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A RANDOMISED CONTROLLED STUDY OF TRACHEAL EXTUBATION RESPONSE FOLLOWING NITROGLYCERINE (NTG) SUBLINGUAL SPRAY IN HYPERTENSIVE PATIENT

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ABSTRACT

The prospective randomized open controlled study was done to compare tracheal extubation response following nitroglycerine (NTG) sublingual spray in hypertensive patients

Keywords-Tracheal extubation response, General Anaesthesia, Nitroglycerine spray, Sublingual, Hypertension

INTRODUCTION

Removal of a tube from the trachea after completion of surgery and anaesthesia is associated with anxiety, airway irritation and difficulty in breathing because of inadequate respiratory efforts and is often associated with a stress response resulting in increased blood pressure and pulse rate. This hypertension and tachycardia can have serious implications, more so in a hypertensive patient. Every possible effort should be made to attenuate this response. Use of sublingual NTG spray can possibly be one such intervention considering its mechanism of action and ease of administration. We undertook this study to compare the tracheal extubation response following nitroglycerine (NTG) sublingual spray versus no intervention in hypertensive patients.

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REVIEW OF LITERATURE

Laryngoscopy, endotracheal intubation as well endotracheal extubation are associated with significant hypertension, tachycardia and arrhythmias. These haemodynamic responses were recognized as early as in 1976 by Robert Stoelting.(1) These haemodynamic changes during extubation can cause cerebrovascular accidents or adverse cardiac events in the form of myocardial ischemia, cardiac dysrhythmias due to exccesive sympathetic responses.

Haemodynamic Effects: The nitrovasodilators promote vascular smooth muscle relaxation(2,3). Low concentrations of nitroglycerin preferentially dilate the veins more than the arterioles. This venodilation decreases left and right ventricular chamber size and end-diastolic pressures but results in little change in systemic vascular resistance. Systemic arterial pressure may fall slightly, and heart rate is unchanged or may increase slightly in response to a decrease in blood pressure.

Pulmonary vascular resistance & cardiac output are slightly reduced. Doses of nitroglycerin that do not alter systemic arterial pressure often produce arteriolar dilation in the face and neck, resulting in a flush, or dilation of meningeal arterial vessels, causing headache.

Higher doses of organic nitrates cause further venous pooling and may decrease arteriolar resistance as well, thereby decreasing systolic and diastolic blood pressure and cardiac output and causing pallor, weakness, dizziness, and activation of compensatory sympathetic reflexes. The reflex tachycardia and peripheral arteriolar vasoconstriction tend to restore systemic vascular resistance; this is superimposed on sustained venous pooling. Coronary blood flow may increase transiently as a result of coronary vasodilatation but may decrease subsequently if cardiac output and blood pressure decrease sufficiently.

The indirect effects of nitroglycerin consist of those compensatory responses evoked by baroreceptors and hormonal mechanisms responding to decreased arterial pressure; this often results in tachycardia and increased cardiac contractility. Retention of salt and water may also be significant, especially with intermediate- and long-acting nitrates.

Various studies have been done with various pharmacological methods to attenuate these haemodynamic responses to endotracheal extubation.

Barkha Bindu, Surender Pasupuleti, and M Bhanu Laxmi [(4)]In 2013 did a double blind, randomized, controlled trial to study the effect of dexmedetomidine on hemodynamic and recovery responses during tracheal extubation which concluded that use of dexmedetomidine before extubation attenuates the hemodynamic response to extubation. It enables smooth extubation of the trachea and provides adequate sedation postoperatively. Dexmedetomidine increases the incidence of bradycardia and hypotension, but does not cause side effects like respiratory depression, laryngospasm, bronchospasm, undue sedation and desaturation.

