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Sublingual Nitroglycerin spray versus normal saline spray in attenuating pressor response to extubation: Changes in heart rate

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Abstract
The sympathetic response involves polysynaptic pathway with Glossopharyngeal and Vagus nerve forming afferent arc to the sympathetic nervous system via brain stem and spinal cord. This causes firing of adrenergic mediators such as norepinephrine and epinephrine which leads to increase in HR and blood pressure. Parasympathetic reflex is monosynaptic and is more common in children. Approval from ethical committee and written informed consent was obtained. A total of 60 patients undergoing surgery under general anaesthesia with endotracheal intubation were included in the study. After having met inclusion and exclusion criteria and having obtained informed consent, patients were randomized based on computer generated randomization table into one of the two groups. Hemodynamic response to extubation increases HR, BP which in turn increases myocardial oxygen demand. Activation of sympathetic nervous system during extubation causes coronary vasoconstriction which in turn reduces coronary blood flow. NTG dilates coronary vessels thereby increases blood flow of coronaries and thus improving oxygen delivery to myocardium which is an added advantage.

Keywords: Nitroglycerin spray, normal saline spray, heart rate

Introduction
The exact mechanism of extubation response is not known but it is believed to involve both sympathetic and parasympathetic systems. The sympathetic response involves polysynaptic pathway with Glossopharyngeal and Vagus nerve forming afferent arc to the sympathetic nervous system via brain stem and spinal cord. This causes firing of adrenergic mediators such as norepinephrine and epinephrine which leads to increase in HR and blood pressure. Parasympathetic reflex is monosynaptic and is more common in children [1, 2].

A study titled "Attenuation of pressor response following intubation: Efficacy of nitroglycerin sub lingual spray done in the year 2016 by Indira Kumari, Uditha Naithani, Vinod Kumar Dadheech, D.S Pradeep, Khemraj Meena, Devendra Verma [3]", 90 patients of ASA I and II, between 18-60 years scheduled for surgeries under general anesthesia were included. Study was prospective randomized controlled trial where patients were randomized to 3 groups with Group C (control group) receiving no Nitroglycerin spray while Group N1 receiving 1 puff of NTG spray whereas Group N2 receiving 2 puffs of NTG spray one minute prior intubation. Patients were pre oxygenated for 3 minutes and intubation was done as per standard general anesthesia technique. Immediately following induction Nitroglycerin spray was administered as one metered spray in Group N1 (400 mcg) and two metered sprays (800 mcg) in group N2 and group C did not receive any drug. Heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were recorded at T1: baseline (before premedication), T2: just before intubation (60 seconds after induction and nitroglycerin spray), T3: just after intubation, T4: 1 min after intubation, T5: 2min after intubation, T6: 5 min after intubation, T7: 10 min after intubation. The study concluded that Nitroglycerin both in a dose of 1 spray or 2 spray which was given 1 minute prior to intubation is effective in attenuating the pressor response in normotensive ASA I and II patients.

In the study "comparison of different doses of Nitroglycerin spray for attenuation of stress response to laryngoscopy" during intubation by Mona Panchal, Upasana Bhatia [4] where 50 ASA I and II patients of either sex aged 20-60 years scheduled for elective surgery were included.

Study design was randomized controlled study where patients were randomized in to, Group I (n=25) received 400 mcg and Group II (n=25) received 800mcg of intranasal nitroglycerin spray 2 minutes before laryngoscopy and endotracheal intubation. General anesthesia was administered as per standard technique and patients were observed after laryngoscopy and intubation every minute till 5 minutes for any complications. Heart rate, systolic blood pressure, diastolic blood pressure were recorded at T1: baseline (before premedication), T2: just before intubation, T3: just after intubation, T4: 1 minute after intubation, T5: 2minute after intubation, T6: 3 minute after intubation, T7:4 minutes after intubation, T8: 5minutes after intubation. Study concluded that Nitroglycerin spray in a dose of 400mcg given 2 minutes prior to induction of general anesthesia is effective in attenuating pressor response to laryngoscopy and intubation where as 800 mcg dose does not have any extra advantage over 400 mcg of nitroglycerin spray.

