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Original Research Article

Evaluation of Haemodynamic Response Attenuation with Intravenous Clonidine Hydrochloride versus Lignocaine Hydrochloride during Laryngoscopy and Endotracheal Intubation

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Abstract

The effectiveness of intravenous bolus dosages of clonidine hydrochloride (0.0025 mg/kg) and lignocaine hydrochloride (1.5 mg/kg) for attenuating the hemodynamic response to laryngoscopy and endotracheal intubation was compared in a double-blind, randomised, controlled research (ETI). Twenty-one patients each administered clonidine, lignocaine, or saline five minutes prior to intubation. The remainder of the process was typical. In comparison to the control group (44.74%) and the lignocaine (38.46%) groups, the clonidine group's PR rise was considerably lower (23.08%) (p=0.003). In the clonidine, lignocaine, and control groups, the rise lasted for 5, 7, and 7 minutes, respectively. At intubation, the SBP rise was reduced for the clonidine group (11.20%) compared to the Control group (25.8%) (p=0.040). In the clonidine and control groups, the rise continued for 3 minutes and 10 minutes, respectively. At intubation, the lignocaine group's SBP increased less (p=0.117) than the control group's (22.4%). The increase in RPP was successfully suppressed by clonidine, which is statistically more effective than lignocaine to do so (p=0.013). While lignocaine was unable to stop this rise in pulse rate, systolic blood pressure, and rate pressure product following intubation, clonidine was able to.

Keywords: Lignocaine, Clonidine, Rate pressure product, Laryngoscopy and endotracheal intubation

Introduction

A crucial component of modern general anaesthesia practise is endotracheal intubation. It is predictable that laryngoscopy and tracheal intubation cause hypertension and tachycardia [1]. The increase in blood pressure and pulse rate is typically brief, unpredictable, and varied. Healthy people typically accept these adjustments without any problems. However, patients with hypertension, coronary artery disease, or intracranial hypertension may die as a result of these

alterations.

The laryngoscopy response may be "blunted" using intravenous lignocaine, but other research have questioned its efficacy in this situation (Miller and Warren, 1990) [2]. Hypotensive medications such as calcium channel blockers, sodium nitroprusside, nitroglycerin, hydralazine, and -blockers have also been proven to be helpful at reducing transitory sympathetic activation.

An [2] agonist called clonidine has been used successfully to reduce the laryngoscopy response [3-6] although the appropriate dosage and timing for an intravenous bolus dose soon before intubation are still unknown. We conducted a study to compare the effects of two commonly used drugs—Clonidine (0.0025 mg/kg) and Lignocaine (1.5 mg/kg)—with a control group for attenuating hemodynamic response.

Material and Methods

120 ASA I & II patients between the ages of 18 and 60 who were scheduled for elective surgery at Department of Anaesthesia and Critical Care, VMMC & Safdarjung Hospital, New Delhi from April 2022 to August 2022 and required general anaesthesia with endotracheal intubation (ETI) participated in this prospective randomised double blind trial. They obtained a thorough history and examination. Patients with known allergies to study drugs, ASA III or higher, autonomic nervous system-affecting medications, significant medical co-morbidities, abnormalities of the airway, anticipated difficulty in intubation, and procedures requiring head/neck manipulations, nasogastric tube insertion, or throat packing during the study period were prohibited.

Using a lottery procedure, the patients were allocated into three groups at random. Group A contains 10cc of control normal saline; Group B contains 1.5 mg/kg of lignocaine; and Group C contains 0.0025 mg/kg of lignocaine diluted in 10cc of normal saline. While the patient was being intubated by the primary investigator, one of my colleagues administered the study drug in accordance with the study protocol, and another colleague kept track of the patient's heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure over time. My coworkers and the principal investigator were not informed about the medication injection. The fourth person prepared the drugs.

