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Comparative study on sublingual nitroglycerine spray with or without iv fentanyl for attenuation of pressor response to laryngoscopy and intubation.

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Abstract

Introduction: Background and Aim: Laryngoscopy and endotracheal Intubations are not only common and necessary medical procedures, but are invasive procedures with the potential to cause dynamic, possibly dangerous hemodynamic pressor responses. They are generally tolerated well by healthy patients. Geriatric and elderly patients have an increased risk of coronary artery disease (CAD), cerebrovascular disease and elevated blood pressure (BP) making them susceptible to swings in BP and heart rate (HR) during Laryngoscopy & endotracheal Intubation (LETI), resulting in the risk of MI, stroke, congestive heart failure (CHF) or sudden death.

Many strategies like reducing the duration of laryngoscopy, administration of drugs like volatile anaesthetics, topical and intravenous lidocaine, opioids, vasodilators, calcium channel blockers, β- lockers and alpha-2 adrenergic agonist before laryngoscopy but none is found to be ideal. So this study compared the efficacy of Glyceryl Trinitrate (Nitroglycerin or NTG) sublingual spray with or without intravenous fentanyl to attenuate the stress response to laryngoscopy and endotracheal intubation in normotensive patients.

Methods: 90 patients of ASA I and II patients of age group 20-60 years posted for elective surgical procedure under general anaesthesia were divided into 3 groups of 30 each. Group I control, Group 2 - NTG sublingual spray (0.4 mg/spray) 1 min before induction and Group 3 Nitroglycerine sublingual spray (0.4 mg/spray) + intravenous fentanyl (2µg/kg)2 min before induction. . Vital parameters like HR, SBP, DBP, MAP were recorded just before intubation and at 1, 3, 5, min. after intubation.

Results: Demographic characteristics and baseline vital parameters in all the groups were comparable. In Group 3 the baseline heart rate came down just before intubation (75.33±12.69 vs 88.57±17.50) and rose at 1 minute after intubation but decreased again at 3 minutes (82.23±12.08) and at 5 minutes (78.43±12.23) after intubation. Group 3 maximum fall was seen just before intubation (73.75±6.63 vs 92.45±7.87) and maximum rise was seen at 1 minute after intubation but blood pressure did not increase to baseline (79.45±7.302).

Keywords: Endotracheal intubation, NTG, Fentanyl, Hemodynamic response.

Introduction:

Laryngoscopy and endotracheal Intubations are invasive procedures with the potential to cause dynamic, possibly dangerous hemodynamic pressor response. A typical pressor response includes a 40-50% increase in blood pressure, a 20% increase in heart rate. The effects usually occur within thirty seconds of intubation and last less than ten minutes and tolerated well by healthy patients. However, these effects can be detrimental to patients with hypertension, ischemic heart disease, history of myocardial infarction or increased intracranial pressure.

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King *et al* [1]also studied the hemodynamic response[2,4] to Laryngoscopy & Endotracheal Intubation (LETI) in 1951 and proposed that the cardiac dysrhythmias , hypertension, and tachycardia related to LETI were the result of either decreased vagal tone or increased sympatho-adrenal activity. Most of the arterial BP response was the result of increased Cardiac output (CO) rather than increased Systemic vascular resistance(SVR). They found that the BP response appeared to be blocked by deeper levels of anesthesia than the increase in HR.

Various measures have been tried to limit the adverse hemodynamic response to laryngoscopy and intubation e.g. limiting the duration of laryngoscopy to less than 15 seconds, administration of volatile anaesthetics before intubation, topical and intravenous lidocaine, opioids, vasodilators like nitroprusside, calcium channel blockers, β- lockers and alpha-2 adrenergic agonist.

Glyceryl trinitrate (Nitroglycerin or NTG) a veno-dilator has been introduced as lingual pump spray or pen spray to attenuate the stress response to laryngoscopy and endotracheal intubation[3]. But administered alone during pre-intubation may not be sufficient and may produce tachycardia. Fentanyl citrate, an opioid can control both heart rate and blood pressure responses but produce respiratory depression and truncal rigidity at higher doses. So this study compares the efficacy of sublingual nitroglycerine spray alone and with intravenous fentanyl to attenuate the pressor response to intubation.

