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A COMPARATIVE OBSERVATIONAL STUDY OF THE EFFICACY OF ORAL CLONIDINE AND 10% LIGNOCAINE OROPHARYNGEAL SPRAY IN ATTENUATING THE HAEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION

Anaesthesiology

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ABSTRACT

Background: Laryngoscopy and tracheal intubation during anaesthesia can trigger significant sympathoadrenal responses, such as tachycardia and hypertension, leading to severe complications like pulmonary edema or cerebral aneurysm rupture. Managing these hemodynamic responses is critical, especially in patients with conditions like hypertension or coronary artery disease. Various interventions, including topical lignocaine, intravenous fentanyl, and beta-blockers, are used to mitigate these effects. This study compares the effectiveness of oral clonidine and 10% lignocaine spray in reducing the hemodynamic response associated with endotracheal intubation. **Methodology:** A comparative observational study was conducted on 52 ASA grade 1 and 2 patients, aged 20-60 years, scheduled for elective surgery under general anaesthesia with endotracheal intubation at A.J. Institute of Medical Sciences & Research Centre, Mangalore, over 24 months. Patients were randomly assigned to receive either oral clonidine (4-5 μg/kg) in Group A or 10% lignocaine spray in Group B. The primary outcomes measured were systolic and diastolic blood pressure, heart rate, and mean arterial pressure, with postoperative sedation assessed as a secondary outcome. Statistical analysis was performed using t-tests, ANOVA, and chi-square tests. **Results:** Before induction, the Clonidine group had significantly lower systolic blood pressure (SBP) compared to the Lignocaine group ($P = 0.019$). At 1, 3 and 5minutes post-intubation, SBP, diastolic blood pressure (DBP), and heart rate (HR) were consistently lower in the Clonidine group, with significant differences ($P \leq 0.001$). xiv Mean arterial pressure (MAP) was also significantly lower in the Clonidine group at these time points ($P \leq 0.05$). **Conclusions:** Oral clonidine (4–5 μg/kg) was more effective than 10% lignocaine spray in maintaining stable hemodynamic parameters during laryngoscopy and intubation. While both drugs had similar effects before induction and during laryngoscopy, the clonidine group returned to baseline hemodynamic parameters by the 5th minute, whereas the lignocaine group experienced significant increases.

KEYWORDS

Laryngoscopy and Endotracheal Intubation, Hemodynamic response, Oral clonidine, 10% lignocaine spray (ASA - American Society of Anesthesiologists, SBP - Systolic Blood Pressure, DBP - Diastolic Blood Pressure, HR - Heart Rate, MAP - Mean Arterial Pressure)

INTRODUCTION

Hemodynamic fluctuations in the form of elevation of systolic and diastolic blood pressure as well as elevated heart rate are seen during intubation. These changes are seen when the tip of the laryngoscope blade touches the base of the tongue for lifting the epiglottis[1].

Airway instrumentation provides an intense noxious stimulus via vagal and glossopharyngeal afferents resulting in a reflex autonomic activation, which is usually manifested as hypertension and tachycardia in adults and adolescents; in infants and small children, autonomic activation may result in bradycardia[2].

Direct laryngoscopy and intubation can lead to increase in heart rate and blood pressure by 20-27% and 30-50% respectively. The hemodynamic response is directly proportional to force exerted to expose glottis[2].

This hemodynamic response is seen seconds after direct laryngoscopes and increases after intubation. It is first seen within 5 s of laryngoscopes, reaching maximum in 45 seconds and normalizes by 5 mins and is proportional to the time taken for intubation[2]

Numerous pharmacological agents have been tried to attenuate this undesired hemodynamic response.

Hemodynamic fluctuations, higher myocardial oxygen demand and cardiac arrhythmia are undesirable and inevitable side effects of laryngoscopy and endotracheal intubation. This can be harmful in patients with coronary artery disease, valvular heart disease, raised intracranial pressure and cerebrovascular disease[3].

Clonidine, an imidazole compound is a selective agonist for α2 adrenoceptors with a ratio of 200:1(α2:α1). Though primarily an antihypertensive, clonidine has been increasingly used for premedication[4].

Clonidine primarily acts on alpha-2 adrenergic receptors in the central nervous system. These receptors are located in the brainstem, particularly in the locus coeruleus. Activation of these receptors inhibits the release of norepinephrine, leading to decreased sympathetic outflow[4].

By stimulating alpha-2 receptors, clonidine reduces the release of norepinephrine and other neurotransmitters involved in the sympathetic nervous system. This results in lower levels of circulating catecholamines (e.g., epinephrine and norepinephrine), which can lead to decreased heart rate and reduced vascular tone[4].

The attenuation of sympathetic outflow by clonidine helps in decreasing the blood pressure and heart rate. This is particularly beneficial during the stress of laryngoscopy and intubation, which often provoke an increase in these parameters due to sympathetic stimulation[4].

During laryngoscopy and endotracheal intubation, there is a reflex sympathetic surge that can cause a transient rise in blood pressure and heart rate. Clonidine helps blunt this response by stabilizing the sympathetic nervous system's reaction to stress[4].

The inhibition of the release of Norepinephrine by the action of Clonidine on alpha-2 receptors results in diminished activity of central nervous system there by resulting in sedative effect[4]

Lignocaine is an amide (-NHCO-) synthetic local anaesthetic. It primarily acts by blocking voltage-gated sodium channels in the neuronal cell membrane. This inhibition prevents sodium ions from entering the nerve cells, which is essential for the initiation and propagation of action potentials. By blocking these channels, lignocaine effectively prevents nerve signal transmission and provides local anaesthesia[5].

