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RANDOMISED CONTROLLED STUDY TO EVALUATE THE EFFECTS OF NITROGLYCERINE SUBLINGUAL SPRAY ON TRACHEAL EXTUBATION RESPONSE IN NORMOTENSIVE PATIENTS UNDERGOING SURGERIES UNDER GENERAL **ANAESTHESIA**



| Anaesthesiology | |
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| Dr Surendra | (MD Anaesthesiology), Professor, Department of Anaesthesiology, Gandhi Medical |
| Kumar Raikwar | College, Bhopal. |
| Dr Anil Kori* | (DA, DNB Anaesthesiology), Department of Anaesthesiology, Gandhi Medical College, Bhopal, *Corresponding Author |

(MD Anaesthesiology), Professor and head, Department of Anaesthesiology, Gandhi Dr Aditya Agarwal Medical College, Bhopal.

ABSTRACT

Tracheal extubation is the translaryngeal removal of a tube from the trachea via the nose or mouth and associated with awakening, pain, anxiety, airway irritation which may cause a cough or difficulties in breathing and may contribute to an increase in haemodynamic response (1) .Several modalities, both pharmacological and nonpharmacological have been tried to decrease this stress response with variable success. We undertook this study to assess the efficacy of NTG spray in decreasing extubation related stress response in normotensive patients undergoing elective surgeries under general anaesthesia.

Material and methods: Sixty normotensive patients were included in study and randomly subdivided into two groups of 30 patients each – group N receiving NTG spray and Group C not receiving NTG spray prior to extubation. Hemodynamic stress response during extubation was noted in both the groups and compared.

Result and conclusion: Extubation was associated with significant rise in systolic, diastolic and mean arterial blood pressure and heart rate in both the groups, but this stress response was significantly less in NTG Group as compared to control group.

KEYWORDS

INTRODUCTION

Tracheal extubation is the translaryngeal removal of a tube from the trachea via the nose or mouth and associated with awakening, pain, anxiety, airway irritation which may cause a cough or difficulties in breathing and may contribute to an increase in haemodynamic response. Therefore, attenuation of this haemodynamic responses to tracheal extubation such as hypertension, tachycardia and arrhythmias is important for an anesthesiologist. Intravenous NTG is used since many years for attenuating raised blood pressure during intraoperative period. We postulated that this spray can be used prior to extubation to attenuate haemodynamic responses during extubation in postsurgical patients.

Hence the present randomized, controlled study was undertaken to evaluate effects of sublingual nitroglycerin spray given prior to reversal of neuromuscular blockade on tracheal extubation response in normotensive patients.

AIMS AND OBJECTIVES

- To evaluate efficacy of NTG spray for attenuating haemodynamic response in normotensive patients in comparison to control cases.
- To note the incidence of side effects it any.

MATERIALS AND METHODS

In this prospective, randomized, controlled, open study, efficacy of NTG sublingual spray on tracheal extubation response was evaluated in 60 ASA I & II normotensive patients, who had undergone elective surgery under general anaesthesia with tracheal Intubation after approval from institutional Ethics Committee for Human research.

All patients under the study were subjected to thorough preanaesthetic assessment including detailed history, clinical examination and necessary investigations.

Patients fulfilling following criteria were included in the study.

ASA status I & II, Age between 20-60 years, Weighing 40 - 80 kg, Undergoing elective surgery under general anesthesia requiring tracheal intubation. The patients having any of the following criteria were excluded from the study:- Unwilling to participate in the study, ASA III, IV & V, Preexisting haemodynamic instability, Having bleeding disorders, Patients on vasodilators e.g. sildenafil, Who requires post operative ventilator support, Pregnant & Lactating females.

A Complete preoperative assessment was carried out with particular attention to haemodynamic parameters and relevant investigations

were checked. Inclusion & exclusion criteria were assessed. Patients who were fulfilling inclusion & exclusion criteria were explained about study. Written informed consent was taken from those who were willing to participate in study. Sixty normotensive patients were included in study and randomly subdivided into two groups of 30 patients each - group A receiving NTG spray and Group B not receiving NTG the spray by chit block method.

After attaching the monitors and recording BP, pulse rate SPO2, temperature probe and ECG, all the patients were premedicated with, Inj. Glycopyrrolate 0.004 mg/kg, inj. Pentoprazole 40 mg, Inj. Midazolam 0.02 mg/kg IV and Inj. Fentanyl 2 μg/kg..

After preoxygenation, anaesthesia was induced with propofol 2 mg/kg IV, Vecuronium 0.08 mg/kg IV, were given. Inj. Lignocaine 1.5mg/kg IV was used to attenuate the intubation response. Under direct laryngoscopic vision intubation was performed, tube was secured, confirmed & fixed.

Anaesthesia was maintained on O2 + N2O + intermittent vecuronium + isoflurane. Haemodynamic parameters i.e. heart rate, blood pressure, O2 saturation, and etco2 were monitored throughout surgery and were maintained within 80-120% of baseline values by adjusting the Isoflurane and fentanyl boluses. All patients received i.v diclofenac 75 mg for postoperative analgesia.

