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Original Research Article

Efficacy of sublingual nitroglycerine spray in attenuation of hemodynamics to tracheal extubation

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ABSTRACT

Background: The present study was undertaken to evaluate efficacy of nitroglycerine (NTG) spray for attenuating haemodynamic response to tracheal extubation in normotensive and hypertensive patients.
Methods: The study enrolling total 120 ASA I and II patients, (60 normotensive and 60 hypertensive) who had undergone elective surgery under general endotracheal anaesthesia. Both these types of patients were randomly subdivided into two groups of 30 patients each -50% receiving NTG spray and 50% not receiving NTG spray.
Results: There was significant increase in heart rate in all four groups after NTG spray. During extubation this increased in heart rate was not statistically significant in group A (Normotensive with NTG) but was significant in group C (hypertensive with NTG) when compared with control groups. Similarly, during extubation there was significant rise in systolic, diastolic and mean arterial blood pressure were noted in all four groups and with use of NTG spray the increase could be significantly attenuated in NTG groups. 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 and normotensive patients who did not receive the NTG spray.
Conclusions: Sublingually administered nitroglycerin spray in a dose of 0.8 mg prior to extubation is an effective, practical, easy and relatively safe method in attenuate haemodynamic response to tracheal extubation.

Keywords: Endotracheal anaesthesia, Haemodynamic response, NTG, Tracheal extubation

INTRODUCTION

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] Therefore, attenuation of these haemodynamic responses to tracheal extubation such as hypertension, tachycardia and arrhythmias is important for an anesthesiologist.

Haemodynamic response occurring during intubation can be attenuated with number of drugs but during extubation we have limited options. The various non-pharmacological methods have been used to attenuate the cardiovascular responses to tracheal extubation but none of them have been proved entirely satisfactory because all 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 and also for controlling hypertension during extubation while studying efficacy of other drugs.[4-9] NTG sublingual spray is a simple, easy to use formulation mainly aimed for treatment of acute anginal episodes. It is also marketed to treat acute hypertensive crisis and also to treat diabetic neuropathic pain with local application. We postulated that this spray can be used prior to extubation to attenuate haemodynamic responses during extubation in postsurgical patients.

Hence the present study was undertaken to evaluate effects of sublingual nitroglycerin spray given prior to reversal of neuromuscular blockade on tracheal extubation response in normotensive and hypertensive patients and to study its efficacy, safety and side effects if any associated with it.

METHODS

This prospective, randomized, controlled, open study enrolling 60 normotensive and 60 hypertensive patients (total 120 patients) of ASA grade I and II, age between 20-60 years and weighing 40-80 kg, who had undergone elective surgery under general anaesthesia with tracheal intubation after approval from institutional Ethics Committee for Human research. Those patients who were unwilling to participate in the study, having ASA grade III, IV and V, preexisting haemodynamic instability, bleeding disorders, patients on vasodilators e.g. sildenafil, patients requires post-operative ventilator support, pregnant and lactating females were excluded from the study. Patients with uncontrolled severe hypertension, associated ischemic heart disease and unstable angina were considered ASA risk III and were therefore not included in the study.

A complete preoperative assessment including detailed history, clinical examination was done with particular attention to haemodynamic parameters and relevant investigations were checked. Written informed consent was obtained from all patients. 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 the 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.

In the operation theatre, intravenous access using an 18 G cannula was secured. The multipara monitor (NGenuity Criticare) was attached to the patient and baseline parameters such as blood pressure, heart rate and SpO2 were recorded. All patients were premedicated with glycopyrrolate 0.004 mg/kg, pentoprazole 40 mg, midazolam 0.02 mg/kg and fentanyl 2 μg/kg. After pre-oxygenation, anaesthesia was induced with propofol 2 mg/kg and vecuronium 0.08 mg/kg. Intravenous injection of lignocaine 1.5mg/kg was used to attenuate the intubation response. Under direct laryngoscopic vision intubation was performed, tube was secured, confirmed and 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 and timing of each were 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 injection glycopyrrolate 0.008 mg/kg and neostigmine 0.06 mg/kg. The control group patients did not receive the sublingual spray prior to reversal agent. Haemodynamic parameters were noted everyone 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 and oxygen 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 all 4 groups, any time during extubation period. A minimal interval of three minutes was maintained between NTG spray and esmolol injection in group A and C. 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.

