Comparison of Effects of Nebulized Lignocaine and Intravenous Lignocaine on the Haemodynamic Response to Endotracheal Intubation

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Abstract:

Background: General anaesthesia with laryngoscopy and intubation activates the sympathoadrenal system, which can lead to untoward complications in patients. As general anaesthesia with endotracheal intubation is widely performed daily, various methods have been adopted to reduce this pressor response to laryngoscopy and intubation. The popular practice is the use of intravenous lignocaine. A nebulized form of lignocaine may be a better alternative to obtund the intubation response. **Methods:** After obtaining ethical committee approval, 196 eligible, consenting adult patients belonging to ASA I and II undergoing surgery under general anaesthesia in a tertiary teaching hospital were recruited and randomised into two groups— group A receiving 0.0375 ml/kg (1.5mg/kg) of nebulized 4% lignocaine and an equivalent volume of normal saline IV and group B receiving preservative-free 2% intravenous lignocaine 0.075 ml/kg (1.5mg/kg) and an equivalent volume of normal saline nebulization. **Results:** The parameters measured were SBP, DBP, MAP, HR, SpO2, duration of intubation and the number of attempts. The baseline vitals among both groups were comparable. At the time of intubation, the rise in all the haemodynamic parameters in group A was significantly lesser than that in group B with SBP of 129.48±7.9 and 134.08±11.55 (t= -3.256 p=0.001), DBP of 75.59±8.75 82.89±12.9 (t= -4.634 p= <0.001), MAP of 93.26±6.87 and 99.95±11.13 (t=5.066 p= <0.001), HR of 80.53±7.73 and 87.72±6.31 (t=7.136 p=<0.001) in group A and group B respectively. The mean duration of intubation was 15.96±3.04s and 16.15±3.55s (t= -0.41 p=0.681) respectively. There were no significant changes in SpO2 in either group. **Conclusion:** We conclude that the rise in haemodynamic response to laryngoscopy and intubation was significantly lower in the nebulized lignocaine group in comparison to the intravenous lignocaine group

Keywords: Nebulized lignocaine, Intravenous lignocaine, Laryngoscopy and intubation response.

Introduction

General anaesthesia with endotracheal intubation is a routine anaesthetic procedure for patients undergoing any surgery. Laryngoscopy and intubation are often associated with an increase in haemodynamic response. Sympathoadrenal response to tracheal intubation mainly arises from stimulation of the supraglottic area during the manoeuvres of elevation of the epiglottis for the exposure of the glottis[1]. Sympathetic stimulation during intubation leads to an elevation in the levels of catecholamine that circulates in the blood and manifests as an increase in heart rate and blood pressure[2]. It can also lead to arrhythmias and increased myocardial oxygen demand. This response is usually initiated within 5 s of laryngoscopy, it peaks in 1–2 min and normalizes in 5 min[3].

These are transient but can be detrimental in certain kinds of patients. In patients with existing co-morbidities like systemic hypertension, cardiovascular disease, and cerebrovascular diseases, the response is more pronounced and unpredictable and any increase in heart rate or blood pressure is deleterious, leading to increased morbidity and mortality.Various measures are undertaken to either minimize or completely abolish this response. It is usually difficult to completely abolish this response but can be attenuated to some degree.

Lignocaine is easily available and routinely used in operation theatres. Different studies have evaluated the effects of lignocaine on the haemodynamic response to intubation[4]. Most of these studies attempted to investigate the effect of intravenous lignocaine in comparison to other drugs or control groups. We aimed to compare the effects of nebulized lignocaine to intravenous lignocaine in attenuating haemodynamic response during laryngoscopy and endotracheal intubation.

Procedure

1.1 Sample Size Calculation

The sample size was calculated based on the data collected by Jokar et al.[5] with a level of significance of 5% and assuming a power of 80%Sample size was found to be 196 with 98 study subjects in each group.

1.2 Patient selection

This trial was in concordance with the Declaration of Helsinki. After obtaining approval from the Institutional Human Ethics Committee and written informed consent, 198 ASA I and II adult patients aged 18–60 years scheduled for surgeries under general anaesthesia in a tertiary care teaching hospital were included in the study. Patients with known allergy to lignocaine, respiratory tract infection, pregnancy, anticipated difficult airway, on medications that affect the cardiovascular response, conduction abnormality in ECG, uncooperative patients, inability to mask ventilate, duration of laryngoscopy and intubation more than 20 s and those who

refused to consent were excluded from the study. 196 patients were randomly divided into two groups (98 patients each) using a computer-generated randomization code and allotted through sequentially numbered opaque envelopes.