At the end of surgery, anaesthetic agents were tapered off & timing was noted. Haemodynamic parameters were recorded every two minutes. When spontaneous respiratory attempts were noticed, the study group was given two NTG sprays (Nitrocin lingual spray pen, Samarth Pharma, India 2 sprays 0.8 mg) through sublingual route. Immediately following this residual neuromuscular blockade was reversed with inj. Glycopyrrolate 0.008 mg/kg & Inj. Neostigmine 0.06 mg/kg. The control group patients did not receive the sublingual spray prior to reversal agent. Haemodynamic parameters were noted every one minute till extubation. Oral suction was done. All Patients were extubated when respiration was adequate, the patients obeyed verbal commands and other general extubation criteria were ful filled.

After extubation heart rate, systolic blood pressure diastolic blood pressure & O2 saturation were noted after every 2 minutes for 10 minutes [0, 2, 4, 6, 8, 10] then after every 5 minutes [15, 20, 25, 30 minutes] in all patients. Incidences of any arrhythmias, ischaemia or any other side effects or complications were noted. Patients were kept in postanaesthesia care unit for two hours and then followed up in post

operatively period for any side effects or adverse events. Intravenous esmolol hydrochloride 0.5 mg/kg was used in any patient as rescue agent to treat acute hypertension (systolic blood pressure> 180 mm Hg) in any patient in both the groups, any time during extubation period. A minimal interval of three minutes was maintained between NTG spray and esmolol injection in Group N. Other possible adverse events like burning sensations in throat, headache, hypotension, occurrence of arrhythmias or ST-T wave changes etc. were looked for and noted if occurred. Coughing and other airway events during extubation were also noted.

A patient was withdrawn from study if intraoperatively haemodynamical instability was noted or if patient required postoperative ventilator support or prolonged intubation.

Following parameters were also noted:

- Time taken from end of isoflurane to extubation.
- Time taken from end of anaesthesia (N2O off) to extubation.
- Time taken from end of anaesthesia to maximum recorded B.P.
- Time taken from sublingual NTG spray to maximum recorded B.P. in NTG groups.
- Patients who required inj. Esmolol during extubation time and dose was recorded.
- Rate Pressure products were also calculated till extubation following NTG sublingual spray in NTG groups and for the same period in control group for comparison.
- Statistical analysis was done using Graphpad statistics calculator and p value <0.05 was considered statistically significant.

RESULTS:

Demograhic parameters (Age, Sex, Weight and ASA Grade) between the two groups were comparable.

Table-I Demographic data for both Groups

| Parameters | Normotensiv | P | |
|---------------------------|-----------------------|--------------------------|--------|
| | Group A (with NTG) | Group B (without NTG) | value |
| Age (Years) Mean ±S.D. | 37.56±13.37 | 37.33±15.79 | 0.95 1 |