Aouad MT,Al-Alami AA,Nasr VG,Souki FG,Zbeidy RA,siddik Sayyid SM [(5)] in 2009, conducted a prospective, randomized, double blind study to evaluate the effect of low dose remifentanil on responses to endotracheal tube during emergence from general anaesthesia, in 60 ASA Grade I & II adult patients presenting for nasal surgery. The patients receiving remifentanil-isoflurane anaesthesia were randomized to receive either low-dose remifentanil infusion or no infusion at the end of surgery. During emergence phase, the remifentanil group had remifentanil reduced to one tenth of the maintenance rate whereas the control group had remifentanil discontinued. Times to awakening and tracheal extubation were similar between the two groups. The remifentanil group (infusion rate 0.014±0.011 µg/kg/min.) had a significant lower incidence (40% vs 80%, p=0.002) and less severe coughing as well as lower incidence of non-purposeful movement (3.3% vs 30%, p=0.006) and slower heart rate compared with control group.

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AIMS AND OBJECTIVES

1) To evaluate haemodynamic responses to tracheal extubaion occurring in hypertensive patients

2) To note the incidence of side effects it any.

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MATERIALS AND METHODS

After obtaining approval from institutional Ethics Committee, 60 hypertensive patients, aged between 20 to 60 years with a body weight between 40 to 80 kg, posted
for elective surgeries under general anaesthesia were included in this study. Patients who refused to enroll for the study, ASA grade I, III , IV & V, haemodynamic instability, bleeding disorders, Patients on vasodilators e.g. sildenafil, patients requiring post operative ventilator support , Pregnant & Lactating females, Patients with uncontrolled severe hypertension, associated ischemic heart disease and unstable angina were excluded from the study. 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 hypertensive patients were included in study. A patient was considered hypertensive if-
1) Known hypertensive on regular antihypertensive treatment or
2) At least 2 readings of blood pressure exceeding 140/90 mm of Hg during preoperative hospitalization period.
Both these types of patients were randomly subdivided into two groups of 30 patients each – Group N receiving NTG spray and Group C 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. 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 fulfilled.
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.

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Statistical analysis was done using Graphpad statistics calculator and p value <0.05 was considered statistically significant.

RESULTS AND DISCUSSION

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

TABLE-1

Parameters	Hypertensive Groups		P value
	Group N (with NTG)	Group C (without NTG)	
Age (Years) Mean ±S.D.	55.10±8.8 1	52.53±9.96	0.295
Weight(kg) Mean ±S.D.	59.53±7.11	62.5±8.46	2.208
Sex(M/F)	18/12	22/8	0.27
ASA I/II	0/30	0/30	-

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

TABLE-2

	Hypertensive Groups		Total
Type of surgeries	Group N (with NTG) n(%)	Group C (without NTG) n(%)	n (%)
abdominal	17(56.7%)	13(43.3%)	59(39.2)
chest	2(6.7%)	2(6.7%)	6(5%)
HNF	1(3.3%)	4(13.3%)	9(7.5%)
neurosurgery	2(6.7%)	0(0%)	10(5%)
orthopedic	4(13.3%)	8(26.7%)	24(20%)
spine	4(13.3%)	3(10%)	11(9.2%)
vascular	0(0%)	0(0%)	1(0.8%)
Total	30(100%)	30(100%)	120(100%)

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

TABLE-3

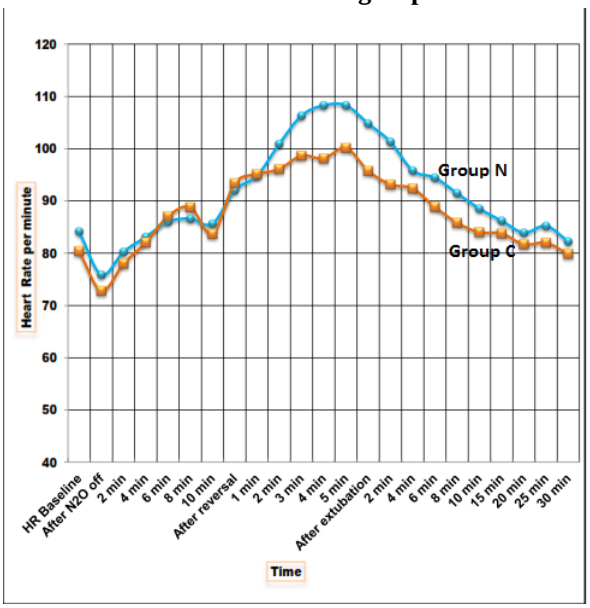
Parametrs	Hypertensive Groups		P value
	Group N (with NTG) Mean±S.D.	Group C (without NTG) Mean±S.D.	
Duration of Surgery (min)	130±58.07	127±34	0.799
Duration of Anaesthesia (min)	164±59.8	164±33.90	0.979
Dose of propofol (mg/hr)	225±57	230±42	0.702

