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ORIGINAL ARTICLE

THE EFFECTS OF NITROGLYCERINE (NTG) SUBLINGUAL SPRAY TO BLUNT THE HAEMODYNAMIC RESPONSE TO ENDOTRACHEAL EXTUBATION IN LUMBAR DISC SURGERY

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ABSTRACT: OBJECTIVE: The aim of this study was to evaluate the effects of nitroglycerine (NTG) Sublingual Spray on prevention of haemodynamic responses to tracheal extubation in patients undergoing lumbar disc surgery. **METHODS:** With approval from the institutional ethical Committee, written consent, 30 patients between 20-60 years of age undergoing elective lumbar disc surgery were randomly placed in either the Group A (n=30) or the Group B Control (n=30).Anaesthesia was induced with 2mg kg-1 propofol, 0.5mg kg-1pentazocin, and 0.1mg kg-1 vecuronium bromide iv, and was maintained with 0.8-1 MAC isoflurane in oxygen-nitrous mixture (40:60). After dressing of the surgical wound, all anaesthetic agents were discontinued and the patients were ventilated with 100% oxygen. Two sublingual NTG sprays (0.8mg) was given to Group A (n=30), after regain of spontaneous respiratory attempts, while no drug given to Group B. Hemodynamic variables were noted before administering study drug, during extubation then at 1, 3, 5, 10, 15 and 20 min after the extubation. **RESULTS:** In the sublingual NTG group, mean arterial pressures decreased significantly after sublingual NTG Spray and were significantly lower than in the control group at exubation and 1,3 and 5min after extubation ($p<0.05$).The heart rate and Rate pressure product (RPP) were comparable in both groups ($p>0.050$). **CONCLUSION:** We concluded that 0.8mg (Two sprays) sublingual NTG before extubation can prevent hypertension caused by extubation in patients undergoing elective lumbar disc surgery without much affecting heart rate and RPP .

KEYWORDS: Nitroglycerine (NTG), Subligual, Extubation, Lumbar disc surgery.

INTRODUCTION: Recovery from general anesthesia and extubation is a period of intense physiological stress for patients. There are several physiological responses to postoperative stress, including increases in oxygen consumption, catecholamine blood levels, blood pressure and heart rate. In most cases blood pressure and heart rate increases gradually as patient awakens. Tracheal extubation causes additional transient increase by 10-30% in arterial pressure and heart rate lasting 5-15 min.[1] it is more hazardous in patients with hypertension, myocardial insufficiency or cerebral vascular diseases. Patient with coronary artery disease experience a 40-50% decrease in ejection fraction.[2]

Therefore, attenuation of haemodynamic responses to tracheal extubation such as hypertension, tachycardia and arrhythmias is important for an anesthesiologist. In order to control haemodynamic changes during tracheal intubation and extubation, local anaesthetics, opioids, beta-blocking agents, and calcium channel blockers have been used with varying success rates.[3-6] all of them require time for preparation and administration.

Nitroglycerine generates NO (Nitric oxide) in vascular smooth muscles which produce vasodilatation leading to decrease in blood pressure.

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Nitroglycerin has been also found to relax tracheal and bronchial smooth muscle and hence it has been used to prevent laryngospasm by some anaesthesiogists.[7,8] NTG sublingual spray is simple and 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.

In this study, our goal was to determine the effects of sublingual nitroglycerin spray on haemodynamic responses during endotracheal extubation in patients undergoing lumbar disc surgery.

METHODS: In this prospective, randomized, controlled, open study, efficacy of NTG sublingual spray on haemodynamic response to tracheal extubation was evaluated in sixty patients, between 20-60 years of age and of American Society of Anesthesiologists (ASA) physical status class 1-2, scheduled for Elective lumbar disc surgery after Institutional Ethics Committee approval.

All patients with refusal for enrolment, allergic to the study drug, those who had significant cardiac, pulmonary, renal, and hepatic diseases, chronic alcohol or drug use, arterial blood pressure below 90/60mmHg or over 180/100mmHg, or those using β-blockers, sympathomimetic agents, calcium channel blockers, or vasodilator were excluded from the study. All the enrolled patients were randomly divided into two groups as control group A (receiving NTG), group-B (Not receiving NTG) of 30 each by computer-generated randomization chart.