At minute 0, patients received 100% oxygen after receiving the experimental medication. Thiopentone sodium 5 mg/kg was delivered intravenously at minute 2. The next dose was injection of vecuronium bromide 0.12 mg/kg. After that, breathing continued for another five minutes at 60% oxygen and N2O. At minute five, a curved Macintosh blade number 3 or 4 was used for direct laryngoscopy, and a 7.0 mm internal diameter endotracheal intubation was performed. Auscultation and capnography confirmed the location of the trachea. A fixed and secured endotracheal tube was used. Fentanyl (0.002 mg/kg) was administered at minute 15. Only after minute 20 was surgery permitted to start.

The following hemodynamic variables were tracked: PR, SBP, DBP, and MAP. These were assessed using a non-invasive blood pressure monitor (NIBP) in manual mode at that specific moment and recorded at minute zero (before to the study drug's administration); then at intervals of one minute up to minute fifteen; and finally, at intervals of five minutes thereafter. We had established the following criteria for the study: 1) SBP less than 20% of the baseline value or 90 mm Hg, whichever was lower, was considered hypotension; 2) SBP more than 20% of the baseline value or 140 mm Hg, whichever was higher, was considered

hypertension; Bradycardia was defined as PR less than 20% of baseline value, whereas tachycardia was defined as HR greater than 20% of baseline value. 5) Any premature ventricular or supraventricular beat or other rhythm other than sinus was deemed an arrhythmia. All of these parameter incidences were noted in each of the three groups.

Fluid challenge was administered if, between minutes 10 and 15, there was hypotension as defined by that time frame. Isoflurane was started if there was hypertension as defined in the aforementioned time frame. Fluid challenge was administered if the tachycardia was linked to hypotension; if it was linked to hypertension, isoflurane was started. Atropine injections were used to treat bradycardia, as defined in the preceding period.

Statistical Analysis

SPSS for Windows and Microsoft Excel were used to examine the data. An ANOVA analysis of the demographic data was followed by an unpaired t test. The student's unpaired t test was used to compare monitored and observed parameters between the groups.

Result

Table 1: Showing means age, weight and sex distribution among groups.

	Group A	Group B	Group C	p value
Age(Yrs.) Mean±Sd	36.82±11.78	36.79±11.5	35.82±10.36	0.904
Weight(Kg) Mean±Sd	49.9±10.58	50.63±9.16	51.52±9.31	0.756
Sex(Male/Female)Number	11/29	11/29	19/21	0.120

The three groups' average ages and weights were comparable. Male and female study participants made up 34% and 66% of the total population, respectively.

Just after administering clonidine, there is a negligible increase in heart rate (1.28%). (PR). Within two minutes, it returned to the baseline. With induction, PR fell in each of the three groups, but it increased with intubation.