TABLE-4
Comparison of Heart Rate

Heart rate	Hypertensive Groups						Unpaired
(per min)	Group N (with NTG)			Group C (without NTG)			t test Pvalue
	N	Mean±S.D	P value (paired)	N	Mean±SD	P value (paired)	
Baseline	30	84.16±11.37		30	80.4±8.18		0.146
After N2O off	30	75.9±11.920	0.00	30	72.8±7.92	0.00	0.24
2 min	30	80.27±13.42	0.06	30	78±9	0.12	0.445
4 min	30	83.13±14.5	0.63	30	82.07±7.89	0.15	0.725
6 min	29	86.03±14.57	0.63	30	87.07±8.44	0.00	0.739
8 min	23	86.61±14.67	0.47	26	88.80±8.96	0.00	0.524
10 min	14	85.64±1 6.63	0.84	9	83.67±9.23	0.02	0.749

At R± NTG	30	92.067±1 3.56	0.01	30	93.4±1 0.7	0.00	0.674
1 min	30	94.83±13.54#	0.00	30	95.13±10.99#	0.00	0.925
2 min	30	100.9±11.87#	0.00	30	96.1±13.42	0.00	0.148
3 min	30	106.33±12.17#	0.00	30	98.67±1 6.83	0.00	0.048
4 min	27	108.29±12.53#	0.00	29	98.14±17.8	0.00	0.017
5 min	16	108.31±11.62#	0.00	12	100.16±18.6	0.00	0.167
Aft extb	30	104.83±12.81#	0.00	30	95.76±15.43	0.00	0.016
2 min	30	101 .33±12.94#	0.00	30	93.16±1 5.14	0.00	0.029
4 min	30	95.83±11.01	0.00	30	92.4±14.46	0.00	0.305
6 min	30	94.47±1 0.98	0.00	30	88.87±12.71#	0.00	0.073
8 min	30	91 .5±11.98	0.00	30	85.83±12.45#	0.03	0.078
10 min	30	88.53±11.6	0.03	30	84.03±9.22#	0.06	0.102
15 min	30	86.23±9.5#	0.25	30	83.8±8.18#	0.05	0.292
20 min	30	83.93±9.43#	0.89	30	81.7±8.73#	0.41	0.345
25 min	30	85.23±9.49#	0.52	30	82±8.58#	0.25	0.172
30 min	30	82.27±9.21#	0.11	30	79.87±7.98#	0.74	0.285

FIGURE-1
Heart rate in two groups



As shown in table-4 and figure-1Mean baseline heart rate was 84.16±11.37 per minute among the group N and 80.4±8.18 per minute among the group C, which were comparable and the difference was not significant.

Compared to baseline, there was a significant increase in heart rate after switching off N2O in both the groups. In the group N, rise was statistically significant after NTG spray and reversal with maximum heart rate noted at 4 minutes after NTG spray. In group C similarly this increase was statistically significant after reversalagent was given. The maximum rise in heart rate was noted at 3 minutes after giving reversal agent in the group C.

Subsequently elevated heart rate started settling down to baseline value by 15 minutes after extubation in group N, and by 20 minutes after extubation in group C. Statistical evaluation between the two groups showed that increase in HR observed in Group N was statistically significant from 2 minutes after NTG spray till 4 minutes after extubation ($p<0.05$), when compared to increase in HR in Group C. However, clinically this difference was minor

