# Anaesthesia Section

# Intraoral Nitroglycerine Spray versus Intraoral Lignocaine Spray to Suppress the Haemodynamic Response to Endotracheal Intubation in Patients Undergoing Elective Surgeries under General Anaesthesia: A Randomised Clinical Trial

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# **ABSTRACT**

**Introduction:** General Anaesthesia (GA) is the keystone in the management of complicated and specialised surgeries, enabling the safe and effective performance of procedures that would otherwise be intolerable or unsuccessful for patients. Airway manipulation during GA, especially laryngoscopy and endotracheal intubation, leads to acute haemodynamic changes that may pose risks in susceptible individuals.

**Aim:** To compare the effect of intraoral Nitroglycerine (NTG) spray versus the intraoral lignocaine spray before laryngoscopy and endotracheal intubation.

Materials and Methods: A single-centre, double-blinded, randomised clinical trial was conducted in the Department of Anaesthesia, Sree Balaji Medical College/BIHER, Chennai, Tamil Nadu, India over 18 months from January 2021 to June 2023. Total of 60, American Society of Anaesthesiologists (ASA) grade I and II patients undergoing elective surgery under GA were randomised into two groups: group A received an intraoral spray of nitroglycerin 400 mcg, and group B received an intraoral spray of 10% lignocaine 20 mg. Haemodynamic parameters were recorded at multiple time points during induction, intubation and at various time intervals post-intubation. Data were analysed using Statistical Package for Social Sciences

(SPSS) software version 23.0 via independent two-tailed t-test and One-way Analysis of Variance (ANOVA) for parametric data and via Chi-square test for non parametric data. A p-value < 0.05 was considered statistically significant.

Results: Among total of 60 participants, 33 (55%) belonged to the age group 20-29 years, and 37 (61.67%) were males. The data showed significant attenuation of Blood Pressure (BP) and Heart Rate (HR) changes during laryngoscopy, intubation and post-intubation in both groups (Mean HR: 85.42 vs 77.22 bpm) {Mean Systolic Blood Pressure (SBP): 124.1 vs 128.53 mmHg} {(Mean Diastolic Blood Pressure (DBP): 78.16 vs 81.27 mmHg} and {Mean Arterial Pressure (MAP): 93.47 vs 97.04 mmHg}, with comparative analysis suggesting that NTG exhibited superior control over blood pressure and the results were statistically significant (p-value <0.05).

**Conclusion:** Both intraoral lignocaine and nitroglycerin sprays effectively attenuate intubation-induced haemodynamic responses, with nitroglycerin providing superior blood pressure control during laryngoscopy and intubation. Nitroglycerin spray may be preferred for patients requiring enhanced haemodynamic stability, especially those with hypertension or coronary artery disease, pending further large-scale studies.

Keywords: Anaesthetic agent, Blood pressure, Heart rate, Laryngoscopy, Sympathetic response attenuation

# **INTRODUCTION**

General Anaesthesia (GA) necessitates secure airway management, and devices such as endotracheal tubes are essential for ensuring patient safety during surgical procedures. Since the seminal work by Reid and Brace, it has been well-established that airway manipulation—including laryngoscopy and tracheal intubation—can provoke significant sympathetic responses, manifested as abrupt increases in HR, BP, and arrhythmias, especially in patients with underlying cardiovascular risk factors such as hypertension or coronary artery disease[1]. These events, driven by catecholamine surges, can precipitate serious complications like myocardial ischaemia [2,3].

Over the years, a variety of pharmacological agents, airway devices, and alternative intubation techniques have been investigated to suppress these haemodynamic responses [4-6]. Lignocaine, applied topically to the airway mucosa, has been widely used for its efficacy in reducing intubation-related discomfort and blunting

sympathetic activation by blocking afferent nerve pathways [7,8]. Similarly, Nitroglycerine (NTG), known for its potent vasodilatory and antianginal properties, has emerged as a possible adjunct, available for intraoral or sublingual administration [9].