Statistical analysis

Data obtained were expressed as mean±SD; among the demographic data, age and weight were analyzed by using student t test and gender distribution between the groups and incidence of complications were analyzed by chi square test. Paired t test was used for intra group analysis of haemodynamic variables at various time intervals Inter group analysis for haemodynamic parameters was done by using unpaired t test. For all statistical comparisons in this study p value of <0.05 was considered as significant. Data with n > 5 was used for graphical presentation at various time intervals.

RESULTS

All the groups were comparable with respect to the demographic characteristics and types of surgeries, duration of surgery, duration of anaesthesia and dose of propofol received with no statistically significant difference, (p value >0.05) (Table 1).

Most of the patients underwent abdominal surgeries (39.2%); smaller number of patients underwent chest (5%), head neck face (7.5%), neuro (5%), orthopedic (20%), spine (9.2), and vascular surgeries (0.8%).

Table 1: Comparison of demographic data, duration of surgery, anaesthesia and dose of propofol required among four groups.

Variables	Normotensive groups			Hypertensive groups		
	Group A with NTG	Group B without NTG	P-value	Group C with NTG	Group D without NTG	P-value
Age (years)	37.56±13.37	37.33±15.79	0.951	55.10±8.81	52.53±9.96	0.295
Weight (kg)	58.23±15.79	59.5±7.38	0.513	59.53±7.11	62.5±8.46	2.208
Sex (Male/Female)	20/10	20/10	1.000	18/12	22/8	0.27
ASA Grade I/II	24/6	21/9	0.37	0/30	0/30	-
Duration of surgery (min)	110±44	129±46	0.113	130±58.07	127±34	0.799
Duration of anaesthesia (min)	142±46	165±50	0.074	164±59.8	164±33.90	0.979
Dose of propofol (mg/hr)	226±63.87	219±51.69	0.643	225±57	230±42	0.702

There was a significant increase in heart rate, systolic, diastolic blood pressure and mean arterial pressure noted after stoppage of N2O in all four groups. In normotensive and hypertensive groups heart rate increased after NTG spray and reversal of neuromuscular blockade. Similarly, both control groups also showed such increase after reversal. Increase in heart rate in normotensive NTG group, was not statistically significant, but was significant in hypertensive NTG group when compared with control groups during extubation. However, clinically this difference was minor (Figure 1).

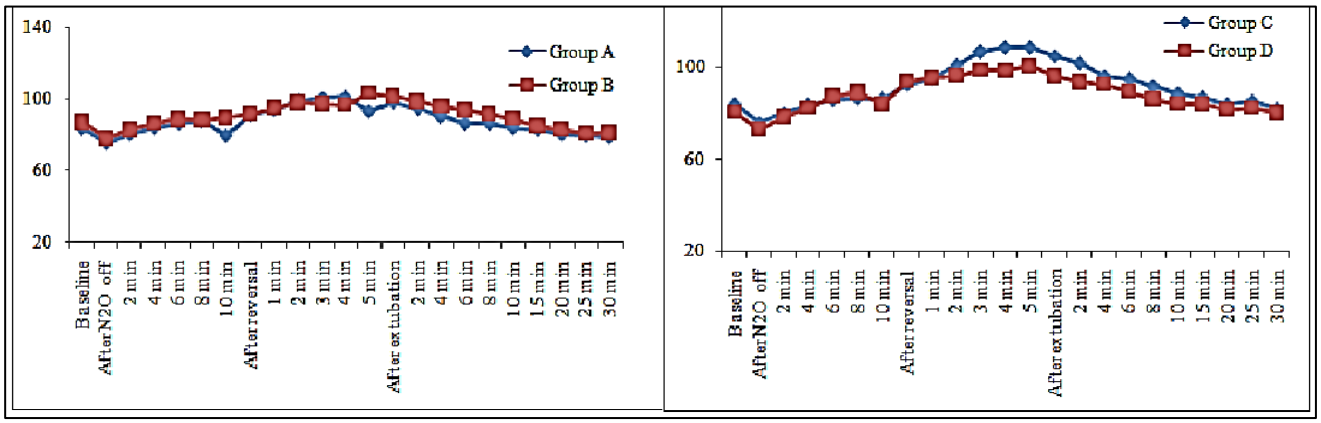

Figure 1: Comparison of heart rate between normotensive groups and hypertensive groups.

During extubation significant rise in systolic, diastolic and mean arterial blood pressure were noted in all four groups, 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, diastolic and mean arterial blood pressure were persistently high during extubation and came to baseline after six minutes of extubation (Figure 2). One patient in group B, two patients in group C and seven patients in group D showed systolic blood pressure higher than 180 mm Hg, which was clinically undesirable and they were immediately treated with intravenous esmolol hydrochloride. Though more number of control patients needed administration of rescue antihypertensive medication which was clinically important, the difference was not statistically significant when the two groups were compared.