TABLE 5-
Systolic Blood Pressure in two groups

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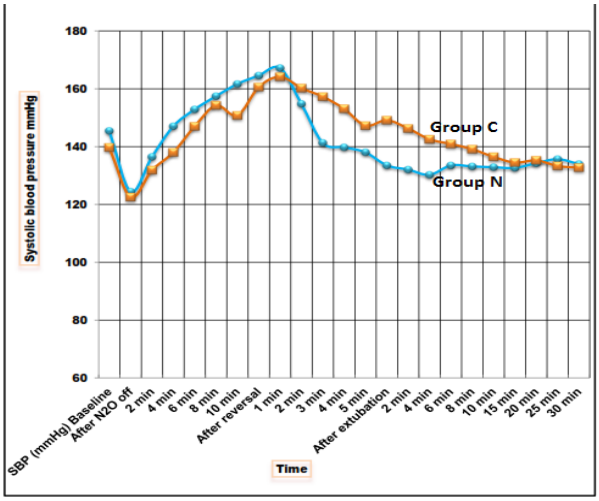
SBP (mmHg)		Hypertensive Group					Unpaired t test P value
		Group N (with NTG)		Group C (without NTG)			
	N	Mean±S.D.	P value (paired)	N	Mean±S.D.	P value (paired)	
Baseline	30	145.47±11.65		30	139.73±7.06		0.025
After N2O Off	30	124.47±12.49	0.000	30	122.53±6.75	0.000	0.459
2 min	30	136.46±16.59	0.020	30	131 .86±8.23	0.000	0.179
4 min	30	147.07±17.82	0.650	30	138±10.28	0.410	0.019
6 min	30	152.9±1 3.57	0.010	30	147.03±1 2.82	0.010	0.091
8 min	23	157.48±13.65	0.01	26	154.26±15.16	0.00	0.443
10 min	13	161 .69±18.5	0.01	9	150.78±21.07	0.07	0.213
At R ± NTG	30	164.6±1 2.91	0.000	30	160.6±1 0.17	0.000	0.188
1 min	30	167.2±12.90	0.00	30	164.17±10.89#	0.00	0.329
2 min	30	154. 8±22.28#	0.06	30	160.27±1 2.76	0.00	0.248
3 min	30	141 .3±21 .97#	0.38	30	157.3±11.1	0.00	0.001
4 min	27	139.77±18.74#	0.16	29	153.10±1 3.39	0.00	0.003
5 min	16	138.06±23.73#	0.14	11	147.27±12.78	0.18	0.253
Aft extb	30	133.53±15.63#	0.00	30	149.16±13.47#	0.00	0.00
2 min	30	132.07±15.49#	0.00	30	146.3±11.64#	0.02	0.00
4 min	30	130.26±14.07#	0.00	30	142.57±10.10#	0.28	0.00
6 min	30	133.53±12.88#	0.00	30	140.93±8.17#	0.59	0.01
8 min	30	133.16±13.59#	0.00	30	139.13±6.19#	0.75	0.033
10 min	30	132.9±11.6#	0.00	30	136.5±5.34#	0.03	0.128
15 min	30	132.67±11.33#	0.00	30	134.5±4.92#	0.00	0.42
20 min	30	134.3±8.44#	0.00	30	135.27±5.93#	0.00	0.599
25 min	30	135.7±7.32#	0.00	30	133.33±4.53#	0.00	0.138
30min	30	134±5.09#	0.00	30	132.73±5.24#	0.00	0.346

FIGURE- 2

SBP IN TWO GROUPS



As shown in table 5,Figure-2 the basal value of mean systolic blood pressure was 145.47±11.65 mm Hg among the group N and 139.73±7.06 mm Hg among the group C, 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. In group N maximum mean systolic pressure was noted at 1 minute after NTG spray. Thereafter the pressure started coming down rapidly to baseline values by 3rd minute after NTG spray. In group C maximum mean systolic pressure was at 1 minute after starting reversal agent. Thereafter the pressure started coming down returned to near baseline values by 8 minutes after extubation in group C.

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 2 minutes of NTG spray. In group C statistically significant decrease in systolic blood pressure was noted after extubation.

Statistical evaluation between the groups showed that systolic arterial blood pressure was statistically significantly lower from 3 minutes after NTG spray till 8 minutes after extubation ($p<0.05$) in group N, when compared to change in systolic arterial blood pressure in Group C. These changes are also depicted in graph 2. Two patients in group N and seven patients in group C showed systolic blood pressure higher than 180 mm Hg, which was clinically undesirable and they were immediately treated with intravenous esmolol hydrochloride.

