetic responses to laryngoscopy and intubation is evident and statistically highly significant at all times.

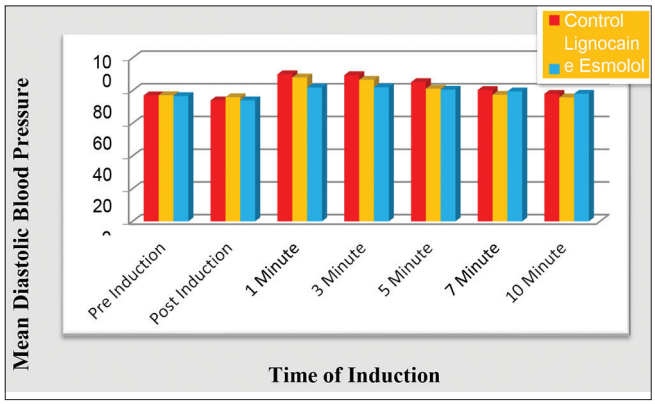
Shende et al.,[6] (2017) conducted a randomized controlled trial to compare the effects of bolus doses of metoprolol



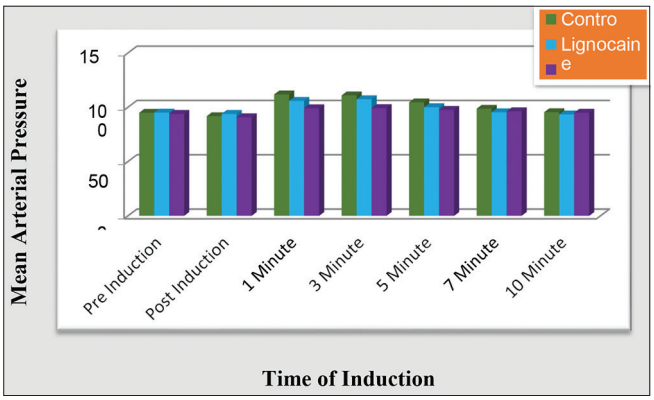
Graph 1: Comparison of heart rates



Graph 2: Comparision of systolic blood pressure



Graph 3: Comparision of diastolic blood pressure



Graph 4: Comparision of mean arterial pressure

and esmolol heart rate, systolic blood pressure, and rate pressure product during laryngoscopy and intubation. Sixty patients of ASA I and II randomly received placebo or study group 1mg/kg of esmolol or 80gμg/kg of metoprolol in 20ml normal saline. Clinically and statistically, they concluded that metoprolol may be a better agent for attenuation of heart rate and esmolol is better choice to attenuate blood pressure.

Mulimani et al.,[7](2019) showed that esmolol in doses of 1.5 mg/kg is effective in attenuating the pressor responses to laryngoscopic intubation in comparison with IV lignocaine 1.5 mg/kg.

Miller et al.,[8] showed that esmolol in doses of 1.5–3.0 mg/kg did not alter stroke volume or depress left ventricular function in patients with preserved cardiac function.

Olatosi et al.,[9] (2016) conducted a study to evaluate and compare the effects of i.v. lignocaine and esmolol on the pressor response as well as determine the occurrence of complications with the use of either agent in Nigerian population. They came to conclusion that i.v. esmolol 2 mg/kg given before laryngoscopy is more effective than i.v. lignocaine 1.5 mg/kg in Nigerian population.

Singh et al.,[10] (2013) conducted a randomized controlled trial on 120 adult patients of ASA I or II undergoing elective surgeries. They came to conclusion that the prophylactic therapy with i.v. esmolol 2 mg/kg when injected 2 min before intubation is significantly more effective than lignocaine 1.5 mg/kg in suppressing hemodynamic changes to laryngoscopy and tracheal intubation in normotensive patients.

In a study by Miller and Warren[11] (1990), patients were allocated randomly to a control group or three treatment groups to receive lignocaine 1.5 mg/kg/i.v. 1, 2, and 3 min before laryngoscopy. The analysis failed to show any significant differences between any of these two groups.

Gupta and Tank[12] (2011) conducted a study on 90 ASA I and II patients posted for elective surgery to compare the effectiveness of single bolus dose of esmolol or fentanyl in attenuating the hemodynamic responses during laryngoscopy and endotracheal intubation. From the study, they came to conclusion that only esmolol provided consistent and reliable protection against increases in both heart rate and systolic blood pressure accompanying laryngoscopy and endotracheal intubation.

Wilson et al.,[13] (1991) studied the effect of varying time of prior doses of lignocaine 1.5 mg/kg on the cardiovascular and catecholamine responses to tracheal intubation. When compared with placebo, there was significant increase in heart rate in all groups but no significant increase in mean arterial pressure in all groups given lignocaine.

Sharma et al.,[14] (1994) designed a study to compare the effectiveness of two bolus doses of esmolol 100 and 200 mg with placebo for blunting of hemodynamic responses to laryngoscopy and intubation in 75 ASA I and II patients. They concluded that in this study, adequate hemodynamic control was obtained with administration of 200mg of esmolol than compared with 100mg.

A study to compare the efficacy of two bolus doses of esmolol in blunting hemodynamic responses during laryngoscopy and tracheal intubation in ASA I and II patients scheduled for elective non-cardiac surgery was conducted by Yuan et al.,[15] (1995).

Singh et al.,[16] (1995) compared the safety and efficacy of lidocaine, esmolol, and nitroglycerine in modifying the hemodynamic response to laryngoscopy and intubation in ASA I and II patients undergoing elective surgery. Esmolol significantly more effective than lignocaine in minimizing the increase in mean arterial pressure.

Mendonca et al., (2017)[17] conducted a study on 56 ASA I and II scheduled for non-cardiac surgery requiring intubation to compare the clinical effects of lidocaine 2 mg/kg and magnesium sulfate 30 mg/kg in attenuating the pressor response to tracheal intubation. They came to conclusion that both have good efficacy and safety for hemodynamic management.

Efficacy of intravenous lignocaine 1.5 mg/kg and two different doses of dexmedetomidine 0.5 μg/kg and 1 μg/kg for attenuating the cardiovascular responses to

laryngoscopy and intubation was evaluated by Gulabani et al., (2015).[18] They concluded that dexmedetomidine 1 μg/kg is effective compared to dexmedetomidine 0.5 μg/kg and lignocaine 1.5μg/kg in attenuating the pressor responses.

Reddy et al.,[19] (2014) conducted a study on 90 ASA I and II scheduled fornon-cardiacsurgeryrequiringin tubiontocomparetheclinicaleffectsofdexmedetomi dine with esmolol to attenuate the pressor response during laryngoscopy. Of the two drugs administered, dexmedetomidine 1.0 μg/kg provides consistent, reliable, and effective attenuation of pressure responses when compared to esmolol 2.0 mg/kg.

Bostanand Eroglu[20] (2012) reported that i.v.esmolol in dose of 1 mg/kg before intubation was effective in suppressing the heart rate and arterial blood pressure.

Limitations of the study

Patients heart rate variability was not assessed.

CONCLUSION

In our study, esmolol is more effective over lignocaine in attenuation of cardiovascular responses to laryngoscopy intubation.

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EPP – Interpreted the results and manuscript preparation; **KSG –** Concept and design of the study and reviewed the literature; **ALA –** Statistical analysis and interpretation;and **RPM –** Preparation of manuscript and revision of manuscript

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