By attenuating the pain and reflex responses, lidocaine spray helps to reduce the increases in heart rate and blood pressure commonly seen with laryngoscopy and intubation. This is particularly beneficial in patients with pre-existing cardiovascular conditions or those who are at higher risk of adverse hemodynamic events[6].

Lidocaine spray helps to mitigate the hemodynamic response to laryngoscopy and intubation by providing local anaesthesia that reduces sensory input, reflexive responses, and overall stress, thereby leading to a more stable cardiovascular response during the Laryngoscopy and Endotracheal intubation[7]

The aim of this study is to compare the efficacy of oral clonidine versus lignocaine spray in attenuating the hemodynamic responses associated with laryngoscopy and endotracheal intubation to identify the superior approach in management of hemodynamic stability in patients undergoing these Laryngoscopy and endotracheal intubation.

Aims And Objectives Of The Study

Aim: The aim of this study is to compare the efficacy of oral clonidine versus lignocaine spray in attenuating the hemodynamic responses associated with laryngoscopy and endotracheal intubation by evaluating the following outcomes.

Primary Outcome:

1. Systolic Blood Pressure
2. Diastolic Blood Pressure
3. Heart Rate
4. Mean Arterial Pressure.

Secondary Outcomes:

Post-operative sedation using Ramsay sedation scale.

MATERIALS AND METHODS

Source Of Data

Study was approved by the Institutional ethical committee and was done among 52 patients aged between 20years -60years scheduled for elective surgery under GA with Endotracheal intubation admitted at A.J. Institute of Medical Sciences & Research Centre, Mangalore over a period of 24 months (July 2022-July 2024) were included in the study.

Study Design

It was an observational, analytical, group comparative study. We assigned the subjects into two groups randomly based on random number allocation system generated by the random number, computer generator applications. Informed consent was taken before the commencement of the study and the patient data was kept confidential. The data was recorded after intervention by the observer.

Selection Criteria

Inclusion Criteria

In this study, we have included adult patients aged between 20 to 60 years of age belonging to ASA grade 1 and 2 of either gender with normal baseline laboratory investigations undergoing surgical procedures under general anaesthesia requiring endotracheal intubation were included in the study.

Exclusion Criteria

We excluded the patients who refused to participate in the study, those belonging to ASA 1 and 2 whose condition was deteriorated ,those with history of Smoking and alcohol, those with cardiovascular disease, bronchospastic disease, cerebrovascular disease, peripheral vascular disease, hepatic and renal impairment, diabetes mellitus, morbid obesity, anticipated difficult airway, those taking vasoactive drugs and beta blockers that are known to affect heart rate, blood pressure or hormonal stress responses, were excluded from the study.

Sample Size

On the basis of the study done by **King et al**[1], to detect a mean difference of Mean Arterial Pressure of 8.9mm of hg after intubation response when checked at 5th minute between control and study groups for suppression of laryngoscopic response.

α=0.05

1-β=90%

Standard deviation (SD) = 8.9mm hg

$$\text{Sample size} = \frac{2SD^2(Z_{\alpha/2}+Z_{\beta})^2}{d^2}$$

Based on this we have calculated the sample size for this study. Further assuming 10% attrition rate, final sample number estimated was 26 patients in each group. Hence, we have included a total of 52 individuals for study.

Sampling Technique

All the patients who were taken up for all elective surgeries under General Anaesthesia meeting the inclusion criteria until the sample size was met were chosen based on convenience sampling.

Study Variables

1. Age
2. Gender
3. ASA GRADE
4. BMI
5. Time taken for Laryngoscopy
6. Type of Laryngoscopy

Variables

Primary Outcome:

1. Systolic blood pressure
2. Diastolic blood pressure
3. Heart rate
4. Mean Arterial Pressure

Secondary Outcome:

Postoperative sedation using Ramsay sedation score

Study Tools

1. Proforma
2. Ramsay sedation scale

Study Procedure And Methodology

A detailed pre-anaesthetic assessment was performed, documenting demographics, baseline vitals, and lab results. Written informed consent was obtained from all patients. Subjects were randomly assigned to two groups:

- Group A: Premedicated with T. Clonidine 100mcg, 2 hours before surgery.
- Group B: Received 10% Lignocaine spray on the posterior pharyngeal wall, 2 minutes before tracheal intubation.

Anaesthesia Procedure

On the day of surgery, intravenous access (18G) was secured, and baseline vitals were recorded after connecting non-invasive monitors. Standard general anaesthesia induction was performed using preoxygenation, midazolam (1mg IV), fentanyl (1-2 mcg/kg IV), and propofol (2 mg/kg IV). After muscle paralysis with vecuronium (2*ED95 dose), patients were intubated using a size 3 or 4 Macintosh blade and PVC tracheal tube (7.0mm for females, 8.0mm for males). Bilateral air entry was confirmed with 5-point auscultation, and ventilation was maintained using oxygen-nitrous oxide (33%/66%) and sevoflurane (1-2% for MAC 1.2-1.5). Muscle relaxation was sustained with cis-atracurium or vecuronium (0.1mg/kg IV). Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MABP), and heart rate (HR) were monitored every 3 minutes.