1.3 Plan of anaesthesia

Institutional protocol for fasting and premedications were followed. Group A was nebulization group and Group B was intravenous group. Saline was used in both groups i.e. nebulization group received intravenous saline and the intravenous group received saline nebulization to aid blinding. Baseline vitals were recorded in the preoperative room. Here, the patients were given 0.0375 ml/kg (1.5mg/kg) of nebulized 4% lignocaine (group A) or equivalent volume of normal saline (group B) 5 minutes prior to shifting to the operation theatre by a preoperative nurse. Inside the operation theatre minimum standard and required monitors were attached. Preoxygenation with 100% oxygen was done for 3 minutes. Induction of anaesthesia was with intravenous fentanyl 2 mcg/kg followed by propofol 2 mg/kg followed by the muscle relaxant vecuronium 0.1 mg/kg. Preservative-free 2% intravenous lignocaine 0.075 ml/kg (1.5mg/kg) (group B) or equivalent volume of normal saline (group A) was injected 90 s before the laryngoscopy by the consultant anaesthesiologist. Laryngoscopy with an appropriate size Macintosh blade was carried out by the consultant anaesthesiologist and the patient was intubated with an appropriate-sized endotracheal tube. The parameters were recorded by the investigator who was blinded. From the time of inducing the patient, the following parameters were recorded every minute for 15 minutes. The parameters that were recorded were systolic blood pressure, diastolic blood pressure, mean arterial pressure, heart rate, SpO2, number of attempts, duration of laryngoscopy and intubation. Intubation time was defined as time from insertion of the laryngoscope, introduction of the endotracheal tube to removal of the laryngoscope blade. Intubation time of more than 20s was excluded from the study. An “Attempt” was defined as insertion of the laryngoscope blade. Patient was not disturbed for 10 min following intubation. There were no changes in the anaesthetic management and no surgical interventions during this period. Further maintenance and reversal of anaesthesia were done according to routine methods followed in the institution and according to the requirements of the surgery.