Methods:

This is a prospective, randomized, double blind study included 90 patients of ASA grade I and II patients aged between 20 and 60 years posted for surgery under general anesthesia with tracheal intubation .They were randomly assigned into three equal groups of 30 each. Patients hypersensitivity to NTG or Fentanyl, predicted difficult laryngoscopy & intubation, unstable hemodynamic status, raised ICT, cardiac and respiratory disease were excluded from the study.

Group-1: Control group- Normal saline infusion.

Group-2:NTG group-Nitroglycerine sublingual sprays (0.4 mg/spray).

Group-3: NTG + intravenous fentanyl group- Nitroglycerine sublingual spray (0.4 mg/spray) + intravenous fentanyl (2µg/kg)

Routine investigations were done and Patients were kept NPO for 8hrs prior to surgery. Patients were advised to take Tab Ranitidine (150mg) and tab alprazolam 0.5mg the night before surgery. In the operation theater base line pulse rate, systolic, diastolic and mean blood pressure were recorded. ECG leads were attached. Injection Ondansetron 0.1mg/kg, Inj. Glycopyrrolate 0.2mg and midazolam 0.05mg/kg IV was administered. Patients were pre-oxygenated with 100% oxygen.

Induction was done with Inj Thiopentone sodium 5mg/kg and Inj vecuronium bromide at dose of 0.1mg/kg as muscle relaxant. Group -1, Normal saline infusion was given 2 min prior to intubation. Patients in Group-2 received sublingual NTG - single spray(0.4mg/spray) one minute before intubation. Patients in Group-3 received injection fentanyl 2µg/kg 2 min. before intubation & sublingual NTG - single spray one minute before intubation. After adequate jaw relaxation intubation was performed. Laryngoscopy was limited to <30 seconds. Anesthesia was maintained with 33% oxygen, 66% nitrous oxide and 1 vol% of isoflurane for up to 5 min after endotracheal intubation. HR, SBP, DBP, MBP were recorded just before intubation and at 1, 3, 5, min. after intubation. After 5 min, fentanyl was administerd in Group 1 & Group 2 patients and Isoflurane was supplemented in titrated doses. Results were analyzed statistically using chi-square ($\chi 2$) test, ANOVA test and Student t test. The critical probability value (p-value) indicating a significant difference was taken as 0.05 or less.

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Observation:

Table 1: Mean age of patients.

Group	Age (years) (Mean±SD)	F-value	P-value
Group 1	35.73 ± 10.03	1.157	0.319
Group 2	39.77 ± 10.15		
Group 3	37.93 ± 10.67		

Table 2: Mean sex of patients and their distributions

	Group 1		Group 2		Group 3	
	No.	%	No.	%	No.	%
Male	17	66.0	14	47.0	15	50.0
Female	13	44.0	16	53.0	15	50.0
Total	30	100	30	100	30	100
$\chi^2 = 0.623$, p = 0.733						

Table 3: Statistical comparison of mean heart rate per minutes ± SD at different time interval before and after intubation with group comparison.

Time Interval	Group 1	Group 2	Group 3	F -value	P -value	Group 1 vs 2, P -value	Group 1 vs 3, P-value	Group 2 vs 3, P-value
Baseline	86.40 ± 14.16	90.60 ± 13.37	88.57 ± 17.50	0.579	0.563	0.242	0.600	0.615
Just before	76.50 ± 10.59	97.63 ± 9.95	75.33 ± 12.69	38.091	<0.001	<0.001	0.701	<0.001
1 min	151.53 ± 12.54	123.17 ± 9.53	89.27 ± 13.56	202.506	<0.001	<0.001	<0.001	<0.001
3 min	145.67±12.95	119.53 ± 9.05	82.23 ± 12.08	231.238	<0.001	<0.001	<0.001	<0.001
5 min	139.70 ±14.76	112.20 ± 10.83	78.43 ± 12.23	174.824	<0.001	<0.001	<0.001	<0.001

Table 4: Mean of systolic blood pressure (mmHg)±SD at different time interval before and after intubation with group comparison.