Parameters Observed

1. Systolic Blood Pressure (SBP)
2. Diastolic Blood Pressure (DBP)
3. Mean Arterial Pressure (MABP)
4. Heart Rate (HR)
5. Ramsay sedation score

Statistical Analysis

Statistical analysis was conducted with GraphPad Prism 10.0. Data normality was checked with the D'Agostino & Pearson test. Continuous variables were analyzed using t-tests or Mann-Whitney U tests, and repeated measures were evaluated with ANOVA or Kruskal-Wallis tests. Post-hoc analysis used Tukey's or Dunn's test. Categorical variables were analyzed using Chi-square or Fisher's exact tests. Pearson's test was used for correlations ($P < 0.1$), and significance was set at $P < 0.05$. Multivariable analysis included age, gender, ASA grade, surgery type, and premedication type, with odds ratios calculated for predictors. The model was considered adequate if the Goodness of Fit test had $P > 0.05$.

RESULTS

The present study was an interventional study conducted in the department of anaesthesiology of tertiary care Hospital-A. J institute of medical sciences after obtaining permission from institutional ethics committee and department of anaesthesiology.

58 patients undergoing surgery under general anaesthesia were

evaluated for the study. Out of them, 6 patients refused to participate in the study. The remaining 52 were analysed as per protocol and randomized into two groups.

The groups did not differ by age, gender, BMI, ASA status, Time of Laryngoscopy and Type of Laryngoscopy. Baseline vitals were comparable.

Both groups received similar anaesthetic techniques with respect general anaesthesia. Baseline vitals were analysed for distribution using Shapiro Wilk test and found normally distributed.

Primary parameters like SBP, DBP, HR and MAP were studied and compared within the group and between the two groups using various statistical analysis and P values were obtained.

Secondary parameters like Ramsay sedation score were studied within the clonidine group.

The parameters were compared within the group at different time intervals using repeat measure of ANOVA and P value obtained. Between the groups, the parameters were compared using t tests.

Variables

1. Age Comparison:

Clonidine group had a mean age of 53.04 ± 6.90 years, while Lignocaine averaged 51.54 ± 5.60 years. The age data was normally distributed, and the unpaired t-test with Welch's correction showed no difference which was statistically significant between the groups (P = 0.39) as shown in Table 1.

Table 1: Mean age of participants

	Number	Mean	SD	t	P value
Clonidine	26	53.04	6.9	0.85	P = 0.39
Lignocaine	26	51.54	5.6		NS

2. Gender Distribution:

In Clonidine group, 65.40% were males and 34.60% were female. Lignocaine group comprised 34.60% males and 65.40% females. Fisher's exact test revealed significant difference in sex distribution (p = 0.02) as shown in Table 2.

Table 2: Distribution of participants according to gender between the groups

	Clonidine		Lignocaine		Total	P value
	Number	Percentage	Number	Percentage		
Males	17	65.4	17	65.4	26	P = 0.9
Females	9	34.6	9	34.6	26	
Total	26	100	26	100	52	

3. American Society of Anaesthesiologists (ASA) Status:

In Clonidine, 38.50% were classified as ASA 1 and 61.50% as ASA 2. Lignocaine group had 50% classified as ASA 1 and 50% as ASA 2. Chi-square test revealed no significant difference in ASA status distribution (P = 0.40) as shown in Table 3.

Table 3: Distribution of participants according to ASA physical status

	Clonidine		Lignocaine		Total	P value
	Number	Percentage	Number	Percentage		
ASA I	10	38.5	13	50	23	P =
ASA II	16	61.5	13	50	29	0.4
Total	26	100	26	100	52	NS

4. Body Mass Index (BMI):

Clonidine had a mean BMI of 24.84 ± 3.50 kg/m², while Lignocaine group averaged 26.88 ± 4.30 kg/m². Unpaired T test showed no significant difference (P = 0.07) as shown in Table 4.

Table 4: Comparison of mean Body Mass Index of participants between the groups

	Number	Mean	SD	t	P value
Clonidine	26	24.84	3.5	-1.83	P = 0.07
Lignocaine	26	26.88	4.3		NS

5. Time taken for Laryngoscopy:

Clonidine group had a mean time taken for Laryngoscopy as 12.12 ± 2.20 seconds, while Lignocaine group averaged 9.85 ± 1.20 seconds. Unpaired T test showed no significant difference (P = 0.***) as shown in Table 5.

Table 5: Comparison of Mean time taken for Laryngoscopy

	Number	Mean	SD	t	P value
Clonidine	26	11.12	2.2	4.51	P = 0.06
Lignocaine	26	10.85	1.2		

6. Type of Laryngoscopy:

In Clonidine group, direct laryngoscopy was performed in 57.7% and Video laryngoscopy in 42.3% of the patients while Lignocaine group has 42.30% patients who underwent Direct Laryngoscopy and 57.7% of patients where Video laryngoscopy was used. Chi-square test revealed no significant difference in ASA status distribution (P = 0.40) as shown in Table 6.

Table 6: Distribution of participants according to type of Laryngoscopy

	Clonidine		Lignocaine		Total	P value
	Number	Percentage	Number	Percentage		
Direct	15	57.7	11	42.3	26	P = 0.4
Video	11	42.3	15	57.7	26	NS
Total	26	100	26	100	52	

Primary Outcome

7. Baseline Systolic Blood Pressure (SBP):

Clonidine group had a mean baseline SBP of 133 ± 2.88 mmHg, while Lignocaine group averaged 134.62 ± 9.08 mmHg. The data was normally distributed and Unpaired t test with Welch's correction indicated no significant difference (P = 0.053) as shown in Table 7.

