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A comparative study of nitroglycerine and nifedipine on cardiovascular response during laryngoscopy and intubation

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Abstract
Laryngoscopy during intubation is associated with significant increase in pulse rate and blood pressure. The present prospective randomized comparative study was conducted at Rama Medical College Hospital and Research Centre to assess the efficacy of Nitroglycerine spray 2 puffs (0.8mg) and 10mg Nifedipine sublingual for attenuation of hemodynamic stress responses in patients undergoing intubation for general anaesthesia. These were compared with the patients receiving premedication only.The study found that the use of Nitroglycerine spray(0.8%) administered intranasal 2 minutes and 10mg. Nifedipine sublingual 20 minutes before induction was associated with blunting of the hypertensive effect but not the tachycardia response of the cardiovascular system to laryngoscopy and intubation.

Keywords: nitroglycerine, nifedipine, general anesthesia, laryngoscopy and intubation

Introduction

The procedure of laryngoscopy and intubation is an integral part of modern day balanced anesthesia. It is performed for most of the major and some minor surgical procedures. The procedure of direct laryngoscopy and intubation is associated with significant hemodynamic changes such as increase in heart rate, arterial pressure and dysarrhythmias in up to 90% of the patients (Asfar SN, and AbdullaWY. (1990) [3]. Transient hypertension and tachycardia are probably of no consequence in healthy individuals but some patients require careful hemodynamic control during anesthesia and intubation of the trachea. Mostly these are patient with known or suspected ischemic heart disease, recent myocardial infarction and those with hypertension. The complications that may occur because of this sudden rise in blood pressure include left ventricular failure (Abou-Madi M N, Kezster H, and Yacoub J M (1977) [1], myocardial ischemia (Adams HA, Bormann BV, Bachmann B, Ratthey K, Hempelmann G (1987) [2] and even sudden death (Dwyer CS, Strout WG, and Thomas PB) [5].These cardiovascular changes had initially been ascribed to be due to vago-vagal reflex or due to stimulation of cardiac response. Subsequently it has been postulated that these reflexes are mediated by increased sympathetic nervous system activity. This is reflected by an increase in the level of circulating catecholamines especially noradrenaline (Fox E, Sklar GS., Hill C, Villanueva R and King B D. (1977) [5]. The stimulation of the sympathetic system occurs due to laryngoscope pressing the base of the tongue or lifting the epiglottis thus stimulating the mechanoreceptors in the proximal part of the trachea. Over the period of time various approaches have been advocated ranging from minimizing the duration of laryngoscopy (to less than 15 second) and the use of various pharmacological agents to reduce the extent of these potentially harmful responses. Lidocaine is the oldest and most widely used drug for the purpose of attenuating pharyngeal and laryngeal reflexes. It is particularly suitable for this purpose because of its rapid onset and short duration of action which is compatible with the duration of this pressor response (Hamill JF, Bedford RF, Weaver D C, and Colohan A R (1981) [6]. It is used topically as laryngotracheal spray or by intravenous route.Other drugs that have been postulated for attenuation of these presser responses include intravenous narcotics like Fentanyl, Alfentanil (KAUTTO 1985) and various antihypertensive agents such as beta blockers (Helfman SM, Gold MI, DeLisser EA, and Herrington CA(1991) [7], ganglion blockers central sympatholytics like clonidine (ORKO *et al* 1987) [9], calcium channel blockers, ACE inhibitors and peripheral vasodilators like nitroprusside and hydralazine (CURRAN 1975 KAMRAS 1986) [4].

None of these pharmacological approaches has proved entirely satisfactory because the response may not be completely blocked or the method itself carries some additional risk. The agent used may have too long action or have unfeasible side effect.

Aims and Objectives

1. The aim of the present study was to study the hemodynamic changes associated with induction of general anesthesia during laryngoscopy and endotracheal intubation.
2. To evaluate the efficacy of 0.8mg of topical Nitroglycerine in the form of intra nasal spray and10mg

Nifedipine sublingual for attenuating stress response during laryngoscopy and intubation

3. To observe any untoward reactions and adverse effects.

Material and Method

The study was conducted from 1st January 2018 to 30th June 2019 in the Department of Anesthesiology and Critical Care, Rama Medical College Hospital and Research Centre, NH-24, Pilkhuwa, Hapur after approval from the hospital ethics committee on 60 normotensive ASA Grade I & II patients. All patients underwent a thorough pre-anesthetic checkup comprising of general physical examination, systemic examination and routine investigations. Other investigations were conducted whenever required. Uncooperative patients, patient suffering from renal, hepatic or psychiatric illness, patients with a history of hypertension, diabetes mellitus, bronchial asthma, patient on medication with any cardio–vascular diseases, patient with addiction to any drugs particularly narcotics were excluded from present study.

