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Original Research Article

Attenuation of Hemodynamic Responses to Laryngoscopy and Endotracheal Intubation: Comparison of Clonidine, Esmolol and Lignocaine for Elective Surgeries under General Anaesthesia

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Abstract:

Background: We compared the effects of intravenous clonidine, esmolol and lignocaine as premedicant in attenuation of hemodynamic response to laryngoscopy and intubation in normotensive patients undergoing elective surgery.

Methods: A total of 90 patients undergoing general anesthesia were enrolled in the study and were randomly allocated into three groups of 30 each. Group 1 patients received intravenous clonidine 2µg/kg 10 minutes before induction and Group 2 patients received intravenous esmolol 1mg/kg 3 minutes before intubation and group 3 received intravenous lignocaine 1.5 mg/kg before intubation.

Results: Heart rate in group 2 at intubation was 95.30±12.4(3.0%) compared to group 1 which was 87.8±13.6 (3.1%) and group 3 had the highest heart rate of 106.2±15.6(26.5%). Group 1 and 2 were comparable but group 3 was not very effective in controlling heart rate. In Group 1, SBP and DBP recorded at the time of intubation was 115.20±17.6 and 80.00±15.00 respectively. In Group 2, SBP and DBP recorded at the time of intubation was 124.60±13.80 and 89.00±11.00. SBP and DBP in group 3 at the time of intubation was133.10±16.20 and 95.00±17.00 which was the highest recorded SBP and DBP when compared to other groups. MAP in Group 1, at the time of intubation was 92.00±16.00 compared to 101.00±12.00 in group 2 and 108.00±16.00 in group 3.

Conclusion: Clonidine is found to be effective in blunting hemodynamic responses to laryngoscopy and intubation, followed by esmolol. Lignocaine was ineffective in attenuating the responses to laryngoscopy and endotracheal intubation.

Keywords: Intravenous, Clonidine, Esmolol, Lignocaine, Intubation Response.

Introduction

The hemodynamic responses to laryngoscopy and endotracheal intubation have been recognized since 1951. Prof King et al (1951) documented myocardial ischemic changes due to reflex sympathoadrenal responses immediately following laryngoscopy and intubation with a mean increase in systolic pressure of 40 mm of Hg even in normotensive individuals. [1]

The induction of anaesthesia, laryngoscopy, tracheal intubation, and surgical stimulation often evoke cardiovascular responses characterized by alteration in systemic arterial blood pressure, heart rate and cardiac rhythm. The response following laryngoscopy and intubation peaks at 1. [2] Minutes and return to baseline within 5 to 10 minutes. [3] Even though the elevation in blood pressure and heart rate due to laryngoscopy and intubation are brief, they may have detrimental effects in high-risk patients including myocardial infarction, cardiac failure, intracranial hemorrhage and increases in intracranial pressure. [4] No single drug or technique is 100% efficient in attenuating intuabation response. [5] Since clonidine, lignocaine and esmolol have been known to blunt sympathetic responses to laryngoscopy and endotracheal intubation, their efficacy has been compared in this study.

Methodology

Institutional ethical committee approval was taken for this prospective, randomised, double blind study. Written informed consent was obtained from the patients. The study was conducted in 90 subjects aged between 15–65 years, ASA I and II patients undergoing elective surgeries under General Anaesthesia. Patients with Diabetes, Hypertension, Cardiovascular, respiratory or

neurological disorders and patients on beta-blockers or calcium channel blockers were excluded.

All the patients included in the study were given Tab. Alprazolam 0.5 mg and Tab. Pantoprazole 40 mg orally, on the night before surgery and was kept nil per oral 6 hours for solids and 2 hours for clear fluids before induction. On arrival to the operation theatre (O.T), intravenous (IV) access was taken using 18G intravenous cannula on the non-dominant hand and an infusion of normal saline was started.