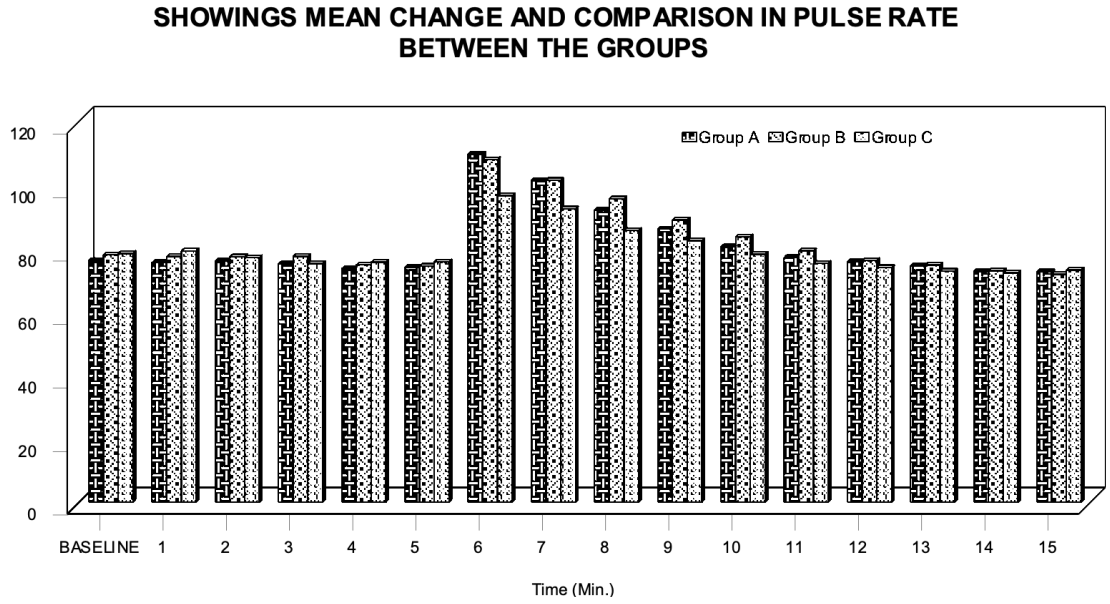

Figure 1: Mean change and comparison in pulse rate between the groups

In comparison to the control group (44.74%) and the lignocaine (38.46%) groups, the clonidine group's PR increased less (23.08%) (p=0.003). In the clonidine, lignocaine, and control groups, the rise lasted for 5, 7, and 7 minutes, respectively.

After administering lignocaine and clonidine, SBP dropped below the initial value. After administering thiopentone to the clonidine, lignocaine, and control groups, SBP further fell from baseline by 13.6%, 9.52%, and 8%, respectively. When compared to lignocaine, this decrease from baseline in the clonidine group was significant (p=0.036). Just after intubation, the SBP rise was less for the lignocaine group (17.46%) than for the control group (22.4%) (p=0.117). Both the lignocaine and control groups experienced the climb for the full three minutes. After treatment, the SBP in the clonidine group significantly decreased; it returned to normal after 3 minutes of intubation. Compared to the lignocaine group, the clonidine group experienced a smaller increase in SBP (11.20%) (p = 0.040).

Table 2: Showing mean change and comparison in systolic blood pressure between the groups.

	Group A Mean±SD	Group B Mean±SD	Group C Mean±SD	pvalue (AVs B)	p value (AVs C)	p value (BVs C)
Baseline	125.25±7.84	125.50±8.23	125.05±9.20	0.891	0.912	0.821
1min	124.50±7.98	123.60±9.72	123.35±11.94	0.657	0.614	0.918
2min	120.67±7.30	121.63±7.92	120.77±16.81	0.580	0.973	0.776
3min	116.77±9.09	119.00±9.99	113.00±14.74	0.307	0.172	0.040
4min	114.47±8.79	117.18±10.63	107.77±13.43	0.223	0.010	0.001
5min INTU	115.40±13.03	113.76±10.25	107.55±14.85	0.541	0.014	0.036
6min	153.07±16.05	147.97±17.00	139.17±19.95	0.177	0.001	0.040
7min	140.12±19.62	136.89±12.99	132.57±16.15	0.397	0.064	0.198
8min	128.95±19.74	128.55±10.04	127.10±13.61	0.912	0.627	0.595
9min	125.32±10.43	124.28±8.92	122.87±14.27	0.640	0.383	0.603
10min	123.42±11.46	122.05±8.28	121.42±10.09	0.548	0.410	0.776
11min	122.07±10.11	120.84±6.75	119.10±9.50	0.531	0.179	0.356
12min	120.60±8.71	119.73±6.89	118.20±10.67	0.630	0.274	0.455
13min	118.10±7.02	118.36±7.01	117.25±9.43	0.866	0.649	0.556
14min	117.37±7.72	116.86±7.74	117.55±11.41	0.773	0.936	0.760
15min	117.12±6.86	117.23±7.62	117.55±10.62	0.946	0.832	0.882

Both the lignocaine and clonidine groups experienced an initial decline in DBP, which was followed by an increase during intubation (returning to baseline) & a subsequent decline. In terms of DBP alterations, there was no discernible difference between the lignocaine and clonidine groups. From the moment of intubation forward, the DBP in the control group was considerably higher than in the lignocaine and clonidine groups.