After obtaining informed consent patients were randomly divided into 3 groups (A, B&C) of 20 each. Uniform premedication was done in all groups with tablet diazepam 5 mg h.s. on the night before surgery and with Inj pethidine 1 mg /kg and Inj Phenergan 0.5 mg / kg I.M. 45 minutes before induction of general anaesthesia. Patient in group A only received the premedication and formed the control group. Patients in group B received topical Nitroglycerine in the form of intra nasal spray in a dose of 0.8 mg. 2 minutes before induction. The drug was administered as 2 puffs of nitroglycerine spray each metered dose of which delivers 0.4 mg. nitroglycerine. Group C patients in this group received 10 mg Nifedipine sublingual 20 Minutes before induction. Baseline parameters were recorded in the operation room. The patients were preoxygenated for 3 minutes with 100% oxygen. Induction was done with inj. thiopentone sodium (3-5 mg/kg) IV followed by injection succinylcholine (1.5 mg / kg) IV. Endotracheal intubation was carried out and maintained with oxygen, nitrous oxide and injection vecuronium (0.08 to 0.1 mg /kg) IV with Bain`s or closed circuit.At the end of surgery reversal was done with injection glycopyrrolate 0.01mg/kg and injection neostigmine 0.05mg / kg IV. Parameters like pulse rate (PR), blood Pressure – Systolic (SBP) and Diastolic (DBP), mean Arterial Pressure (MAP), SPO_2, E.C.G were observed for the study.

The readings were recorded just before giving drugs (baseline values, B.V), after giving drugs (before induction, B.I), after induction, (A.I)just after laryngoscopy and intubation, (L&I), post intubation at 1st (I_1), 3rd (I_3), 5th (I_5)·10th (I_{10}), 15th (I_{15}) and 30th (I_{30}) minuteintervals. Adverse effects if any were recorded. All the above information was recorded in a proforma. After completion of the study observations were tabulated, qualitatively and quantitatively analyzed using proper statistical methods.

Observations

The present study was conducted on 60 patients of both sexes age 20 to 60 years, after approval of the ethical committee schedule for elective surgery under general anesthesia at Rama Medical College Hospital & Research Centre, Pilkhuwa, Hapur.

Table 1: Mean pulse rate in all groups at relevant recording time

Group		B.V.	V.I.	A.I.	L&I	I_1	I_3	I_5	I_{10}	I_{15}	I_{30}
A (Control)	Mean	87.05	87.05	99.95	103.65	119.65	109.05	100.40	98.85	89.75	87.55
	S.D	7.69	7.69	5.51	5.82	9.03	9.81	5.91	5.40	5.50	5.61
B (Nitroglycerine Spray)	Mean	97.90	99.20	98.00	104.10	109.50	100.90	96.90	96.60	94.80	97.45
	S.D	14.73	14.12	25.23	12.34	11.57	11.52	12.22	11.70	12.08	14.27
C(Sublingual Nifedipine)	Mean	88.55	95.70	98.95	102.50	109.60	101.35	93.10	93.00	90.20	88.50
	S.D	14.68	14.41	14.75	15.05	15.56	16.07	13.97	11.85	14.21	14.65

Table 2: Statistical analysis of mean pulse rate in all groups at relevant recoding time and their comparison with baseline value

Group		B.V-B.I	B.V-A.I	B.V-L&I	B.V-I_1	B.V-I_3	B.V-I_5	B.V-I_{10}	B.V-I_{15}	B.V-I_{30}
A (Control)	P. Value	--	<0.00	<0.00	<0.00	<0.00	<0.05	<0.05	>0.05	>0.05
	Significance	--	H.S.	H.S.	H.S.	H.S.	S.	S.	N.S.	N.S.
B (Nitroglycerine Spray)	P. Value	> 0.05	> 0.05	<0.00	<0.00	< 0.05	> 0.05	> 0.05	> 0.05	> 0.05
	Significance	N.S.	N.S	H.S.	H.S.	S	N.S	N.S	N.S	N.S
C(Sublingual Nifedipine)	P. Value	<0.05	<0.05	<0.05	<0.00	<0.00	<0.05	<0.05	>0.05	>0.05
	Significance	S.	S.	S.	H.S.	H.S.	S.	S.	N.S	N.S

s=significant, n.s. = non-significant, h.s. = highly significant

In Group a (Control) the rise in mean pulse rate was statistically highly significant after induction, at laryngoscopy and intubation, 1 & 3 minutes post intubation and was significant at 5 & 10 minutes post intubation. While at other intervals the changes were statistically non-significant.