Previous studies were largely focused on intravenous lignocaine and intravenous NTG in different clinical contexts, and their individual roles in cardiovascular modulation were well-documented [7-9]. However, there was limited evidence directly comparing intraoral NTG and intraoral lignocaine sprays specifically for attenuation of haemodynamic responses during endotracheal intubation [10,11]. The existing gap lies in the lack of robust, direct comparative studies assessing these two agents in this context. Furthermore, the optimal choice for patients at increased cardiovascular risk remains unclear, highlighting a need for focused investigation. Hence, this study was planned to address these gaps and to identify which agent offers better haemodynamic control. Therefore, the present study aimed to compare the efficacy of intraoral spray of lignocaine and NTG in

suppressing the haemodynamic stress response (HR and BP levels) to laryngoscopy and endotracheal intubation in patients undergoing elective surgeries under GA. The primary outcomes measured in the study were: Heart Rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP). The secondary outcomes measured were: Mean oxygen saturation levels (SpO<sub>2</sub>) and Mean Arterial Pressure (MAP).

# MATERIALS AND METHODS

This was a single-centre, double-blinded, randomised clinical trial conducted in the Department of Anaesthesia, Sree Balaji Medical College/BIHER, Chennai, Tamil Nadu, India over 18 months from January 2021 to June 2023.. The study adhered to the principles outlined in the Declaration of Helsinki. Institution Review Board and Human Ethics Committee approved this study as per the reference number 002/SBMCH/IHEC/2020/1366 dated 19.08.2020. The trial was not registered in the clinical registry due to the heightened clinical burden during the Coronavirus Disease 2019 (COVID-19) pandemic (2020-2021).

Sample size calculation: The sample size was calculated using data from Kumari I et al., who studied the use of NTG spray in attenuating pressor responses to laryngoscopy [12]. Their reported DBP values showed a standard deviation of approximately 6-9 mmHg. Assuming an effect size of 6.5 mmHg difference between groups,  $\alpha = 0.05$ , and power = 80%, the required sample size was 27-31 patients per arm. Hence, 30 patients per group and a total of 60 patients were recruited for this study to provide adequate statistical power.

Inclusion criteria: Patients in the age group of 18-60 years, classified under ASA grade I and II, without gender-specific, posted for elective general surgical, Ear, Nose, Throat (ENT) department, and Orthopaedic procedures, with normal Electrocardiogram (ECG) rhythm, and without anticipated difficult intubation were included for this study.

Exclusion criteria: Patients with known allergy to any medications, any anticipated difficulty in intubation, patients with morbid obesity, Body Mass Index (BMI>35 kg/m²), patients who were on antipsychotic medications, ASA grade more than II, existing hepatic/ cardiac/renal diseases, post-COVID infection were excluded.

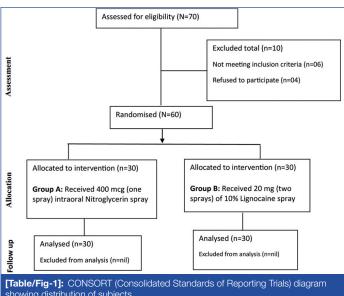
Among the 70 screened candidates scheduled for elective surgery under GA, 60 eligible patients were enrolled after applying exclusion criteria. Written informed consent was obtained from all participants and were randomised into two groups by using a computergenerated random sequence with a 1:1 allocation ratio [Table/Fig-1]. Allocation concealment was achieved using sequentially numbered opaque sealed envelopes prepared by an independent consultant. Double-blinding was done to minimise bias and to ensure that participants, surgeons, anaesthesiologists, nursing staff, and outcome assessors remained unaware of the group assignments throughout the study.

- Group A (n=30): Received 400 mcg (one spray) intraoral NTG
- Group B (n=30): Received 20 mg (two sprays) of 10% lignocaine

The selected doses of NTG (400 µg) and 10% lignocaine spray (20 mg) were based on previously published trials that demonstrated their safety and efficacy in attenuating pressor responses during intubation [13].

# **Study Procedure**

Preoperative and intraoperative management protocol: Once the patient was transferred into the operating room, Intravenous (i.v.) access was established with a 16/18-G i.v. cannula, and Ringer's lactate infusion was started at a rate of 15-20 mg/kg/hour. Premedication with inj.midazolam 0.02 mg/kg and inj.glycopyrrolate



showing distribution of subjects

0.01 mg/kg was given as per the Institution protocol. Vital sign monitors, ECG, HR, Non Invasive Blood Pressure (NIBP), SpO<sub>2</sub>, End-tidal Carbon Dioxide (EtCO<sub>2</sub>), and temperature probe were connected for continuous intraoperative monitoring. Patients were pre oxygenated for 5 minutes with 100% oxygen, then induced with inj.fentanyl (2 mcg/kg), inj.propofol (2.5 mg/kg) and muscle relaxant inj.vecuronium (0.1 mg/kg) was given for intubation facilitation. Airway instrumentation was done 1 minute post-NTG spray or post-lignocaine spray as per the order in the concealed envelope, and intubation of trachea and confirmation was done within 20-25 seconds in all the cases.