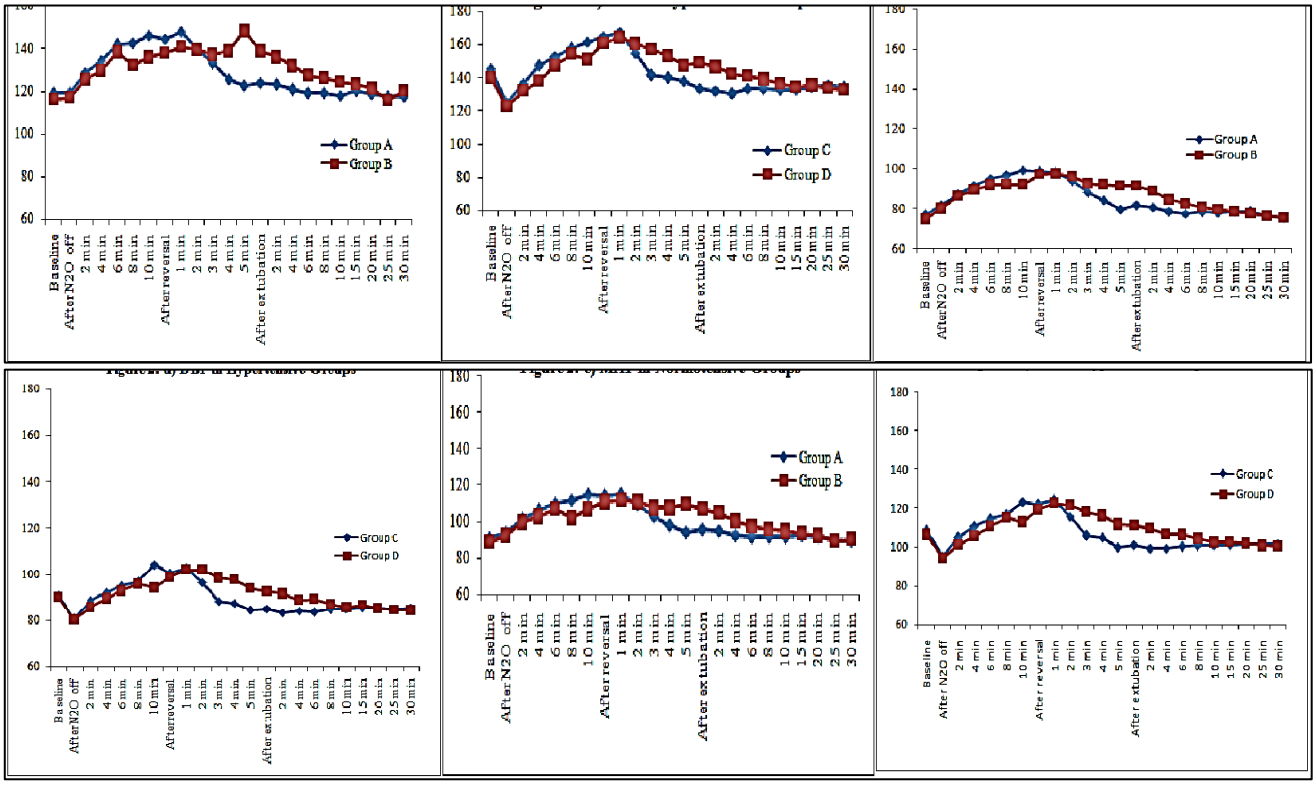

Figure 2: Comparison of SBP, DBP and MAP between normotensive groups and hypertensive groups.

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 and normotensive 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.

One patient in group A and one patient in group C had burning sensations in mouth, two patients in group C had headache after extubation. One patient in group C had ventricular premature contraction but reversed with blood pressure control. No complications were found in control groups. No patient in any of the four groups showed any other side effects like, hypotension, ST-T changes or major cardiac arrhythmia.

DISCUSSION

The basic 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-minutes 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. Iwasaka et al also found similar time gaps for peak plasma concentrations after intranasal administration.[10] 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 intravenously

and hence, the current dose of 0.8 mg was used in the current study.