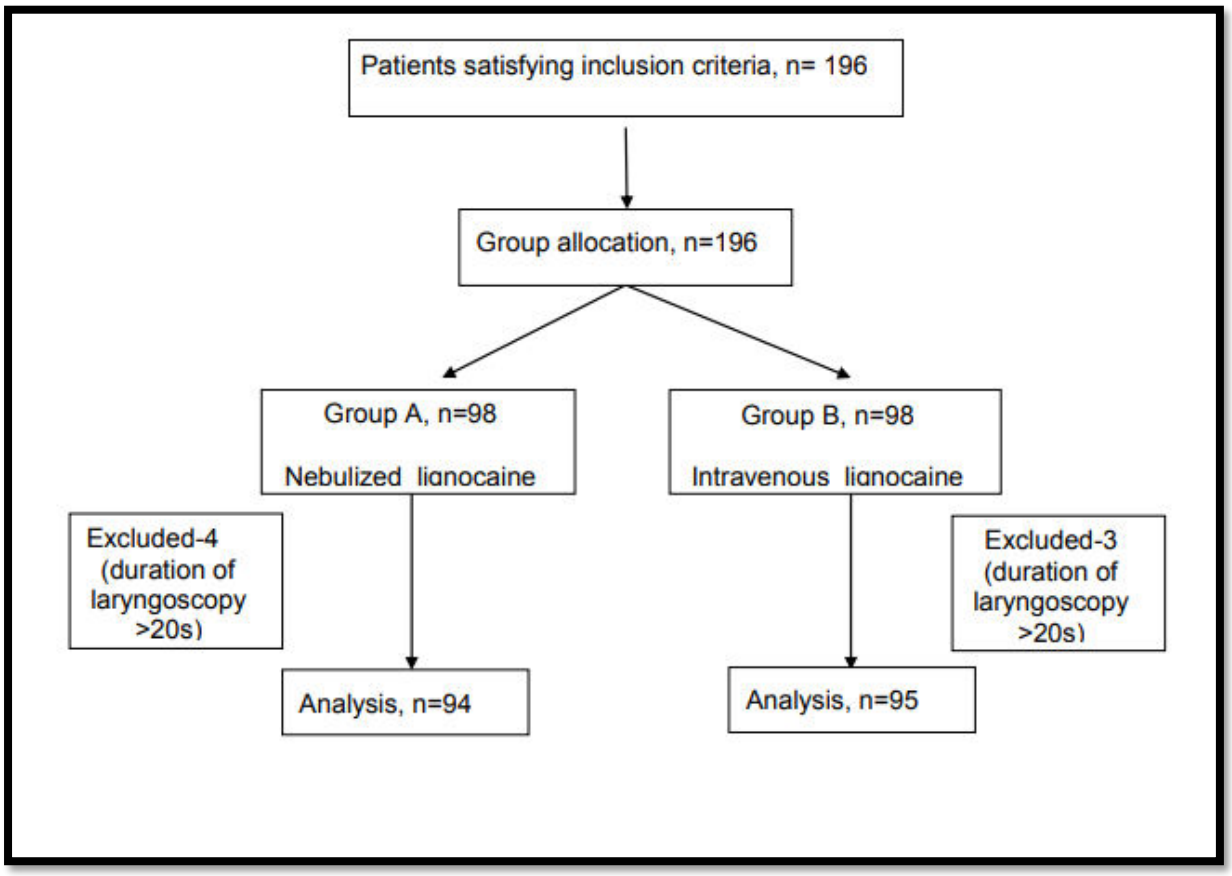
Statistical analysis

Qualitative variables were presented using frequency or percentages. Quantitative data were presented using mean, standard deviation, and confidence interval. The data were compared using Student’s t-test and Chi-Square test. A *p*-value of <0.05 was considered statistically significant. Statistical Package for the Social Sciences (SPSS) software version 25 was used for data analysis.

Results

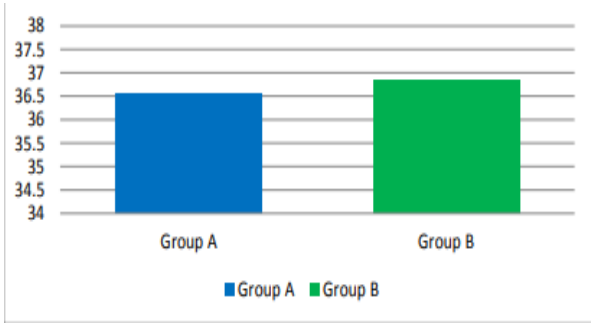
A total of 196 patients between the ages of 18 and 60 years were included in the study divided into 2 groups of 98 each in nebulized lignocaine group and intravenous lignocaine group. *p*-value < 0.05 was considered statistically significant.

Figure 1- Consort Flow Chart

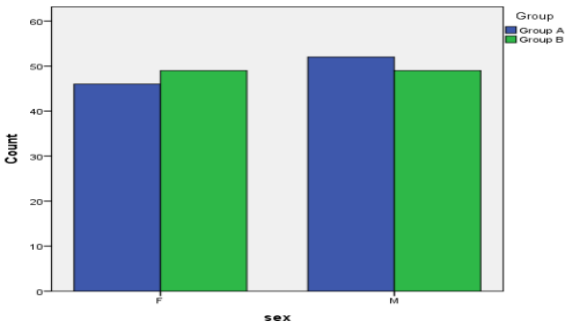


Mean of the age was about 36 years and was comparable between group A and group B. Mean age difference between the groups were not statistically significant. It was observed that 46.9% of the study participants were female and 53.1% were male in group A whereas in group B, 50% and 50% were female and male respectively. Statistically the difference between the genders were not significant.

Figure 2- Demographic details- (a) Age; (b) Gender



a



b

Table 1- Types of surgeries

Procedure	**Group A (*t*)**	**Group B (*t*)**	**TOTAL**
Craniotomy	0	1	1
FESS	20	16	36
Hemithyroidectomy	3	0	3
Modified Radical Mastoidectomy	8	15	23
Tympanoplasty	24	23	47
Fibroadenoma excision	1	0	1
Septoplasty	27	29	56
Total thyroidectomy	11	11	22
TOTAL	94	95	189
Chi- Square Tests			
Pearson Chi-Square	**Value**	**df**	***p*- value**
	11.407	10	0.327

It was observed that baseline SBP, DBP, MAP, HR and SpO2 were comparable in both groups.

Table 2- Baseline Vitals

Baseline Vitals	**Column A (*t*)**	**Column B (*t*)**	**t**	***p*- Value**
SBP	124.14±8..68	122±10.35	1.249	0.213
DBP	71.08±10.59	69.1±7.33	1.521	0.13
MAP	86.66±9.08	86.94±6.89	1.495	0.137
HR	74.8±9.41	76.13±8.89	-1.022	0.308
SpO_2	100±0	100±0		

The rise in SBP and DBP was significantly lesser in group A compared to group B during the minute of intubation and remained so for the next 6 min.

