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Original Research Article

A prospective study evaluating the effect of nebulised lidocaine on haemodynamic responses during nasotracheal intubation

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ABSTRACT

Background: Laryngoscopy and endotracheal intubation result in a significant increase in haemodynamic stress response which is well tolerated by healthy patients but in patients with significant coronary artery or cerebrovascular diseases, if it is not prevented adequately may lead to myocardial ischemia and cerebral haemorrhage.

Objectives: This prospective comparative study was conducted between August 2019-July 2020 to study the effect of nebulised lidocaine on haemodynamic stress responses (primarily mean arterial blood pressure also heart rate, systolic blood pressure and diastolic blood pressure) during nasotracheal intubation.

Materials and Methods: 94 patients who underwent head and neck surgery under general anaesthesia requiring nasotracheal intubation were randomised into two groups using a computational random number, Group A (control group): was nebulised with 5 ml of normal saline. Group B: was nebulised with 5ml of Lidocaine 4% solution. Heart rate(HR), systolic blood pressure(SBP), diastolic blood pressure(DBP), mean arterial blood pressure(MAP), and SpO2 were observed before and after nebulisation, just before intubation, immediately after intubation and at 3, 5 10 min after intubation.

Results: On comparing SBP, DBP, MAP and heart rate immediately after intubation with pre-intubation values, there was a significant surge in both groups but an increase in the control group was more in comparison to the lidocaine group($p<.05$). Thereafter MAP, SBP, DBP and HR gradually decreased till the duration of study i.e. 10 minutes.

Conclusion: The administration of nebulised 4% Lidocaine inhalation before induction attenuates cardiovascular response (primarily in terms of MAP also SBP, DBP and HR) that occurs due to nasotracheal intubation.

1. Introduction

Nasotracheal intubation (NTI) is one of the commonest methods used to provide anaesthesia for surgeries on the head and neck region. NTI involves the tracheal tube passing through the nose hence allowing better isolation and good surgical access for intraoral procedures. In 1951, King described significant reflex circulatory changes caused by laryngoscopy and endotracheal intubation.[1] These changes are initiated by a laryngoscope pressing on the base of the tongue and lifting of epiglottis. Although such a response would likely be tolerated well by healthy patients, these changes may be associated with myocardial ischemia and cerebral haemorrhage in those with significant coronary artery or cerebrovascular diseases.[2] Nasotracheal intubation results in a more severe and sustained hypertensive response in comparison to orotracheal intubation.[3] Commonly used techniques include increasing the depth of anaesthesia by

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heavy pre-medication, potent narcotics such as fentanyl and inhalational anaesthetic agents.[4–6] Others include intravenous (IV) and topical lidocaine, clonidine, calcium channel blockers and magnesium sulphate.[7–10] Lidocaine is one of the most frequently used local anaesthetics and is available in multiple dosage forms. Nebulised lidocaine has been used in clinical practice for a variety of indications. It has been tried in patients with bronchial asthma to decrease airway reactivity.[11] Also, it has been found in various studies that the use of nebulised lidocaine preoperatively decreases the haemodynamic responses during laryngoscopy and orotracheal intubation.[12–15] In this study we have studied the effects of nebulised lidocaine on haemodynamic stress responses during nasotracheal intubation and compared it with the control group. The primary objective of this study was to compare mean arterial pressure changes after nasotracheal intubation between two groups. The secondary objectives were to compare other haemodynamic parameters (heart rate, systolic blood pressure and diastolic blood pressure) between the two groups.

2. Material and Methods

After getting approval from the Ethical Committee (ECR/262/Inst/UP/2013/RR-16) of our University, this prospective comparative study was conducted in a tertiary health care centre from August 2019-July 2020. A total of 94 patients classified as American Society of Anaesthesiologists' physiologic status Classes I- II belonging to 18-65 years planned for head and neck surgery were included in the randomized control double-blind study. Hypertensive patients, patients allergic to local anaesthetics, history of convulsion, pregnant females, anticipated difficult intubation, patients requiring a second attempt at intubation, at high risk of aspiration, and patients with a history of recent URTI were excluded from the study.