The patient was connected with the multi-parameter monitor, which records heart rate (HR), non- invasive measurements of systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and continuous ECG monitoring and oxygen saturation (SpO_2). The baseline systolic blood pressure, diastolic blood pressure, mean arterial pressure, heart rate and oxygen saturation were recorded.

All the patient were pre-oxygenated with 100% oxygen for 3 minutes and pre-medicated with Inj. Midazolam (0.02 mg/kg body weight), Inj. Glycopyrrolate (0.01 mg/kg bodyweight), Inj. Fentanyl (1.5 mcg/kg body weight), Inj. Ondansetron (0.1mg/kg body weight) three minutes before induction. Group 1 was given intravenous Clonidine (2µg/kg body weight) ten minutes before induction. Group 2 was given intravenous Esmolol (1 mg/kg body weight) three minutes before intubation. Group 3 was given intravenous Lignocaine (1.5mg/kg body weight) three minutes before intubation. Induction of general anaesthesia for all patients was done with Injection Propofol 2mg/kg. This will be followed by an intubating dose of injection Vecuronium bromide 0.1mg/kg. Patients then were bag and mask ventilated for three minutes. Intubation condition was assessed by Krieg scale. [6]

Endotracheal intubation was done using appropriate size cuffed endotracheal tube. After confirming bilateral equal air entry, cuff inflated, tube fixed, connected to circuit and positive pressure ventilation continued. Recordings of HR, SBP, DBP, MAP and SPO_2 were taken at basal (before premedication), after induction, at laryngoscopy and intubation and at 1 min, 5min, and 10 min post intubation. Anaesthesia was maintained with Oxygen (33%) + Nitrous oxide (66%) + volatile anesthetic (sevoflurane or isoflurane) and further neuromuscular blockade was maintained using vecuronium bromide at a dose of 0.01mg/kg and IPPV. Adequacy of ventilation was monitored clinically and using SpO_2 monitoring.

Results

Table 1: Demography of the patients

Parameters	Group 1	Group 2	Group 3	P value
No. of patients	30	30	30	**-**
Age (years)	22.87 + 5.077	22.87+5.204	22.87+5.204	**1.00**
BMI(Kg/m^2)	24.5+ 1.757	24.00 +1.554	24.00 +1.554	**0.236**
Sex (M/F)	15/15	15/15	15/15	**-**
ASA Grade I	24	23	23	**0.935**
ASA Grade II	6	7	7	

Table 1 shows demographic data – age, BMI, gender and ASA grade which were comparable between the three groups.

Table 2: Distribution of subjects according to KREIG among three groups

	Group 1		Group 2		Group 3	
	N	**%**	**N**	**%**	**N**	**%**
KREIG I	24	80.0%	23	76.7%	24	80.0%
KREIG II	6	20.0%	7	23.3%	6	20.0%

P-value -0.935, there was no statistically significant difference found between three groups with respect to Kreig scale.

Table 3: Comparison of mean heart rate at various time interval

	Group 1			Group 2			Group 3			p-value
	Mean	**SD**	**% diff**	**Mean**	**SD**	**% diff**	**Mean**	**SD**	**% diff**	
Basal	85.2	14.2	-	92.4	15.6	-	83.9	14.8	-	0.063
After Induction	82.5	14.6	-3.1	84.0	13.2	-9.0	93.3	15.9	11.2	0.061
At Intubation	87.8	13.6	3.0	95.3	12.4	3.1	106.2	15.6	26.5	<0.001
1 min after Intubation	84.7	12.9	-0.5	89.5	11.0	-3.1	97.7	15.3	16.4	<0.001
5 min after Intubation	80.8	12.2	-5.1	87.5	12.3	-5.3	92.0	13.5	9.6	0.004
10 min after Intubation	76.4	11.2	-10.3	86.0	12.2	-6.9	87.1	13.9	3.8	0.002