Table-III Heart rate in normotensive groups

| (per min) Group A(with NTG) Group B(without NTG) N Mean+ SD P value N Mean+ SD P value Baseline 30 83.5±12.179 30 86.8±13.11 O.001 After N20 Off 30 75.4±11.616 0.002 30 77.8±13.21 0.001 2 min 30 80.43±14.381 0.260 30 82.7±14.76 0.086 4 min 30 83.83±1 6.28 0.917 30 86.27±1 5.12 0.847 6 min 30 86.67±1 8.59 0.375 30 88.6±1 3.35 0.462 8 min 27 87.85±20.76 0.494 24 88.2 1±8.41 0.776 10 min 13 80±24.16 0.397 12 89.33±9.46 0.462 At R ± NTG 30 91.17±16.91 0.033 30 91.3±12.41 0.115 1 min 30 94±18.34# 0.007 30 95.03±12.82# 0.003 2 min 30 98.67±17.47# 0.000 <th>Unpaired T</th> | Unpaired T | |
|--|--------------|--|
| Baseline 30 83.5±12.179 30 86.8±13.11 After N20 Off 30 75.4±11.616 0.002 30 77.8±13.21 0.001 2 min 30 80.43±14.381 0.260 30 82.7±14.76 0.086 4 min 30 83.83±1 6.28 0.917 30 86.27±1 5.12 0.847 6 min 30 86.67±1 8.59 0.375 30 88.6±1 3.35 0.462 8 min 27 87.85±20.76 0.494 24 88.2 1±8.41 0.776 10 min 13 80±24.16 0.397 12 89.33±9.46 0.462 At R ± NTG 30 91.17±16.91 0.033 30 91.3±12.41 0.115 1 min 30 94±18.34# 0.007 30 95.03±12.82# 0.003 2 min 30 98.67±17.47# 0.000 30 97.93±11.94# 0.000 | test P value | |
| Baseline 30 83.5±12.179 30 86.8±13.11 After N20 Off 30 75.4±11.616 0.002 30 77.8±13.21 0.001 2 min 30 80.43±14.381 0.260 30 82.7±14.76 0.086 4 min 30 83.83±1 6.28 0.917 30 86.27±1 5.12 0.847 6 min 30 86.67±1 8.59 0.375 30 88.6±1 3.35 0.462 8 min 27 87.85±20.76 0.494 24 88.2 1±8.41 0.776 10 min 13 80±24.16 0.397 12 89.33±9.46 0.462 At R ± NTG 30 91.17±16.91 0.033 30 91.3±12.41 0.115 1 min 30 94±18.34# 0.007 30 95.03±12.82# 0.003 2 min 30 98.67±17.47# 0.000 30 97.93±11.94# 0.000 | | |
| After N20 Off 30 75.4± 11.616 0.002 30 77.8±13.21 0.001 2 min 30 80.43±14.381 0.260 30 82.7±14.76 0.086 4 min 30 83.83±1 6.28 0.917 30 86.27±1 5.12 0.847 6 min 30 86.67±1 8.59 0.375 30 88.6±1 3.35 0.462 8 min 27 87.85±20.76 0.494 24 88.2 1±8.41 0.776 10 min 13 80±24.16 0.397 12 89.33±9.46 0.462 At R ± NTG 30 91.17±16.91 0.033 30 91.3±12.41 0.115 1 min 30 94±18.34# 0.007 30 95.03±12.82# 0.003 2 min 30 98.67±17.47# 0.000 30 97.93±11.94# 0.000 | | |
| 2 min 30 80.43±14.381 0.260 30 82.7±14.76 0.086 4 min 30 83.83±1 6.28 0.917 30 86.27±1 5.12 0.847 6 min 30 86.67±1 8.59 0.375 30 88.6±1 3.35 0.462 8 min 27 87.85±20.76 0.494 24 88.2 1±8.41 0.776 10 min 13 80±24.16 0.397 12 89.33±9.46 0.462 At R ± NTG 30 91.17±16.91 0.033 30 91.3±12.41 0.115 1 min 30 94±18.34# 0.007 30 95.03±12.82# 0.003 2 min 30 98.67±17.47# 0.000 30 97.93±11.94# 0.000 | 0.317 | |
| 4 min 30 83.83±1 6.28 0.917 30 86.27±1 5.12 0.847 6 min 30 86.67±1 8.59 0.375 30 88.6±1 3.35 0.462 8 min 27 87.85±20.76 0.494 24 88.2 1±8.41 0.776 10 min 13 80±24.16 0.397 12 89.33±9.46 0.462 At R ± NTG 30 91.17±16.91 0.033 30 91.3±12.41 0.115 1 min 30 94±18.34# 0.007 30 95.03±12.82# 0.003 2 min 30 98.67±17.47# 0.000 30 97.93±11.94# 0.000 | 0.458 | |
| 6 min 30 86.67±1 8.59 0.375 30 88.6±1 3.35 0.462 8 min 27 87.85±20.76 0.494 24 88.2 1±8.41 0.776 10 min 13 80±24.16 0.397 12 89.33±9.46 0.462 At R ± NTG 30 91.17±16.91 0.033 30 91.3±12.41 0.115 1 min 30 94±18.34# 0.007 30 95.03±12.82# 0.003 2 min 30 98.67±17.47# 0.000 30 97.93±11.94# 0.000 | 0.549 | |
| 8 min 27 87.85±20.76 0.494 24 88.2 1±8.41 0.776 10 min 13 80±24.16 0.397 12 89.33±9.46 0.462 At R ± NTG 30 91.17±16.91 0.033 30 91.3±12.41 0.115 1 min 30 94± 18.34# 0.007 30 95.03±12.82# 0.003 2 min 30 98.67±17.47# 0.000 30 97.93±11.94# 0.000 | 0.551 | |
| 10 min 13 80±24.16 0.397 12 89.33±9.46 0.462 At R ± NTG 30 91.17±16.91 0.033 30 91.3±12.41 0.115 1 min 30 94±18.34# 0.007 30 95.03±12.82# 0.003 2 min 30 98.67±17.47# 0.000 30 97.93±11.94# 0.000 | 0.645 | |
| At R ± NTG 30 91.17±16.91 0.033 30 91.3±12.41 0.115 1 min 30 94±18.34# 0.007 30 95.03±12.82# 0.003 2 min 30 98.67±17.47# 0.000 30 97.93±11.94# 0.000 | 0.93 8 | |
| 1 min 30 94± 18.34# 0.007 30 95.03±12.82# 0.003 2 min 30 98.67±17.47# 0.000 30 97.93±11.94# 0.000 | 0.224 | |
| 2 min 30 98.67±17.47# 0.000 30 97.93±11.94# 0.000 | 0.972 | |
| | 0.801 | |
| 3 min 29 100.65+16.025# 0.000 29 96.89+11.76# 0.005 | 0.85 | |
| 3 mm 2) 100.05±10.025# 0.000 2) 90.05±11.70# 0.005 | 0.3 13 | |
| 4 min 26 101.5±14.79# 0.000 26 96.42±11.75 0.012 | 0.177 | |
| 5 min 13 93.38±14.86 0.002 13 103.08±14.56# 0.015 | 0.106 | |
| 6 min 2 95±24.04 0.563 3 94.33±16.56 0.703 | 0.972 | |
| Aft extb 30 97.97±16.11# 0.000 30 101.37±13.29# 0.000 | 0.376 | |
| 2 min 30 94.5±1 6.22 0.001 30 98.6±13.5# 0.001 | 0.292 | |
| 4 min 30 90.37±1 5.76 0.016 30 95.43±14.13 0.014 | 0.195 | |
| 6 min 30 86.2±1 5.60 0.278 30 93.5±1 3.16 0.044 | 0.055 | |
| 8 min 30 86±1 5.45 0.315 30 91 .5±14.06 0.140 | 0.155 | |
| 10 min 30 83.77±13.99# 0.904 30 88.93±1 3.53 0.499 | 0.151 | |
| 15 min 30 83.033±14.46# 0.845 30 84.57±9.97# 0.406 | 0.634 | |
| 20 min 30 80.8±12.79# 0.259 30 83.4±9.67# 0.180 | 0.378 | |
| 25 min 30 80.07±13.42# 0.185 30 80.93±9.02# 0.019 | 0.77 | |
| 30 min 30 78.73±9.88# 0.011 30 81.1±8.55# 0.007 | | |