For all patients, heart rate (HR), systolic arterial pressure (SBP), diastolic arterial pressure (DBP), mean arterial pressure (MBP), peripheral oxygen saturation (SpO2), and end-tidal CO2 (ETCO2) were monitored. A standard anaesthesia technique was used for all patients. Anaesthesia was induced with 2mg/kg propofol, 0.5mg kg-1pentazocin, and 0.1mg kg-1 vecuronium bromide IV, and after endotracheal intubation, it was maintained with 40: 60 mixture of oxygen and nitrous, 0.8 -1 MAC isoflurane. Controlled mechanical ventilation was adjusted to maintain ETCO2 pressure between 30-35mmHg.

After dressing of the surgical wound, all anaesthetic agents were discontinued and the patients were ventilated with 100% oxygen. When spontaneous respiratory attempts were noticed, the study group A Two NTG sprays (Nitrocin lingual spray pen, Samarth Pharma, India 2sprays = 0.8mg) was given through sublingual route. Residual muscle paralysis was reversed with neostigmine (0.05mg/kg) and glycopyrrolate (0.01mg/kg).Once patient became conscious and responded to verbal commands extubation was performed after aspiration of oropharyngeal secretions. Hemodynamic variables were noted before administering study drug when spontaneous respiratory attempts were noticed (Ts) and then during extubation (TE) then at 1, 3, 5, 10, 15 and 20 min (T1, T2, T3, T4, T5 and T6) after the extubation.

Patients were kept in post-anaesthesia care unit for two hours and then followed up in post-operatively period for any side effects or adverse events. Atropine sulphate 0.6mg for bradycardia (HR <50 beat min-1), 5mg ephedrine for hypotension (Systolic arterial pressure<100), and 0.5mg/kg esmolol hydrochloride IV for hypertension (Systolic arterial pressure >180mmHg) were used as rescue drug.

Patients who required rescue drug during extubation time and dose was recorded. Rate Pressure products were calculated from returning of spontaneous ventilation till 5 min after extubation in NTG groups and for the same period in other group for comparison. Beside this other possible adverse events like burning sensations in throat, headache, hypotension, occurrence of arrhythmias or ST–T wave changes etc. were noted if occurred.

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STATISTICAL ANALYSIS: Statistical analysis was done using SPSS version 17.0. Data are presented as mean (standard deviation) or number (%). The qualitative data was compared by applying Chi-square test. The values for normal distribution blood pressure and HR were analyzed using ANOVA test. Non-parametric data were analyzed using Chi-square test. Statistical significance was accepted at $p<0.05$.

RESULTS: No statistically significant differences were found between the both groups in demographic data, duration of anaesthesia and surgery (Table1).

Parameters	Group A	Group B	P value
Age (Years)	47.56±13.37	46.12±14.79	0.951
Sex(M/F)	20/10	22/8	0.899
Weight (kg)	68±8.11	63.5±9.18	0.98
Anaesthesia duration (min)	159±57.8	154±43.90	0.779
Duration of surgery (min)	130±38.0	128±34.97	0.88

Table 1: Demographicdata, duration of anaesthesia and surgery in two study group

The MBP in the sublingual NTG group was found to be significantly lower than those of the control group during extubation and at 1, 3 and 5min after extubation. No significant difference was found after 10 minutes ($p>0.05$).However, HR and RPP were comparable between both groups ($p>0.05$) (Table2).

TIME	HR			MAP			RPP		
	Group A	Group B	P value	Group A	Group B	P value	Group A	Group B	P value
T0	82.5±11.179	86.8±13.11	0.32	91.84±8.19	86.56±6.80	0.25			
Ts	91.17±16.91	91.3±12.41	0.92	113.85±12	111.31±7.33	0.029	13181±2745	12618±1726	0.290
Te	97.87±15.11	101.37±12.3	0.36	*94.14±12.04	109.47±9.04	0.001	13912±3179	13312±2005	0.396
T1	92.5±13.22	96.6±12.5	0.34	*93.71±12.38	105.25±8.83	0.000	13544±3428	13680±1884	0.615
T2	88.2±13.60	95.5±1 3.16	0.06	*94.80±10.8	104.49±7.86	0.000	13539±2645	13564±2242	0.89
T3	87±13.35	91 .5±13.06	0.16	*90.67±9.6	98.25±8.93	0.008	12709±2857	13897±2077	0.45
T4	82.23±14.46	84.67±8.97	0.63	89.88±7.88	94.61±6.21	0.132	11599±2576	15315±3203	0.63
T5	80.32±12.79	83.98±9.77	0.36	92.50±7.9	93.55±5.84	0.563			
T6	77.75±9.86	81.98±8.48	0.37	90.7±7.3	92.18±6.43	0.722			

Table 2: Hemodynamic data in two study group

T0: Preoperative, Ts: spontaneous respiration, Te: During extubation, T1: 1 min after extubation, T2: 3 min after extubation, T3: 5min after extubation, T4: 10 min after extubation. T5:15min after extubation, T6: 20min after extubation Group A: Receiving NTG Spray, Group B: Control Group (not receiving NTG Spray, $p>0.05$ non-significant, *$p<0.05$ significant, MAP: Mean arterial pressure, HR: Heart rate, RPP: Rate pressure product.

