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Comparative Study of Intravenous Lignocaine and Sublingual Nitroglycerine to Attenuate Stress Response to Laryngoscopy

Sunil A.[1], Lt Col (Dr) Krishna Prasad G.V.[2], Lt. Col Abhinav Tewari[3], Lt Col (Dr) Ritu Grewal[4]

[1]Divisional Medical Officer (Anaesthesiologist), South Western Railway Gadag Road, Hubli, Karnataka- 580007, India. [2,3,4]Classified Specialist (Anaesthesiology), Military Hospital, Jaipur, Rajasthan 302016, India.

Abstract

Introduction: Laryngoscopy and intubation is associated with a reflex sympathetic pressor response resulting in elevated heart rate (HR) and blood pressures (BP). This may prove detrimental in high risk patients and may be in normal patients also. Several drugs Nitroglycerine (NTG), Lignocaine, Beta-blockers, Opioids, Calcium Channel blockers and Adrenergic agonists, have been used for attenuating the stress response. NTG sublingual spray is a new introduction to attenuate the stress response to intubation. *Aims*: Aim of this study was to compare the effects of sublingual NTG spray and intravenous (iv) Lignocaine on the haemodynamic response following laryngoscopy and intubation. *Patients and Methods:* Randomised control study involving sixty ASA I and II patients who are aged between 20 to 40 years posted for elective surgery were divided randomly into two groups of thirty each. 'Z' test was used for statistical analysis. All patients received premedication with Glycopyrrolate (0.01mg/kg), Midazolam (0.02 mg/kg)iv. Patients were induced with Thiopentone 5 mg/kg iv and muscle relaxant was used in the form of Vecuronium (0.1 mg/kg)iv. First group received iv Lignocaine 1.5 mg/kg, 5 min before intubation and second group received two puffs of NTG sub lingual spray, 400mcg/spray. HR and BP were recorded noninvasively before induction, post-induction, at intubation (0 min), 1,3,5,7 and 10 min from the onset of laryngoscopy. Pair wise comparison between the groups was done by `z' test. For all tests a `z' value of 1.96 was considered significant and a `p' value of 0.05 was considered significant. *Results*: In group N, the rise in systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) was not significant at 1, 3 and 5 min after laryngoscopy, the attenuation was statistically highly significant with p values of < 0.001. Where as in group L, there was significant increase in SBP, DBP and MAP till 7 min post laryngoscopy, after which the values reached the pre induction values. *Conclusions*: Pre-treatment with sublingual NTG spray provides a consistent and reliable attenuation of pressure response to laryngoscopy and intubation when compared to iv Lignocaine.

Keywords: Attenuation; Laryngoscopy; Intubation; Nitroglycerine; Lignocaine.

Introduction

Endotracheal intubation has become an integral part of anaesthetic management and critical care since its description in 1921 by Row Botham and Magill. In 1940, Reid and Brace first described the hemodynamic response to laryngoscopy and intubation is noxious stimuli of the upper airway [1]. The rise in the pulse rate and blood pressure is usually transient occurring 30 seconds after intubation, lasting for less than 10min [2]. Usually these changes are well tolerated by healthy individuals. However, these changes may be fatal in Patients with Hypertension [3], Coronary artery disease [4], or Intracranial hypertension and also in normal patients. Numerous agents have been utilized to blunt these stimulatory effects on the Cardiovascular system induced by laryngoscopy and endotracheal intubation such as deepening of anaesthesia, pretreatment with vasodilators such as Nitroglycerin(NTG) [5], Lignocaine [6], Beta-blockers[7], Opioids [8], Calcium Channel blockers[9] and Alpha Adrenergic agonists [10].

Corresponding Author: Lt Col (Dr) Krishna Prasad G.V., Classified Specialist (Anaesthesiology), Military Hospital, Jaipur, Rajasthan 302016, India.
E-mail: drkaypee99@gmail.com

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Lignocaine iv has traditionally been used to minimize the stress response. Hence, it is important to find an effective means of attenuating sympathetic responses to laryngoscopy and tracheal intubation. Many strategies have been advocated to minimise these hemodynamic responses and aimed at different levels of the reflex arc are topical application and infiltration of local anaesthetic to superior laryngeal nerve, block of central mechanism of integration and sensory input: i.e Fentanyl, Morphine, Block of efferent pathway and effector sites iv Lignocaine, Beta blockers, Calcium channel blockers, NTG. No single drug or technique is satisfactory [11].