In Group B (Nitroglycerine Spray) the increase in mean pulse rate was statistically highly significant on laryngoscopy and intubation, at1minute post intubation and was significant at 3 minutes post intubation, while at other intervals the changes were non-significant.

In Group C (sublingual Nifedipine) the rise in means pulse rate was statistically significant as compare to the basal value, after administration, induction, laryngoscopy and intubation which progressed to a highly significant increase at 1& 3 minutes post intubation followed by a significant increase at 5 & 10 minutes post intubation. While at other intervals the changes were statistically non-significant.

Table 3: Mean systolic blood pressure in all group at relevant recording time

Group		B.V.	B.I.	A.I.	L & I	I_1	I_3	I_5	I_{10}	I_{15}	I_{30}
A (Control)	Mean	128.80	128.80	127.30	139.40	165.40	145.00	134.30	130.30	129.10	127.70

	S.D	10.29	10.29	13.30	11.46	16.44	8.17	9.61	8.74	8.32	9.59
B (Nitroglycerine Spray)	Mean	136.50	136.00	126.30	134.30	148.80	138.80	134.90	134.00	134.70	135.20
	S.D	8.58	11.37	9.80	8.95	9.99	10.07	6.03	5.31	7.12	7.77
C (Sublingual Nifedipine)	Mean	127.80	127.40	119.70	129.10	152.20	150.50	126.50	126.10	123.50	128.10
	S.D	11.57	15.19	12.77	31.21	12.86	72.76	12.63	10.90	8.10	11.58

In group A (control) the rise in mean systolic blood pressure was highly significant after laryngoscopy and intubation and at 1min. post intubation and significant at 3 & 5 min. post intubation.
In group B (Nitroglycerine spray) the fall in mean systolic blood pressure after induction and at 1 minute post intubation respectively were both statistically highly significant.
In GROUP C (sublingual Nifedipine) the fall in mean systolic blood pressure after induction was significant while increase at 1 min. post intubation was highly significant.

Table 4: Mean diastolic blood pressure in all groups at relevant recording time

Group		B.V.	B.I.	A.I.	L&I	I_1	I_3	I_5	I_{10}	I_{15}	I_{30}
A (Control)	Mean	77.50	77.50	76.50	81.95	96.40	87.50	81.70	79.40	76.30	75.30
	S.D	6.39	6.39	5.91	9.62	8.62	3.78	6.03	5.73	4.91	4.65
B(Nitroglycerine Spray)	Mean	81.50	83.40	77.70	80.10	90.10	84.80	80.30	79.10	83.60	83.00
	S.D	5.39	5.70	4.99	5.33	5.29	6.07	5.36	4.42	5.13	4.47
C (Sublingual Nifedipine)	Mean	76.60	77.70	70.70	83.60	94.60	84.90	78.50	79.30	77.20	76.80
	S.D	7.82	7.09	17.75	9.08	8.83	9.55	6.89	7.23	6.20	7.38

In group A (control) there was a highly significant increase in the mean diastolic blood pressure at 1 & 3 minutes post intubation and significant increase subsequent to laryngoscopy, intubation and at 5 minutes post intubation.
In group B (Nitroglycerine spray) there was a significant fall in mean diastolic blood pressure after induction and at 3 minutes post intubation respectively, while at 1 minute post intubation the increase was highly significant as compared with the baseline value.
In group C (Sublingual Nifedipine) the rise in mean diastolic blood pressure was statistically significant after laryngoscopy, intubation, at 3 minutes post intubation and was highly significant at 1min. post intubation.