Figure 4- Intraoperative Systolic Blood Pressure showing a rise immediately post-intubation

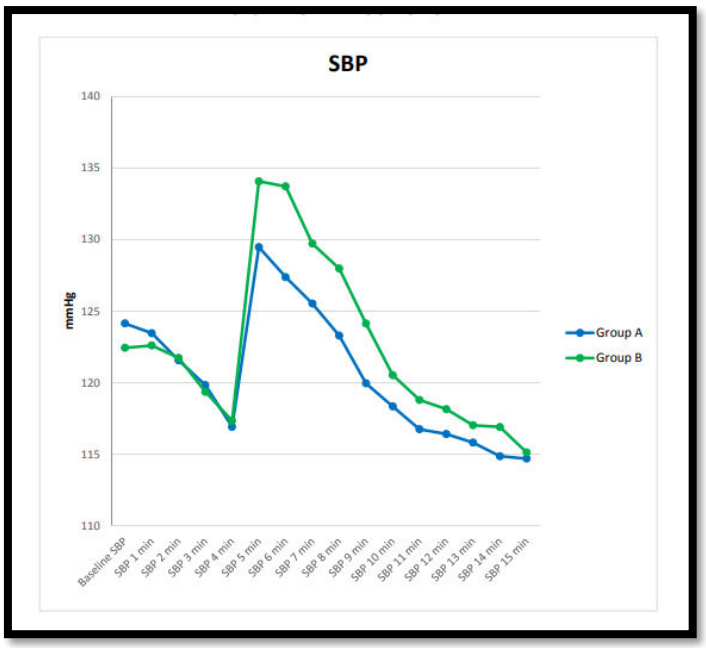
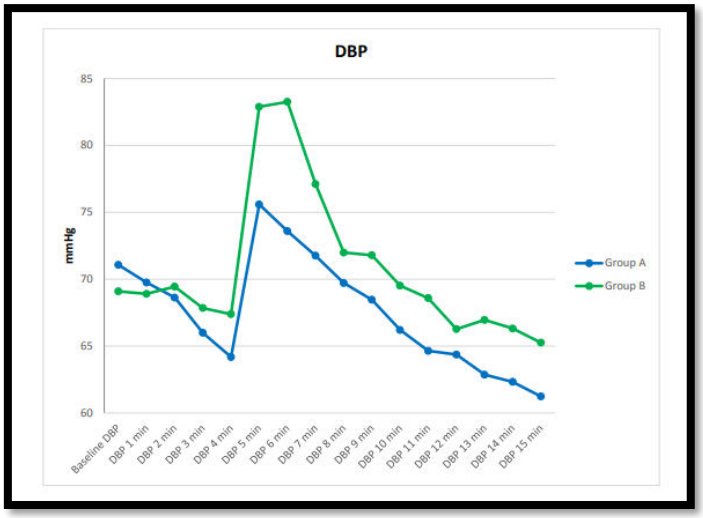
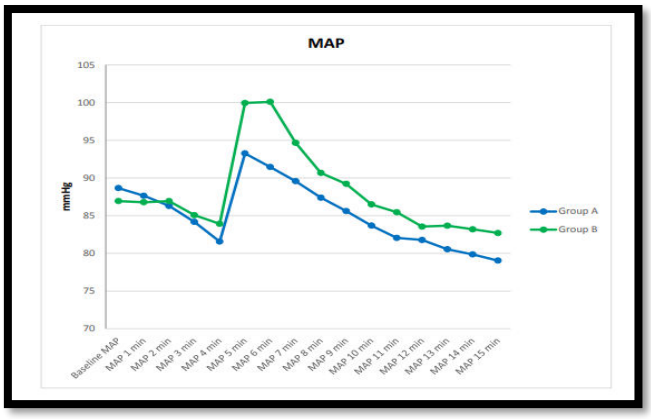