NTG was the first practical explosive ever produced that was stronger than black powder. NTG was first synthesized by the chemist Ascanio Sobrero in 1846, who observed that a small quantity placed on tongue elicited severe headache. Sobrero initially called his discovery Pyroglycerine, and warned vigorously against its use as an explosive. It was later adopted as a commercially useful explosive by Alfred Nobel. Nobel experimented with several safer ways to handle the dangerous NTG. Following the discovery that Amyl nitrite helped alleviate chest pain, Dr William Murrell experimented with the use of NTG to alleviate angina pectoris and to reduce the blood pressure. He began treating his patients with small doses of NTG in 1878 [12]. NTG sublingual spray is a metered dose spray containing NTG. This product delivers NTG (400 mcg per spray) in the form of spray droplets under the tongue.

Aim

The purpose of the present study was to compare the effect of NTG sublingual spray with Lignocaine iv on the increase of blood pressure following laryngoscopy and intubation prior to surgery. The objectives of the present study were:

To compare the effect of NTG sublingual spray and Lignocaine iv in attenuating the stress response to laryngoscopy and intubation, with respect to changes in the heart rate (HR), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Mean arterial blood pressure(MAP). And to evaluate any side effects associated with the use of these drugs.

Subjects and Methods

A randomized control study of attenuation of sympathetic response to laryngoscopy and intubation was done in 60 patients posted for elective surgery. General anaesthesia was provided with endotracheal intubation for all patients. Patients undergoing various orthopaedic, ENT, General Surgical and Laparoscopic procedures were selected.

Ethical committee approval was obtained as per the protocol of the Ethical Committee Review Board of the institution. Informed consent was obtained from all the subjects included in the study. The Inclusion criteria were: Patients scheduled for elective surgeries, Age between 20 to 40 years, Patients with ASA grade I or II. The Exclusion criteria were: Unwilling patients, Emergency surgeries, Anticipated difficult intubation, Patients with ASA grade III or higher, Patients with cardiovascular diseases. Patients were selected after thorough preanaesthetic assessment. 60 cases were divided into two groups of 30 each. Group-L: Lignocaine group. In this group lignocaine iv, 1.5mg/kg was administered for attenuating sympathetic response to laryngoscopy and intubation. Group-N: NTG group. Here patients received sublingual NTG spray, 2 puffs of 400mcg each, before laryngoscopy and intubation. Anaesthesia was given after pre-oxygenation (6 liter/min) for 3 minutes. Midazolam (0.02mg/kg) and Fentanyl (2mcg/kg) was administered as premedication and induction with Thiopentone (5mg/kg). Vecuronium (0.1mg/kg) was injected after disappearance of eyelash reflex. At this time, patients in group L received Lignocaine intravenous (1.5mg/kg) 5min before intubation. Patients in group N, received NTG sub lingual spray two metered sprays (400mcg/spray) under the tongue, just prior to intubation by opening mouth and retracting the tongue to expose the ventral aspect of the tongue. The rest of the procedure was same for all patients, 3min after oxygenation with mask, patients were intubated by using Macintosh laryngoscope with PVC tube. Anesthesia was maintained in both groups equally using 1-1.5 MAC of isoflurane, N_2O and O2 (2: 1). HR, SBP and DBP, MAP were measured before induction, after intubation at 0,1,3,5,7,10min interval. During the surgery, occurrences of any types of arrhythmia, or cardiovascular complications were recorded. HR and BP values were taken from the monitor record by an independent observer who was blinded to the technique used in the patient. An observation was made related to adverse effects of drugs and anaesthesia related problems and were attended appropriately.

Descriptive data presented as Mean ± standard deviation in percentage. Pair wise comparison between the groups was done by 'z' test. For all

tests a 'z' value of 1.96 was considered significant and a 'p' value of 0.05 was considered significant. Statistical analysis were performed using the Statistical Package for the Social Sciences, version 19.0 (SPSS, Inc., Chicago, IL, USA).

Results

The mean value of age was 29.7±7.51 and 30.3±6.43 for group L and group N respectively. There was no significant difference between the two groups (p>0.05). No significant difference was observed in sex wise distribution between the two groups (p>0.05).