Time Interval	Group 1	Group 2	Group 3	F -value	P -value	Group 1 vs 2, P -value	Group 1 vs 3, P-value	Group 2 vs 3, P-value
Baseline	120.33 ± 11.807	122.60 ± 14.45	123.47 ± 11.78	0.495	0.611	0.502	0.298	0.799
Just before	111.50 ± 12.99	92.27 ± 11.53	96.90 ± 7.57	25.257	<0.001	0.001	<0.001	0.071
1 min	178.77 ± 14.58	132.70 ± 14.99	112.43 ± 6.61	216.205	<0.001	<0.001	<0.001	<0.001
3 min	171.03 ± 14.54	125.70 ± 12.55	107.77 ± 5.78	237.657	<0.001	<0.001	<0.001	<0.001

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5 min	162.60 ± 12.80	119.93 ± 11.07	104.30 ± 5.83	255.854	<0.001	<0.001	<0.001	<0.001

Table 5:Mean of diastolic blood pressure (mmHg)±SD at different time interval before and after intubation with group comparison.

Time Interval	Group 1	Group 2	Group 3	F -value	P -value	Group 1 vs 2, P -value	Group 1 vs 3, P-value	Group 2 vs 3, P-value
Baseline	79.23 ± 12.02	77.63 ± 8.13	78.27 ± .564	0.217	0.805	0.548	0.712	0.757
Just before	71.87 ± 12.36	59.10 ± 5.74	63.23 ± 7.27	16.015	<0.001	<0.001	0.002	0.018
1 min	112.77 ± 7.61	84.47 ± 10.65	70.47 ± 7.57	182.685	<0.001	<0.001	<0.001	<0.001
3 min	107.73 ± 6.12	77.87 ± 10.21	67.40 ± 7.24	202.987	<0.001	<0.001	<0.001	<0.001
5 min	101.43 ± 5.64	73.60 ± 9.16	65.33± 7.87	178.415	<0.001	<0.001	<0.001	<0.001

Table 6:Mean of mean blood pressure (mmHg)±SD at different time interval before and after intubation with group comparison.

Time Interval	Group 1	Group 2	Group 3	F -value	P -value	Group 1 vs 2, P -value	Group 1 vs 3, P-value	Group 2 vs 3, P-value
Baseline	91.95±11.736	93.75±7.552	92.45±7.870	0.33	0.968	0.910	0.896	0.782
Just before	87.10±22.351	69.95±8.835	73.75±6.632	22.686	<0.001	<0.001	<0.001	0.017
1 min	147.75±14.686	100.95±12.886	84.40±8.840	236.559	<0.001	<0.001	<0.001	<0.001
3 min	141.45±11.450	94.90±11.350	81.70±7.428	270.920	<0.001	<0.001	<0.001	<0.001
5 min	136.40±12.215	89.85±10.629	79.45±7.302	277.630	<0.001	<0.001	<0.001	<0.001

Discussion:

Patients with hypertension, ischemic heart disease or cerebrovascular disease are susceptible to adverse events due to large swings of blood pressure and heart rate during laryngoscopy and tracheal intubation. Tachycardia and hypertension increases myocardial oxygen requirements and can produce myocardial ischemia or infarction. Studies support the hypothesis that controlling per operative stress including that of laryngoscopy and tracheal intubation improve outcome in high risk patients.

Nitroglycerine is one of the commonly used drug to blunt the hemodynamic response. Kamra*et al*.[13] used topical injection nitroglycerine equivalent to 30 mg nitroglycerine. Fassoulaki and Kaniaris.[3] used nitroglycerine in a dose of 60 mg. and Gupta PK *et al*.[9] used nitroglycerine as continuous infusion. Swami *et al*.[17] used 30 microgram/kg of nitroglycerine 5 minutes prior to intubation. Anant and Waghray[14] used intranasal NTG spray for attenuation of pressor response to intubation.

Dahlgren *et al*.[4] used fentanyl 15 microgram/kg intravenously three and a half minutes prior to intubation. Kautto.[5] used fentanyl in a dose of 2 microgram/kg and 6 microgram/kg. Iyer and Russel[6] reported that more than 10 microgram/kg of intravenous fentanyl was necessary to keep heart rate below

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baseline during laryngoscopy. Helfman*et al*. used fentanyl in a dose of 3 microgram/kg intravenously and reported that it attenuates blood pressure but not the heart rate. Ebert *et al*.[7] administered fentanyl intravenously in a dose of 0.8 microgram/kg/minute and found that fentanyl decreased heart rate, systolic blood pressure, diastolic blood pressure and means blood pressure below the baseline.