TABLE -6

DBP in two groups

DBP (mmHg)	Hypertensive Groups						Unpaired t test P value
	Group C (with NTG)			Group D (without NTG)			
	N	Mean±S.D.	P value (paired)	N	Mean±S.D.	P value (paired)	
Baseline	30	91±4.42		30	89.93±5.29		0.400
Af off N2O	30	80.53±7.93	0.000	30	80.13±6.34	0.000	0.830
2 min	30	88.8±9.72	0.201	30	85.63±8.28	0.007	0.180
4 min	30	92.23±1 0.84	0.530	30	89.4±8.81	0.749	0.271
6 min	30	95.16±9.58	0.021	30	92.8±8.56	0.166	0.317
8 min	23	96.56±11.79	0.023	26	95.69±8.08	0.007	0.762
10 min	13	104.15±20.22	0.026	9	94.11±8.18	0.254	0.176
Af st R & NTG	30	100.6±8.55	0.000	30	98.66±7.95	0.000	0.368
1 min	30	102.73±8.63#	0.000	30	101.87±10.17#	0.000	0.723
2 min	30	96.46±1 3.18	0.028	30	102.03±9.06#	0.000	0.062
3 min	30	88.23±12.34#	0.256	30	98.33±7.64	0.000	0.000
4 min	27	87.59±12.52#	0.210	29	97.72±7.18	0.000	0.000
5 min	16	84.5±13.81#	0.132	11	93.72±7.93	0.214	0.057
Af extb	30	84.86±8.97#	0.003	30	92.63±9.23#	0.155	0.002
2 min	30	83.2±9.07#	0.000	30	91.53±7.47#	0.335	0.000
4 min	30	84.06±9.59#	0.001	30	88.66±7.67#	0.486	0.045
6 min	30	83.43±7.53#	0.000	30	89.13±6.19#	0.572	0.002
8 min	30	84.66±8.95#	0.001	30	87.03±5.77#	0.053	0.228
10 min	30	84.86±6.5#	0.000	30	85.56±4.95#	0.001	0.641
15 min	30	85.43±7.01#	0.000	30	86.6±4.73#	0.009	0.453
20 min	30	85.16±6.84#	0.000	30	85.13±4.32#	0.000	0.982
25 min	30	84.8±5.72#	0.000	30	84.56±4.22#	0.000	0.858
30 min	30	85.47±5.78#	0.000	30	84.26±4.06#	0.000	0.356

FIGURE-3 DBP in two groups

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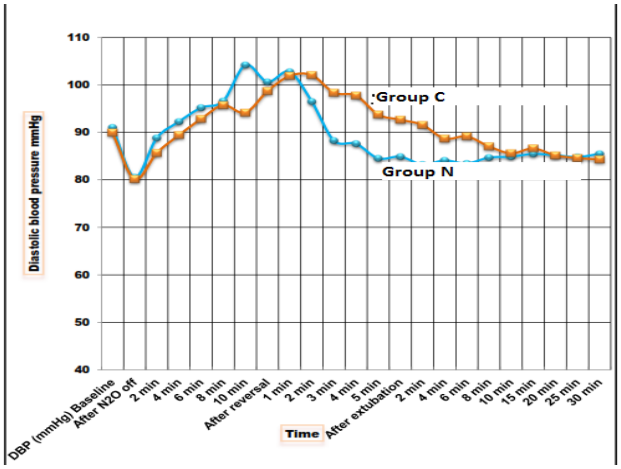


As shown in table 6 and graph 3, the basal value of mean diastolic blood pressure was 91±4.42 mm Hg among the group N and 89.93±5.29 mm Hg among the group C, which were comparable and the difference was not significant. There was a significant increase in diastolic blood pressure from the baseline after switching of N2O in both the groups. In group N mean diastolic pressure was maximum at 1 minute after NTG spray and reversal agent. Thereafter the pressure started coming down returned to near baseline values by 3rd minute after NTG spray in N group. In group C, mean diastolic pressure was maximum at 2 minute after starting reversal agent. Thereafter the pressure started coming down returned to near baseline values by 6 minutes after extubation in C group.