Mean value of weight is 61.33±7.17. In NTG group, mean of 61.6±7.95. No significant difference were observed between the two groups (p>0.05).

Heart rate (Figure 1): In the group L, pre induction HR was 91.18±8.23, after induction HR was 96.18±10.69. At onset of laryngoscopy (0 min) the rate was 98.2±8.4. At 1 min from onset of laryngoscopy the heart rate increased to 120±10 and remained higher till 3min with mean of 114.20 ±11.77. Subsequently decreased from 5min to 10min post laryngoscopy, 99.46±13.18 at 5 min, 98.94±11.47 at 7 min and 10 min it was 94.87±8.64. In the group N, the heart rate pre-induction was 89.3±6.80, post induction it was 91.76±6.27. At laryngoscopy the heart rate was 93.8±6.4 and 1 min after that the rate increased to 119.74±8.09 and remained high till 3min (113.48±8.74). Subsequently the mean heart rate decreased to 93.60±6.20 at 5min and to 92.6±9.86 at 7min and to 91.96±5.78 at 10min post laryngoscopy. The difference in heart rates between the two groups was statistically not significant (p > 0.05).

Systolic Blood Pressure (Figure 2): In group L, the mean pre induction values of SBP was 119.88±10.86

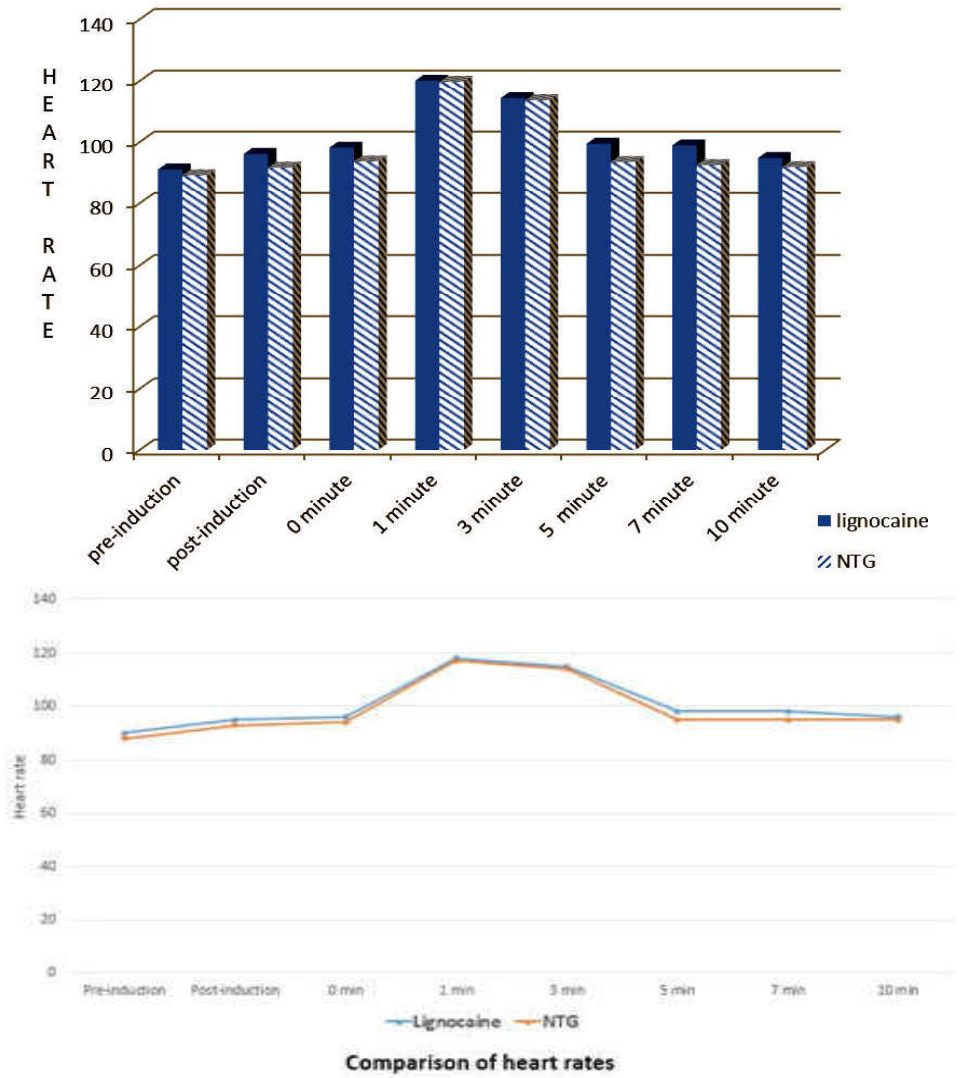


Fig. 1: Comparison of heart rates

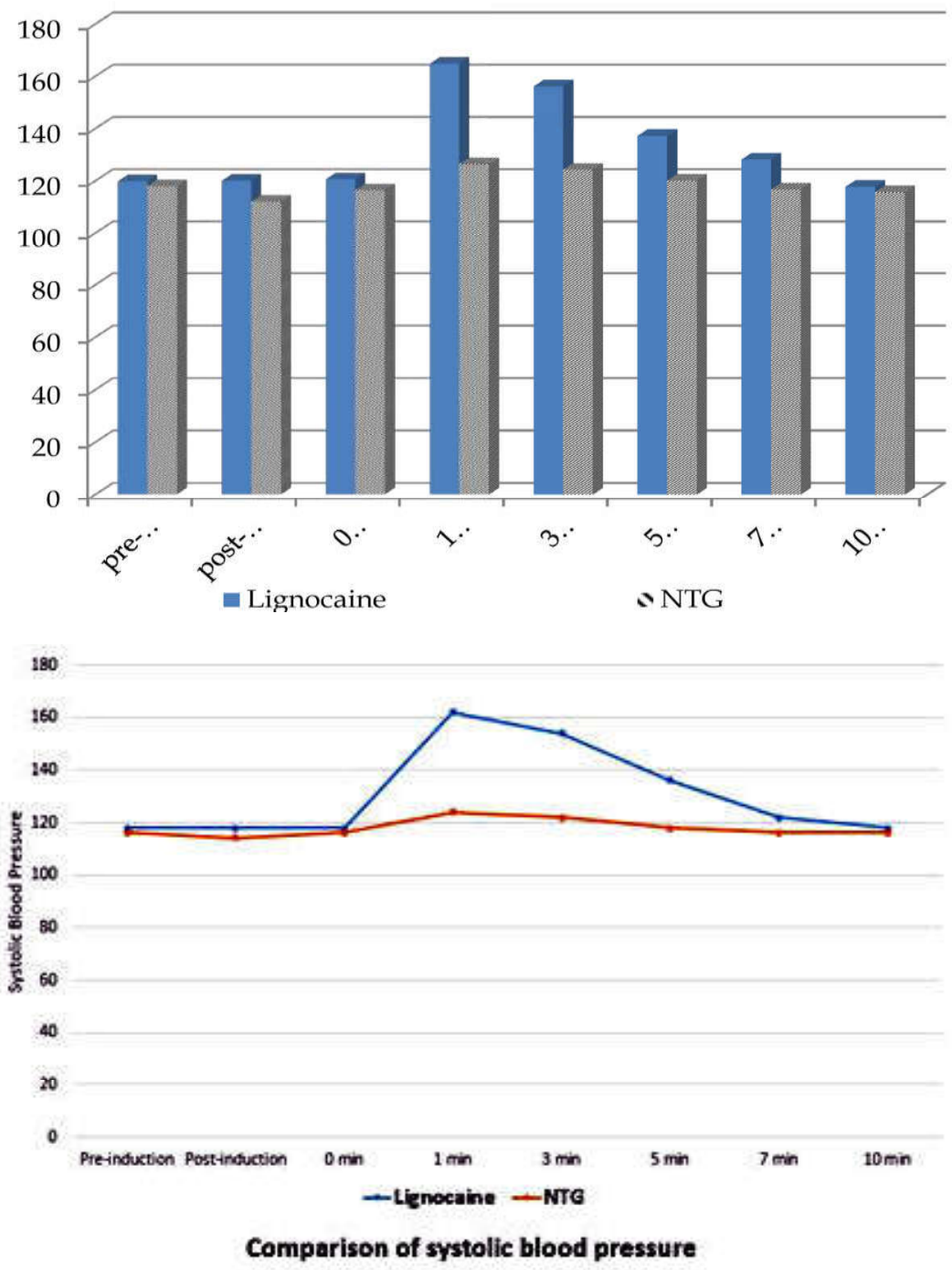


Fig. 2: Comparison of systolic blood pressure

and after induction it was 120.10±11.70. At onset of laryngoscopy (0 min) pressure was 120.64±10.60. At 1 min after the onset the pressure increased to 164.90±11.48 and at 3min it was 156.10±11.64. By 5 min the pressure started reduced 137.21±13.09, then at 7min it was 128.14±11.13 and at 10min it was 117.72± 10.01. In group N, the mean