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**ORIGINAL ARTICLE**

# Comparative Study on the Effects of Lignocaine Nebulization with I/V Lignocaine on Stress Response to Laryngoscopy and Tracheal Intubation

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## ABSTRACT

**Aim:** To determine the frequency of any immediate side effects associated with the use of lignocaine in patients.
**Methodology:** Randomized control trial. Sindh Institute of Urology and Transplantation, Karachi from 1st December 2021 to 31st May 2022. Ninety patients enrolled for laryngoscopy and endotracheal intubation. Patients were randomly allocated into three groups on the basis of the treatment. Thirty patients in group I was treated with 2% lignocaine 1.5mg/kg was given by intravenous route, 30 in group N was received 4% lignocaine 1.5mg/kg was given by nebulization and 30 in groups C treated as control group in whom normal saline placebo. The hemodynamic response and side effect was recorded in all patients.
**Results:** The mean heart rate was not statistically significant among groups at baseline and 1 min, 3min to 8 min, while it was statistically significant at 2 min and 9 min among the groups. Mean atrial BP was statistically significant among groups during 2 min to 6 min and then 8 min. regarding immediate side effects, the frequency of side effects were lower in group N and group I than in group C. However, the rate of drowsiness, tremors, and hypoxia was significantly higher in group C compare to group N and group I.
**Conclusion:** Lignocaine is a safe drug and proved to be safe and effective method for the improvement of hemodynamic response to intubation and laryngoscopy.
**Keywords:** Lignocaine, Nebulization of 4%lignocaine, Hemodynamic response, Endotracheal intubation

## INTRODUCTION

Securing the airway to ensure adequate ventilation for the patient undergoing surgical intervention is one of the major obligations of an anesthesiologist[1]. Endotracheal intubation is the gold standard technique[2] widely preferred among anesthesiologists to be the safest of all. However, the use of a laryngoscope and tracheal intubation after inducing anaesthesia is almost always associated with a hemodynamic surge due to reflex sympathetic excitation caused by laryngopharyngeal stimulation. This raised sympatho-adrenal venture results in hypertension, tachycardia, and arrhythmias[3].

This transient, fluctuating, and unstable rise in blood pressure and heart rate is apparently of less significance in healthy individuals. Moreover, both are perhaps a constant risk to patients with hypertension, cerebrovascular diseases, myocardial insufficiency, intracranial lesions, and penetrating eye injuries. This laryngoscopic response in corresponding patients is prone to incidents like pulmonary oedema, myocardial deficits, and cerebrovascular mishaps. At least in such individuals, it is essential to attenuate these detrimental hypertensive and rate-responses[4].

Lignocaine is the chief example of an amino-amide local anaesthetic used as a general anaesthetic adjuvant. Lignocaine competently reduces nociception and cardiovascular sympathomimetic responses to the surgical strain, postoperative pain, and analgesic demands[6]. It is classified as an anti-arrhythmic drug that could prove substantial for cardiac smooth-muscle action potential and help in myocardial conduction. It also invades membrane receptors to reduce the permeability of Na ions by preventing both the initiation and conduction of impulses. The maximum safe dose for topical use is 3mg/kg, as recommended by the British National Formulary for Children, and for intravenous use, it is 1.5–2.0mg/kg[7]. Considering the previous estimate of MAP at 5 min observed as 86.60±9.10 in the IV group and 94.63±10.061 observed in the control group, No significant difference was observed in all three treatment groups, and MAP was smaller in group 1 as compared to group 2. Common side effects that can be observed are dizziness, nausea, and drowsiness. Hypoxia, bradycardia, tremors, twitching, and convulsions also sometimes occur at higher levels.

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The rationale of this study is that endotracheal intubation is associated with activation of the sympathetic system, which results in tachycardia and hypertension. A higher incidence of mortality and morbidity was also reported in patients with cerebrovascular disease. The use of lignocaine in nebulization proves substantial with fewer side effects. The study can be beneficial when it is proven that nebulization of lignocaine is as effective as or more effective than IV lignocaine in relieving sympathetic stimulation. According to the existing studies, the effect of lidocaine is not fully understood in controlling hemodynamic response. Also, keeping in mind the health condition and living standards of our population, there is a paucity of local data, therefore we are conducting this study.

The IV group showed lower heart rate, while the nebulization group had significantly higher systolic and diastolic blood pressure and lower complications incidence compared to the control group.