When this data was compared before and after NTG spray and reversal, in group N statistically significant decrease in diastolic blood pressure was noted after 3 minutes of NTG spray. But in group C statistically significant decrease in diastolic blood pressure was noted 2 minutes after extubation

Statistical evaluation between the groups showed that variation in diastolic arterial blood pressure was statistically significant from 3 minutes after NTG spray till 6 minutes after extubation ($p<0.05$) in group N, when compared to change in diastolic arterial blood pressure in Group C.

TABLE -7

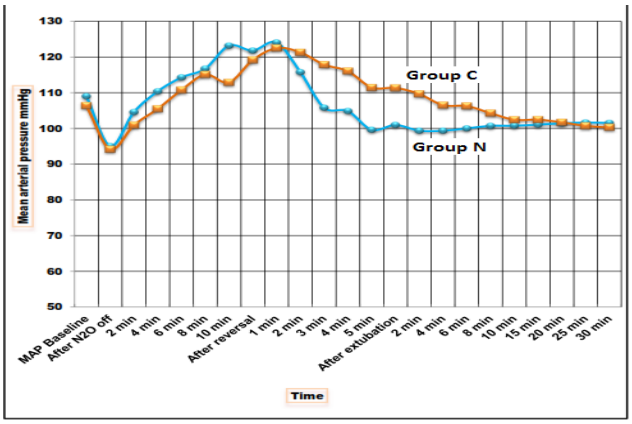
MAP in two groups

MAP	Hypertensive Group N (with NTG)			Groups Group C(without NTG)			Unpaired t test P value
	N	Mean±S.D.	P value (paired)	N	Mean±S.D.	P value (paired)	
Baseline	30	109.05±5.47		30	106.43±5.08		0.059
After N2O off	30	95.08±8.34	0.000	30	94.17±5.2	0.000	0.614
2min	30	104.58±11.25	0.040	30	100.94±7.28	0.000	0.142
4 min	30	110.40±12.24	0.544	30	105.49±7.91	0.519	0.070
6 min	30	114.29±9.88	0.005	30	110.76±9.29	0.035	0.159
8 min	23	116.75±11.42	0.005	26	115.10±9.71	0.000	0.587
10 min	13	123.21±18.68	0.013	9	112.887±11.49	0.120	0.157
AtR± NTG	30	121.81±8.32	0.000	30	119.19±7.82	0.000	0.214
1 min	30	124.09±8.55#	0.000	30	122.51±9.63#	0.000	0.502
2 min	30	115.79±14.68#	0.025	30	121 .32±9.55	0.000	0.089
3 min	30	105.81±14.59#	0.283	30	117.87±7.86	0.000	0.000
4 min	27	104.88±14.01#	0.161	29	116.06±8.31	0.000	0.001
5 min	16	99.62±20.7#	0.092	11	111.46±9.03	0.164	0.088
Aft extb	30	100.98±10.43#	0.001	30	111.36±10.34#	0.025	0.000
2 min	30	99.3 8±8.46#	0.000	30	109.67±8.2#	0.088	0.000
4 min	30	99.36±10.47#	0.000	30	106.52±7.39#	0.956	0.003
6 min	30	100.03±8.64#	0.000	30	106.29±5.92#	0.926	0.002
8 min	30	100.73±9.88#	0.000	30	104.29±4.77#	0.107	0.080
10 min	30	100.77±7.51#	0.000	30	102.44±4.37#	0.001	0.298
15 min	30	101 .07±7.57#	0.000	30	102.46±4.15#	0.001	0.382

20 min	30	101 .44±6.87#	0.000	30	101 .74±4.34#	0.000	0.841
25 min	30	101 .66±5.72#	0.000	30	100.72±3.75#	0.000	0.453
30 min	30	101 .54±4.8#	0.000	30	100.32±3.8#	0.000	0.279

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

FIGURE 4
Comparison of Mean Blood Pressure



Mean blood pressure in hypertensive groups are shown in table 7. The baseline value of mean arterial pressure was 109.05±5.47 mm Hg among the group N and 106.43±5.08 mm Hg among the group C, which were comparable and the difference was not significant. There was a significant increase in mean arterial pressure from the baseline after switching of N2O in both the groups. In group N mean arterial pressure was maximum at 1 minute after NTG spray. There after the pressure started coming down below baseline value after extubation. In group N mean arterial pressure maximum value was noted at 1minute after reversal. There after the pressure returned to near baseline values by 4 minutes after extubation in group N.