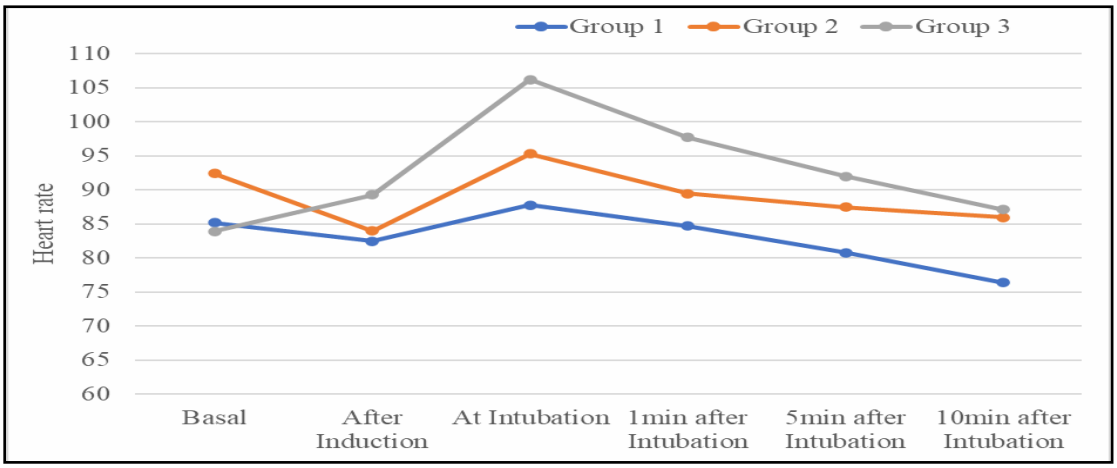

Figure 1:

In Group 1, highest HR recorded at the time of intubation was 87.80±13.60 and 1 minute after intubation was 84.70±12.90, which is significantly less when, compared to group 3. In Group 2, the highest HR recorded at the time of intubation was 95.30±12.4 and at 1 minute and at 5 minutes was 89.5±11.0 and 87.5±12.3 respectively which is significantly less when compared to group 3. In Group 3, HR was increased throughout induction and intubation compared to its baseline and when compared to Group 1. Highest HR in group 3 recorded at time of intubation was 106.2±15.6 and at 1 min after intubation was 97.7±15.3 was highest recorded HR when compared to group 2.

Table 4: Comparison of mean SBP at various time interval

	Group 1			Group 2			Group 3			P value
	Mean	SD	% Diff	Mean	SD	% Diff	Mean	SD	% Diff	
Basal	120.7	11.2	-	121.7	10.9	-	117.9	9.6	-	0.372
After Induction	102.1	21.4	-15.4	109.8	12.4	-9.8	108.8	10.5	-7.7	0.119
At Intubation	115.2	17.6	-4.6	124.6	13.8	2.4	133.1	16.2	12.9	<0.001
1 min after Intubation	108.2	16.0	-10.4	117.5	12.5	-3.5	120.3	16.0	2.0	0.006
5 min after Intubation	102.0	15.7	-15.5	112.7	10.0	-7.4	110.8	13.9	-6.0	0.006
10 min after Intubation	98.9	12.7	-18.1	111.5	9.3	-8.4	107.8	12.6	-8.6	<0.001