Parameters like HR. SBP. DBP and MAP were recorded at baseline. during induction, at intubation, and 1, 3, 5 and 10 minutes postintubation. The duration of surgeries varied from 2-3 hours, based on the surgical procedures.

The GA was maintained with O<sub>2</sub>:N<sub>2</sub>O (50:50) and sevoflurane at 1-1.5 Minimum Alveolar Concentration (MAC). Reversal was achieved with glycopyrrolate (0.01 mg/kg) and neostigmine (0.05 mg/kg) after confirming spontaneous respiratory effort. All patients were extubated following full recovery and transferred to the recovery unit.

## STATISTICAL ANALYSIS

Data analysis was conducted using SPSS version 23.0 (SPSS Inc., Chicago, IL, USA., 2011) and Microsoft Excel. Parametric data were evaluated via Independent two-tailed t-tests, ANOVA or Levene's test; non parametric data were assessed using the Chi-square test. Type I and II errors were set at 0.05 and 0.20, respectively. A p-value < 0.05 was considered statistically significant.

# **RESULTS**

Baseline demographic and clinical statuses of both the groups were comparable and statistically non significant. Oxygen saturation was monitored continuously in all the patients and maintained around 99.5% to 99.6% [Table/Fig-2].

Heart rate variability was comparable in both groups, but HR increase was statistically significant in the group that received NTG spray 400 mcg than in the group that received 20 mg of 10% lignocaine spray during intubation (p-value=0.005), 1 min after intubation (p-value=0.034) and 3 mins after intubation (p-value=0.057) [Table/Fig-3].

Systolic blood pressure remained stable after laryngoscopy and intubation in both groups, but patients who received NTG spray demonstrated better control compared to those given lignocaine spray. Statistical significance was found during intubation (p-value=0.013), 1 min after intubation (p-value=0.019), 3 mins after intubation (p-value

<0.0001), 5 mins after intubation (p-value <0.0001), and 10 mins after intubation (p-value=0.002) [Table/Fig-4].

Parameters	Group A (n %)	Group B (n %)	Chi- square	p-value
Age (in years)				
20-29	17 (56.7%)	16 (53.3%)	1.004	0.605
30-39	8 (26.7%)	11 (36.7%)		
40-49	5 (16.4%)	3 (10%)		
Gender and weight				
Male	18 (60%)	19 (63.33%)	0.07	0.790
Female	12 (40%)	11 (36.67%)		
Mean Weight (kg) (Mean±SD)	50.7±7.3	51.3±7.7		0.756
ASA grading				
ASA I	13 (43.33%)	14 (46.67%)	0.00	0.795
ASA II	17 (56.67%)	16 (53.33%)	0.06	
Oxygen saturation				
Mean SpO <sub>2</sub> (Mean±SD)	99.56±0.44	99.62±0.38		1.00
				(1.1.00)

[Table/Fig-2]: Comparison of demographic profiles among the study groups (N=60) p-value <0.05- Statistically significant; Chi-square test was used for categorical variables; Independent t-test was used for continuous variables

Heart Rate	Group A (Mean±SD)	Group B (Mean±SD)	p-value
Baseline	78.43±13.94	79.57±13.17	0.241
During induction	88.87±14.02	86±12.49	0.085
During intubation	89.4±14.54	84.4±12.12	0.0054
1 min after intubation	85.93±15.75	82.9±12.78	0.034
3 mins after intubation	83.4±16.49	79.5±13.41	0.057
5 mins after intubation	80.37±13.62	78.23±11.24	0.076
10 mins after intubation	79.27±16.01	78.93±10.69	0.096
Grand mean	85.42±14.91	77.22±12.27	0.043

**[Table/Fig-3]:** Comparison of heart rate (mmHg) among the study groups (N=60). A p-value <0.05 - Statistically significant, Independent t-test was applied to compare means between groups

Parameters	Group A (Mean±SD)	Group B (Mean±SD)	p-value
Baseline	124.93±3.51	125.73±4.19	0.234
During induction	122.03±5.71	124.27±5.75	0.013
During intubation	128.73±5.91	134.07±5.84	0.031
1 min after intubation	126.27±9.57	130.2±9.46	0.019
3 mins after intubation	124.17±5.37	136.93±2.03	<0.0001
5 mins after intubation	114.4±5.99	126.6±5.26	<0.0001
10 mins after intubation	124.2±9.89	131.67±8.19	0.0023
Grand mean	124.1±6.56	128.53±5.81	0.002

[Table/Fig-4]: Comparison of systolic blood pressure (mmHg) among the study groups.