We noted that, as compared to baseline, there was a significant increase in heart rate, systolic blood pressure, diastolic blood pressure, after termination of anaesthesia in all the patients, these changes were found to be more marked in hypertensive groups than normotensive groups. During extubation, heart rate was found to be increased in NTG groups, it was not statistically significant in normotensive group, but was found to be significant in hypertensive group when compared with control group. The systolic, diastolic and mean arterial blood pressure was found to be significantly lower in NTG groups as compared to control groups during extubation. After NTG, systolic, diastolic and mean arterial blood pressure were under control within two minutes of medication and remained close to baseline during extubation, whereas in control group systolic, diastolic and mean arterial blood pressure were found to be persistently high during extubation, coming to baseline after six minutes of extubation.

In present study, the increase in heart rate following the administration of NTG was modest. This may be partly attributable in hypertensive patients to their preoperative antihypertensive therapy which in most cases involved beta-blockers and/or calcium antagonists. In addition, injection neostigmine and injection glycopyrrolate were given intravenously simultaneously and as both the drugs affect the heart rate, the change produced by NTG was masked and the combine effect was noted. The principal advantage of the drug is that while a desirable and transient reduction in blood pressure is achieved, cardiac output is unlikely to decrease due to increase in heart rate.

In present study, SBP>180 mm Hg was considered dangerous and injection esmolol hydrochloride was used as a rescue drug to control hypertension. Ten patients - one patient in normotensive control group, two patients in hypertensive NTG and seven patients in hypertensive control group-showed such high blood pressure and required inj. esmolol. Even though statistically this numbers were not significant between the groups, clinically it suggests that high blood pressure may occur during extubation and there are increased instances where there was need to provide medication to control blood pressure, especially in hypertensive patients. Some of these instances can be reduced by prophylactic administration of a drug like NTG spray.

Nitroglycerine produces reduction in blood pressure but increases heart rate. So, to evaluate the net effect on myocardial oxygen consumption, calculation of RPP is important. In the present study rate pressure product was calculated before and for five minutes after the NTG spray when its maximum clinical effect was seen. The RPP was not found to be much altered in NTG groups when compared with control groups. Similar results were found in Kamara et al and Dich-Niels et al.[4,5] Several of patients in both hypertensive groups showed very high RPP at extubation. In general, all patients had higher RPP attributable to a combined effect of pain, anxiety and consequent catecholamine release, though no patient showed any evidence of myocardial ischaemia or complained of chest pain postoperatively.

In a patient with compromised coronary perfusion, the haemodynamic responses to intubation or extubation that predispose patients to ischaemia include increases in heart rate, mean arterial pressure, and pulmonary capillary wedge pressure, and decreased ejection fraction. These responses are thought to be a result of sympathetic nervous system response. Diseased epicardial arteries respond to sympathetic activation with vasoconstriction. This vasoconstriction can be abolished by NTG. It has been shown in the setting of catecholamine release that ischaemia can be reversed by NTG in doses too small to affect global haemodynamics (i.e. rate pressure product) but sufficient to reverse vasoconstriction. This may be the basis for present findings of NTG in the prevention of ischaemia during stress of extubation.

In one hypertensive NTG group patient arrhythmias (occasional ventricular ectopics) were noted associated with severe hypertension. Though there were no electrocardiographic evidences, these may be secondary to myocardial ischemia.[11] The changes were transient and subsided two minutes after NTG spray. However, blood pressure needed to be controlled with esmolol. Though lignocaine (1.5 mg/kg) found to provide protection against cardiac arrhythmias, it was used only during intubation in our study, and the effect would not last till extubation. One normotensive and one hypertensive patient who received NTG had burning sensation in their mouth and two hypertensive patients who received NTG had headache postoperatively. Similarly, Nyberg et al also observed headache in six (out of nine) patients after oral nitroglycerin.[12] No patient in any group showed respiratory adverse events. Actually, nitroglycerine in higher doses has been used to treat perioperative laryngospasm successfully though we have not come across such observation.[5,13]

Limitations of this study use of invasive arterial line would have been more accurate method for measurement of blood pressure. However, this was not needed for the type of procedures that these patients underwent and hence such additional invasive monitoring was not justified.

A double-blind study would have eliminated some bias from subjective data. However, this was not possible due to non-availability of placebo spray pen at the starting time of the study. This limitation was reduced by use of objective parameters for the statistical analysis. A study involving much larger number of patients would have been preferred for more reliable results.

CONCLUSION

The 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 and provides a more comfortable recovery. Incidence of hypertension is more in hypertensive patients during extubation and hence prophylactic use of NTG spray can be recommended to prevent such hypertensive episodes. In normotensive patients probably it would be appropriate to use NTG spray if rising trend of blood pressure noticed.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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