pre induction values of SBP was 117.96±12.22 and after induction 112.03±10.98. At onset of laryngoscopy (0 min) pressure was 116.42±11.60. At 1 min after the onset the pressure increased to 126.35±10.55 and at 3 min it was 124.22±10.13. By 5 min the pressure reduced 120.02±9.83, then at 7 min it was 116.67±9.49 and at 10 min it was 115.04±9.40. No significant variation was noted in both the groups at pre induction, post induction and at laryngoscopy (0 min). In

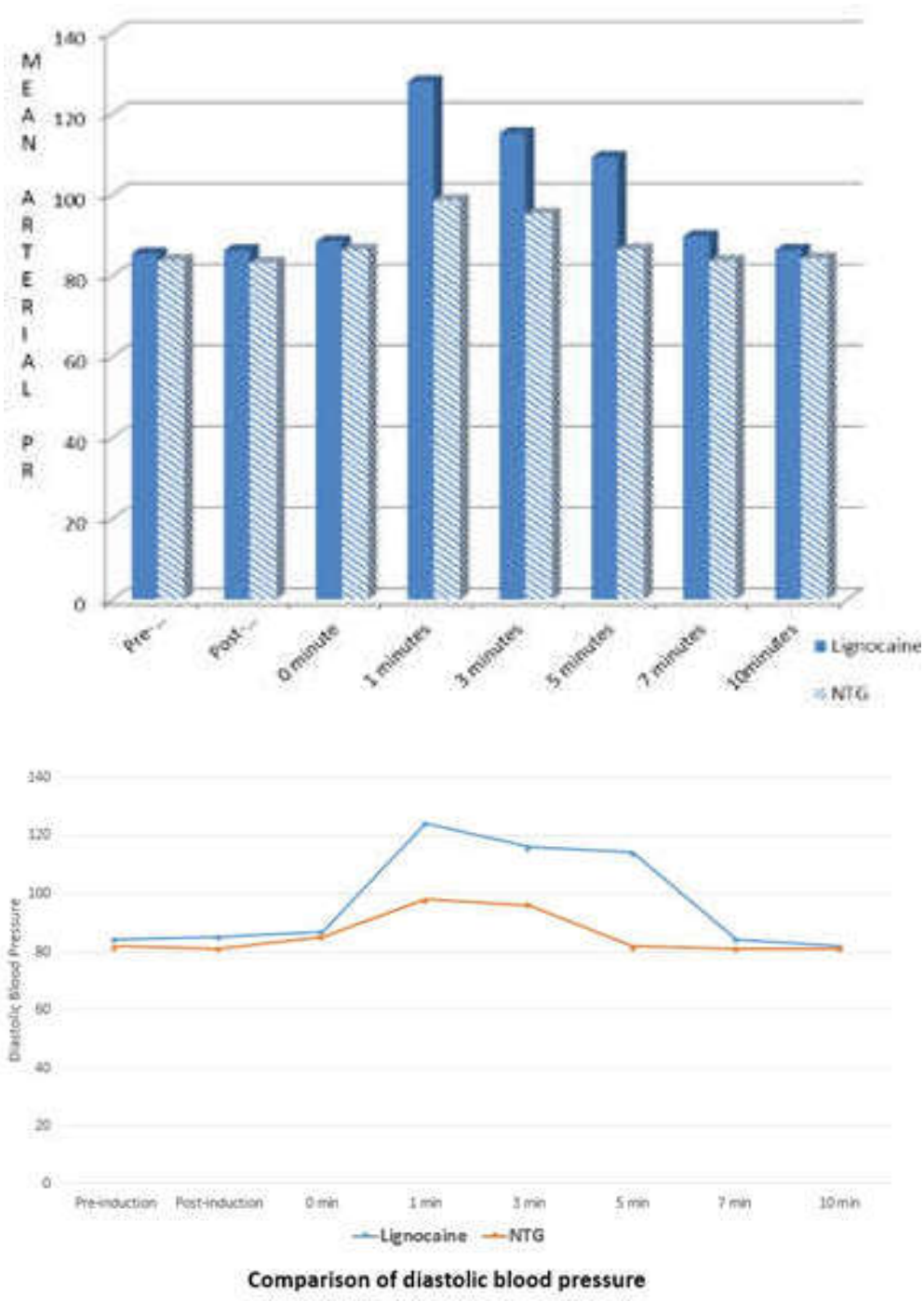
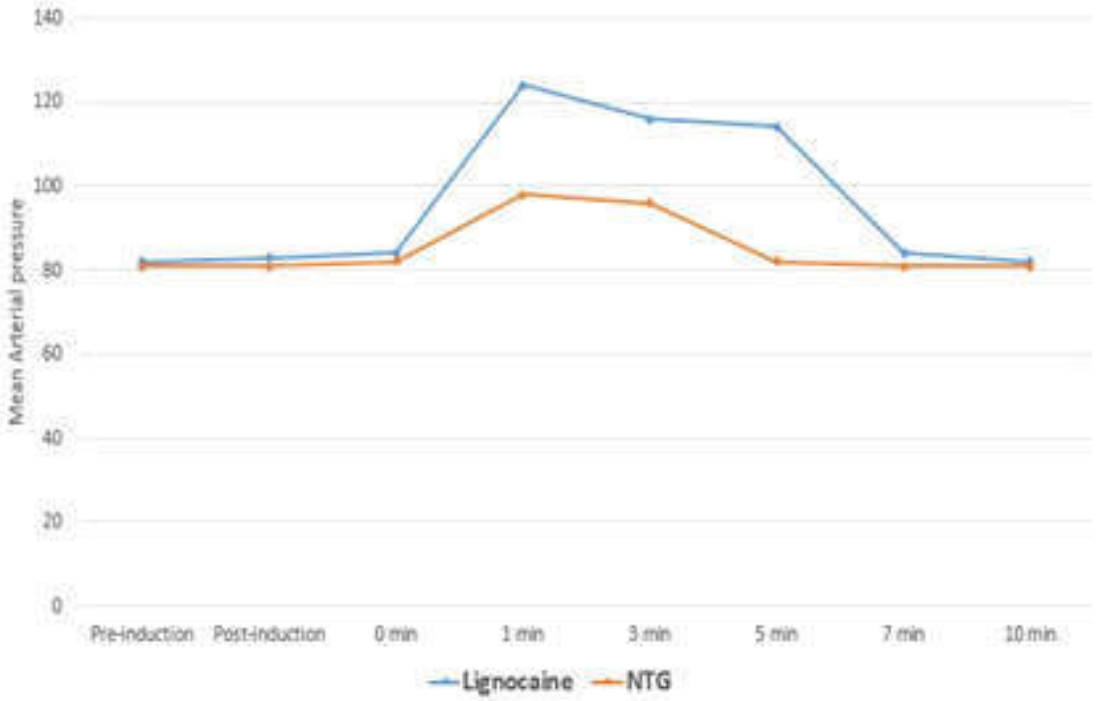