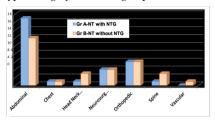
P value <0.05, Significant. # -p value<0.05, significant (paired t test applied before and after drug)

| Weight (Kg) | 58.23±15.79 | 59.5±7.3 8 | 0.5 13 |
|-------------|-------------|------------|--------|
| Mean±S.D. | | | |
| Sex(M/F) | 20/10 | 20/10 | 1.000 |
| ASA I/II | 24/6 | 21/9 | 0.37 |

p value >0.05, Not-significant

Both the groups were also comparable with respect to the types of surgeries performed.

Graph-I Type of surgery in both the groups



Also, the length of surgery, anaesthesia and dose of Isofluane were comparable between the two groups.

Table-II Duration of surgery, anaesthesia, and dose of propofol for normotensive groups

| Parameters | | Normotensive Groups | | | | P |
|------------|-------------|---------------------|-------------|---------------|-------------|-------|
| | | Grou | рΑ | GroupB | | value |
| | | (With NTG) | | (Without NTG) | | |
| | | Mean∃ | S.D. | Mea | $1 \pm S.D$ | |
| Durat | Duration of | | ± 44 | 129 | ± 46 | 0.113 |
| Surger | y (min) | | | | | |
| Duration | of | 142 | ± 46 | 165 | ± 50 | 0.074 |
| (min) | Anaesthesia | | | | | |
| Propofol | Requirement | 226 | ± 63.87 | 219 | ± 51.69 | 0.643 |
| (mg/kg/h) | | | | | | |

^{*}p value > 0.05, Not-significant

Variations in mean heart rates at various times are depicted in table III and Graph II.

Mean baseline heart rate was 83.5 ± 12.17 per minute in the group A and 86.70 ± 13.11 per minute in the group B, which were comparable and the difference was not significant (p>0.05). Compared to baseline, there was a significant increase in heart rate at the end of surgery, after switching off N2O in both the groups as clinically expected. In the group A, this rise was statistically significant after NTG spray and reversal with the maximum heart rate noted at 4 minutes after NTG spray. In group B, similarly this increase was statistically significant after reversal agent was given. The maximum rise in heart rate was noted at the time of extubation in the group B. However at both these times, the difference between the groups was not statistically significant. (p>0.05)

After that, a gradual decrease was noted in both the groups and after 10 minutes of extubation, the difference from baseline was clinically non significant. There was no significant difference (p>0.05) between the two groups.

Graph II Heart Rate Variation

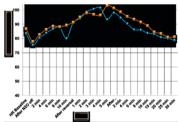


Table-IV Systolic blood pressure Variation

As shown in table IV and Graph III, the basal value of mean systolic blood pressure was 119.1±9.82 mm Hg in the group A and 116.3±9.44 mm Hg in the group B, which were comparable and the difference was not significant. There was a significant increase in systolic blood pressure from the baseline after switching of N2O in both the groups throughout the extubation phase (p< 0.05). In group A maximum systolic pressure was noted at 1 minute after NTG spray.

Thereafter the systolic pressure started coming down and returned to near baseline values by 6th minute after extubation in group A.

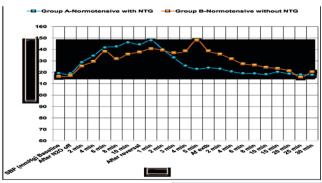
In group B maximum systolic pressure was noted at 1 minute after starting reversal agent. Thereafter the pressure started coming down returned to near baseline values by 25 minutes after extubation in group B. When this data was compared before and after NTG spray and reversal, in group N statistically significant decrease in systolic blood pressure was noted after 3 minutes of NTG spray. In group B statistically significant decrease in systolic blood pressure was noted after 4 minutes of extubation.