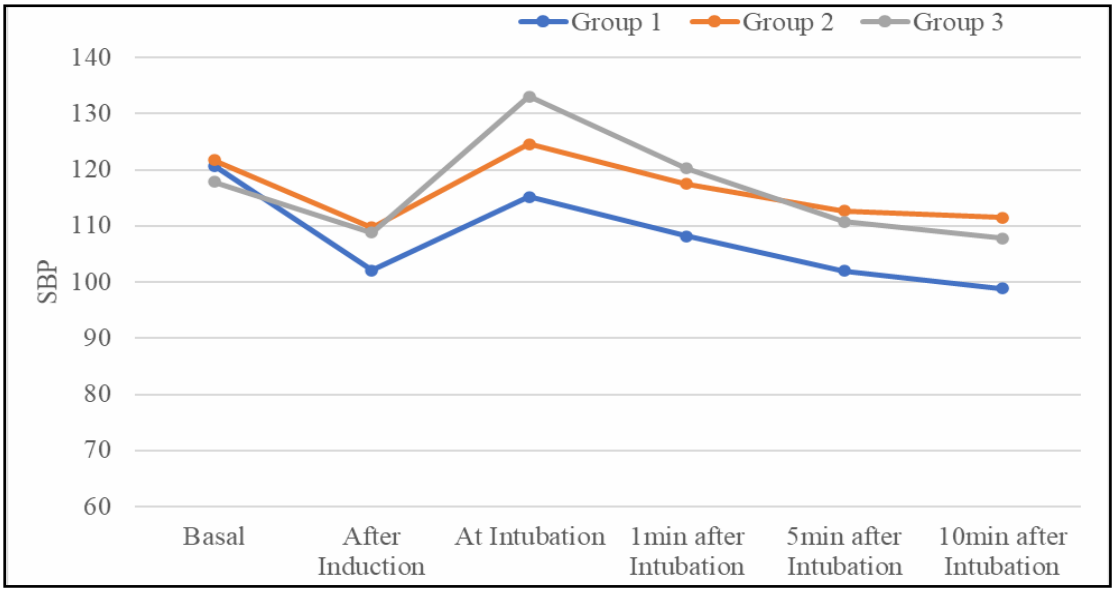

Figure 2:

There was no significant difference in baseline systolic blood pressure values (p=0.372) among the three groups. Even at induction, there was no difference in systolic blood pressure of all the groups (p =0.119). At intubation, there was a sudden increase in systolic blood pressures in all three groups. In Group 1, highest SBP was recorded at the time of intubation (115.20±17.6)

and 1 minute after intubation (108.2±16.00). In Group 2, the highest SBP was recorded at the time of intubation (124.60±13.80) and 1 minute after intubation (117.5±12.50). Highest SBP in group 3 was recorded at the time of intubation (133.10±16.20) and at 1 minute after intubation (120.30±16.00) which was the highest recorded SBP when compared to other groups.

Table 5: Comparison of mean DBP at various time interval

	Group 1			Group 2			Group 3			P value
	Mean	SD	% Diff	Mean	SD	% Diff	Mean	SD	% Diff	
Basal	81	9		80	8		78	8		0.509
After Induction	70	12	-13.6	75	10	-6.3	74	11	-5.1	0.203
At Intubation	80	15	-1.2	89	11	11.3	95	17	21.8	<0.001
1 min after Intubation	74	13	-8.6	83	8	3.8	84	13	7.7	0.003
5 min after Intubation	68	13	-16.0	78	8	-2.5	84	13	7.7	0.002
10 min after Intubation	65.63	11	19.0	76.8	7.4	4	73.3	13.0	6.02	<0.001