In group B two patients showed systolic blood pressure higher than 180mm Hg, one at the time of extubation and another at 3 minutes after reversal which was treated with inj. esmololhydrochloride. In group A, none of the patient showed hypertension requiring any rescue drug. The difference was not significant ($p>0.05$) when the two groups were compared (Table3).

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	Group A N (%)	Group B N (%)	Total N (%)
Esmolol given	1(3.3%)	0(0%)	1(1.7%)
Burning sensation	0(0%)	1(3.3%)	1(1.7%)
Hypotension	1(3.3%)	0(0%)	1(1.7%)
Headache	2(6.7%)	0(0%)	2(3.3%)

Table 3: Rescue drug esmolol required and adverse event in both study groups

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

One patient in group A had burning sensation in mouth after extubation and two had headache in postoperative period, No adverse effect noted in group B. No other adverse events like arrhythmia or hypotension (SBP<25% of baseline) noted in any of the two group.

DISCUSSION: Intubation and extubation both are associated with various cardiovascular and airway responses but attention has been paid to attenuate these changes during intubation when compared with extubation. However, extubation is an equally important part of general anaesthesia as intubation, but is often not given due attention 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.[9]

Although the mechanism of changes occurring in the cardiovascular system during extubation remains to be elucidated, it is associated with increased release of catecholamines as a result of the stress response.[10]

In this study, we compared the hemodynamic changes and adverse events with sublingual NTG during extubation and upto twenty min thereafter .We found that after NTG, mean blood pressure were under control during and after extubation and it remained close to baseline, whereas in control group, mean arterial blood pressure were found to be persistently high during extubation, coming to baseline after ten minutes of extubation. However, increase in heart rate was comparable in both groups.

Though there is minimal data about nitroglycerine for extubation response, it has been effectively used as a rescue drug for controlling hypertension during extubation while studying other drugs.[10]The drug has also been used by several authors during tracheal intubation with favorable haemodynamic effects. S. Kamra et al.[11] 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. Similarly, Anant S et al.[12] and J. Dich-Niels et al.[13] found significant attenuation of hypertensive response to laryngoscopy and intubation following intranasal NTG spray without significant increase in heart rate. Firoozbakshetal.[14] also reported similar result with intravenous nitroglycerine during intubation. Results of the present study also confirm similar haemodynamic changes with sublingual nitroglycerine spray used during tracheal extubation.

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In the present study rate pressure product was calculated at time of NTG spray and for five minutes after the extubation when its maximum clinical effect was seen.

In our study the RPP was not found to be much altered in NTG groups when compared with control groups. Similar results were found in J. Dich-Nielset al.[13] study suggesting that NTG did not increase myocardial oxygen demand to make the patient prone to ischaemia. However, Kamara et al.[12] observed that RPP rise was more than double in the control group as compared to the NTG group suggesting that NTG administration actually reduces the MVO2. Besides, by dilating the coronary vessels NTG increases the coronary blood flow and oxygen delivery to myocardium and is primarily indicated to treat the acute myocardial ischaemia. Thus tachycardia is not a major concern in these patients. Though NTG causes compensatory tachycardia, NTG spray may benefit the ischaemic myocardium by its known vasodilator properties, thus facilitating oxygen delivery to the myocardium.

The previously reported side effects of NTG spray such as nausea, dizziness, congestion, palpitations and hypotension were not observed in any of our patients, but one patient who received NTG had burning sensation in their mouth and two had headache postoperatively. G. Nyberg et al.[15]also observed headache in six (Out of nine) patients after oral nitroglycerin.

In the present study no patient in any group showed respiratory adverse events. Actually nitroglycerine in higher doses has been used to treat perioperative laryngospasm successfully.[7,8] though we have not come across such observation.

Our study has some limitations. First, 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 and second 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.

CONCLUSIONS: To conclude, in patients undergoing lumbar disc surgery, sublingually administered nitroglycerin spray in a dose of 0.8mg 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 and RPP during extubation.

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