COMPARISON OF DIFFERENT DOSES OF NITROGLYCERINE SPRAY FOR ATTENUATION OF STRESS RESPONSE TO LARYNGOSCOPY

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Abstract

Background The study was done to evaluate the efficacy of NTG intranasal spray in attenuation of laryngoscopy and intubation induced hemodynamic responses and to elucidate the optimum dose.

Material and methods Prospective randomized controlled study was conducted in 50 ASA physical status I and II patients of both sexes, aged 20-60 years who were scheduled for elective surgery. patients were divided into 2 groups(n=25), group I received 400µg and group II received 800µg intranasally 2 minutes before laryngoscopy and endotracheal intubation after standard general anaesthesia technique and its effects on heart rate , systolic, diastolic, and mean arterial blood pressure were noted before and after premedication and 1-5 minutes after intubation.

Results Baseline mean heart rate in group I was 97.4 ± 28.91 and 81.80 ± 6.22 in group II . There was highly significant ($P < 0.01$) increase in heart rate as compared to base line values in two groups after laryngoscopy and intubation. There was statistically significant fall in MAP after 30 seconds in Gp I which remained consistently decreased till 5 min post laryngoscopy and intubation. There was 9.97 % increase in mean arterial pressure in group II after laryngoscopy

and intubation compared to baseline value, and decreased to 4.34% of baseline at 3 min after post-laryngoscopy and intubation.

Conclusions NTG spray in dose of 400 µg given 2 min before general anesthesia is effective in attenuating the pressor response to laryngoscopy and intubation in normotensive patients, 800 µg does decrease the mean arterial blood pressure but does not have an extra advantage over 400µg. NTG does not attenuate the rise in HR.

keywords Nitroglycerine intranasal spray; General anesthesia; hemodynamic responses.

INTRODUCTION

The stress response to laryngoscopy and endotracheal intubation activates the sympathetic nervous system, which may increase myocardial oxygen demand by increasing heart rate and arterial blood pressure. Activation of the sympathetic nervous system may also cause coronary artery vasoconstriction reducing the supply of oxygen to the myocardium, which in turn would predispose to myocardial ischaemia. Therefore, attenuation of haemodynamic response to tracheal intubation such as hypertension, tachycardia and arrhythmias is important for an anaesthesiologist.(1-4)

In 1940, Reid and Brace first described a hemodynamic response to laryngoscopy and intubation.(**5)** It leads to an average increase in blood pressure by 40-50% and 20% increase in heart rate (HR).(**6)**

A wide variety of pharmacological agents were used to attenuate the hemodynamic responses to laryngoscopy and endotracheal intubation like lignocaine(**7),** fentanyl(8), alfentanil (9), remifentanil (9) nifedipine(10), beta-blockers(11), Gabapentin (12), magnesium sulfate(13), verapamil, nicardipine and diltiazem (14) with varying results. The non-pharmacological methods like,appropriate premedication, smooth rapid and gentle intubation, blocking the

glossopharyngeal nerve and superior laryngeal nerve have been used to attenuate the cardiovascular responses to tracheal intubation. None of these above mentioned approaches have been proved entirely satisfactory. All of them require time for preparation and administration.(**15)**

Glyceryl trinitrate (nitro-glycerin or NTG) relaxes vascular smooth muscles with venous dilation predominantly over arterial dilation(16), NTG had been administered intranasally (17), or parenterally as a bolus(18) or infusion(19) to attenuate hemodynamic responses during laryngoscopy and intubation but preparation, standardization and stabilization of such solution is not without problem and cost effectiveness has been questioned. (12,20,21)

Intravenous and inhalational anaesthetic agents have no appreciable effects on stress response. Nitroglycerine generates NO (nitric oxide) in vascular smooth muscles which produce vasodilatation leading to decrease in blood pressure. 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.(22-24)

Our aim was to observe the various pressor responses to laryngoscopy and intubation in normotensive patient undergoing elective surgery under general anesthesia and use of two different attenuating doses (400, 800 mcg) of intranasal nitroglycerine administered two minutes before laryngoscopy and intubation, to observe its efficacy and safety .