A p-value <0.05 - Statistically significant, Independent t-test was applied to compare means between groups

Diastolic blood pressure was more stable in patients receiving NTG spray and had minimal changes to manipulation via laryngoscopy and intubation. Statistical significance was found during induction (p-value=0.02), during intubation (p-value=0.04), 1 min after intubation (p-value=0.002), 3 mins after intubation (p-value=0.003), 5 mins after intubation (p-value=0.001), and 10 mins after intubation (p-value <0.0001) [Table/Fig-5].

Mean arterial pressure also showed statistically significant control during laryngoscopy and intubation in the patient group receiving NTG spray than lignocaine. Statistical significance was found during induction (p-value <0.0001), during intubation (p-value=0.001), 1 min after intubation (p-value=0.002), 3 mins after intubation (p-value=0.003), 5 mins after intubation (p-value <0.001), and 10 mins after intubation (p-value=0.002) [Table/Fig-6].

Parameters	Group A (Mean±SD)	Group B (Mean±SD)	p-value
Baseline	78.66±3.72	79.2±4.44	0.243
During induction	76.53±5.27	80.8±5.08	0.02
During intubation	77.8±7.4	81.27±5.34	0.04
1 min after intubation	77.73±4.89	81.33±6.71	0.02
3 mins after intubation	79.47±3.1	82.93±4.52	0.0034
5 mins after intubation	79.07±4.91	84.33±4.2	0.001
10 mins after intubation	78.6±1.19	82.03±3.89	<0.0001
Grand mean	78.16±3.58	81.27±1.96	0.001

[Table/Fig-5]: Comparison of diastolic blood pressure (mmHg) among the study groups.

A p-value <0.05 - Statistically significant, Independent t-test was applied to compare means between groups

Parameters	Group A (Mean±SD)	Group B (Mean±SD)	p-value
Baseline	92.4±1.22	93.71±3.77	0.076
During induction	91.69±2.73	95.29±4.68	<0.0001
During intubation	95.44±3.08	98.87±4.86	0.001
1 min after intubation	93.91±1.96	97.62±2.84	0.002
3 min after intubation	94.10±1.78	99.39±4.66	0.003
5 mins after intubation	95.51±3.08	97.08±4.86	<0.0001
10 mins after intubation	93.8±1.23	99.89±3.58	0.002
Grand mean	93.47±2.82	97.04±2.22	<0.0001

[Table/Fig-6]: Comparison of mean arterial pressure (mmHg) among the study groups.

A p-value < 0.05 - Statistically significant, Independent t-test was applied to compare means between groups

#### DISCUSSION

Various anaesthetic methods have been introduced and used to attenuate the haemodynamic response due to laryngoscopy and tracheal intubation, with varying results. The goal of any anaesthesiologist is to achieve tracheal intubation via laryngoscopy with as minimal haemodynamic response as possible. The present study was done to assess whether NTG spray (400 mcg/dose) or lignocaine two sprays (10 mg/spray) was better in attenuating this haemodynamic response to laryngoscopy and intubation.

The effect of laryngoscopy and tracheal intubation was studied by King BD et. al., [14]. Burstein King and colleagues suggested that the majority of electrocardiographic changes observed during endotracheal intubation stem from the activation of cardioaccelerator fibres, which provoked a sympathetic surge rather than a vasovagal response as previously suggested by Reid LC and Brace DE [1].

Since then, various anaesthetic approaches and drug regimens have been evaluated for their ability to dampen these cardiovascular responses during laryngoscopy and intubation. In this current study, the focus was on comparing two intraoral medications, nitroglycerin spray (400 mcg/dose) or lignocaine spray 20 mg (2 sprays of 10% metered dose), to determine which drug more effectively controls the haemodynamic changes during laryngoscopy and intubation. Studies with the geriatric population reported notable haemodynamic fluctuations during laryngoscopy [15]. To limit age-related variability in responses, participants between 18 and 60 years of age were included. Reports from the research conducted by Kumari I et al., [12] as well as Madhuri Gopal V and Sangitha D., [16] showed that both 400 mcg and 800 mcg doses of NTG spray were efficacious to attenuate the intubation response. Hence, the present study adopted the NTG spray of 400 mcg, for evaluation.