All enrolled patients were allocated into one of the two groups by a computer-generated random number. (Diagram 1) Patients were premedicated the night before surgery with tablet alprazolam 0.5mg. After transferring to the operating room blood pressure, mean arterial pressure (MAP), heart rate (HR), ECG, and oxygen saturation (SPO2) were continuously monitored. Intravenous (IV) access was secured with an 18G cannula and baseline SBP, DBP, and HR were recorded. All patients were given injection glycopyrrolate 0.2mg iv and 0.1% oxymetazoline nasal drops were instilled in both the nasal passage. Afterwards, all the patients were randomly nebulised by study drug according to a sequence generated by a computer. Group A patients (control group) were nebulised with 5 ml of normal saline. Group B patients were nebulised with 5ml(200 mg) of Lidocaine 4%(40 mg/ml) solution. The primary anaesthesiologist blinded to the assignments administered nebulisation to patients in all groups. The second anaesthesiologist who was unaware of group allocations recorded the haemodynamic changes. The study drug was prepared by a third anaesthesiologist. Thus, participants as well as anaesthesiologists preparing the drug, administering the drug, and recording outcomes were blinded to the study. The drug was administered as an aerosol through nebulisation. Nebulisation was done with a nebuliser by a gas (100% oxygen at a flow rate of 10 L/min from a wall mount oxygen port) through a 200 cm tubing connected from the oxygen port to the face mask attached with a nebulizer. Nebulisation was continued until the complete solution in the nebulizer got aerosolized (10–12 min). After completion of nebulisation, all the patients were given 2 microgram/kg of fentanyl before induction. All patients received 10 ml/kg of Ringer lactate solution over a 10-min period before induction of anaesthesia and thereby maintenance infusion continued. Thereafter, all patients were pre-oxygenated with 100% oxygen for 3 minutes and induced with injected Propofol 1.5-2.5mg/kg until loss of verbal response followed by muscle relaxant vecuronium 0.1 mg/kg. After 3 min of the bag and mask, ventilation was done with 100% o2 @ 6 l/min, patients were intubated nasally with the appropriate size endotracheal tube by direct laryngoscopy technique using Macintosh Blade. Anaesthesia was maintained with O2:N2O(1:1) and 2% Sevoflurane. Tidal volume was set at 6 mg/kg, the respiratory rate was set at 12/min, and the inspiration/expiration ratio was set at 1:2. All parameters were observed before induction (baseline), just before intubation, immediately after intubation, at 3, 5 and 10 min after intubation.

2.1. Sample size and statistics

The sample size was calculated from PASS 15 software. For each group to achieve a power of 80% and a level of significance of 5% (two-sided) for detecting a true difference in mean arterial pressure between the test and reference group of -7(i.e. 44-51) units, and with the standard deviation of 12 mmHg, the sample size of 47 patients(i.e. a total sample size of 94) was calculated. Statistics were done using SPSS software(version 24). P- value less than 0.05 was considered significant. Categorical data were analysed using chi-square. For other data, an unpaired t-test was used for comparing independent variables and paired t-test was used for dependent variables. Continuous data variables were analysed using ANOVA.

3. Results

This study was conducted in a tertiary health care centre from August 2019-July 2020. A total of 147 patients ASA I- II belonging to 18-65 years planned for head and neck surgery were assessed for eligibility out of which 16 patients declined to participate in the study so 94 patients were

