Original article:

A randomised controlled study of tracheal extubation response following nitroglycerine (NTG) sublingual spray in normotensive and hypertensive patients

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Abstract

Tracheal extubation is as important part of general anaesthesia as that of intubation. The purpose of this paper to evaluate haemodynamic responses to tracheal extubation occurring in normotensive and hypertensive patients and to evaluate efficacy of NTG spray for attenuating haemodynamic response in normotensive & hypertensive patients in comparison to control cases.This study consider 120 patient undergoing general anaesthesia with trachel intubation divided into two groups of 30 patients each - 50% receiving NTG spray and 50% not receiving NTG the spray by chit block method using groups of 20 chits. This study concluded that, Sublingually administered nitroglycerin spray in a dose of 0.8 mg prior to extubation is an effective in attenuate haemodynamic response to tracheal extubation.

Keywords: Nitroglycerine, Normotensive, Hypertensive, Tracheal extubation

Introduction

Tracheal extubation is as important part of general anaesthesia as that of intubation.Tracheal extubation is associated with increase in haemodynamic response[1,2]. The haemodynamic changes during tracheal extubation occur due to reflex sympathetic discharge caused by epipharyngeal and laryngopharyngeal stimulation. This increase in sympathoadrenal activity may result in hypertension, tachycardia and arrhythmias[1]. This increase in blood pressure and heart rate are usually transitory, variable and unpredictable. It is more hazardous in a patient with hypertension, myocardial insufficiency or cerebrovascular diseases[1,3,4]. Therefore, attenuation of this haemodynamic responses to tracheal extubation such as hypertension, tachycardia and arrhythmias is important for an anesthesiologist. During extubation we have limited options, as the agents to be used to attenuate haemodynamic response. should be -

Therefore sometimes intravenous agents like esmolol, lignocaine and diltiazem which fulfill these criteria are used in patients who are likely develop hypertension at the time of extubation[1,5] The non-pharmacological methods like, smooth and gentle extubation, blocking the glossopharyngeal nerve and superior laryngeal nerve have been used to attenuate the cardiovascular responses to tracheal extubation. None of these above mentioned approaches have been proved entirely satisfactory. All of them require time for preparation and administration. Hence, the search for an ideal agent to attenuate the haemodynamic responses is still continuing.

Intravenous NTG is used since many years for attenuating raised blood pressure during intraoperative period. Intravenous or sublingual NTG has been used for attenuating hypertensive response during laryngoscopy, tracheal intubation[6,7,8] & also for controlling hypertension during extubation while

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studying efficacy of other drugs.[5,9,10] Nitroglycerine generate NO (Nitric oxide) in vascular smooth muscle which produce vasodilatation leading to decrease in blood pressure.[11,12,13] Nitroglycerin has been also found to relax tracheal and bronchial smooth muscle and hence it has been used to prevent laryngospasm by some anaesthesiogists. NTG sublingual spray is a simple, easy to use formulation mainly aimed for treatment of acute anginal episodes 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 & hypertensive patients.

Materials and methods

In this randomized controlled study efficacy of NTG sublingual spray on tracheal extubation response was evaluated in 120 ASA I & II normotensive and hypertensive patients, who had undergone elective surgery under general anaesthesia with tracheal intubation.

A Complete preoperative assessment was carried out with particular attention to haemodynamic parameters and relevant investigations were checked. Written informed consent was taken from those who were willing to participate in study. Sixty normotensive patients and 60 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 - 50% receiving NTG spray and 50% not receiving NTG the spray by chit block method using groups of 20 chits.

After the patient was taken on OT table, a multipara monitor was attached, blood pressure, heart rate and SpO2 were checked & noted. Intravenous (IV) access was obtained. A standard anaesthesia technique was used for all patients. Intravenous Premedication with, Inj. Glycopyrrolate 0.004 mg/kg, inj.Pentoprazole 40 mg, Inj. Midazolam 0.02 mg/kg IV, Inj. Fentanyl 2 µg/kg, were given to all patients.

After preoxygenation, anaesthesia was induced with propofol 2 mg/kg IV, neuromuscular blocking agent 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 + Propofol infusion. 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 propofol infusion and fentanyl boluses. All patients received per rectal diclofenac 100 mg for postoperative analgesia .

At the end of surgery, anaesthetic agents were gradually tapered off –first propofol and postoperatively, after oral suctioning nitrous oxide & timing of each 43 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) was given 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

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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

Observations and results

Sixty normotensive patients were divided into two groups of 30 each. A group (n=30) received sublingual nitroglycerine spray before reversal of neuromuscular blockade after surgery where as Group B (n=30) served as control and did not receive the NTG spray. Similarly, 60 hypertensive patients were also divided randomly to group C (n=30) receiving NTG spray and Group D (n=30) not receiving the spray.