Statistical evaluation between the groups A and B showed that difference in systolic arterial blood pressure was statistically significantly lower from 4 minutes after NTG spray till 10 minutes after extubation (p<0.05) in group A, as compared to change in systolic arterial blood pressure in Group B. One patient in group B showed a systolic blood pressure higher than 180 mm Hg from the time of reversal upto 4 minutes after reversal. Two dosage of rescue medication esmolol required one at starting of reversal and nother at 3 minutes after reversal for blood pressure control.

| SBP | | Normotensive Groups | | | | | | | | |
|---------------|----|---------------------------|------------------|----|----------------------------|------------------|-------|--|--|--|
| (mmHg) | | GROUP A (with N | ΓG) | | Group B (without NTG) | | | | | |
| | N | Mean±S.D. | P value (paired) | N | Mean±S.D. | P value (Paired) | | | | |
| Baseline | 30 | 119.06±9.82 | | 30 | 116.3±9.44 | | 0.270 | | | |
| After N2O off | 30 | 118.9313.35 | 0.968 | 30 | 117.07±8.77 | 0.761 | 0.525 | | | |
| 2 min | 30 | 128.67±17.08 | 0.015 | 30 | 125.43±13.08 | 0.007 | 0.414 | | | |
| 4 min | 30 | 134.43±14.66 | 0.000 | 30 | 129.47±1 5.73 | 0.000 | 0.211 | | | |
| 6 min | 30 | 141 .6±15.32 | 0.000 | 30 | 138.23±14.35 | 0.000 | 0.383 | | | |
| 8 min | 27 | 142.52±11.31 | 0.000 | 24 | 131 .87±11.65 | 0.000 | 0.002 | | | |
| 10 min | 13 | 146±13.33 | 0.000 | 13 | 135.85±11.99 | 0.000 | 0.052 | | | |
| At R± NTG | 30 | 144.33±13.14 | 0.000 | 30 | 137.7±13.59 | 0.000 | 0.060 | | | |
| 1 min | 30 | 147.83±13.84 [#] | 0.000 | 30 | 140.63±15.38 [#] | 0.000 | 0.062 | | | |
| 2 min | 30 | 140.13±22.01 | 0.000 | 30 | 139.33±14.52 | 0.000 | 0.869 | | | |
| 3 min | 29 | 132.86±22.83 [#] | 0.003 | 29 | 137±1 6.56 | 0.000 | 0.433 | | | |
| 4 min | 26 | 125.69±18.79 [#] | 0.081 | 27 | 138.67±1 3.5 | 0.000 | 0.006 | | | |
| 5 min | 14 | 122.86±18.58 [#] | 0.334 | 13 | 148±17 | 0.000 | 0.001 | | | |
| Aft extb | 30 | 123.9±18.21# | 0.142 | 30 | 138.76±14.01 | 0.000 | 0.001 | | | |
| 2 min | 30 | 122.97±15.61 [#] | 0.179 | 30 | 135.87±10.44 | 0.000 | 0.000 | | | |
| 4 min | 30 | 120.63±13.84 [#] | 0.529 | 30 | 131 .77±11.02 [#] | 0.000 | 0.001 | | | |
| 6 min | 30 | 119±12.76 [#] | 0.974 | 30 | 127.33±8.59 [#] | 0.000 | 0.004 | | | |
| 8 min | 30 | 118.9±12.2# | 0.938 | 30 | 126.33±9.65# | 0.000 | 0.011 | | | |
| 10 min | 30 | 118.2±10.8 [#] | 0.656 | 30 | 124.33±8.68 [#] | 0.000 | 0.018 | | | |
| 15 min | 30 | 120.2±10.9# | 0.603 | 30 | 123.33±8.53# | 0.003 | 0.220 | | | |
| 20 min | 30 | 118.63±10.08 [#] | 0.817 | 30 | 121 .23±9.54 [#] | 0.030 | 0.309 | | | |
| 25 min | 30 | 117.93±9.95# | 0.541 | 30 | 115.83±21.86 [#] | 0.913 | 0.634 | | | |
| 30 min | 30 | 117.6±7.82 [#] | 0.374 | 30 | 120.43±7.37 [#] | 0.037 | 0.154 | | | |

 $P\ value < 0.05, Significant.\ \#-p\ value < 0.05, significant\ (paired\ t\ test\ applied\ before\ and\ after\ drug)$

Graph- III Systolic blood pressure Variation



A similar trend was observed in Diastolic Blood Pressure (Table V and graph IV) and Mean Arterial Pressure (table VI and Graph V) between the two groups.