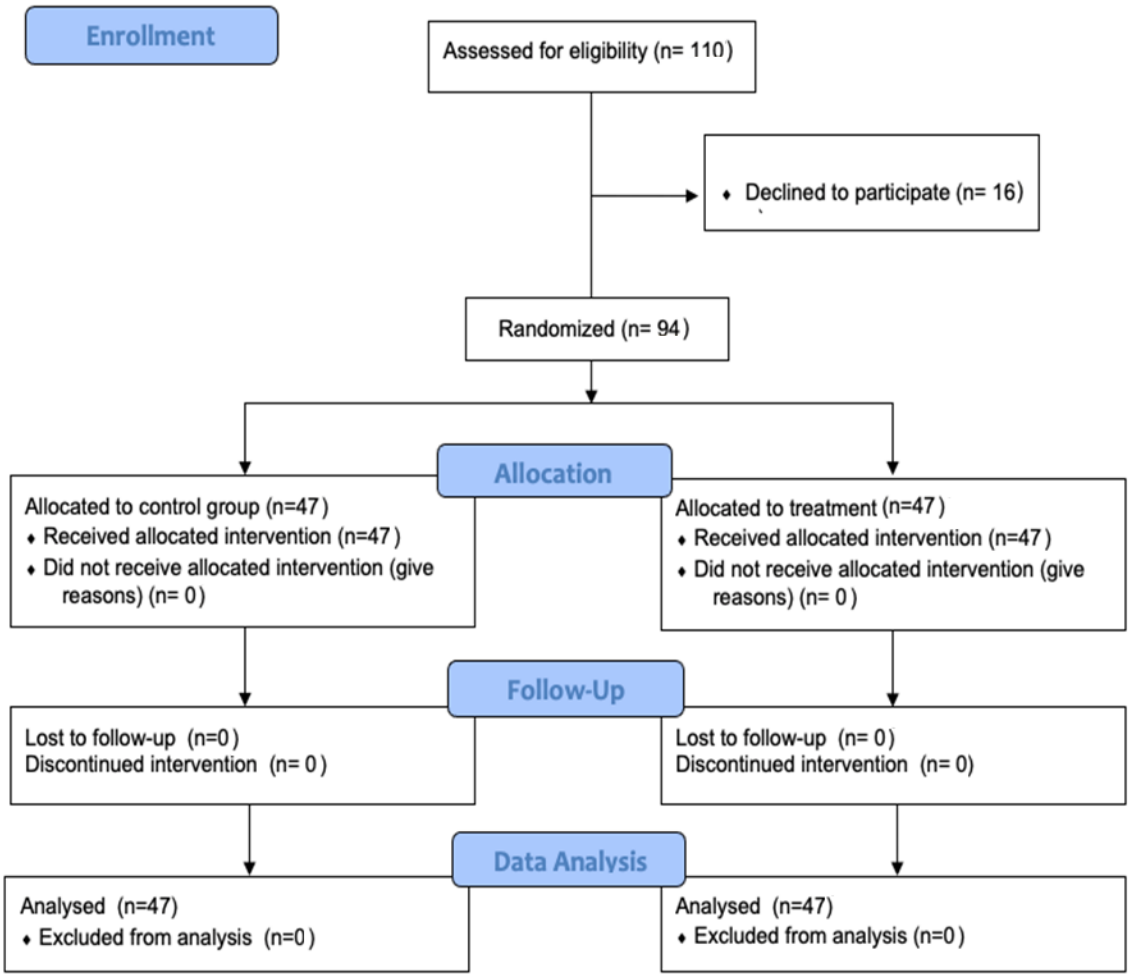

Diagram 1: Consort flow chart

randomized for the study. (Flow chart 1). Demographic profile was comparable between the two groups (Table 1). On comparing SBP, DBP, MAP and HR immediately after intubation with pre-intubation values, there was a significant surge in both groups but the rise in the control group was more in comparison to the lidocaine group($p< .05$). In the control group rise in MAP was more than 20% but in lidocaine group, it was 12%. For SBP rise were 25% and 16% in the control group and lidocaine group respectively. For DBP increase was 25% & 8% in the control group and lidocaine group respectively. HR was increased to 18% in the control group and 4% in the lidocaine group. Thereafter MAP, SBP, DBP and HR gradually decreased in both groups at 3, 5 and 10 min. (Tables 2, 3, 4 and 5). In the intergroup comparison of MAP and SBP both were significantly lower in the lidocaine group in comparison to the control group from immediately before intubation till the duration of the study (10 minutes after intubation)($p<.05$). DBP was significantly lower in lidocaine group before intubation, immediately after intubation and at 3 minutes after intubation. Heart rate was significantly lower in the lidocaine group immediately after intubation and at 3 minutes after intubation.