Figure 5- Intraoperative Diastolic Blood Pressure



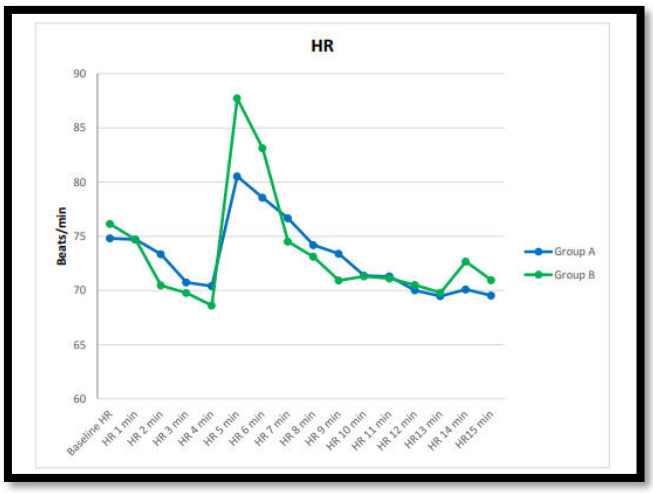
The MAP in Group A was lesser compared to Group B post-intubation.

Figure 6- Intraoperative Mean Arterial Pressure



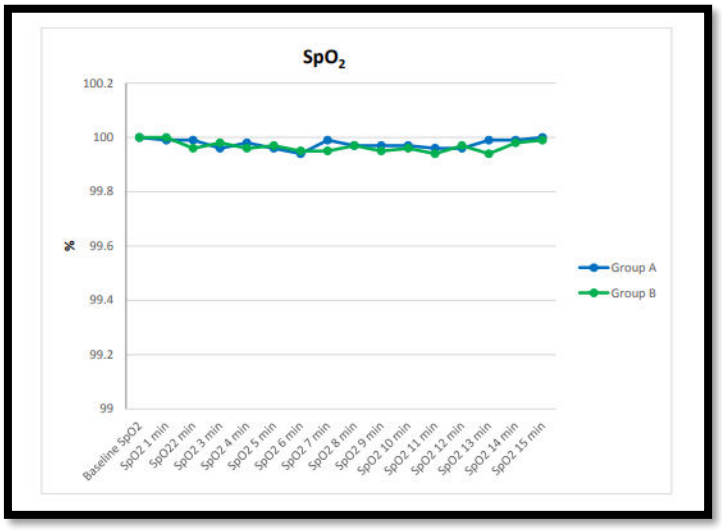
The HR was comparatively lesser in Group A compared to Group B immediately after intubation and statistically significant.

Figure 7- Heart Rate



It was observed that there was no desaturation in any patient.

Figure 8- Oxygen Saturation



Mean and SD of duration of intubation (s) were 15.96 and 3.04 in Group A where as in Group B, mean and SD of age were 16.15 and 3.55. Mean duration of intubation between the groups was not statistically significant.

Table 3: Duration of intubation

Duration of intubation (s)	Group A (N=94)	Group B(N=95)	t	P VALUE
	15.96±3.04	16.15±3.55	-0.411	0.681

The number of single attempts in both the groups were same for 185 patients. 4 patients required 2 attempts of intubation.

Table 4: Number of Intubation attempts

		Group		Total
		Group A N (%)	Group B N (%)	
Number of attempts	1	92 (98%)	93 (98%)	185 (98%)
	2	2 (2%)	2 (2%)	4 (2%)
Total		94 (100%)	95 (100%)	189 (100%)

Discussion

The commonest procedure for most patients undergoing general anaesthesia is endotracheal intubation with positive pressure ventilation. Hence intubation and its response become an inevitable issue for all the cases undergoing such procedure. Performing laryngoscopy and intubation causes activation of sympathoadrenal response. The mechanism of this response is not completely clear but may be attributed to the stretching and tissue tension produced in the epipharynx and laryngopharynx during laryngoscopy. This noxious stimulus produces a wide spectrum of haemodynamic and stress responses such as tachycardia, hypertension, laryngospasm, bronchospasm, raised intracranial pressure and intraocular pressure, etc.

The response is initiated as early as 5 s after laryngoscopy, peaks in 1–2 min, and returns to normal levels within 5 min. This might be well tolerated in normal healthy individuals but the response may be exaggerated and detrimental in patients with hypertension, coronary artery disease, cerebrovascular disease, raised ICP, raised IOP,

etc. It can lead to harmful effects like myocardial ischaemia, ventricular dysrhythmias, ventricular failure and pulmonary oedema. It can also lead to cerebrovascular accidents in patients with known cerebrovascular disease.