Fig. 3: Comparison of diastolic blood pressure

comparison with lignocaine, nitroglycerine group showed a statistically significant attenuation of systolic blood pressure at 1 min, 3 min and 5 min after onset of laryngoscopy with p values of <0.001 and by 5 min the values were almost equal to basal values.

Diastolic Blood Pressure (Figure 3): In the group L, the mean pre induction values of diastolic blood pressure was 68.28±6.12 and after induction it was 70.32±6.40. At onset of laryngoscopy (0min) pressure was 72.00±6.20. At 1 min after the onset the pressure increased to 109.40±5.18 and at 3 min it was 94.60±6.11. By 5 min the pressure started reduced 89.84±5.20, then at 7 min it was 76.60±5.47 and at 10 min it was 74.68±5.52.In the group N, the mean pre induction values of diastolic blood



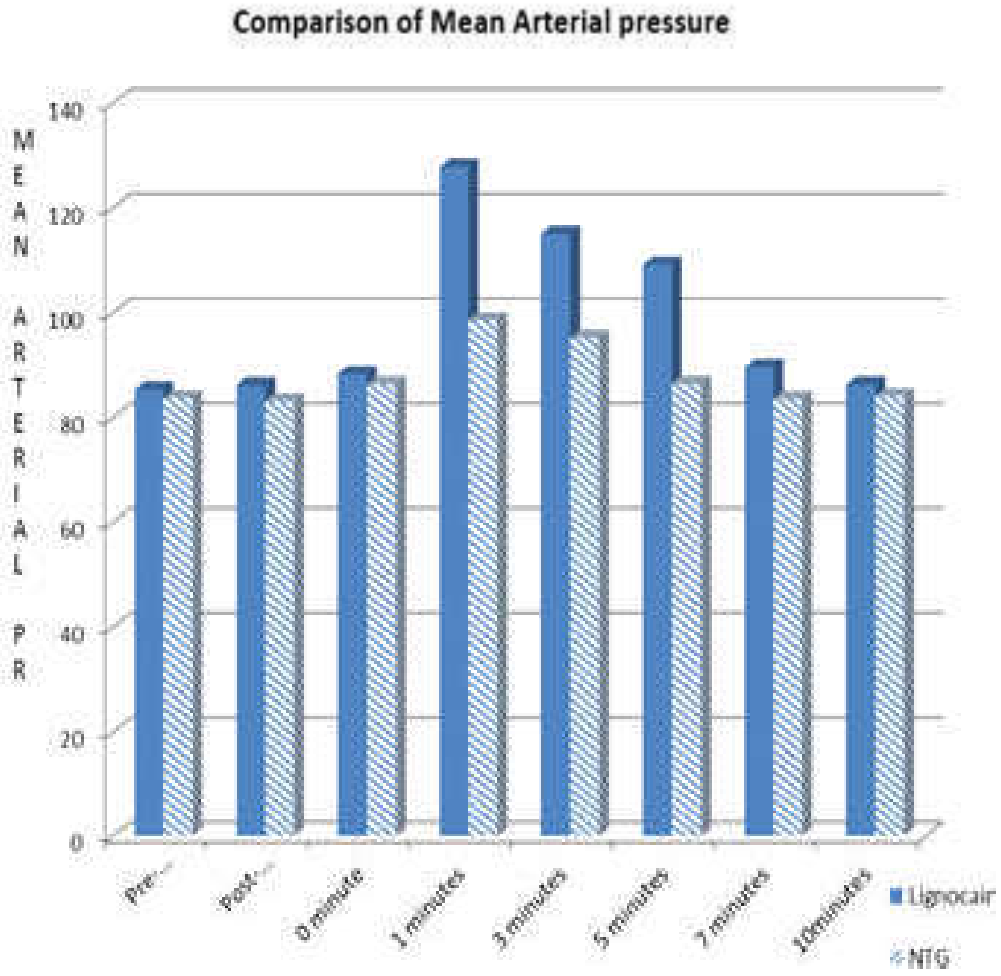


Fig. 4: Comparison of mean arterial blood pressure

pressure was 66.72±5.77 and after induction it was 68.82±5.37. At onset of laryngoscopy (0 min) pressure was 70.74±5.40. At 1 min after the onset the pressure increased to 84.92±5.22 and at 3 min it was 79.78±4.28. By 5 min the pressure started reduced 69.80±5.52, then at 7 min it was 67.10±4.80 and at 10 min it was 68.14±4.40. No significant difference was noted in diastolic blood pressure at pre induction, post induction and at onset of laryngoscopy. However the attenuation of diastolic systolic blood pressure with Nitroglycerine was statistically highly significant at 1 min, 3 min and at 5 min after the onset of laryngoscopy.

Mean Arterial Pressure (Figure 4)

In the group L, the mean arterial pressure before induction was 85.5±6.68 and after induction were 89.25±6.62. At laryngoscopy(0 min) the mean arterial pressure was 88.42±6.42. At 1 min after onset of laryngoscopy the map increased to 127.9±6.17 and subsequently the pressure at 3min was 115.20±6.17, at 5 min was 109.31±6.86 and by 7 min it was 89.75±6.33 almost equal to basal values and at 10 min it was 86.2±5.89.In the group N, the mean arterial pressure before induction was 83.80±5.75. After induction it was 83.17±5.16 and at laryngoscopy the pressure was 86.42±5.40. At 1 min, the mean arterial pressure increased to 98.61±5.24 subsequently at 3 min it was 95.34±4.72. At 5 min it was 86.5±4.66 reached almost to basal levels at 7 mins it was 83.62±4.42 and by 10 min it was 84.20±4.17.No significant difference was noted in mean arterial blood pressure at pre induction, post induction and at onset of laryngoscopy (0 min). However attenuation of mean arterial pressure with nitroglycerine was statistically highly significant attenuation at 1 min, 3 min and 5 min after onset of laryngoscopy.