There was no significant difference in initial heart rate between the groups(p =0.563). In Group 2, heart rate continued to rise after intubation and gradually came down but did not reach the baseline value(90.60±13.37 vs 112.20±10.83) .Whereas in Group 1 and Group 3, heart rate came down below baseline just before intubation. Rise of heart rate was maximum in all the groups at 1 minute after intubation. Rise of heart rate in Group 2 was in accordance with studies conducted by Dutta*et al*.[8] The heart rate in Group 1 did not reach the baseline even at 5 minutes after intubation (139.70±14.76 vs 86.40±14.16). These observations were in accordance with King *et al*.[1], Wycoff [10].In Group 3 the baseline heart rate came down just before intubation (75.33±12.69 vs 88.57±17.50) and rose at 1 minute after intubation . Heart rate decreased again at 3 minutes (82.23±12.08) and at 5 minutes (78.43±12.23) after intubation but it was never above baseline. Kautto[5] also stated that fentanyl 2 microgram/kg significantly attenuated heart rate and blood pressure response. Ebert *et al*.[7] also reported fentanyl intravenously decreased heart rate below baseline.

Rise of heart rate in the Group 2 where nitroglycerine spray alone was due to systemic vasodilation leading to hypotension and a baroreceptor reflex producing tachycardia. So there was a transient fall of blood pressure in Group 2 before intubation yet blood pressure increased significantly after intubation which may be explained by the short duration action of NTG. Optimal control of heart rate in Group 3 where both NTG spray and intravenous fentanyl were used can be explained by the bradycardia producing property of fentanyl which neutralizes the tachycardia of NTG.

Baseline blood pressures were comparable in all the three groups (SBP p value 0.611, DBP p value 0.805). Systolic and diastolic blood pressures in Group 1 decreased just before intubation to rise at 1 minute after intubation. Systolic and diastolic blood pressure did not return to baseline even at 5minute after intubation(SBP 162.60±12.80 vs120.33±11.807 and DBP 101.43±5.64 vs 79.23±12.02). In Group 2 systolic and diastolic blood pressure decreased significantly before intubation. After intubation systolic and diastolic blood pressure were maximum at 1minute and again decreased gradually below the base line after 5 min(SBP 119.93±11.07 vs 122.60±14.45 and DBP 73.60±9.16 vs 77.63±8.13). Kamra*et al.*[13] reported that the increase in systolic blood pressure lasted only for 1minute following intubation. In Group 3 post intubation blood pressures did not rise above base line (SBP 112.43±6.61 vs123.47±11.78 and DBP 70.47±7.57 vs 78.27±0.564). Ebert *et al.*[7] reported that the systolic and diastolic blood pressure remained below base line after intubation using intravenous fentanyl. Helfman*et al.* and Kautto[5] reported that intravenous fentanyl attenuated pressor response. Ebert *et al*.[7] also reported that fentanyl decrease the diastolic blood pressure below baseline.

Mean blood pressures were comparable in all the three groups (p =0.805). In Group 1 the mean blood pressure decreased before intubation and increased maximally at 1 minute after intubation (147.75±14.686 vs 91.95±11.736) and did not reach baseline even at 5 minutes after intubation (136.40±12.215). In Group 2, mean blood pressure decreased from baseline just before intubation (69.95±8.83 vs 93.75±7.55). Maximum rise was seen at 1 minute after intubation (100.95±12.88) and gradually came down below the baseline at 5 minutes. In Group 3 maximum fall was seen just before intubation (73.75±6.63 vs 92.45±7.87) and maximum rise was seen at 1 minute after intubation but blood pressure did not increase to baseline (79.45±7.302). Results were in accordance with study done by Ebert *et al*.[7] using intravenous fentanyl.

So intravenous fentanyl and nitroglycerine spray combination was more effective than NTG alone in controlling the pressor response to laryngoscopy and intubation during general anesthesia in healthy patients undergoing e surgeries

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