The greatest MAP increase for the control group occurred right after intubation and was 26.88%. After administration, the lignocaine group's MAP decreased by 7.45%, however there was a noticeable increase (20.21%) from the time of intubation onwards for the next three minutes. Following administration, the clonidine group's MAP significantly decreased (15.63%) before returning to baseline within 3 minutes of intubation and then decreasing once more.

Table 3: Showing mean change and comparison in mean blood pressure between the groups.

	Group A Mean±SD	Group B Mean±SD	Group C Mean±SD	p value (A Vs B)	p value (A Vs C)	p value (B Vs C)
Baseline	93.22±7.88	93.89±7.41	95.50±5.96	0.700	0.149	0.294
1min	91.62±7.64	93.60±8.41	94.25±7.18	0.279	0.117	0.716
2min	90.05±8.24	91.55±9.11	90.22±11.24	0.447	0.937	0.569
3min	85.95±8.38	89.94±10.51	85.70±10.78	0.066	0.908	0.082
4min	84.35±7.34	87.47±9.10	82.12±12.65	0.099	0.339	0.036
5min INTO	84.87±10.65	86.65±11.47	81.40±12.55	0.479	0.186	0.058
6min	118.27±15.70	113.34±14.61	108.22±16.73	0.156	0.007	0.155
7min	109.15±12.74	101.73±17.77	101.97±12.95	0.057	0.015	0.946
8min	99.85±10.09	97.63±9.02	98.55±11.41	0.310	0.591	0.695
9min	93.45±9.09	93.94±9.08	94.80±11.50	0.810	0.562	0.718
10min	92.57±8.58	93.55±8.07	93.62±8.75	0.606	0.589	0.970
11min	91.30±8.49	90.86±7.42	91.45±8.04	0.812	0.936	0.741
12min	88.35±8.17	89.68±7.09	90.70±9.34	0.444	0.240	0.596
13min	86.05±7.88	89.31±6.67	89.82±9.29	0.052	0.054	0.783
14min	86.30±6.82	86.76±6.78	89.05±9.55	0.765	0.142	0.229
15min	86.15±7.04	85.97±7.80	89.65±9.75	0.917	0.069	0.071

At intubation, the rate pressure product (RPP) rose to its highest level in the control group (70%). In the lignocaine group, RPP rose throughout intubation, reaching a peak at 6 minutes (60%) and continuing through 9 minutes. Following the administration of clonidine, the RPP in the clonidine group significantly dropped (20%); the RPP returned to baseline with intubation; the maximum rise was significantly increased (40%); and it again decreased at 11 minutes following intubation.