Table 7: Comparison of Mean Systolic Blood Pressure of participants at different time intervals between the groups

		Number	Mean	SD	t	P Value
Before Induction	Clonidine	26	133	2.88	-0.96	P = 0.053
	Lignocaine	26	134.62	9.08		NS
0 Minute	Clonidine	26	137.46	2.56	-1.16	P = 0.25
	Lignocaine	26	139.65	9.2		
1 Minute	Clonidine	26	133.31	2.82	-5.3	P =
	Lignocaine	26	143.08	8.9		0.001**
3 Minute	Clonidine	26	129.38	2.9	-9.26	P =
	Lignocaine	26	145.85	8.5		0.001**
5 Minute	Clonidine	26	125.62	2.65	-9.3	P =
	Lignocaine	26	140.85	7.8		0.001**

Inference: Before induction, the Systolic Blood Pressure (SBP) in the Clonidine group was marginally lower than in the Lignocaine group, but this difference was not statistically significant (P = 0.053). At 0 minute, the SBP remained lower in the Clonidine group, though still not significant (P = 0.25). At the 1st, 3rd, and 5th minutes, the SBP in the Clonidine group was significantly lower than in the Lignocaine group, with all differences being statistically significant (P = 0.001).

8. Baseline Diastolic Blood Pressure (DBP):

Clonidine group had a mean baseline DBP of 85.42 ± 4.70 mmHg, while Lignocaine group averaged 83.92 ± 5.20 mmHg. The data was normally distributed and the unpaired t-test with Welch's correction showed no significant difference (P = 0.28) as shown in Table 8.

Table 8: Comparison of Mean Diastolic Blood Pressure of participants at different time intervals between the groups

		Number	Mean	SD	t	P value
Before Induction	Clonidine	26	85.42	4.7	1.07	P = 0.28
	Lignocaine	26	83.92	5.2		NS
0 Minute	Clonidine	26	89.96	4.5	1.45	P = 0.15
	Lignocaine	26	87.92	5.5		NS
1 Minute	Clonidine	26	86	3.8	-4.2	P =
	Lignocaine	26	91.81	5.7		0.001**
3 Minute	Clonidine	26	82.23	3.5	-10.2	P 0.001**
	Lignocaine	26	95.31	5.4		
5 Minute	Clonidine	26	78.35	3.1	-9.9	P =
	Lignocaine	26	91.08	5.6		0.001**

Inference: Before induction, the Diastolic Blood Pressure (DBP) in

the Clonidine group was higher than in the Lignocaine group, but this difference was not statistically significant (P = 0.28). At 0 minute, the DBP remained higher in the Clonidine group, though still not significant (P = 0.15). At the 1st, 3rd, and 5th minutes, the DBP in the Clonidine group was significantly lower than in the Lignocaine group, with all differences being statistically significant (P = 0.001).

9. Baseline Heart Rate:

Clonidine group had a mean baseline heart rate of 74.77 ± 5.10 beats per minute, while Lignocaine group averaged 77.19 ± 6.04 beats per minute. The data was normally distributed, and the unpaired t-test with Welch's correction showed no significant difference (P = 0.12) as shown in Table 9.

Table 9: Comparison of Mean Heart rate of participants at different time intervals between the groups

		Number	Mean	SD	t	P value
Before Induction	Clonidine	26	74.77	5.1	-1.5	P = 0.12 NS
	Lignocaine	26	77.19	6.04		
0 Minute	Clonidine	26	79.81	5.3	-1.14	P = 0.25 NS
	Lignocaine	26	81.65	6.2		
1 Minute	Clonidine	26	75.08	5.3	-6.69	P = 0.001**
	Lignocaine	26	85.81	6.1		
3 Minute	Clonidine	26	70.92	5.4	-12.11	P 0.001**
	Lignocaine	26	89.92	5.8		
5 Minute	Clonidine	26	66.12	6.1	-12.3	P = 0.001**
	Lignocaine	26	86.54	5.7		

Inference: Before induction, the mean Heart Rate (HR) in the Clonidine group was lower than in the Lignocaine group, but this difference was not statistically significant (P = 0.12). At 0 minute, the HR remained lower in the Clonidine group, though still not significant (P = 0.25). At the 1st, 3rd, and 5th minutes, the HR in the Clonidine group was significantly lower than in the Lignocaine group, with all differences being statistically significant (P = 0.001).

10. Baseline Mean Arterial Pressure (MAP):

Clonidine group had a mean baseline MAP of 74.77 ± 5.10 mmHg, while Lignocaine group averaged 77.19 ± 6.04 mmHg. The data was normally distributed, and the unpaired t-test with Welch's correction revealed no significant difference (P = 0.12) as shown in Table 10.