4. Discussion

In our study, it was observed that pre-intubation MAP, SBP, and DBP were significantly lower in the lidocaine group in comparison to the control group. It might be because of the absorption of lidocaine in systemic circulation and its subsequent effect on the peripheral system. Although the effect of lidocaine on the peripheral vascular system is biphasic. At low concentration it causes vasoconstriction and at high concentration, it has a vasodilating effect.[16] Weinberg L et al also observed that intravenous lidocaine 1.5 mg/kg loading dose followed by an infusion of 1.5mg/hr reduces volatile anaesthetic requirements and lowers blood pressure and heart rate in patients undergoing open radical prostatectomy.[17]

Table 1: Demographic characteristics of patients

	Group C (n= 47)	Group L (n= 47)	p-value
Male(n,%)	6 (12.8)	9 (19.1)	0.398#
Female(n,%)	41 (87.2)	38 (80.9)	
Age in years (Mean ± SD) (Range)	47.8 ± 6.4 (23 – 65)	50.9 ± 10.0 (24 – 65)	0.080#
BMI (Mean ± SD)	25.1 ± 3.5 (19.3 – 34.2)	26.2 ± 4.2 (18.7 – 37.4)	0.155#
ASA I(n,%)	30 (63.8)	29 (61.7)	0.831#
ASAII(n,%)	17 (36.2)	18 (38.3)	
Nasotracheal Intubation Duration in sec (Mean ± SD)	55±16 (30 – 86)	58±18 (30 – 90)	0.342#

*p value< .05= significant, #p value > .05= significant

Table 2: Mean difference of changes in mean arterial blood pressure (MAP) between two group

MAP (mm of Hg)	Group C Mean±SD (n= 47)	Group L Mean±SD (n= 47)	t-value	p-value
Baseline	94.1±4.7	93±4.7	1.097	0.276#
Just before intubation	81.5±5.2	77.9±4.1	1.288	0.001*
Immediately after intubation	101.9±3.6	86.9±4.4	17.997	0.001*
At 3 min	92.4±5.3	82.3±4.6	9.844	< 0.0001*
At 5 min	88.1±6.7	83.8±5.1	3.519	0.001*
At 10 min	87.0±6.3	82.7±5.1	3.664	< 0.0001*

*p value< .05= significant, #p value > .05= significant

Table 3: Mean difference of changes in Systolic blood pressure (SBP) between two groups

SBP (mm of Hg)	Group C Mean±SD (n= 47)	Group L Mean±SD (n= 47)	t-value	p-value
Baseline	127±7.3	123.4±8.1	2.269	0.026*
Just before intubation	108.2±8.7	102.9±6.9	3.238	0.002*
Immediately after intubation	136.1±6	119.1±8.4	11.325	< 0.0001*
At 3 min	128.5±9.2	113.4±8.8	8.143	< 0.0001*
At 5 min	122.6±11	112.7±7.4	5.110	< 0.0001*
At 10 min	121.8±11.3	110.3±7	5.961	< 0.0001*

*p value< .05= significant,#p value > .05= significant

Table 4: Mean difference of changes in diastolic blood pressure(DBP) between two groups

DBP (mm of Hg)	Group CMean±SD (n= 47)	Group LMean±SD (n= 47)	t-value	p-value
Baseline	77.6±5.3	77.8±5.6	-0.190	0.850#
Just before intubation	67.5±5.8	65.4±4.3	2.042	0.044*
Immediately after intubation	84.7±3.9	70.9±4	17.032	< 0.0001*
At 3 min	74.3±6.4	66.8±4.2	6.756	< 0.0001*
At 5 min	70.9±7.7	69.3±6.6	1.038	0.302#
At 10 min	69.5±6.6	68.8±6.7	0.512	0.610#

*p value< .05= significant,#p value > .05= significant

Table 5: Mean difference of change s in heart rate between two groups

Heart Rate(per minute	Group CMean±SD (n= 47)	Group LMean±SD (n= 47)	t-value	p-value
Baseline	82±12	85.5±11.5	-1.421	0.159#
Just before intubation	70.7±11	73.6±11.4	-1.231	0.222#
Immediately after intubation	83.7±10	76±11.9	3.404	0.001*
At 3 min	78.6±9.8	73±11.4	2.540	0.013*
At 5 min	77.3±8.5	75±12.7	1.014	0.313#
At 10 min	76.4±8.9	75.5±12.9	0.390	0.698#