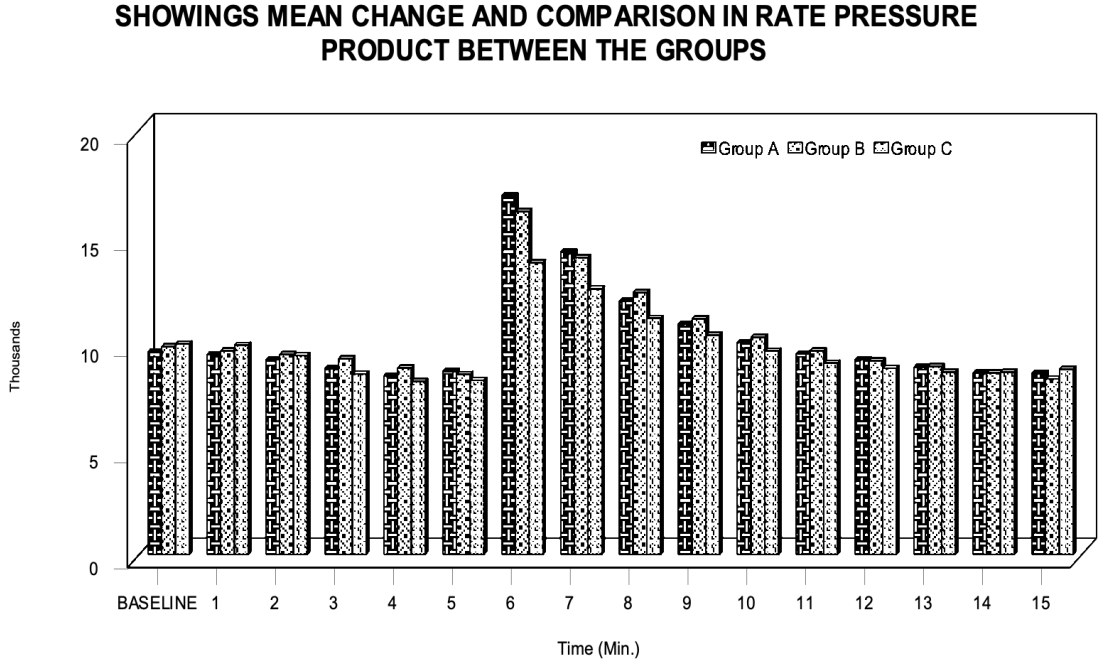

Figure 2: Mean change and comparison in rate pressure product between the groups

After intubation, 75% of patients in the control group experienced tachycardia, and 67.5% experienced hypertension. Eight (20%) of these patients needed halothane to treat this unexpected increase in blood pressure and pulse rate. After intubation, 55% of patients in the lignocaine group experienced tachycardia, and 47.5% experienced hypertension. The abrupt increase in blood pressure and pulse rate in patient 3 (7.5%) was treated with halothane.

15 (37.5%) of the patients in the clonidine group exhibited both tachycardia and hypertension. Two (5%) of these patients needed isoflurane to reduce an increase in blood pressure and pulse rate. During the intubation period, bradycardia and hypotension were experienced by 7 (15%) and 17 (42.5%) patients, respectively. Of these, 3 (7.5%) of the patients needed intravenous atropine, and 6 (15%) needed a fluid challenge to keep their blood pressure and pulse rate stable, respectively. In the groups receiving lignocaine or clonidine, nothing disastrous happened.

Discussion

Endotracheal intubation is linked to a response in the cardiovascular system that includes increased heart rate and blood pressure, sporadic dysrhythmias, cough reflexes, elevated intracranial pressure, and elevated intraocular pressure. Depending on the induction technique, the PR can increase from 26% to 66% if specific precautions are not taken to prevent a haemodynamic reaction.

SBP can rise from 36% to 45% [7-10], etc. In our study, the control group experienced a rise in PR of 44.74% and a rise in SBP of 22.4%. These reactions to intubation are well tolerated in individuals with ASA grades I and II, but they may lead to fatal events in patients with atherosclerotic heart disease, cerebral lesions, or possibly piercing eye injuries. When no specific measures are taken to prevent it, almost 50% of patients with coronary artery disease develop episodes of myocardial ischemia while being intubated.

According to several research, lignocaine given intravenously can reduce the rise in heart rate, blood pressure, intracranial pressure, and intraocular pressure. In a study by Yukioka *et al* [11] from 1985, it was demonstrated that 2 mg/kg of intravenous lignocaine administered two minutes before intubation totally controlled the cough reflex.

However, recent researches have questioned the effectiveness of lignocaine. In the studies by Singh *et al* [8] 1995, van den Berg *et al* [12] 1997, and Kindler *et al* [13] 1996, intravenous lidocaine 1.5 mg/kg given soon before intubation was ineffective in reducing the acute haemodynamic reaction after laryngoscopy and intubation. In our study also, in lignocaine group there was significant rise in SBP for 3 minutes after ETI; SBP increased up to 17.46%; rise in PR was present for 5 minutes after ETI; PR increased up to 38.46%. We injected lignocaine 5 minutes before intubation.