Table 5: Mean of arterial blood pressure in all groups at relevant recording time

Group		B.V.	B.I.	A.I.	L&I	I_1	I_3	I_5	I_{10}	I_{15}	I_{30}
A(Control)	Mean	94.70	94.70	93.50	101.10	119.50	106.60	99.25	96.45	93.95	92.75
	S.D	6.83	6.83	7.19	9.54	10.25	4.03	5.73	5.38	5.16	5.77
B (Nitroglycerine Spray)	Mean	99.80	100.85	93.95	98.30	109.65	102.65	98.45	97.40	100.65	100.45
	S.D	5.28	5.82	5.92	5.69	5.70	5.97	5.18	4.25	4.31	4.77
C(Sublingual Nifedipine)	Mean	93.65	94.15	86.95	98.65	113.75	106.75	94.50	94.75	92.60	93.90
	S.D	8.54	8.89	14.62	14.52	9.65	26.51	7.55	6.73	5.88	8.21

In group A the increase in mean arterial blood pressure from basal was observed which was significant at laryngoscopy, intubation, and 5 min post intubation and highly significant at 1 & 3 min post intubation.
In group B there was a statistically highly significant decrease in mean arterial blood pressure after induction and significant increase at 1 & 3 minute post intubation respectively. Sinus tachycardia was seen in all cases and no other abnormality was seen in ECG throughout the study. In all the cases SPO_2 was 95 % or more throughout the study.
In GROUP C there was a significant decrease in mean arterial blood pressure after induction and a highly significant increase at 1 & 3 min post intubation respectively.

ECG Changes
Sinus tachycardia was seen in all cases and no other abnormality was seen in ECG throughout the study.

SPO_2 Changes
In all the cases SPO_2 was 95 % or more throughout the study.

Complication
No adverse effect of any drug and no complication was observed in the study.

Discussion
The aim of the present study was to compare the hemodynamic effects of nitroglycerine spray and sublingual Nifedipine in healthy normotensive patients during general anesthesia and to study the hemodynamic and electrocardiographic responses to laryngoscopy and tracheal intubation.
In group A (CONTROL GROUP), after induction there was a highly significant increase in PR, a non-significant decrease in the SBP, DBP and MAP.Just after laryngoscopy and intubation there was a highly significant increase in PR, SBP, DBP and MAP. At 1 min post intubation a highly significant increase was observed in all the parameters from the basal value.
At 3 min post intubation there was highly significant increase in PR, DBP, and MAP, though a decrease was seen in the SBP. It was still significantly higher than the basal value. At 5 minutes post intubation a gradual decline was seen in all the parameters with SBP, DBP and MAP reaching the basal value by 10 minutes post intubation and PR by 15 minutes post intubation.
In group B (nitroglycerine spray), after pre-treatment a statistically non-significant changes were observed in all the recorded parameters. After induction a statistically non-significant increase was observed in PR while there was a

highly significant decrease in SBP & MAP and a significant decrease in DBP. Just after laryngoscopy and intubation there was a statistically highly significant increase in PR and a steady rise in the rest of parameters which was statistically non-significant. At 1 minute after laryngoscopy and intubation statistically highly significant changes occurred in all the parameters from the baseline value. At 3 minutes post intubation PR, DBP and MAP remained above the basal value and were statistically significant while SBP increased from the baseline and it was non-significant. At 5 minutes post intubation all the parameters had reached the baseline value and non-significant changes were observed in all the recorded parameters.

In Group C (Sublingual Nifedipine), after pre-treatment with sublingual Nifedipine a statistically significant increase was observed in the PR while the changes in the rest of the parameters from the baseline were non-significant. After induction there was a significant increase in PR while a statistically significant fall was observed in SBP and MAP and a non-significant increase was seen in DBP. Just after laryngoscopy and intubation there was a significant increase in PR, DBP while a non-significant increase in the rest of the parameters. At 1 min post intubation there was a highly significant increase in all the parameters. At 3 minutes post intubation there was still a highly significant increase in the PR and a significant increase in DBP, MAP. At 5 minutes post intubation there was a persistent significant increase in PR while the rest of the parameters had decreased but were still higher than the basal value by a non-significant difference. Thereafter there was a non-significant change from the baseline in the rest of the recording at the remaining intervals.

Conclusion

In the present study the following conclusion are drawn

In control Group maximum increases in parameters occur at 1 min post intubation with values returning to baseline at 10 min post intubation in case of pulse rate and at 5 minutes post intubation in case of systolic, diastolic and mean arterial pressure. Nitroglycerine spray administered intranasal 2 minutes before induction effectively attenuate the hypertensive effect but not the tachycardia response of the cardiovascular system to laryngoscopy and intubation.

Sublingual Nifedipine given 20 minutes before induction effectively attenuate the increases in blood pressure but caused significant tachycardia which was further exaggerated following laryngoscopy and intubation.

The drug studied are helpful in attenuating the hypertensive effect of cardiovascular system to laryngoscopy and intubation but not very effective in attenuating the tachycardia response and it is more with Nifedipine when used in proper dosage and at a proper time.

Conflict of interest: None
Acknowledgement: None

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