When this data was compared before and after NTG spray and reversal, in group N statistically significant decrease in mean arterial pressure was noted after 2 minutes of NTG spray. But in group N statistically significant decrease in mean arterial pressure was noted after extubation.

Statistical evaluation between the groups showed that variation in mean arterial blood pressure was statistically significant from 3 minutes after NTG spray till 6 minutes after extubation ($p<0.05$) in group N, when compared to change in systolic arterial blood pressure in Group D.

As nitroglycerine is known to cause tachycardia while reducing blood pressure, we were concerned about the increased myocardial oxygen consumption and hence the rate pressure products (RPP) were calculated during the most susceptible time i.e. before and after the sublingual NTG spray, every minute till extubation and at similar times in the non-spray groups and are shown in the following table 8 and figure 5.

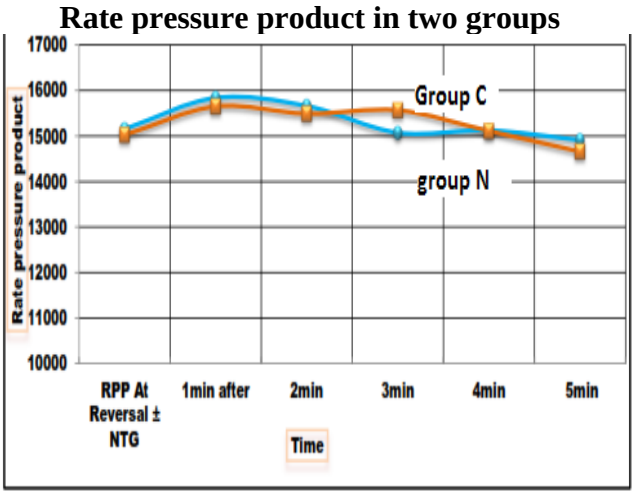
Table -8
Rate pressure product in two groups

Rate pressure Product			Hypertensive	Groups			Unpaired t test P value
	Group N (with NTG)			Group C (without NTG)			
	N	Mean±S.D.	P value	N	Mean±S.D.	P value	

			(paired)			(paired)	
RPP At R±NTG	30	151 55±2589		30	15022±2081		0.827
1min after	30	15838±2528	0.000	30	15649±2262	0.000	0.762
2min	30	15660.5±3060	0.291	30	15490±3021	0.324	0.830
3min	30	15072±3096	0.869	30	15565±2976	0.320	0.532
4min	27	15124±2627	0.814	29	15111±3508	0.719	0.988
RPP 5min	15	14912±3004	0.223	11	14658±3708	0.892	0.849

p value <0.05, Significant.

Figure 5



In hypertensive patients, RPP in group N at the time of starting NTG spray and reversal agent was 15155±2589 mm Hg per minute, and increased to 15838±2528 mm Hg per minute after 1 minute.

RPP at the time of starting reversal agent in group C was 15022±2021mm Hg per minute which increased to maximum RPP of 15649±2262 mmHg per minute at 1 minute. This rise was statistically significant. Thereafter the RPP were close to before reversal value. The difference, however, was not significant (p>0.05) when the two groups were compared. Thus, increase in heart rate along with reduction in blood pressure seen after NTG spray did not produce significant increase in RPP as compared to hypertensive patients who did not receive the NTG spray. However RPP noted in these immediate postoperative patients were higher than commonly seen in general nonsurgical population.

TABLE.9:
Rescue drug esmolol required in hypertensive groups.

	Hypertensive Groups		Total n(%)
	Group N (with NTG) n(%)	Group C (without NTG)n(%)	
Esmolol given	2(6.7%)	7(23.3%)	9(15%)

p value <0.05, Significant

In contrast, as shown in the above table, in group N, two patients and in group C, seven patients required inj. esmolol as a rescue drug to control hypertension once each. Most patients responded to the medication and a repeat dose was not needed. Though more number of patients needed administration of rescue antihypertensive medication which is clinically important, the difference, however, was not statistically significant (p>0.05) when the two groups were compared.