## MATERIALS AND METHODS

This randomized control trial was conducted at the Sindh Institute of Urology and Transplantation, Karachi, from December 1st, 2021, to May 31st, 2022 after IRB permission and 90 participants were enrolled. All patients age 18–65 years old, both genders, ASA Grade I, Mallampati scored 1 and 2, single attempt of laryngoscopy, duration of laryngoscopy less than 15 seconds recorded by stopwatch, and giving informed consent were included. Patients with comorbidities such as diabetes, hypertension, cardiovascular disease, kidney and liver diseases, respiratory diseases, recent respiratory infection, pregnancy, allergy to lignocaine, limited mouth opening, and edentulus were excluded. After history and examination of the patient, an equal number of patients were taken into three groups: Group I was allotted to patients in whom 2% lignocaine 1.5mg/kg was given by intravenous route, Group N was allotted to patients in whom 4% lignocaine 1.5 mg/kg was given by nebulization, and Group C, the control group, was allotted to patients in whom normal saline placebo was given, as control was no drug given before and after surgery. The randomization was performed using the SNOSE protocol.

A pre-operative assessment of patients was done prior to the surgical day, and the weight of the patient was recorded during a fast of more than 6 hours by a properly balanced weighing machine. To measure height, the patient stands straight on the scale with his back to the measuring bar. The bar was lowered so

that it lightly touched the top of the patient's head. The height was recorded in centimeters. To measure BMI, the following formula was used: Calculation: [weight (kg) / height (cm)] x 10,000.

A detailed pre-anaesthetic evaluation, including a history of previous illnesses, previous surgeries, a general physical examination, and a detailed examination of the cardiovascular system, respiratory system, and other relevant systems, was taken. Patients were brought to operation theatres 30 minutes before surgery, and their rhythm was continuously monitored using a visual display of ECG lead 2, non-invasive blood pressure readings, and SpO2. On the operating table, the intravenous line was secured with an 18G cannula, and a ringer lactate 10 mL/kg/hour infusion started. Patients were connected to non-invasive monitoring with a 3-lead electrocardiograph (ECG lead II), pulse oximeter, and non-invasive BP monitor (oscillotonometer) and recorded. All patients were pre-medicated with Inj. Midazolam 1mg IV to allay anxiety. A face mask for pre-oxygenation was also used on all patients for 3 minutes.

Anaesthesia was induced with an injection of propanol (2 mg/kg). All patients will receive a 0.1 mg/kg injection of Nalbuphine IV for analgesia. After loss of verbal response and confirmation of ventilation, ET was facilitated with a non-depolarizing muscle relaxant injection of Atracurium 0.5 mg/kg IV loading dose. Laryngoscopy was performed using a Macintosh laryngoscope blade size 3 or 4. On visualisation of the vocal cords, a cuffed ET was passed to the trachea. Anaesthesia was administered by an oxygen/air mixture (FiO2-40%) and isoflurane 1%. The following hemodynamic response was recorded in all patients: heart rate (HR) in beats per minute (BPM), systolic blood pressure (SBP) in mmHg, diastolic blood pressure (DBP) in mmHg, and mean arterial pressure (MAP) in mmHg. The above hemodynamic responses were noted as below basal before giving any study drugs and premedication, at one-minute intervals for 10 consecutive minutes after laryngoscopy and intubation, and any immediate side effects noted were mentioned. Data was entered and analysed using SPSS-24.0. The ANOVA test was applied, and $P<0.05$ was considered significant.

## RESULTS

The average age of the patients was 35.92±9.87 years. The mean age, weight, height, and body mass index are shown in Table 1. There were 41(45.6%) males and 49 (54.4%) females, and the Mallampthi classification of the patients is presented in Table 2. The mean heart rate was not statistically significant among groups at baseline and 1 min, 3 min, and 8 min, while it was statistically significant at 2 min and 9 min (Table 3). The mean systolic BP was also not significant among groups at baseline and 1 min, but it was statistically significant among groups during 2–6 min, and after 6 min, it was stable at all points (Table 4). Mean diastolic BP was also not significant among groups at baseline and 1 min, but it was statistically significant among groups during 2 min to 6 min and then 8 min; however, it was not statistically significant at 7 min, 9 min, and 10 min (Table 5). Similarly, mean atrial BP was also not significant among groups at baseline and 1 min, but it was statistically significant among groups during 2–6 min and then 8 min; however, it was not statistically significant at 7 min to 10 min (Table 6). Regarding immediate side effects, the frequency of side effects was lower in groups N and I than in group C, but the rate of drowsiness, tremors, and hypoxia was significantly higher in group C as compared to groups N and I, as shown in Table 7.