Table-V Diastolic blood pressure Variation

| DBP (mmHg) | | Normotensive | | | Groups | | | |
|---------------|----|--------------------------|------------------|-----------------------|-------------------------|------------------|----------------|--|
| | | Group A (with NT) | G) | Group B (without NTG) | | | T test P value | |
| | N | Mean±S.D. | p value (paired) | N | Mean±S.D. | P value (paired) | | |
| Baseline | 30 | 76.86±7.89 | | 30 | 74.83±6.5 | | 0.280 | |
| After N2O off | 30 | 81 .73±7.67 | 0.028 | 30 | 79.93±4.59 | 0.00 1 | 0.275 | |
| 2 min | 30 | 87.33±10.46 | 0.000 | 30 | 86.5±3.97 | 0.000 | 0.685 | |
| 4 min | 30 | 91 .7±9.53 | 0.000 | 30 | 89.43±8.69 | 0.000 | 0.340 | |
| 6 min | 30 | 95.03±12.89 | 0.000 | 30 | 91 .83±8.0 1 | 0.000 | 0.253 | |
| 8 min | 27 | 96.55±11.2 | 0.000 | 26 | 91 .96±5.9 | 0.000 | 0.069 | |
| 10 min | 13 | 99.46±11.12 | 0.000 | 13 | 92±6.87 | 0.000 | 0.051 | |
| At R ± NTG | 30 | 98.46±8.04 | 0.000 | 30 | 97.13±5.16 | 0.000 | 0.448 | |
| 1 min | 30 | 98.03±9.34 | 0.000 | 30 | 97.56±7.21 | 0.000 | 0.829 | |
| 2 min | 30 | 93.9±14.62 | 0.000 | 30 | 96.3±8 | 0.000 | 0.434 | |
| 3 min | 29 | 88.20±12.42 [#] | 0.000 | 29 | 92.75±6.3 | 0.000 | 0.084 | |
| 4 min | 26 | 84.34±12.18 [#] | 0.010 | 27 | 91 .96±7.5 | 0.000 | 0.008 | |
| 5 min | 14 | 79.92±9.62 [#] | 0.25 1 | 12 | 91 .66±7.85 | 0.219 | 0.003 | |
| Aft extb | 30 | 81.76±12.37 [#] | 0.066 | 30 | 91 .66±6.75 | 0.000 | 0.000 | |
| 2 min | 30 | 80.86±9.62 [#] | 0.059 | 30 | 88.96±8.1 [#] | 0.000 | 0.001 | |
| 4 min | 30 | 78.7±9.41 [#] | 0.373 | 30 | 84.66±8.29 [#] | 0.000 | 0.012 | |
| 6 min | 30 | 77.7±8.91 [#] | 0.619 | 30 | 82.66±7.28# | 0.000 | 0.021 | |
| 8 min | 30 | 78.46±8.32 [#] | 0.3 87 | 30 | 80.66±5.83 [#] | 0.000 | 0.241 | |
| 10 min | 30 | 78.26±9.47 [#] | 0.456 | 30 | 79.9±6.69 [#] | 0.00 1 | 0.444 | |
| 15 min | 30 | 78.8±8.15 [#] | 0.223 | 30 | 78.8±6.43 [#] | 0.019 | 1.000 | |
| 20 min | 30 | 78.4±9.03 [#] | 0.394 | 30 | 77.8±6.42 | 0.078 | 0.768 | |
| 25 min | 30 | 76.5±8.39# | 0.820 | 30 | 76.36±4.79 | 0.272 | 0.940 | |
| 30 min | 30 | 75.63±5.94 [#] | 0.418 | 30 | 75.7±4.92 | 0.603 | 0.962 | |

p value <0.05, Significant. #-p value<0.05, significant (paired t test applied before and after drug)

Graph- IV Diastolic blood pressure Variation

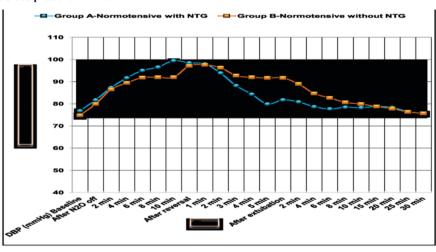


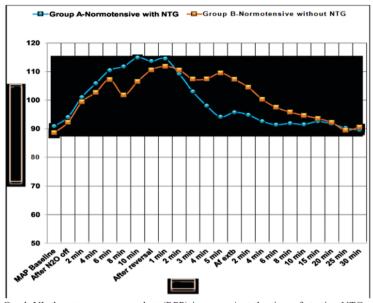
Table-VI Mean arterial pressure Variation

| MAP | | Normotensi | ve | | Unpaired T test P value | | | |
|----------------|----|---------------------------|------------------|----|-------------------------|------------------|-------|--|
| | | Group A (with 1 | NTG) | (| Group B (without NTG) | | | |
| | N | Mean±S.D. | P value (paired) | N | Mean±S.D. | P value (paired) | | |
| Baseline | 30 | 90.84±8.19 | | 30 | 88.56±6.80 | | 0.246 | |
| After N2O off | 30 | 94.03±8.86 | 0.028 | 30 | 92.21±4.06 | 0.016 | 0.311 | |
| 2 min | 30 | 101 .01±11.85 | 0.000 | 30 | 99.37±5.9 | 0.000 | 0.502 | |
| 4 min | 30 | 105.83±1 0.74 | 0.000 | 30 | 102.67±9.94 | 0.000 | 0.241 | |
| 6 min | 30 | 110.44±13.28 | 0.000 | 30 | 107.19±8.92 | 0.000 | 0.270 | |
| 8 min | 27 | 111.76±10.29 | 0.000 | 26 | 101.78±13.49 | 0.000 | 0.004 | |
| 10 min | 13 | 114.85±11.01 | 0.000 | 13 | 106.50±6.87 | 0.000 | 0.029 | |
| At $R \pm NTG$ | 30 | 113.64±8.77 | 0.000 | 30 | 110.54±5.99 | 0.000 | 0.116 | |
| 1 min | 30 | 114.51±10.2 | 0.000 | 30 | 111.81±8.33 | 0.000 | 0.265 | |
| 2 min | 30 | 109.20±16.46 | 0.000 | 30 | 110.53±8.25 | 0.000 | 0.693 | |
| 3 min | 29 | 102.98±14.65 [#] | 0.000 | 29 | 107.39±7.82 | 0.000 | 0.158 | |
| 4 min | 26 | 98.03±13.72 [#] | 0.010 | 27 | 107.42±7.62 | 0.000 | 0.003 | |
| 5 min | 14 | 94.14±12.04 [#] | 0.251 | 12 | 109.47±9.04 | 0.000 | 0.001 | |