In a study done by V. Madhuri Gopal titled "Comparative study of pressor response to laryngoscopy and intubation with oral spray of Nitroglycerin and Oropharyngeal spray of lignocaine [5]" done in the year 2017 where 60 patients belonging to either sex aged between 18-60 years belonging to ASA I and II with Mallampati class I and II were included. Study design was prospective randomized study where study population were randomized into 30 patients in each group. Anaesthesia was induced as per general anesthesia guidelines and endotracheal intubation was done with appropriate size endotracheal tube. Group L-Lignocaine group (n=30) received oropharyngeal Lignocaine 10% spray 100mg 3 minutes before induction, Group N – Nitroglycerin group (n=30) received oral nitroglycerin spray 0.8mg 30 seconds before induction. Heart rate, systolic and diastolic blood pressure were recorded at baseline, at induction, 1, 3, 5 and 10 minute interval after laryngoscopy. The study concluded that Nitroglycerin spray group was better in attenuating pressor response to laryngoscopy and intubation without side effects compared to Lignocaine spray group.

"A comparative study to evaluate the effects of NTG and Esmolol on hemodynamic parameters in controlled hypertensive patients during emergence from anaesthesia and extubation" a study undertaken by R. Vacchani, Rahul Gulati [6] published in 2017 in which 60 controlled hypertensives were included. Patients belonged to ASA status II and III, aged 30-65 years were randomly divided into group I (NTG infusion 0.5mcg/kg/min) and group II (Esmolol 100mcg/kg/min). After completion of surgery and before reversal, the study drug was started and continued during extubation. Data were recorded at following stages-pre-operatively, just before reversal, just after reversal, at the time of extubation, 1 and 3 minutes after extubation. Statistical comparison of drugs was done by student's t tests. It was noted that there was increase in HR in both the groups. Study concluded that intravenous Esmolol had better hemodynamic stability but both attenuate extubation response without any adverse effects and complications.

Methodology

Inclusion Criteria

- Patient who provided consent.
- ASA I and II.
- Age - 18 to 60 years.
- Patients scheduled for elective surgeries under general anaesthesia with endotracheal intubation.

Exclusion Criteria

- Hypertensive patients.
- ASA grade III and IV
- Patients allergic to study drug
- Patients with difficult airway

Approval from ethical committee and written informed consent was obtained. A total of 60 patients undergoing surgery under general anaesthesia with endotracheal intubation were included in the study.

After having met inclusion and exclusion criteria and having obtained informed consent, patients were randomized based on computer generated randomization table into one of the two groups.

Group A: where patients received 1 puff of sublingual nitroglycerin spray 1 minute after administration of reversal.

Group B: where patients received 1 puff of sublingual normal saline spray 1 minute after administration of reversal.

A thorough pre-anaesthetic evaluation was done on day before surgery. Detailed medical history was elicited and detailed physical examination was carried out. Patients were kept nil per orally for 8 hours prior to surgery. Preoperatively investigations like CBC, RBS and Sr. Creatinine were done. ECG and CXR were done if patient was more than 40 years of age.

Results

There were 15 patients in Group A who were ASA I patients where as 15 patients were ASA II. Where as group B had 19 patients who were ASA I while 11 were of ASA II status. When compared, difference was statistically not significant with p value 0.297.

Table 1: Distribution of ASA

	Group a	Group b	Total
ASA i	15	19	34
ASA ii	15	11	26
Total	30	30	60

Table 2: Heart Rate

	Group a		Group b			
	Mean	S.d.	Mean	S.d.	P value	Inference
TR	89.05	12.67	90.47	5.36	0.5730	NS
T0	91.01	12.66	92.47	5.35	0.5630	NS
T1	91.03	11.88	92.07	4.57	0.6582	NS
T2	92.00	9.50	93.13	4.29	0.5536	NS
T3	93.03	9.73	96.00	3.45	0.1209	NS

T4	94.03	10.49	94.13	3.79	0.9610	NS
T5	91.93	10.54	95.33	3.91	0.1030	NS
T6	91.00	10.34	94.60	4.01	0.0807	NS
T7	90.00	9.71	93.07	3.54	0.1097	NS
T8	90.97	9.30	94.20	3.84	0.0836	NS
T9	90.07	9.68	96.17	4.22	0.0112	S
T10	89.87	9.78	96.00	5.48	0.0340	S

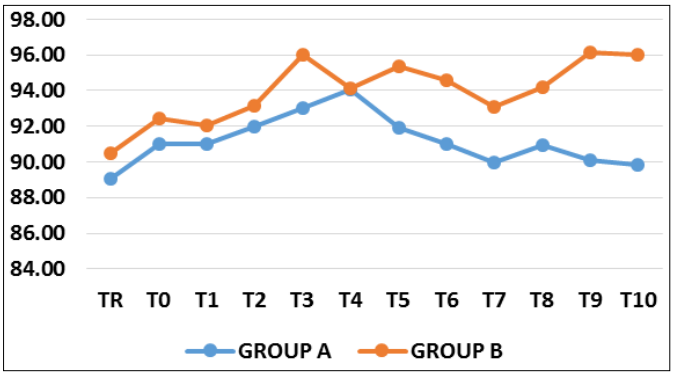

Fig 1: Mean HR

In Group A

Mean HR at the time of administration of reversal was 89.05+12.67 (TR) and at the time of administration of NTG spray was 91.01+12.66 (T0).