Table.10:
Adverse events in hypertensive groups.

Adverse Events	Hypertensive Groups		Total n(%)
	Group N with NTG) n(%)	Group C (without NTG) n(%)	
Burning sensations	1(3.3%)	0(0%)	1(1.7%)

Headache	2((6.7%)	0(0%)	2(3.3%)
Arrhythmias	0(0%)	0(0%)	0(0%)
Hypotension	0(0%)	0(0%)	0(0%)

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

In group N, one patient had burning sensations in mouth and two patients had headache after extubation. No adverse effects noted in group C. The difference, however, was not significant (p>0.05) when the two groups were compared. No adverse events like headache, hypotension (SBP<25% of baseline) noted in any of the two group. One patient in group N showed ventricular premature contractions but disappeared after two minutes of NTG spray. Other side effects like, ST-T changes or major cardiac arrhythmia were not noted in any of the groups.

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 hypertensive patients undergoing elective surgeries under general anaesthesia.

Extubation is as important part of general anaesthesia as intubation, but is often not given equal care leading to several problems. The stimulation of the airway due to suctioning, coughing and straining associated with emergence from anaesthesia to lighter planes are often associated with increase in heart rate and blood pressure. In addition, the process of tracheal extubation itself often provokes hypertension and tachycardia just like tracheal intubation due to reflex sympathetic discharge caused by pharyngeal and laryngeal stimulation. During these periods a 26-66% increase in heart rate and a 36-45% increase in systolic blood pressure are reported when no pretreatment is used to prevent this haemodynamic response. Although the precise mechanism responsible for tachycardia and hypertension following tracheal extubation is unknown, these haemodynamic changes may be associated with the release of catecholamines during this period.

These cardiovascular responses to tracheal extubation though normally do not cause major consequences, they can be more hazardous in some select group of patients like hypertensive patients.

Especially in susceptible patients like hypertensive patients, ischaemic heart disease or cerebral vascular disease patients, these circulatory perturbations occasionally may lead to arrhythmias, myocardial ischaemia, heart failure, coughing, laryngospasm, bronchospasm or cerebrovascular accidents.

A new way of administration, nitroglycerin lingual spray retain the advantages of rapid absorption via the oral mucosa.[7] 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.

SUMMARY AND CONCLUSION

Tracheal extubation is as important part of general anesthesia as that of intubation. During extubation we have limited options for attenuating haemodynamic response, as the agents to be used should be

1) Non anaesthetic & Non sedative
2) Shorter acting
3) No respiratory depressant action.

Therefore sometimes intravenous agents like NTG, lignocaine & esmolol which fulfill these criteria are used in patients who are likely to develop hypertension at the time of extubation.

NTG sublingual spray is a simple formulation used for treatment of acute anginal episodes and also recommended for controlling hypertensive crises. We postulated that this spray can be used prior to tracheal extubation to attenuate haemodynamic responses during extubation in hypertensive patients.

There was a significant increase in heart rate, systolic, diastolic blood pressure and mean arterial pressure noted after stoppage of N2O in both groups, increase in heart rate was significant in hypertensive NTG group when compared with control groups during extubation. However, clinically this difference was minor.

During extubation significant rise in systolic, diastolic and mean arterial blood pressure were noted in group C, and with use of NTG spray the increase could be significantly attenuated in NTG groups.

After NTG, systolic blood pressure, diastolic blood pressure, mean arterial blood pressure were under control within two minutes, remaining close to baseline during extubation, whereas in control group systolic blood pressure, diastolic blood pressure, mean arterial blood pressure were persistently high during extubation and came to baseline after six minutes of extubation.

Hence we conclude from this study that, sublingually administered nitroglycerin spray in a dose of 0.8 mg prior to extubation in ASA grade 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, hence prophylactic use of NTG spray can be recommended to prevent such hypertensive episodes as these patients are more prone to ischemia during perioperative period.

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