| Aft extb | 30 | 95.71±13.38 [#] | 0.066 | 30 | 107.25±7.83 | 0.000 | 0.000 |
|----------|----|---------------------------|-------|----|--------------------------|-------|--------|
| 2 min | 30 | 94.80±10.8 [#] | 0.059 | 30 | 104.49±7.86 [#] | 0.000 | 0.000 |
| 4 min | 30 | 92.58±10.22 [#] | 0.373 | 30 | 100.26±8 [#] | 0.000 | 0.002 |
| 6 min | 30 | 91.37±9.64 [#] | 0.619 | 30 | 97.45±6.93 [#] | 0.000 | 0.007 |
| 8 min | 30 | 91.85±8.79 [#] | 0.387 | 30 | 95.79±6.3 [#] | 0.000 | 0.05 1 |
| 10 min | 30 | 91.4862±8.86 [#] | 0.456 | 30 | 94.61±6.21 [#] | 0.000 | 0.118 |
| 15 min | 30 | 92.50±7.9 [#] | 0.223 | 30 | 93.55±5.84 [#] | 0.004 | 0.563 |
| 20 min | 30 | 91.7±8.5 [#] | 0.394 | 30 | 92.18±6.43 [#] | 0.035 | 0.813 |
| 25 min | 30 | 90.2±8.3 [#] | 0.820 | 30 | 89.43±8.35 [#] | 0.640 | 0.7 16 |
| 30 min | 30 | 89.53±5.90 [#] | 0.418 | 30 | 90.52±4.45 [#] | 0.223 | 0.467 |

p value < 0.05, Significant. #-p value < 0.05, significant (paired t test applied before and after drug)

Graph-V Mean arterial pressure Variation



As shown in table VII and Graph VI, the rate pressure product (RPP) in group A at the time of starting NTG spray and reversal agent was 13151 ± 2745 mm Hg per minute, and maximum RPP after that was 13912 ± 3179 mm Hg per minute. RPP at the time of starting reversal agent in group B was 12518 ± 726 mm Hg per minute and maximum RPP after that was 13584 ± 1777 mmHg per minute. Thus in both the groups RPP was significantly increased after reversal with or without NTG spray. The difference was statistically not significant (p>0.05) for first four minutes between the two groups. At fifth minute, however the RPP was significantly lower in group A as compared with group B.

Table-VII: Rate pressure product Variation

| Rate pressure | ate pressure Normotensive Groups | | | | | | |
|---------------|----------------------------------|------------|------------------|----|------------------|------------------|----------------|
| product | Group A (with NTG) | | | | Group B (without | NTG) | t test P value |
| Ī | N | Mean±S.D. | P value (paired) | N | Mean | P value (paired) | |
| At R± NTG | 30 | 13151±2745 | | 30 | 12518±1726 | | 0.290 |
| 1min after | 30 | 13912±3179 | 0.000 | 30 | 13312±2005 | 0.001 | 0.386 |
| 2min | 30 | 13837±3328 | 0.037 | 30 | 13584±1777 | 0.001 | 0.715 |
| 3min | 29 | 13309±2795 | 0.682 | 29 | 13275±2232 | 0.027 | 0.960 |
| 4min | 26 | 12803±2867 | 0.112 | 26 | 13397±2017 | 0.042 | 0.392 |
| RPP 5min | 13 | 11599±2576 | 0.052 | 13 | 15315±3203 | 0.001 | 0.003 |

p value <0.05, Significant.

Graph-VI Rate pressure product Variation

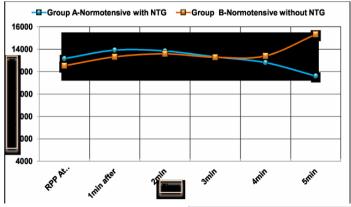


Table-VIII Rescue drug esmolol required in both groups.

| | Normote | Normotensive Groups | | | | | |
|---------|--------------------|-----------------------|------------|--|--|--|--|
| | Group A (with NTG) | Group B (without NTG) | | | | | |
| | n(%) | n(%) | Total n(%) | | | | |
| Esmolol | 0(0%) | 1(3.3%) | 1(1.7%) | | | | |
| Given | | | | | | | |

p value < 0.05, Significant.