Table 10: Comparison of Mean Arterial Pressure of participants at different time intervals between the groups

		Number	Mean	SD	t	P value
Before Induction	Clonidine	26	100.27	3.66	-0.445	P = 0.65 NS
	Lignocaine	26	100.85	5.4		
0 Minute	Clonidine	26	105.88	3.3	0.56	P = 0.57 NS
	Lignocaine	26	105.12	6.03		
1 Minute	Clonidine	26	99.9	3.07	-1.96	P = 0.04*
	Lignocaine	26	103.6	7.4		
3 Minute	Clonidine	26	98.54	4.6	0.76	P = 0.05*
	Lignocaine	26	101.46	5.3		
5 Minute	Clonidine	26	93.85	4.3	-1.96	P = 0.049*
	Lignocaine	26	98.04	5.3		

Inference: Before induction and at 0 minute, the Mean Arterial Pressure (MAP) in the Clonidine group was similar to that in the Lignocaine group, with no statistically significant difference (P = 0.65 and P = 0.57, respectively). However, at 1 minute, 3rd minute, and 5th minute, the MAP in the Clonidine group was significantly lower than in the Lignocaine group, with these differences being statistically significant (P = 0.04, P = 0.05, and P = 0.049, respectively).

The visual representations (Figures x-y) are provided for each comparison.

In summary, this comprehensive analysis of demographic and physiological parameters revealed no statistically significant differences between the two groups across all measured variables. This suggests that the groups were well-matched in terms of age, gender, ASA status, BMI, Time taken for Laryngoscopy, Type of Laryngoscopy and baseline cardiovascular measurements.

Comparison of SBP, DBP, HR and MAP within Clonidine group at different time intervals

1. Systolic Blood Pressure:

It was found that there was an increase in SBP from before induction to during induction. which reduced at 1st minute, 3rd minute and 5th minute respectively. This difference in mean SBP was found to be statistically significant (P = 0.001). (Table 11.1) A post hoc test adjusted using Bonferroni's correction revealed a statistically significant difference in mean SBP between before induction vs. during induction (P = 0.001), during induction vs. at 1st minute (P = 0.001), 1st minute vs. 3rd minute (P = 0.001), 3rd minute vs. 5th minute (P = 0.001), and between 5th minute vs. before induction (P = 0.001). (Table 11.2)

Table 11.1: Comparison of Mean Systolic Blood Pressure at different time intervals in the Clonidine group

	Number	Mean	SD	F	P value
Before Induction	26	133	2.88	246.5	P = 0.001**
At 0 minute	26	137.46	2.56		
At 1st minute	26	133.31	2.8		
At 3rd minute	26	129.38	2.92		
At 5th minute	26	125.62	2.65		

Table 11.2: Pairwise comparison within the group

	Mean	SD	MD	P value
Before Induction	133	2.88	-4.4	P = 0.001**
At 0 minute	137.46	2.56		
At 0 minute	137.46	2.56	4.15	P = 0.001**
At 1 minute	133.31	2.8		
At 1 minute	133.31	2.8	3.92	P = 0.001**
At 3 minutes	129.38	2.92		
At 3 minutes	129.38	2.92	3.76	P = 0.001**
At 5 minutes	125.62	2.65		
At 5 minutes	125.62	2.65	-4.38	P = 0.001**
Before Induction	130	2.88		

2. Diastolic Blood Pressure:

It was found that there was an increase in DBP from before induction to during induction. which reduced at 1st minute, 3rd minute and 5th minute respectively. This difference in mean DBP was found to be statistically significant (P = 0.001). (Table 12.1)

Table 12.1: Comparison of Mean Diastolic Blood Pressure at different time intervals in Clonidine group

	Number	Mean	SD	F	P value
Before Induction	**26**	**85.42**	**4.7**	173.9	P = 0.001**
At 0 minute	**26**	**89.96**	**4.5**		
At 1st minute	**26**	**86**	**3.8**		
At 3rd minute	**26**	**82.23**	**3.5**		
At 5th minute	**26**	**78.35**	**3.1**		

Table 12.2: Pairwise comparison within the group

	Mean	SD	MD	P value
Before Induction At 0 minute	85.42 89.96	4.4 4.5	-4.5	P = 0.001**
At 0 minute At 1 minute	89.96 86	4.5 3.8	3.96	P = 0.001**
At 1 minute At 3 minutes	86 82.23	3.8 3.5	3.76	P = 0.001**
At 3 minutes At 5 minutes	82.23 78.35	3.5 3.1	3.88	P = 0.001**
At 5 minutes Before Induction	78.35 85.42	3.1 4.7	-7.07	P = 0.001**

A post hoc test adjusted using Bonferroni's correction revealed a statistically significant difference in mean DBP between before induction vs. during induction (P = 0.001), during induction vs. at 1st minute (P = 0.001), 1st minute vs. 3rd minute (P = 0.001), 3rd minute vs. 5th minute (P = 0.001), and between 5th minute vs. before induction (P = 0.001). (Table 12.2)

3. Heart Rate:

It was found that there was an increase in HR from before induction to during induction. which reduced at 1st minute, 3rd minute and 5th minute respectively. This difference in mean HR was found to be statistically significant (P = 0.001). (Table 13.1)

Table 13.1: Comparison of Mean Heart rate at different time intervals in the Clonidine group

	Number	Mean	SD	F	P value
Before Induction	26	74.77	5.11	310.1	P = 0.001**
At 0 minute	26	79.81	5.3		
At 1st minute	26	75.08	5.3		
At 3rd minute	26	70.92	5.4		
At 5th minute	26	66.12	6.1		

A post hoc test adjusted using Bonferroni's correction revealed a statistically significant difference in mean SBP between before induction vs. during induction (P = 0.001), during induction vs. at 1st minute (P = 0.001), 1st minute vs. 3rd minute (P = 0.001), 3rd minute vs. 5th minute (P = 0.001), and between 5th minute vs. before induction (P = 0.001). (Table 13.2)