*p value< .05= significant,#p value > .05= significant

Laryngoscopy and endotracheal intubation require manipulation and instrumentation of the airway which may cause several complications, such as increased heart rate and blood pressure due to sympathetic nerve stimulation and increased serum catecholamines. Such responses are exaggerated during nasotracheal intubation. Nasotracheal intubation also stimulates the nasal cavity and nasopharynx which doesn't occur during orotracheal intubation.[18] Moreover in nasotracheal intubation duration is prolonged than orotracheal intubation.[3] In our study, we used lidocaine 4% in nebulisation form, an amide local anaesthetic to blunt the haemodynamic response during nasotracheal intubation. Lidocaine is a cheap and easily available drug and has been used in various forms like spray,[10] intravenous and nebulised forms to abolish the stress response during laryngoscopy and intubation during orotracheal intubation.[19–24] But studies evaluating the effect of nebulised lidocaine on haemodynamic responses during nasotracheal intubation are sparse. Gupta A et al and Gansesan P et al have compared nebulised lidocaine with intravenous lidocaine and they observed that nebulised lidocaine was able to attenuate haemodynamic responses better than intravenous lidocaine.[25,26] The primary objective of our study was to compare MAP between the two groups & the other objectives of our study were to compare SBP, DBP and HR between the two groups. In our study, we have observed that rise in MAP, SBP, DBP & HR immediately after intubation was lesser in the lidocaine group in comparison to the control group. Also, similar findings were observed by Lee S Y et al. who found that MAP and HR at 2.5 and 5 min after orotracheal intubation were significantly higher in the control group than in the lidocaine group where 10% lidocaine was sprayed on a laryngoscope blade or trachea.[7] Venus B et al conducted a study in which topical anaesthesia of the oropharynx with lidocaine aerosol (6ml of 4% for 5min) was given to assess the stress response of laryngoscopy and orotracheal intubation and they reported that a rise in Mean BP, SBP and HR was significantly less than that of their control group.[13] Also our findings are supported by a study done by Jokar A et al in which they compared 4% lidocaine which was sprayed around the patient's epiglottis and larynx with intravenous lidocaine 2% (7.5 mg/kg) and control group and they observed that MAP and HR in two groups (i.v vs lidocaine) were lower than the control group which was statistically significant.23 Patil V et also observed that 4% lidocaine nebulization was effective in attenuating haemodynamic response to direct laryngoscopy and oral intubation.[27] In their study they compared 2% and 4% lidocaine in nebulization. Similar findings were observed by Kumar A et al who observed that nebulised 4% lidocaine in combination with fentanyl was effective in attenuating haemodynamic responses to intubation in comparison to fentanyl or nebulization alone.[28] In our study, MAP was significantly lower in the lidocaine group in comparison to the control group at all intervals post-intubation. (p<.05). Similar to our study Soenarto R et al also found out that MAP was higher in the NaCl group as compared to the 1.5 mg/kg nebulised lidocaine group at all-time intervals post-intubation.[18]

There are some limitations of our study as we have not measured the plasma concentration of lidocaine which might provide more about the safety of inhalation lidocaine. Parkes SB et al observed that inhalation of nebulised lidocaine at a dose of 6 mg/kg produces peak plasma lidocaine concentrations which are well below the toxic threshold of 5 mg/l.[29] In our study we used 5ml 4% lidocaine which is quite below the recommended dosage according to the weight range used in our study. The other limitation of our study was that we used automated blood pressure monitoring for continuous blood pressure monitoring rather than invasive blood pressure monitoring. Invasive blood pressure monitoring is more sensitive and could provide more accurate data. Another limitation of the study is that we have not collected the data on the amount of propofol used in each patient. In our study propofol was used in a varied dose of 1.5-2.5 mg/kg until loss of verbal response, so this would affect the result of our study.

To be concluded, administration of nebulised 4% Lidocaine inhalation before induction attenuates cardiovascular response (MAP also SBP, DB and HR) and sympathetic stimulation that occurs due to nasotracheal intubation.

5. Source of Funding

None.

6. Conflict of Interest

None.

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