As shown in table IX, groups A and B were comparable with respect to intervals between discontinuation of anaesthetic agent and extubation time for propofol and N2O. Statistically significant difference was found in interval between discontinuation of anaesthetic agent and maximum rise in blood pressure when the two groups were compared (p<0.05).

Table. IX: Intervals for normotensive groups.

| | | Normotensive Groups | | | | | |
|----------------------|-------|---------------------|-------|----------------|-------|--|--|
| Intervals | Group | A | Group | В | P | | |
| | NTG) | (without) | NTG) | (without) | value | | |
| | N | Mean±S.D | N | Mean±S.D | | | |
| Discontinuation of | 30 | 27.93±5.02 | 30 | 28.3±6.2 | 0.802 | | |
| Propofol | | | | | | | |
| and extubation time. | | | | | | | |
| Discontinuation of | 30 | 13.46±2.5 | 30 | 13.16±2.73 | 0.659 | | |
| N2O and | | | | | | | |
| Extubation | | | | | | | |
| Discontinuation of | 30 | 9.36±2.36 | 30 | 10.93 ± 2.78 | 0.022 | | |
| anaesthetic agent & | | | | | | | |
| maximum increase | | | | | | | |
| in blood pressure. | | | | | | | |

p value < 0.05, Significant.

No significant adverse event (table X) was noted in any of the groups. One patient in group N had burning sensation in mouth after extubation. No adverse effect noted in group B. (p>0.05) when the two groups were compared. No adverse events like headache, arrhythmia or hypotension (SBP<25% of baseline) noted in any of the two group.

Table-X Adverse events in normotensive groups.

| | 8 1 | | |
|-------------------|-----------------------------|--------------------------------|-------------|
| | Normotensive Groups | | |
| Adverse events | Group A N (%) (with NTG) | Group B n (%) (without NTG) | Total n (%) |
| Burning sensation | 1(3.3%) | 0(0%) | 1(1.7%) |
| Headache | 0(0%) | 0(0%) | 0(0%) |
| Arrhythmias | 0(0%) | 0(0%) | 0(%) |
| Hypotension | 0(0%) | 0(0%) | 0(0%) |

Pearson Chi-Square. p value >0.05, not significant

DISCUSSION

The present, prospective, randomized, controlled, open study was done to assess efficacy of sublingual nitroglycerin spray given at reversal of neuromuscular blocking agent on tracheal extubation response in normotensive patients undergoing elective surgeries under general anaesthesia.

Nitroglycerine is a commonly used intravenous agent in treatment of hypertension during anaesthesia. The rapid sublingual absorption of nitroglycerine is almost equal to intravenous injection as noted by Blumenthal et al (2) plasma nitroglycerine levels were almost instantaneously achieved after the 0.3 mg nitroglycerin sublingual tablet, reaching about 1 ng/ml at the first measured data point (3 min). A new way of administration, nitroglycerin lingual spray avoids these problems and may retain the advantages of rapid absorption via the oral mucosa. NTG sublingual spray is having faster onset of action (2-3 minutes), higher peak response, shorter duration of action, no need to prepare and is easy to administer as compared to any other preparation. The half-life of 4-5 minutes gives us a convenient alternative to intravenous administration when prolonged therapy is not anticipated as in the situation of endotracheal intubation or extubation. It does not have any anaesthetic, sedative or respiratory depressant action making it a good choice of drug when a patient is recovering from anaesthesia. Though there is minimal data about nitroglycerine for extubation response, it has also been effectively used as a rescue drug for controlling hypertension during extubation while studying other drugs . The drug has also been used by several authors during tracheal

intubation with favourable haemodynamic effects.

S. Kamra et al (5) examined the effects of 2% nitroglycerin ointment rubbed on the forehead prior to intubation and found that the rise in systolic arterial pressure was significantly lower as compared to the control group (p<0.001). The increase in pulse rate was not significant. Anant S et al (1) found significant attenuation of hypertensive response to laryngoscopy and intubation following intranasal NTG spray. The increase in heart rate was comparable with the control patients. Firoozbaksh et al (6) found that following tracheal intubation mean arterial pressure and systolic blood pressure increased to a significantly lesser extent in patients receiving intravenous nitroglycerine. J. Dich-Niels et al (7) found similar effects with intranasally administered nitroglycerin (NTG) on the cardiovascular response to laryngoscopy and intubation. Results of the present study also confirm similar haemodynamic changes with sublingual nitroglycerine spray used during tracheal extubation in both normotensive and hypertensive patients.

CONCLUSION

Hence we conclude from this study that, sublingually administered nitroglycerin spray in a dose of 0.8 mg prior to extubation in ASA grade I and II patients is an effective, practical, easy and relatively safe method of protecting patient from the hypertension and complications related with hypertension without much affecting heart rate and RPP during extubation. After surgery it stabilizes haemodynamics, allows easy extubation, provides a more comfortable recovery.

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