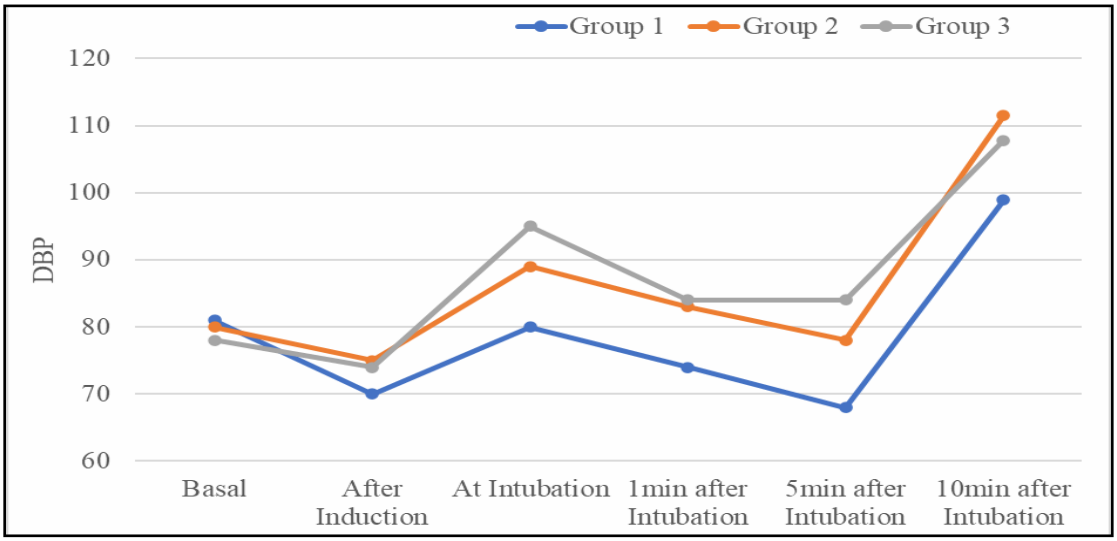

Figure 3:

There was no significant difference in baseline mean diastolic blood pressure among the three groups (p = 0.509). During induction of anaesthesia, groups did not show significant difference in diastolic blood pressure (p = 0.203). After intubation, there was a sudden increase in diastolic blood pressure in all the three groups. In Group 1, highest DBP was recorded at the time of intubation (80.00±15.00) and 1 minute after intubation (74.00±13.00). In Group 2, the highest DBP was recorded at the time of intubation (89.00±11.00) and 1 minute after intubation (83.00±8.00). Highest DBP in group 3 was recorded at the time of intubation (95.00±17.00) and at 1 minute after intubation (84.00±13.00) which was the highest recorded DBP when compared to other groups.

Table 6: Comparison of mean MAP at various time interval

	Group 1			Group 2			Group 3			P value
	Mean	SD	% Diff	Mean	SD	% Diff	Mean	SD	% Diff	
Basal	94	10		94	9		91	8		0.437
After Induction	81	15	-13.8	87	11	-7.4	85	11	-6.6	0.165
At Intubation	92	16	-2.1	101	12	7.4	108	16	18.7	<0.001
1 min after Intubation	85	14	-9.6	94	10	0.0	93	14	2.1	<0.001
5 min after Intubation	79	14	-16.0	90	9	-4.3	86	13	-5.5	0.003
10 min after Intubation	77	11	-18.1	88	8	-6.4	85	13	-6.6	<0.001

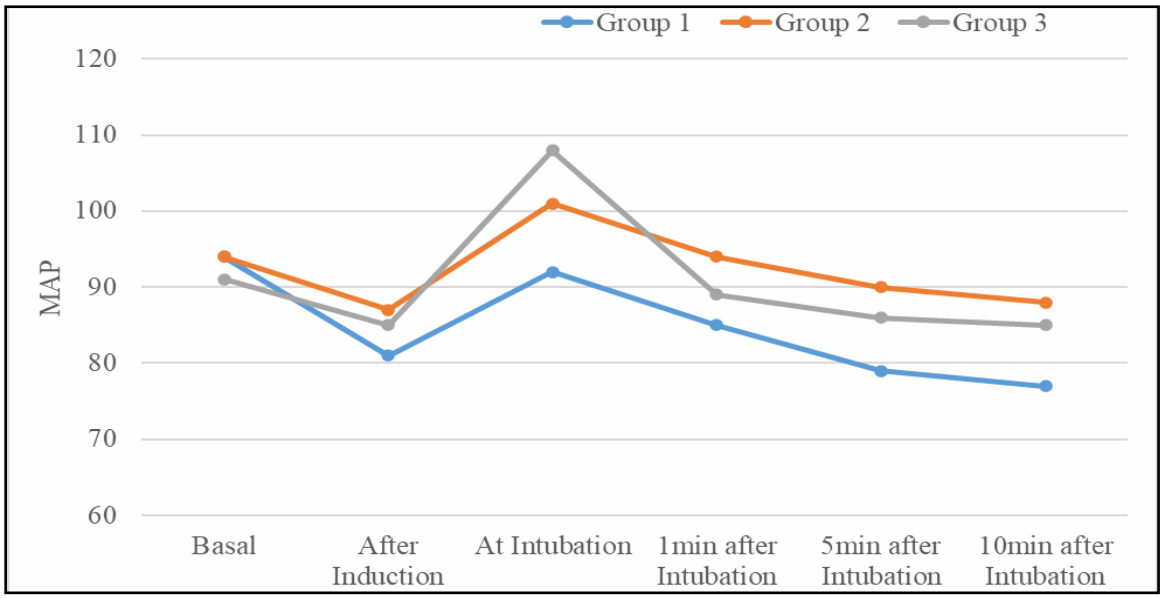

Figure 4:

There was no significant difference in baseline mean arterial pressure among the three groups (p=0.437). During induction of anaesthesia, the groups did not show significant difference in mean arterial pressure (p = 0.165). After intubation, there was a sudden increase in mean arterial pressures in all the three groups**.** In Group 1, highest MAP was recorded at the time of intubation (92.00±16.00) and 1 minute after intubation (85.00±14.00). In Group 2, the highest MAP was recorded at the time of intubation (101.00±12.00) and 1 minute after intubation (94.00±10.00). Highest MAP in group 3 was recorded at the time of intubation (108.00±16.00) and at 1 minute after intubation (93.00±14.00) which was the highest recorded MAP when compared to other groups.

Discussion

Laryngoscopy and endotracheal intubation produce hemodynamic stress responses characterized by hypertension and tachycardia. These neuroendocrine responses can cause a variety of complications in patients with cardiac disease due to imbalance of myocardial oxygen supply and demand like ischemic changes, ventricular arrythmias and cardiac failure. [7]

Many drugs have been reported to have beneficial effects in partially attenuating sympathoadrenal responses to endotracheal intubation. Injection lidocaine, esmolol, fentanyl, calcium channel blockers have been extensively studied by many authors. Alpha 2 agonist clonidine by oral route has also been observed to attenuate intubation response, but there are very few studies using intravenous clonidine.

Clonidine is a α2 adrenergic agonist, stimulates α2A subtype of α2 adrenergic receptors in the brainstem resulting in a reduction in sympathetic outflow from central nervous system thus causing lowering of arterial pressure by an effect on both cardiac output and peripheral resistance. By its central sympatholytic action, it tends to attenuate the hemodynamic response to any surgical nociceptive stimulus and to improve overall perianesthetic cardiovascular stability. [8]

Esmolol hydrochloride is a relatively new cardioselective, i.v. beta adrenoceptor antagonist. It has a rapid onset of action, exerts a peak haemodynamic effect within minutes and possesses a short elimination half-life of 9 min [9]. Consequently, it should prove ideal for control of the short-lived haemodynamic sequelae associated with laryngoscopy and intubation [10]. Lignocaine is one of the commonly used drug for reducing hemodynamic response and post-operative pain. Lignocaine has been administered in various forms like intravenous, gargle with viscous, spray and nebulization among patients undergoing intubation. Intravenous route was the most common route used in clinical practice and has been researched extensively. [11] The difference in heart rate between group 1 and group 3 matches with study conducted by Ghignone et al [12] (1987) which proved clonidine was more effective than lignocaine in attenuating pressor response to endotracheal intubation. Our study results with regard to heart rate matches with Vucevic et al [13] which proved efficacy of esmolol and Carabine et al [14] which proved the efficacy of clonidine. Inefficiency of lignocaine in attenuating rise in heart rate in our study can be explained by comparing it with Singh et al [15], Van der begh et al [16] and Kindlers et al [7] all of whom questioned lignocaine's efficacy. The heart rate in group 1 and group 2 stayed significantly lower than group 3 even at 5 minutes after intubation (p value

= 0.004), but in group 1 it stayed significantly lower than group 2 till 10 minutes after intubation (p value = 0.011). After 10 minutes there was no significant difference among group 2 and 3 (p value = 1.00) which can be explained by the short duration of action of esmolol. Thus, it is inferred that though clonidine and esmolol are equally effective in blunting rise in heart rate immediately following intubation, clonidine provides a better heart rate control over esmolol for a longer duration following intubation.