Discussion

Laryngoscopy and intubation is associated with rise in heart rate, blood pressure and incidence of cardiac arrhythmias. These potentially dangerous changes disappear within 5min of onset of laryngoscopy [13]. Although these responses of blood pressure and heart rate are transient and short lived they may prove to be detrimental in high risk patients especially in those with cardiovascular disease [4], increased intracranial pressure or anomalies of the cerebral blood vessels. An average rise in MAP of 25mmHg and 47.7mmHg has been documented [14]. A rise in mean heart rate of 29.9 beats/min has also been noted [2]. Many factors influence the cardiovascular changes associated with laryngoscopy like age, drugs, depth of anaesthesia, hypoxia, hypercarbia, etc., variations in HR decrease with age, young patients show more extreme changes [15]. Therefore we opted an optimal age group of 20–40 years.

Patients on antihypertensive drugs may exhibit a decrease in pressor response. We excluded the patients on antihypertensive medications from our study. Different drugs used for premedication, induction, relaxation, maintenance of anaesthesia influence the sympathetic response to laryngoscopy and intubation. Midazolam at a dose of 0.2mg/kg iv decreases the blood pressure and increases the HR similar to Thiopentone [16].

However premedication with of Midazolam has no effect on sympathetic response to laryngoscopy and intubation. Glycopyrrolate premedication can moderately increase the HR. Thiopentone was selected for induction since it still continues to be the most popular agent for induction. In normovolemic patients Thiopentone 5mg/kg iv can transiently decrease 10-20mm Hg of BP and increase the HR by 15-20 beats/min. There is increase in catecholamine levels, both Noradernaline and Adrenaline [17]. Nitrous oxide may increase the tone of sympathetic nervous system, Nitrous attenuates pressor response but did not affect the tachycardia response [18].

Laryngoscopy alone may produce most of the cardiovascular responses reported after laryngoscopy and tracheal intubation during anaesthesia [19].

The most significant laryngoscopic factor influencing cardiovascular responses is found to be the duration of laryngoscopy [13]. A linear increase in HR and MAP during the first 45 seconds has been observed. Further prolongation has little effect. The force applied during laryngoscopy has only minor effect [20].

Attenuation of sympathetic response during laryngoscopy and intubation is of prime concern. Many strategies have been recommended but, no single drug or technique is satisfactory.

Each technique has advantages and disadvantages, the most obvious being that the prevention often outlasts the stimulus.

Bachofen M [21], stated the criteria for selection appropriate drug to prevent sympathetic response. The drug must be applicable regardless of patient collaboration, Prevent impairment of cerebral blood flow and avoid arousal of the patients, It should

neither be time consuming nor affect the duration and modality of ensuing anaesthesia.

In our study, both sublingual NTG spray and iv Lignocaine appear to fulfil the above criteria. Lignocaine though failed to attenuate cardiovascular response to laryngoscopy in a study by Miller and Warren [22], its efficacy was noted by others [6]. Its recommended dose 1.5mg/kg iv, optimum time is 3 min before intubation. NTG has been used intravenous [23], intranasal [24], topical [25] and sublingual tablets [26] successfully in a dose of up to 1mg to attenuate the laryngoscopic stress response.

In the present study NTG attenuated the increase in SBP and prevented a rise in DBP following intubation, though it failed to attenuate inotropic response to intubation. The reason for this could have been the tendency of NTG to cause tachycardia. This finding is similar to that of Singh et al [23] and Vanden Berg et.al [27], who also reported failure of NTG to attenuate increase in HR following intubation. One of the limitations of the present study is that the population enrolled comprised healthy patients of ASA grade I and II. Further studies are required to rule out any other short term or long term adverse effects in especially patients with comorbidities like hypertension, cardiovascular disease and intracranial pathology.

Conclusion

Pre-treatment with sublingual NTG spray provides a consistent and reliable attenuation of pressure response to laryngoscopy and intubation when compared to iv Lignocaine.

Acknowledgement

Conflicts of Interest: Nil

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