Table 1: Descriptive statistics of the patients according to groups (n=90)

| Variable | Group N (n=30) | Group I (n=30) | Group C (n=30) |
|---|---|---|---|
| Age (Years) | 38.37±10.02 | 34.97±10.13 | 34.43±9.29 |
| Weight (kg) | 64.03±10.19 | 62.83±11.73 | 65.83±10.69 |
| Height (cm) | 160.13±7.01 | 162.2±9.63 | 162.87±8.02 |
| Body mass index ($kg/m^2$) | 24.993±3.95 | 24.01±4.64 | 24.817±3.68 |

Table 2: Demographic information of the patients (n=90)

| Variable | Group N (n=30) | Group I (n=30) | Group C (n=30) |
|---|---|---|---|
| **Gender** | | | |
| Male | 11 (36.67%) | 14(46.67%) | 16 (53.33%) |
| Female | 19 (63.33%) | 16 (53.33%) | 14(46.67%) |
| **Mallampthi score** | | | |
| I | 13 (43.33%) | 17 (56.67%) | 14 (46.67%) |
| II | 17 (56.67%) | 13 (43.33%) | 16 (53.33%) |

Table 3: Comparison of mean heart rate among the groups (n=90)

| Heart Rate | Group N (n=30) | Group I (n=30) | Group C (n=30) | P value |
|---|---|---|---|---|
| BL | 85.60±10.59 | 85.27±15.49 | 81.60±8.10 | 0.35 |
| 1min | 87.73±10.67 | 87.43±16.37 | 84.90±7.95 | 0.64 |
| 2 min | 83.10±10.13 | 75.13±11.72 | 80.90±11.33 | 0.02* |
| 3 min | 81.47±8.74 | 75.67±12.37 | 79.27±13.04 | 0.15 |
| 4 min | 80.83±8.69 | 77.13±12.68 | 80.20±12.96 | 0.42 |
| 5 min | 80.67±8.57 | 78.80±12.29 | 81.73±12.46 | 0.59 |
| 6 min | 80.67±8.51 | 79.77±11.72 | 80.07±10.97 | 0.94 |
| 7 min | 76.10±9.62 | 78.20±12.28 | 80.50±11.24 | 0.31 |
| 8 min | 77.50±10.40 | 76.77±12.68 | 80.47±10.49 | 0.41 |
| 9 min | 73.30±12.99 | 73.23±13.39 | 80.53±11.88 | 0.04* |
| 10 min | 75.00±12.07 | 73.77±13.15 | 80.27±12.33 | 0.11 |

Table 4: Comparison of mean systolic BP among the groups

| SBP | Group N (n=30) | Group I (n=30) | Group C (n=30) | P value |
|---|---|---|---|---|
| BL | 127.33±12.71 | 125.57±9.60 | 126.83±11.10 | 0.82 |
| 1min | 123.77±13.48 | 123.77±12.11 | 124.07±11.58 | 0.99 |
| 2 min | 104.70±9.90 | 122.70±14.32 | 110.03±10.25 | 0.0005 |
| 3 min | 100.33±8.67 | 116.87±14.47 | 10.20±13.76 | 0.0005 |
| 4 min | 97.67±9.16 | 111.83±12.95 | 103.63±13.90 | 0.0005 |
| 5 min | 96.27±9.25 | 110.07±12.27 | 102.40±14.60 | 0.0005 |
| 6 min | 94.63±7.95 | 107.60±12.49 | 100.50±13.25 | 0.0005 |
| 7 min | 123.30±13.65 | 123.30±10.89 | 119.77±11.99 | 0.43 |
| 8 min | 111.67±13.67 | 112.40±10.73 | 113.37±13.98 | 0.87 |
| 9 min | 108.70±13.76 | 108.50±12.68 | 106.67±13.35 | 0.81 |
| 10 min | 104.63±12.24 | 103.83±10.40 | 102.33±11.80 | 0.74 |

Table 5: Comparison of mean diastolic BP among the groups

| DBP | Group N (n=30) | Group I (n=30) | Group C (n=30) | P value |
|---|---|---|---|---|
| BL | 79.63±7.60 | 77.73±8.94 | 77.13±8.51 | 0.48 |
| 1min | 78.07±7.89 | 77.03±7.67 | 76.73±8.65 | 0.79 |
| 2 min | 65.00±6.19 | 76.93±9.96 | 69.07±8.31 | 0.0005 |
| 3 min | 61.80±5.89 | 72.30±9.39 | 65.97±9.08 | 0.002 |
| 4 min | 60.73±7.61 | 69.03±9.54 | 63.60±8.96 | 0.0005 |
| 5 min | 57.97±5.49 | 66.33±9.23 | 60.83±7.43 | 0.0005 |
| 6 min | 56.40±5.61 | 64.63±8.31 | 60.30±8.23 | 0.0005 |
| 7 min | 76.70±8.01 | 75.10±9.51 | 72.73±9.44 | 0.23 |
| 8 min | 77.87±5.06 | 74.60±10.19 | 72.30±7.99 | 0.030 |
| 9 min | 68.90±8.34 | 67.20±9.24 | 66.97±10.24 | 0.681 |
| 10 min | 66.10±8.45 | 63.73±11.33 | 62.97±10.23 | 0.458 |