Group 1 had least rise in systolic blood pressure which when compared with group 2 (p value =0.039) and group 3 (p value <0.001) were statistically significant at intubation. Even after 5 minutes of intubation, group 1 differed from group 2 (p = 0.008) and group 3 (p=0.037) showing a sustained attenuation of pressor response. At 5 minutes and 10 minutes, there were no statistically significant differences in systolic blood pressure among groups 2 and 3 (p value 1.00 and 0.637 respectively). Probably due to shorter duration of action, group 2 could not show much difference from group 3 at 5 minutes and 10 minutes interval.

Attenuation of pressor responses by group 2 in our study matches with studies conducted by Yuan et al [17] and Helfman et al. [18] the difference between group 1 and group 2 matches with study conducted by Zalunardo MP et al [19] in 2001 which proved clonidine was more effective than esmolol in attenuating pressor response to endotracheal intubation. The difference between group 1 and group 3 matches with study conducted by Ghignone et al [12] (1987) which proved clonidine was more effective than lignocaine in attenuating pressor response to endotracheal intubation.

Group 1 had least rise in diastolic blood pressure which when compared with group 2 (p value=0.014) and group 3 (p value <0.001) were statistically significant at intubation. Even after 5 minutes, group 1 differed from group 2 (p value <0.001) and group 3 (p value <0.01) showing a sustained attenuation of pressor response. At 5 minutes and 10 minutes, there were no statistically significant difference in both diastolic blood pressure among groups 2 and 3 (p value 0.719 and 0.633 respectively). Again, probably due to shorter duration of action, group 2 did not show much difference from group 3 at 5 minutes and 10 minutes interval. Attenuation of pressor responses by group 2 in our study matches with studies conducted by Yuan et al [17] and Helfman et al [18]. The difference between group 1 and group 2 matches with study conducted by Zalunardo MP et al [19] in 2001 which proved clonidine was more effective than esmolol in attenuating pressor response to endotracheal intubation. The difference between group 1 and group 3 matches with study conducted by Ghignone et al [12] in 1987 which proved clonidine was more effective than lignocaine in attenuating pressor response to endotracheal intubation. Inefficiency of lignocaine in attenuating rise in SBP in our study can be explained by comparing it with Singh et al, [15] van der Begh et al [16] and Kindlers et al [7] all of whom questioned lignocaine's efficacy.

Group 1 had least rise in mean arterial pressure which when compared with group 2 (p value=0.016) and group 3 (p value <0.001) were statistically significant at intubation. Even after 5 minutes, group 1 differed from group 2 (p value 0.002) and group 3 (p value 0.049) showing a sustained attenuation of pressor response. At 5 minutes and 10 minutes, there were no statistically significant difference in both diastolic blood pressure and mean arterial pressure among groups 2 and 3 (p value 0.714 and 0.534 respectively). Again, probably due to shorter duration of action, group 2 did not show much difference from group 3 at 5 minutes and 10 minutes interval. Attenuation of pressor responses by group 2 in our study matches with studies conducted by Yuan et al [17] and Helfman et al [18]. The difference between group 1 and group 2 matches with study conducted by Zalunardo MP et al [19] in 2001 which proved clonidine was more effective than esmolol in attenuating pressor response to endotracheal intubation. The difference between group 1 and group 3 matches with study conducted by Ghignone et al [12] (1987) which proved clonidine was more effective than lignocaine in attenuating pressor response to endotracheal intubation. Inefficiency of lignocaine in attenuating rise in SBP in our study can be explained by comparing it with Singh et al, [15] van der Begh et al [16] and Kindlers et al [7] all of whom questioned lignocaine's efficacy.

Conclusion

Clonidine is found to be effective in blunting hemodynamic responses to laryngoscopy and intubation, followed by esmolol. Lignocaine was ineffective in attenuating the responses to laryngoscopy and endotracheal intubation.

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