On the haemodynamic response to laryngoscopy and endotracheal intubation, we reviewed a variety of papers. It was determined that the basis for taming these reactions is a sufficient depth of anaesthesia and a swift, fluid laryngoscopy. Adrenergic medications that may be hazardous haemodynamic reactions during laryngoscopy and tracheal intubation are reduced, such as clonidine or dexmedetomidine.

Carabine *et al* [14] 1992 showed that administering 0.625 and 1.25 g/kg of clonidine intravenously 15 minutes before inducing anaesthesia attenuated the haemodynamic response to laryngoscopy and intubation in noncardiac ASA physical status I patients. In contrast, Wright *et al* [15] 1991 found that under nearly

comparable circumstances, 1.25 g/kg of intravenous clonidine was ineffective in noncardiac ASA physical status I patients. In addition, Laurito CE *et al* [16] 2001 demonstrated that 4 kg/kg clonidine administered orally to patients undergoing general surgery was unable to reduce the reactivity to laryngoscopes lasting more than 15 seconds.

The effect of clonidine on peripheral - adrenoceptors [17] limits the drug's maximal dose. In a 1992 study by Lawrence CJ *et al* [18], it was discovered that clonidine administered intravenously at doses more than 3 μg/kg enhanced peripheral resistance and cardiac output while also raising arterial blood pressure. We used this dose in our work to reduce the laryngoscopy response because, in humans, 2.5 μg/kg clonidine was administered without relevant symptoms of peripheral stimulation (Brenda C. McClain, 1996) [19].

Different oral dosages and infusion formulations of clonidine have been attempted. As an intravenous bolus dosage in our investigation. We use the intravenous method of administration because bioavailability after oral ingestion varies between 70% and 90%, allowing us to more closely tie pharmacodynamic effects to this dose [20]. In our patients, the safety of the intravenous bolus of clonidine was demonstrated. In order to determine its effectiveness for reducing the haemodynamic response through intravenous bolus dose, our study was created.

In our study, we discovered that 2.5 μg/kg of intravenous clonidine administered five minutes prior to intubation was helpful in reducing the increase in PR following intubation. Lignocaine (1.5 mg/kg) did not accomplish this. To reduce this increase in PR, clonidine is statistically more effective than lignocaine. Clonidine is an effective attenuator of the increase in SBP that occurs during laryngoscopy and intubation. Additionally, statistically speaking, clonidine prevents the rise in SBP better than lignocaine. Lignocaine given 5 min prior to intubation was not able to prevent this rise in SBP. Both clonidine and lignocaine were effective in attenuating the rise in DBP and there was no statistical difference between the two groups. MAP is important in relation to the auto- regulatory responses of the heart, brain and kidneys.

Clonidine considerably reduces the MAP rise after endotracheal intubation, whereas lignocaine had little impact. One of the resulting parameters, RPP, which is the result of PR and SBP, has been linked to the development of angina. It also has a correlation with myocardial oxygen demand. Both clonidine and lignocaine above the cut-off value of 12000, however clonidine was more successful in preventing the rise in RPP and is statistically more significant than lignocaine to do so.

The possibility of unfavourable side effects is crucial when assessing the general safety of clonidine. Bradycardia and hypotension may counteract the positive effect of α_2 agonists that could otherwise exist. According to the current investigation, hypotension is possible. This hypotensive effect has been documented in several investigations using either oral doses of 4 or 5 μg/kg or clonidine administered intravenously [21,22]. However, hypotension did occur in the current investigation, which may have been brought on by the high induction dose of thiopentone sodium (5 mg/kg) utilised. Although we did not record recovery time (i.e., response to verbal command), clonidine did not affect time to extubation.

Conclusion

Our results' interpretation may be constrained by our sample size, which was quite small. However, the findings of this study should support the widespread usage

of clonidine to lessen the haemodynamic reaction to laryngoscopy. Clonidine may help a wide spectrum of patients by improving hemodynamics.

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