MATERIAL AND METHODS

After institutional ethical committee approval, a prospective randomized controlled study was conducted in 50 ASA physical status I and II patients of both sexes, aged 20-60 years scheduled for elective surgery under general anesthesia. Study was undertaken to observe

and compare the attenuating effects of two different doses of nitroglycerine spray administered intranasally before laryngoscopy and endotracheal intubation in normotensive patients on heart rate changes, systolic, diastolic, and mean arterial blood pressure changes . Doses of intranasal nitroglycerine used were 400 and 800 µ given two minutes prior to laryngoscopy and intubation and observed till 5 minutes after laryngoscopy and intubation every minute. Patients were watched for any complication like tachycardia, hypotension, arrhythmias, bronchospasm

All the patients under study were subjected to a detailed preanesthetic evaluation to rule out any anatomical or systemic disorders. Informed consent from each patient was taken. History of past, prolonged illness and drug therapy was elicited. Routine and relevant special investigations were carried out. patients with baseline heart rate <60 beats per minute, baseline blood pressure <100/50 mm of Hg, reactive airways disease, history of cardiac disease and hypertensive patient, treatment with adrenergic augmenting or depleting drug, contraindication to use of nitroglycerine and patient requiring two or more attempt for laryngoscopy and intubation were excluded from the study.

Patients were randomly divided into two groups of 25 each. Group I received (1 metered dose) 400 µg and group II received (2metered doses) 800 µg of intranasal nitroglycerine spray two minutes before laryngoscopy and intubation. Anaesthesia technique was standardised for both the groups. On the day of surgery, in the operation theatre intravenous line was secured, pulse oxymeter, NIBP, ECG monitor were applied. Baseline parameters heart rate, systolic BP, diastolic BP were noted before administration of any drugs. Crystalloid fluid was started. All the patients were pre-medicated with inj. glycopyrolate 0.04 mg/kg, inj. ondansetron 0.15 mg/kg, and inj. fentanyl 2 µg /kg intravenously. Nitroglycerine spray was done according to group. Patients were induced with inj. pentothal (6-7 mg/kg) i.v. and inj. suxamethonium (2 mg/kg) i.v. followed by laryngoscopy and intubation. vitals were noted

If intubation took more than 30 s or more than 1 attempt , it was excluded from the study. Anesthesia was maintained on 50% N_2O and 50% O_2 ,1.5% MAC sevoflurane and inj.

vecuronium bromide.

HR, SBP, DBP were recorded at T1: baseline(before premedication), T2: just before intubation, T3: just after intubation, T4:1 min after intubation, T5: 2 min after intubation, T6: 3 min after intubation, T7: 4 min after intubation, T8: 5 min after intubation. at the end of surgery patients were reversed with Inj. Neostigmine 0.05mg/kg and glycopyrolate 0.01mg/kg.

Patients were watched for any complication like tachycardia, hypotension, arrhythmias, bronchospasm.

Data were entered and analyzed .Qualitative or categorical data were presented as number (proportion) and compared using Chi-square test. Quantitative or continuous variables were presented as mean ± standard deviation and compared using Student's *t*-test and analysis of variance. $P < 0.05$ was considered as statistically significant.

Results

Patient's age, weight, sex, ASA grade and type of surgery were statistically comparable in three groups, $P > 0.05$

In our study baseline mean heart rate in group I was 97.4 ± 28.91 and 81.80 ± 6.22 in group II . There was highly significant ($P < 0.01$) increase in heart rate as compared to base line values in two groups after laryngoscopy and intubation. It went to 28.8% increase in Group I and 27.13 % increase in GroupII after one minute post intubation **Table 4**

There was significant hypotension ($P < 0.05$) in both the groups one minute after laryngoscopy and intubation compared to baseline value and consistent hypotension in group I till 5 minutes after intubation and laryngoscopy. **Table 5**

There was significant decrease in diastolic blood pressure in both the group immediately after laryngoscopy and intubation as compared to baseline value, which remained consistently significantly decreased up till 5 min after intubation and laryngoscopy. **Table 6**