Heart Rate (HR): Heart rate variability was higher in the patient group that received NTG spray 400 mcg than in the patient group that received 10% lignocaine spray of 20 mg. This tachycardiac effect was likely a reflex response to the vasodilatory impact of NTG. These results echoed findings from researchers such as

Madhuri Gopal V, and Sangitha D., [16], Verma G and Sharma A et al., [17], and Balasandya P and Aswini G [18], Asif M et al., [19]. But, contrasting outcomes were reported by Varshney RK et al., [10], who observed greater HR elevation in the lignocaine group. Similarly, Datla S et al., also concluded that the increase in the HR of the lignocaine group was higher when compared to the NTG group [11]. The reason behind this was pointed out by Manjunath HG and Ravi L , that lignocaine 10 mg/single spray did not adequately anaesthetise the trachea below the vocal cords, which led to an HR rise following intubation and cuff-inflation [20]. Based on this finding, lignocaine, two sprays (20 mg), was adapted in this study for evaluation.

Blood Pressure (BP): In the present study, though there was a rise from the baseline recordings across both groups, systolic and diastolic BP remained within a clinically acceptable range (120/70 to 130/80 mmHg). However, reductions in BP were more substantial in the NTG group. Systolic Blood pressure was on the lower side and did not show an increase in SBP post-laryngoscopy and intubation in patients receiving NTG spray. Diastolic blood pressure was more stable in patients receiving NTG spray and had minimal changes to manipulation via laryngoscopy and intubation. Research by Varshney RK et al., [10] corroborated these findings, noting a significant rise in SBP between the first and fourth minute post-intubation, with values returning near baseline around the sixth to eighth minute after extubation, which was also observed in the present study.

Mean Arterial Pressure (MAP): In the current study, NTG spray was associated with a statistically significant reduction in MAP during laryngoscopy and tracheal intubation, compared to lignocaine in terms of managing cardiovascular stress responses. MAP was constant and showed minimal variation during laryngoscopy and intubation in the patient group receiving Nitroglycerin spray. Nath S and Manjusha JR et al., were also documented that NTG spray is the superior agent to attenuate the pressor responses during endotracheal intubation [21,22]. These studies reinforced the present study's inference that NTG spray is a more effective agent than lignocaine in attenuating sympathetic cardiovascular response to laryngoscopy and intubation.

#### Limitation(s)

The study was conducted exclusively on normotensive patients categorised under ASA I or II, by excluding individuals with comorbid illness. Regarding the conduct of GA, the Institution protocol was followed for premedication (Glycopyrolate-antisialogauge and Ondansetron-antiemetic) in both groups, so that this would not confound study results. Induction and intubation were carried out using propofol and vecuronium due to the restricted availability of other induction agents such as etomidate. A Macintosh laryngoscope was used for all cases; advanced tools like video laryngoscopes were not employed. Haemodynamic monitoring relied on a NIBP device, which constrained the evaluation of certain vital parameters like rate pressure product, cardiac output, and stroke volume.

#### CONCLUSION(S)

In this randomised clinical trial, both intraoral NTG and lignocaine sprays were found to effectively attenuate haemodynamic responses to endotracheal intubation in patients undergoing elective surgeries under general anaesthesia. Nitroglycerin spray demonstrated superior control over systolic and diastolic blood pressure during laryngoscopy and intubation, with statistically significant differences at multiple time points. The tachycardic effect noted with nitroglycerin was likely attributable to reflex responses secondary to its vasodilatory action. Heart rate increases, although present in both groups, were generally more pronounced following NTG use. Overall, blood pressures remained within clinically acceptable ranges, and both agents were safe and well-tolerated. The study

suggests nitroglycerin spray may be especially beneficial in patients requiring enhanced blood pressure control, such as those with hypertension or coronary artery disease, though larger trials are needed to confirm these findings.

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#### PLAGIARISM CHECKING METHODS: [Jain H et al.]

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• Manual Googling: Sep 13, 2025

• iThenticate Software: Sep 16, 2025 (6%)

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**EMENDATIONS:** 6

#### AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
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