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TABEL1. HEART RATE IN NORMOTENSIVE GROUP

Heart rate (per min)	Normotensive Groups						Unpaired t test P value
	Group A(with NTG)			Group B(without NTG)			
	N	Mean± SD	P value (Paired)	N	Mean± SD	P value (Paired)	
Baseline	30	83.5±12.179		30	86.8±13.11		0.317
After N_20 off	30	75.4± 11.616	0.002	30	77.8±13.21	0.001	0.458
2 min	30	80.43±14.381	0.260	30	82.7±14.76	0.086	0.549
4 min	30	83.83±16.28	0.917	30	86.27±15.12	0.847	0.551
6 min	30	86.67±18.59	0.375	30	88.6±13.35	0.462	0.645
8 min	27	87.85±20.76	0.494	24	88.21±8.41	0.776	0.938
10 min	13	80±24.16	0.397	12	89.33±9.46	0.462	0.224
At R ± NTG	30	91.17±16.91	0.033	30	91.3±12.41	0.115	0.972
1 min	30	94± 18.34#	0.007	30	95.03±12.82#	0.003	0.801
2 min	30	98.67±17.47#	0.000	30	97.93±11.94#	0.000	0.85
3 min	29	100.65±16.025#	0.000	29	96.89±11.76#	0.005	0.313
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±16.22	0.001	30	98.6±13.5#	0.001	0.292
4 min	30	90.37±15.76	0.016	30	95.43±14.13	0.014	0.195
6 min	30	86.2±15.60	0.278	30	93.5±13.16	0.044	0.055
8 min	30	86±15.45	0.315	30	91.5±14.06	0.140	0.155
10 min	30	83.77±13.99#	0.904	30	88.93±13.53	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	0.325

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

Variations in mean heart rates at various times are depicted in table 1. Mean baseline heart rate was 83.5±12.17 per minute in the A group and 86.70±13.11 per minute in the B group, 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 A group, 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

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was given. The maximum rise in heart rate was noted at the time of extubation in the B group. 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.

TABEL2. HEART RATE IN HYPERTENSIVE GROUP

Heart rate (per min)	Hypertensive Groups						Unpaired t test P value
	Group C (with NTG)			Group D (without NTG)			
	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 N_2O 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±16.63	0.84	9	83.67±9.23	0.02	0.749
At R± NTG	30	92.067±13.56	0.01	30	93.4±10.7	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±16.83	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±15.14	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±10.98	0.00	30	88.87±12.71#	0.00	0.073
8 mln	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 mln	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

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SBP (mmHg)	Normotensive Groups						Unpaired t test P value
	GROUP A (with NTG)			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±15.73	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±16.56	0.000	0.433
4 min	26	125.69±18.79#	0.081	27	138.67±13.5	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)

As shown in table 3. The basal value of mean systolic blood pressure was 119.1±9.82 mm Hg in the A group and 116.3±9.44 mm Hg in the B group 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 A group. 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 B group. When this data was compared before and

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after NTG spray and reversal, in group A 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

TABEL 4.SYSTOLIC BLOOD PRESSURE IN HYPERTENSIVE GROUP

SBP (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	145.47±11.65		30	139.73±7.06		0.025
After N_2O 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±13.57	0.010	30	147.03±12.82	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±12.91	0.000	30	160.6±10.17	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±12.76	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±13.39	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

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There was a significant increase in systolic blood pressure from the baseline after switching of N2O in both the groups. In group C 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 D 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 D group.When

In group A mean diastolic pressure was maximum at the time of NTG spray. Thereafter the diastolic pressure returned to near baseline values by 6th minute after extubation in A group. In group B mean diastolic pressure was maximum at 1 minute after starting reversal agent, thereafter the pressure started coming down slowly and returned to near baseline values much later, by 30 minutes after extubation.

When this data was compared before and after NTG spray and reversal, in group A statistically significant decrease in diastolic blood pressure was noted after 3 minutes of NTG spray. In group B 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 C, when compared to change in diastolic arterial blood pressure in Group D.

Discussion

Nitroglycerine is a commonly used intravenous agent in treatment of hypertension during anaesthesia 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 The basic

this data was compared before and after NTG spray and reversal, in group C statistically significant decrease in systolic blood pressure was noted after 2 minutes of NTG spray. 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 C, when compared to change in systolic arterial blood pressure in Group D

idea of using any drug for attenuating the hypertensive response to tracheal extubation is that its peak effect should correspond to that of the stimulus. A 2-3 minute time gap is needed between administration of NTG sublingual spray and tracheal extubation as done in the present study, as this time interval was found to be satisfactory after preliminary clinical trials.Thus the choice of the drug, route of administration and the timing used in present study seem to be justified. Though wide range of doses of NTG are used to control blood pressure(0.3-0.5mg), satisfactory blood pressure control has been observed with 0.8-1.2 mg sublingually or intranasally and hence, the current dose of 0.8 mg was used in the present study. Significant increase in heart rate, systolic blood pressure, diastolic blood pressure, after termination of 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[5,9,10.] The drug has also been used by several authors during tracheal intubation with favourable haemodynamic Anant S et al 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.

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

Sublingually administered nitroglycerin spray in a dose of 0.8 mg prior to extubation 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. It stabilizes haemodynamics, allows easy extubation, provides a more comfortable recovery.

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