Table 13.2: Pairwise comparison within the group

	Mean	SD	MD	P value
Before Induction	74.77	5.11	-5.03	P = 0.001**
At 0 minute	79.81	5.3		
At 0 minute	79.81	5.3	4.7	P = 0.001**
At 1 minute	75.08	5.3		
At 1 minute	75.08	5.3	4.1	P = 0.001**
At 3 minutes	70.92	5.4		
At 3 minutes	70.92	5.4	-3.84	P = 0.001**
At 5 minutes	66.12	6.1		
At 5 minutes	66.12	6.1	-8.6	P = 0.001**
Before Induction	74.77	5.1		

4. Mean Arterial Pressure:

It was found that there was an increase in MAP from before induction to during induction. which reduced at 1st minute, 3rd minute and 5th minute respectively. This difference in mean MAP was found to be statistically significant (P = 0.001). (Table 14.1) A post hoc test adjusted using Bonferroni's correction revealed a statistically significant difference in mean SBP between before induction vs. during induction (P = 0.001), during induction vs. at 1st minute (P = 0.001), 1st minute vs. 3rd minute (P = 0.001), 3rd minute vs. 5th minute (P = 0.001), and between 5th minute vs. before induction (P = 0.001). (Table 14.2)

Table 14.1: Comparison of Mean Arterial Pressure at different time intervals in the Clonidine group

	Number	Mean	SD	F	P value
Before Induction	26	100.27	3.66	114.8	P = 0.001**
At 0 minute	26	105.88	3.37		
At 1st minute	26	99.9	3.07		
At 3rd minute	26	98.54	4.69		
At 5th minute	26	93.85	4.35		

Table 14.2: Pairwise comparison within the group

	Mean	SD	MD	P value
Before Induction At 0 minute	100.27 105.88	3.66 3.37	-5.61	P = 0.001**
At 0 minute At 1 minute	105.88 99.9	3.37 3.07	5.9	P = 0.001**
At 1 minute At 3 minutes	99.9 98.54	3.07 4.69	1.36	P = 0.03**
At 3 minutes At 5 minutes	98.54 93.04	4.69 4.35	5.5	P = 0.001**
At 5 minutes Before Induction	93.04 100.17	4.35 3.66	-7.2	P = 0.001**

Comparison of SBP, DBP, HR and MAP within Lignocaine group at different time intervals

1. Systolic Blood Pressure:

It was found that there was an increase in the SBP from before induction to during induction and till 3rd minute following which there was a reduction in SBP at the 5th minute. The difference in mean SBP was found to be statistically significant (p = 0.001). (Table 15.1).

Table 15.1: Comparison of Mean Systolic Blood Pressure at different time intervals in Lignocaine group

	Number	Mean	SD	F	P value
Before Induction	26	134.62	9.08	301.7	P = 0.001**
At 0 minute	26	139.65	9.2		
At 1st minute	26	143.08	8.9		
At 3rd minute	26	145.85	8.5		
At 5th minute	26	140.85	7.8		

A post hoc test adjusted using Bonferronis correction revealed a statistically significant difference between before induction vs. during induction (P = 0.001), during induction vs. at 1st minute (P = 0.001), 1st minute vs. 3rd minute (P = 0.001), a significant decrease from 3rd minute vs. 5th minute (P = 0.001), and an increase between 5th minute vs. before induction (P = 0.001). (Table 15.2)

Table 15.2: Pairwise comparison within the group

	Mean	SD	MD	P value
Before Induction	134.62	9.08	-5.03	P = 0.001**
At 0 minute	139.65	9.2		
At 0 minute	139.65	9.2	-3.4	P = 0.001**
At 1 minute	143.08	8.9		
At 1 minute	143.08	8.9	-2.7	P = 0.001**
At 3 minutes	145.85	8.5		
At 3 minutes	145.85	8.5	5	P = 0.001**
At 5 minutes	140.85	7.8		
At 5 minutes	140.85	7.8	6.2	P = 0.001**
Before Induction	134.62	9.08		

2. Disatolic Blood Pressure:

It was found that there was an increase in the DBP from before induction to during induction and till 3rd minute following which there was a reduction in SBP at the 5th minute. The difference in mean DBP was found to be statistically significant (p = 0.001). (Table 16.1).

Table 16.1: Comparison of Mean Diastolic Blood Pressure at different time intervals in Lignocaine group

	Number	Mean	SD	F	P value
Before Induction	26	83.92	5.2	174.32	P = 0.001**
At 0 minute	26	87.92	5		
At 1st minute	26	91.81	5.7		
At 3rd minute	26	95.31	5.4		
At 5th minute	26	91.08	5.6		

A post hoc test adjusted using Bonferronis correction revealed a statistically significant difference between before induction vs. during induction (P = 0.001), during induction vs. at 1st minute (P = 0.001), 1st minute vs. 3rd minute (P = 0.001), a significant decrease from 3rd minute vs. 5th minute (P = 0.001), and an increase between 5th minute vs. before induction (P = 0.001). (Table 16.2)

Table 16.2: Pairwise comparison within the group

	Mean	SD	MD	P value
Before Induction	83.92	5.2	-4	P = 0.001**
At 0 minute	87.92	5		
At 0 minute	87.92	5	-3.85	P = 0.001**
At 1 minute	91.81	5.7		
At 1 minute	91.81	5.7	-3.5	P = 0.001**
At 3 minutes	95.31	5.4		
At 3 minutes	95.31	5.4	4.2	P = 0.001**
At 5 minutes	91.08	5.6		
At 5 minutes	91.08	5.6	7.1	P = 0.001**
Before Induction	83.92	5.2		

3. Heart Rate:

It was found that there was an increase in the HR from before induction to during induction and till 3rd minute following which there was a reduction in HR at the 5th minute. The difference in mean HR was found to be statistically significant (p = 0.001). (Table 17.1).