There was statistically significant fall in MAP after 30 seconds in Gp I which remained consistently decreased till 5 min post laryngoscopy and intubation There was 9.97 % increase in mean arterial pressure in group II after laryngoscopy and intubation compared to baseline value, and decreased to 4.34% of baseline at 3 min after post-laryngoscopy and intubation. ($P < 0.05$) **Table 7**

Discussion

Nitroglycerine is a commonly used intravenous agent in treatment of hypertension during anaesthesia NTG is having faster onset of action (2-3 minutes), higher peak response, shorter duration of action, no need to prepare and is easy to administer as compared to any other preparation. The half-life of 4-5
minutes gives us a convenient alternative . The idea of using any drug for attenuating the hypertensive
response to tracheal intubation is that its peak effect should correspond to that of the stimulus. A 2-3 minute time gap is needed between administration of NTG spray and tracheal intubation as done in the
present study, as this time interval was found to be satisfactory.(15)
The magnitude of pressor response can be assessed by observing the rise in HR (demand), SBP (afterload), DBP (preload), and MAP. We observed that NTG spray does not attenuate the rise in HR.

The principal advantage of using NTG is that, while a desirable and transient hypotension is achieved, cardiac output is not likely to decrease. Preload reduction and accompanying decrease in ventricular end-diastolic pressure(21) reduces myocardial oxygen demand and increases endocardial perfusion by dilating the coronary vessels, NTG may increase the

coronary blood flow and oxygen delivery to the myocardium. Because of its predominantly venodilatory action, it seems to be the best choice in patients with low cardiac output and moderately elevated resistance. (16)

Myocardial oxygen consumption or demand (as measured by the pressure-rate product, tension-time index, and stroke-work index) is decreased by both the arterial and venous effects of NTG resulting in a more favorable supply-demand ratio. (21)

our findings coincided with study done by Fassoulaki A, Kaniaris P. in 1983 who gave nitroglycerine before induction of anesthesia. In comparison with the control group who received placebo, systolic blood pressure did not increase significantly immediately after intubation ($P > 0.005$); while the heart rate increased significantly in both groups ($P < 0.001$). According to the results of this study, nitroglycerine had an effective influence on post intubation blood pressure diminution, with no effect on heart rate (18)

Previous studies (14,21 25 -27) have also documented that NTG does not attenuate the rise in HR after intubation which can be attributed to reflex tachycardia produced by vasodilation which correlated with our study where HR increases significantly in both the groups post laryngoscopy and intubation .

Other studies have reported effective attenuation of pressor response by NTG used intravenously as bolus injection,([14,19,20,28)] and IV infusion.(29 30) .We have documented a blunting of pressor response by the intra nasal spray of NTG in doses of 400 and 800 µg. There was a trend toward fall in mean arterial blood pressure in group I from 4.98 % to 17 .20 % at 5 min and the fall in the mean arterial blood pressure started decreasing 2 min post laryngoscopy intubationie. 0.43 % to 8.11 % at 5 min which was clinically significant.

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Conclusions

We conclude that NTG spray in dose of 400 µg given 2 min before general anesthesia is effective in attenuating the pressor response to laryngoscopy and intubation in normotensive ASA I-II patients where 800 µg does decrease the mean arterial blood pressure but does not have an extra advantage over 400µg. NTG does not attenuate the rise in HR.

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Tables

Table 1 : Age distribution (yrs)				
	Group 1 (no of patients)	%	Group II (no of patients)	%
15-24	6	24	10	40
25-34	6	24	7	28
35-44	4	16	3	12
45-54	5	20	4	16
55-64	4	16	1	4
Total	25		25	

Table 2 : Sex Distribution (no of patients)				
	Group I		Group II	
	no of patients	%	no of patients	%
Male	13	52	12	48
Female	12	48	13	52

Table 3 : weight distribution (kgs)				
	Group I		Group II	
	No of patients	%	No of patients	%
40-49	6	24	13	52
50-59	6	24	8	32
60-69	8	32	4	16
70-79	5	20	1	4