Maximum increase in HR was seen at 4 minutes which was 94.03+10.49. The HR subsequently reduced gradually reaching baseline at 10 minutes.

In Group B

Mean HR at the time of administration of reversal was 90.47+5.36 (TR) and at the time of administration of saline spray (T0) was 92.47+5.35.

Subsequently HR increased with maximum increase in HR seen at 3 minutes, with mean HR being 96.00+3.45.

The HR remained high till 10 minutes and when compared with Group A the increase in HR was found to be statistically insignificant till 8 minutes.

Discussion

Laryngoscopy and extubation is the most crucial part of general anaesthesia. It was in 1940; Reid and Brace [7] first described hemodynamic changes to intubation. This lead to a large number of studies to attenuate the stress response to intubation. Extubation is associated with patient awakening, pain, anxiety and airway irritation which causes similar increase in heart rate and blood pressure as during intubation what is known as pressor response to extubation. This Pressor response to extubation may be well tolerated in ASA I patients but is deleterious in patients with history of cardiovascular disease, hypertension and arrhythmias.

Pressor response to extubation causes transient increase in "heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure" due to increased sympathoadrenergic activity caused by epipharyngeal and laryngopharyngeal stimulation [8].

Numerous methods were tried to attenuate this response to extubation such as non pharmacological methods like_ extubation in deeper planes of anesthesia, using supraglottic airway devices etc. Various drugs such as magnesium sulphate, preservative free lignocaine, beta blockers such as esmolol, calcium channel blockers such as verapamil, diltiazam, remifentanyl, fentanyl, dexmedetomidine and nitroglycerin have been used to attenuate hemodynamic response to extubation [9].

Extubation in deeper planes of anesthesia causes decreased cardiovascular stimulation as there is reduced incidence of coughing and straining on the tube. However, there is chance of respiratory complication which is found to be greater after extubation under deep anesthesia, irrespective of the type of surgery where as supraglottic airway devices insertion might be difficult in some patients. Fentanyl, Remifentanyl and Dexmedetomidine even though effective, have sedating effect due to which even though we can use them during intubation but these cannot be used to attenuate pressor response during extubation as following extubation an awake patient capable of maintaining patent airway is of paramount importance [10].

Intravenous nitroglycerin is commonly used in anesthesia to treat hypertension while NTG spray was basically used to abort anginal attack. NTG relaxes vascular smooth muscles, predominantly venous dilatation over arterial dilatation.

Hemodynamic response to extubation increases HR, BP which in turn increases myocardial oxygen demand. Activation of sympathetic nervous system during extubation causes coronary vasoconstriction which in turn reduces coronary blood flow. NTG dilates coronary vessels thereby increases blood flow of coronaries and thus improving oxygen delivery to myocardium which is an added advantage.

NTG has faster onset of action (2-3 minutes) and shorter duration of action with plasma half life 4 – 5 minutes. Sublingual Nitroglycerin spray is cost effective as well as can be easily administered.

Present study titled "Efficacy of sublingual nitroglycerin spray versus normal saline spray in attenuating pressor response during extubation: A one year hospital based randomized controlled trial" attempted to study the effects of sublingual nitroglycerin spray to attenuate pressor response to extubation. In this study 60 patients who belonged to ASA physical status I and II were randomized into Group A and Group B with 30 patients in each group. Group A received 1 puff of sublingual nitroglycerin spray 1 minute after reversal of neuromuscular blockade whereas Group B received 1 puff of sublingual normal saline spray 1 minute after reversal of neuromuscular blockade. Heart rate, systolic blood pressure,, diastolic blood pressure and mean blood pressure, oxygen saturation were noted before intervention (T0) and there after every minute i.e " T1, T2, T3, T4, T5, T6, T7, T8,T9 and T10" till 10 minutes. Time of extubation was noted.

Conclusion

We observed that HR increased till 3rd minute in Group A and thereafter had better hemodynamic control of pressor response to extubation compared to baseline and returning to baseline after 9 minutes. Whereas in Group B, HR increased progressively till 10 minutes.

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