The methods adopted are a reduced duration of laryngoscopy, deeper planes of anaesthesia, inhalational anaesthesia, and intravenous drugs. Intravenous lignocaine has been compared to various other intravenous agents. We aimed to compare the effects of intravenous lignocaine to 4% nebulized lignocaine on the haemodynamics to laryngoscopy and intubation and conducted this study in 196 ASA 1 and 2 patients posted for elective surgeries under general anaesthesia with endotracheal intubation.

Stoelting[6] found that this response can be minimal when limited to short and fast durations of laryngoscopy ideally < 15 s in combination with lignocaine. We excluded cases which required >20 s from our study. We selected ASA I and II patients and excluded those with any cardiovascular or cerebrovascular diseases so the implementation of the study protocol would not result in any undesired adverse effects. Bedford et al.[7] in their study showed that administration of lignocaine 1.5 mg/kg about 1.5 min produces a mean blood lignocaine level of 3.2 μg/ml before laryngoscopy and intubation which had sufficiently prevented cardiovascular response. Veigas and Stoelting[8] have shown that the blood lignocaine levels after laryngotracheal instillation gradually reached a peak of 1- 2.7 μg/ml at 4 –15 min after the instillation. The patients in group B were hence given 1.5 mg/kg of lignocaine 90 s before laryngoscopy and intubation. Hence, after the nebulisation was given it was made sure that the process of intubation was carried out within 15 min.

Independent t-test and chi-square test were used for statistical analysis. *p*-value < 0.05 was considered statistically significant. These mean age, gender and other demographic variables were comparable in both groups. The baseline vitals were also comparable in both groups with no statistically significant difference. The mean SBP at the minute of intubation was significantly lower in group A (129.48±7.9) when compared to group B (134.08±11.55). The rise in SBP following intubation was significantly less in group A in comparison to group B for 6 mins following intubation. The mean HR at the time of intubation was significantly lower in group A (80.53±7.73) when compared to group B (87.72±6.31) and remained so till the 3rd min post-intubation. This was similar to the study conducted by Venus et al.[9] where aerosolized lignocaine had significantly lower SBP and HR at intubation till 5 min following it compared to the control group which received aerosolised saline. The changes in heart rate were also similar to the study done by Ganesan et al.[10].The increase in HR at intubation was more with intravenous lignocaine compared to nebulized lignocaine which was statistically significant ($p< 0.05$). The HR in group A attained the baseline values at the 4th min post-intubation. The mean DBP at the time of intubation was significantly lower in group A (75.59±8.75) compared to group B (82.89±12.9) which remained significantly lower till the 6th min post-intubation. There was a rise in the DBP in both the groups post-intubation which came down to the baseline value at the

3rd min post-intubation in the nebulisation group and the 4th min in the intravenous group. This was similar to the study conducted by Ganesan et al.[10] wherein both the groups reached the baseline value in the 2nd min post-intubation. The mean MAP was lower in group A (93.26±6.87) when compared to group B (99.95±11.13) at the minute of intubation continuing for 10 min and this was statistically significant. Jokar et al.[5] in their study told that the MAP in the nebulized lignocaine group was lower in comparison to the intravenous group but the difference was not significant and the average reduction in MAP over time was faster in the nebulized group as compared to the control group. Lee et al.45 conducted a study where 10% lidocaine spray was used either on the laryngoscope blade or on the trachea. They found that MAP at 1 min post-intubation was significantly lower in the group where lidocaine was used than in the group where it wasn't. Our study also showed similar results where both the groups had lower MAP 1 min post intubation with the nebulization group having lesser MAP than the intravenous group. There was no significant hypotension in either of the groups but SBP, DBP, MAP and HR remained lower than the baseline value in both groups, the values of which were similar in both groups at the end of 10 min post-intubation. In a study conducted by Venus et al.[9], the incidence of PVCs was lesser in the nebulised lignocaine group in comparison to the saline group. In our study, there were no adverse effects seen with either of the groups, a possible reason being the inclusion of ASA 1 and 2 patients and the use of 4% lignocaine given according to body weight rather than a fixed volume for all patients.

The possible mechanism of attenuation with lignocaine nebulisation is blockade of vagal receptors and reduction of reflex sympathetic discharge along with the systemic absorption which probably provided an added effect and hence better attenuation of the sympathoadrenal response to laryngoscopy.

Conclusion

In this study, we found that the rise in the haemodynamics with nebulized lignocaine in comparison to intravenous lignocaine following laryngoscopy and intubation was significantly lesser. As this response is an inevitable part of intubation, among the various methods tried to attenuate it, nebulized lignocaine is a better, safer and easily accessible alternative in comparison to intravenous lignocaine.

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