Table 4 : Heart Rate changes Mean ± SD					
	Group I		Group II		P value
		%		%	

		Increase /decrease from base line (increase ÷original × 100)		Increase / decrease from base line(increase ÷original × 100)	
Before premedication	97.4 ± 28.91	Baseline	81.80 ± 6.22	baseline	<0.05
After premedication	107.1 ± 27.74	9.95	88.5 ± 6.83	8.19	<0.01
After intubation					
30 seconds	125.09 ± 22.33	28.4	102.50 ±9.25	25.30	<0.01
1 min	125.47 ± 20.95	28.8	104 ± 9.5	27.13	<0.02
2 min	124.66 ± 19.06	27.98	102.55 ± 8.22	25.36	<0.03
3 min	122.14 ± 18.18	25.40	98.7 ± 7.13	20.66	<0.04
4 min	115 ± 17.02	18.06	96.50 ± 6.99	17.97	<0.05
5 min	113.28 ± 16.28	16.30	95.15 ± 5.10	16.32	<0.06

Table 5: Systolic blood pressure changes Mean ± SD					
	Group I		Group II		P value
		% Increase /decrease from base line (increase ÷original × 100)		% Increase /decrease from base line (increase ÷original × 100)	
Before premedication	135.71 ± 16.22	baseline	120.7 ± 7.40	baseline	<0.01
After premedication	127 ± 15.24	-6.41	123 ± 7.87	1.90	0.29
After intubation					
30 seconds	133.57 ± 21.93	-1.57	131.15 ± 7.11	8.65	0.64
1 min	121.23 ± 24.94	-10.66	132.8 ± 7.46	10.02	0.06
2 min	110.90 ± 24.13	-18.28	126.20 ± 7.57	4.55	<0.05
3 min	112 ± 18.90	-17.47	122.55 ±7.27	1.5	<0.05
4 min	111.71 ± 20.95	-17.68	118.70 ± 6.46	-1.65	0.15
5 min	113.33 ± 18.07	--16.49	114.95 ± 5.52	-4.7	0.6

Table 6: Diastolic blood pressure changes Mean ± SD					
	Group I		Group II		P value
		% Increase /decrease from base line (increase ÷original × 100)		% Increase /decrease from base line (increase ÷original × 100)	
Before premedication	86.57 ± 9.13		76.80 ±3.96		<0.01
After premedication	83.23 ± 12.01	-3.8	77.40 ± 3.43	0.7	<0.05
After intubation					
30 seconds	85.19 ±17.16	-1.5	85.25 ± 4.63	11.00	0.99
1 min	74.61 ± 18.78	-13.81	84.75 ± 4.29	10.35	<0.05
2 min	69.57 ±19.45	-19.63	79.70 ± 4.91	3.77	<0.05
3 min	68.52 ± 16.47	-20.85	76.5 ± 5.35	-0.39	<0.05
4 min	68.19 ± 16.24	-21.23	71.85 ± 4.31	-6.44	0.4
5 min	71.2 ± 18.27	-17.75	68.55 ± 4.16	-10.74	0.4

Table 7: mean arterial blood pressure changes Mean ± SD					
	Group I		Group II		P value
		% Increase /decrease from base line (increase ÷original × 100)		% Increase /decrease from base line (increase ÷original × 100)	
Before premedication	102.95±11.49	Base line	91.43 ±5.10	Base line	<0.01
After premedication	97.82± 13.08	-4.98	92.6 ±4.91	1.27	<0.05
After intubation					
30 seconds	101.31±18.75	- 1.59	100.55 ±5.45	9.97	.87
1 min	90.15±20.83	- 12.43	100.76 ±5.34	10.20	<0.05
2 min	83.34±21.01	- 19.04	95.2	4.12	<0.05

			±5.79		
3 min	83.01±17.28	- 19.36	91.83 ±5.99	0.43	<0.05
4 min	82.69±17.81	- 19.67	87.46 ±5.02	- 4.34	.31
5 min	85.24±18.20	- 17.20	84.01 ±4.61	-8.11	.46

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