Table 17.1: Comparison of mean Heart rate at different time intervals in the Lignocaine group

	Number	Mean	SD	F	P value
Before Induction	26	77.19	6.04	492.04	P = 0.001**
At 0 minute	26	81.65	3.2		
At 1st minute	26	85.81	6.1		
At 3rd minute	26	89.92	5.8		
At 5th minute	26	86.54	5.7		

A post hoc test adjusted using Bonferronis correction revealed a statistically significant difference between before induction vs. during induction (P = 0.001), during induction vs. at 1st minute (P = 0.001),

1st minute vs. 3rd minute (P = 0.001), a significant decrease from 3rd minute vs. 5th minute (P = 0.001), and a significant increase between 5th minute vs. before induction (P = 0.001). (Table 17.2)

Table 17.2: Pairwise comparison within the group

	Mean	SD	MD	P value
Before Induction	77.19	6.04	-4.46	P = 0.001**
At 0 minute	81.65	3.2		
At 0 minute	81.65	3.2	-4.1	P = 0.001**
At 1 minute	85.81	6.1		
At 1 minute	85.81	6.1	-4.1	P = 0.001**
At 3 minutes	89.92	5.8		
At 3 minutes	89.92	5.8	3.38	P = 0.001**
At 5 minutes	86.54	5.7		
At 5 minutes	86.54	5.7	9.3	P = 0.001**
Before Induction	77.19	6.04		

4. Mean Arterial Pressure:

It was found that there was a fluctuation in the MAP that involved an increase from before induction to during induction following which there was a decrease at 1st minute, 3rd minute, and 5th minute. The difference in mean MAP was found to be statistically significant (p = 0.001). (Table 18.1).

Table 18.1: Comparison of Mean Arterial Pressure at different time intervals in the Lignocaine group

	Number	Mean	SD	F	P value
Before Induction	26	100.85	5.4	125.5	P = 0.001**
At 0 minute	26	105.12	6.03		
At 1st minute	26	103.6	7.4		
At 3rd minute	26	101.46	5.4		
At 5th minute	26	98.04	5.3		

A post hoc test adjusted using Bonferroni correction revealed a statistically significant increase between before induction vs. during induction (P = 0.001), a significant decrease from during induction vs. at 1st minute (P = 0.035), a significant increase from 1st minute vs. 3rd minute (P = 0.01), a significant decrease from 3rd minute vs. 5th minute (P = 0.001), and between 5th minute vs. before induction (P = 0.01). (Table 18.2)

Table 18.2: Pairwise comparison within the group

	Mean	SD	MD	P value
Before Induction	100.85	5.4	-4.2	P = 0.001**
At 0 minute	105.12	6.03		
At 0 minute	105.12	6.03	1.56	P = 0.035*
At 1 minute	103.6	7.4		
At 1 minute	103.6	7.4	2.14	P = 0.01**
At 3 minutes	101.46	5.4		
At 3 minutes	101.46	5.4	3.4	P = 0.001**
At 5 minutes	98.04	5.3		
At 5 minutes	98.04	5.3	-2.81	P = 0.01**
Before Induction	100.85	5.4		

Secondary Outcome

Comparison Of Ramsay Sedation Scoring Within Clonidine Group:

In the Clonidine group, the distribution of Ramsey Sedation Scores among participants was analysed. It was observed that the majority of participants, 55.6%, had a sedation score of 2. A smaller proportion, 29.6%, were assigned a sedation score of 3, indicating moderate sedation levels. Only 14.8% of participants achieved a sedation score of 4, suggesting deeper sedation. These findings highlight the predominance of mild sedation in the group. The detailed distribution is given in Table 19.

Table 19: Distribution of participants according to Ramsey Sedation Scores

	Number	Percentage
Score 2	15	55.6
Score 3	8	29.6
Score 4	4	14.8

DISCUSSION

Instrumentation of the upper airway using laryngoscopy and intubation acts like a noxious stimulus that causes the release of catecholamines due to the stimulation of the sympatho adrenergic system[8]. These result in an increase in blood pressure, heart rate, and serum catecholamines due to centrally mediated sympathetic reflex secondary to stretching of laryngeal and pharyngeal tissue.[9,10] These pressor responses are transient ranging from 15 seconds to 10 minutes, often well tolerated by healthy patients, however, can have severe consequences among patients with hypertension and pre-existing heart conditions like coronary artery disease and cerebrovascular diseases[11,12]. Therefore, it is essential to attenuate these pressor responses to avoid any intraoperative adverse events that might not be favourable for the patient.

In the present prospective comparative study, we evaluated and compared the efficacy of oral clonidine (4 – 5 µg/kg) and 10% lignocaine oropharyngeal spray in attenuating the hemodynamic response to laryngoscopy and intubation. We found that hemodynamic parameters (SBP, DBP, HR) were significantly lower among participants in the oral clonidine group when compared to 10% lignocaine spray from 1st minute to 5th minute. There was no statistically significant difference in MAP between the two medications except at 1st minute where MAP was significantly lower among participants in the 10% lignocaine group. In addition, it was found that there was no statistically significant difference between oral clonidine and 10% lignocaine spray before induction and during intubation.