Table 6: Comparison of mean arterial BP among the groups

| MAP | Group N (n=30) | Group I (n=30) | Group C (n=30) | P value |
|---|---|---|---|---|
| BL | 96.07±8.84 | 94.23±8.10 | 93.47±8.70 | 0.48 |
| 1min | 93.37±9.24 | 93.17±8.61 | 92.27±8.88 | 0.87 |
| 2 min | 78.23±6.92 | 92.43±10.71 | 82.87±8.29 | 0.0005 |
| 3 min | 74.80±6.14 | 87.03±10.28 | 79.57±10.34 | 0.0005 |
| 4 min | 72.60±6.54 | 83.27±10.08 | 77.37±10.71 | 0.0005 |
| 5 min | 70.67±6.18 | 81.23±9.02 | 74.73±9.76 | 0.0005 |
| 6 min | 69.30±5.45 | 79.00±8.83 | 73.63±10.02 | 0.0005 |
| 7 min | 91.23±10.66 | 91.80±9.08 | 90.30±8.10 | 0.82 |
| 8 min | 90.20±10.55 | 91.00±8.58 | 88.77±7.66 | 0.62 |
| 9 min | 83.07±13.10 | 83.90±9.95 | 82.67±9.67 | 0.91 |
| 10 min | 77.07±9.48 | 80.37±10.27 | 77.37±7.32 | 0.30 |

Table 7: Comparison of frequency of any immediate side effects among the groups

| Side Effect | Group N (n=30) | Group I (n=30) | Group C (n=30) | P value |
|---|---|---|---|---|
| Nausea | 6 (20%) | 7 (23.3%) | 10(33.3%) | 0.46 |
| Drowsiness | 6 (20%) | 5 (16.7%) | 14(46.7%) | 0.018 |
| Dizziness | 8 (26.7%) | 4 (13.3%) | 10(33.3%) | 0.186 |
| Shivering | 3 (10%) | 4 (13.3%) | 4 (13.3%) | 0.902 |
| Muscular twitching | 4 (13.3%) | 6 (20%) | 7 (23.3%) | 0.602 |
| Tremors | 2 (6.7%) | 1 (3.3%) | 7 (23.3%) | 0.031 |
| Convulsions | 4 (13.3%) | 2 (6.7%) | 7 (23.3%) | 0.181 |
| Bradycardia | 4 (13.3%) | 5 (16.7%) | 5 (16.7%) | 0.919 |
| Hypoxia | - | - | 6 (20%) | 0.002 |
| Circulatory collapse | - | - | - | NA |

## DISCUSSION

Patients with ischemic heart diseases have shown a significant reduction in hemodynamic responses after endotracheal intubation and laryngoscopy. Deleterious effects are also frequently reported in patients with intracanial aneurysms, cerebral haemorrhage, pulmonary oedema, hypertension, and myocardial dysrhythmias. [9-11] Lignocaine has been extensively used to normalise the hemodynamic response because of various significant properties, including cough suppressant, anti-arrhythmic, vasodilation, and laryngospasm. 13-15 In our study, the average age of the patients was 35.92±9.87 years. There were 45.6% males and 54.4% females. Samuel et al[16] reported that the mean age was 39.19±12.45 years.

In the present study, heart rate was recorded in all study groups. The heart rate appeared to be lower in the IV group, and a significant difference was observed compared to the other groups. The smaller difference was observed in the nebulized group, possibly due to the higher lidocaine used in these studies.[12-14] Systolic and diastolic blood pressure were significantly decreased, and the results of the present study are also comparable to previously published data.[15] Blood pressure was observed to be normal in the nebulized and control groups, and this could be done because of using a face mask for nebulization administration and a lower dose of drug. The author[16] showed that a lower difference in blood pressure was observed in the group that was treated with lidocaine as compared to the group treated with fentanyl. Therefore, the results suggested that lignocaine inhalation leads to a reduction in MAP compared to the IV-injection group.

Several studies have suggested that the use of lignocaine spray results in a lower MAP in the case group compared to the control group[17]. Elective surgery for the evaluation of esmolol was also conducted by, which indicates no change in hemodynamic response in the lignocaine group. IV lignocaine has also been used for the treatment of cough and other responses, including bronchoconstriction and hyperactivity during laryngospasm and tracheal intubation. Proven effects of IV-lignocaine appear to be more suitable to minimise the stress response[18-20].

## CONCLUSION

Heart rate appeared to be lower in the IV group, whereas systolic and diastolic blood pressure in the nebulization group were significantly higher in the control group as compared to the IV group. Complications' incidence was also lower in the nebulization group in contrast to the control group.

**Authorship and contribution declaration:** Each author of this article fulfilled following Criteria of Authorship:

1. Conception and design of or acquisition of data or analysis and interpretation of data.
2. Drafting the manuscript or revising it critically for important intellectual content.
3. Final approval of the version for publication.

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