Clonidine is an α2 adrenoreceptor agonist with a central sympatholytic effect. It is available as a tablet that is rapidly absorbed with a bioavailability of almost 100% and has a peak plasma concentration within 60-90 minutes of administration[13,14]. It is a hypotensive agent that stimulates α2 adrenergic receptors in the vasomotor centre of the medulla and pre-synaptically at the peripheral nerve terminals by blocking the release of norepinephrine and leads to hypotension and bradycardia[15]. The results from the present study were in line with studies conducted by Priyamargavi et al, [16] Raval et al[17], Gupta et al, [18] Sung et al,[19] Talebi et al[20] and Kishneni et al[21] who reported that oral clonidine attenuated hemodynamic parameters when compared to control groups. In addition, Islam et al reported the attenuating effect of oral clonidine among hypertensive patients.[22]

Various authors have compared the attenuating properties of oral clonidine with other pharmacological agents that are commonly used. Koti et al conducted a study to compare oral clonidine with oral atenolol (0.75 mg/kg) among 50 participants and found that atenolol is more effective in attenuating hemodynamic response within 5 minutes of laryngoscopy and intubation.[23] Parveen et al conducted a randomized double-blind study to compare the efficacy between oral clonidine and oral pregabalin (150 mg) among 80 participants. They found oral clonidine to be more effective in lowering blood pressure and heart rate than oral pregabalin. However, pregabalin had better post-operative analgesia, lesser bradycardia, and more sedation when compared to clonidine.[24] Gupta et al conducted a randomized controlled trial to compare oral clonidine and oral melatonin and found that both Clonidine and melatonin were excellent pharmacological agents in attenuating hemodynamic response after laryngoscopy and intubation[18].

Jamadar Khana et al[30]. presented limited yet indicative evidence supporting clonidine's effectiveness in ICU sedation, particularly for managing sympathetic overactivity and withdrawal syndromes. Clonidine, an imidazoline compound and alpha-2 adrenoceptor agonist, has notable sedative properties, enhancing its value in the ICU. The study demonstrated that clonidine decreases the requirement for other sedatives and analgesics, ensures hemodynamic stability, and results in minimal respiratory depression.

Lignocaine is one of the oldest, cheapest, and most easily available agents used to attenuate hemodynamic response to laryngoscopy[25]. Multiple studies have documented the beneficial effects of lignocaine on pressor response. Mahajan et al reported that topical application of Xylocaine (10%) was more effective than IV

Lidocaine in attenuating the pressor response to direct laryngoscopy and intubation. [26] Mostafa et al conducted a randomized study to compare the efficacy of topical lignocaine spray when used directly on the larynx/trachea immediately before intubation and when used as Oro laryngeal lignocaine spray before the induction of anaesthesia. The authors concluded that the administration of topical lignocaine

spray before the induction of anaesthesia is more effective in reducing pressor response to laryngoscopy and intubation.[27]

In the present study, we observed that lignocaine spray could not attenuate hemodynamic parameters when compared to oral clonidine. Though topical applications of lignocaine spray were more effective when compared to lignocaine administered intravenously, [26] a randomized double-blind placebo-controlled study by Varshney et al reported the efficacy of Nitro-glycerine to be more effective than lignocaine spray.[28] Similar results were given by Verma and Sharma who compared nitro-glycerine and lignocaine spray with controls and found that lignocaine spray was more effective in preventing the rise of heart rate while Nitro-glycerine was more effective in attenuating pressor response.[29]

In the present study, we also attempted to compare the changes in hemodynamic parameters at different time intervals for oral clonidine and 10% lignocaine spray. We found a significant increase in all hemodynamic parameters from before induction to during intubation followed by a gradual reduction from 1st minute to 3rd minute and to 5th minute that was statistically significant with an additional post operative sedative effect which was evaluated using Ramsay sedation score. On the contrary, we observed a gradual and significant rise in hemodynamic parameters among participants in the 10% lignocaine spray group with no sedative effect.

Limitations Of The Study

1. Sample size was too small to apply to the entire population.
2. The nature of illness- like diagnosis, type of surgery, duration of procedure, history of previous surgeries was not considered in the groups.
3. Fixed dose of drug was used, not compared to other doses.
4. Comorbidities like diabetes which may be associated with autonomic neuropathy was not excluded from study group.
5. Drug administered by different anaesthetists, administration of drug was monitored by different observers, hence may cause discrepancy.
6. Laryngoscopy performed by different anaesthetists, which may influence the response to different induction agents could not be compared as uniform induction protocol were followed.
7. As hypertensive patients, IHD patients were excluded from the study, influence of these comorbidities could not be evaluate.

CONCLUSION

From the parameters of the present study, it can be concluded that oral clonidine (4 - 5µg/kg) was more effective in maintaining a stable hemodynamic parameter when compared to 10% lignocaine spray. The effect of both drugs on hemodynamic parameters was comparable before induction and during laryngoscopy. In addition, hemodynamic parameters in the oral clonidine group were restored to baseline values at the 5th minute. On the contrary, there was a significant increase in hemodynamic parameters in the 10% lignocaine spray. Additionally, clonidine exhibited a sedative effect postoperatively, further enhancing its clinical utility.

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