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A Study of Pressor Response to Laryngoscopy and Intubation and Its Attenuation by Nitroglycerine

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Abstract
This study evaluated 100 adult patients of either sex belonging to ASA grade 1; aged 20 to 40 years were randomly allocated into 4 groups of 25 each. Group 1- acted as control group (not receiving any pretreatment), group 2- Nitroglycerine intranasal group, group 3- Nitroglycerine topical group, group 4- Nitroglycerine intravenous group. All the patients were prepared by 12 hour preoperative fasting and overnight sedation with 10 mg diazepam orally at bedtime. Patients received 10/c mg diazepam 2 hours before surgery. After checking the patient's blood pressure, heart rate and ECG, at basal stage, pretreatment was started. Group 2 was pretreated with 2 ml solution 2mg nitroglycerine tablet dissolved in 2ml of distilled water (1 ml in each nostril) 3 minutes before induction of anesthesia. Group 3 was pretreated with 30 mg of 2% nitroglycerine ointment applied by spreading and rubbing on an area of 10 to 15 cm over the forehead using a specially designed dose measuring applicator 20 minutes prior to induction of anesthesia. Group 4 was pretreated with slow intravenous nitroglycerine at the rate of 200mg per minute to be given till the systolic arterial blood pressure fell down by 20-30%. Patients were again checked for heart rate, blood pressure and ECG. This stage of recording was termed pre-induction stage. Patients belonging to all the groups were anaesthetized by routine conventional methods i.e. 3 minutes pre-oxygenation was followed by induction by 4 to 5 mg per kg body weight of sodium thiopentone intravenously followed by suxamethonium 1 to 1.5 mg per kg body weight intravenously. Without any undue delay endotracheal intubation was performed and the drug in Group 3 was immediately removed with a gauze piece. Patients were again checked for heart rate, blood pressure and ECG. This stage of recording was termed intubation stage. For the next 15 minutes these recordings were again taken after every 5 minutes. Anaesthesia was maintained on nitrous oxide, oxygen, 0.5% isoflurane and a long acting muscle relaxant. All the four groups showed highly significant increase in heart rate during laryngoscopy and intubation as compared to basal stage. Hence nitroglycerine had no role in bringing down increased heart rate during intubation. Except for control group no group showed significant rise in systolic and diastolic blood pressure. This suggests that nitroglycerine via various routes safely and effectively attenuates hypertensive response secondary to laryngoscopy and tracheal intubation. ECG changes were observed in all the four groups, most significant being sinus tachycardia. Thus nitroglycerine does not alter cardiac rhythm occurring in response to laryngoscopy and tracheal intubation. It is thus concluded that nitroglycerine can be recommended in patients of cerebral and cardiovascular diseases, where major complications occurring as a result of significant hemodynamics changes are apprehended.

Keywords: Laryngoscopy, endotracheal intubation, nitroglycerine, pressor response

Introduction
Laryngoscopy and tracheal intubation are potent stimuli that increase heart rate and blood pressure (pressor response) as has been recognised since 1951 (King and Harris, 1951) [10]. These are produced due to sympathetic reflex provoked by stimulation of epipharynx and laryngapharynx (Tomori and Widdicombe, 1969) [17]. Reid and Brace (1940) [14] first described the effect of endotracheal intubation on electrocardiograph which were of the nature of premature ventricular beat, nodal rhythm, sinus bradycardia, etc (Burstein, *et al*, 1950 a) [2]. The sensitive receptor area of epiglottis when mechanically stimulated by instrumentation evokes reflex response (Reid and Brace, 1940; King, *et al*, 1951; Brustein, *et al*, 1950 and Takeshime, *et al*, 1964) [14, 10, 2, 16]. Measurements of the plasma catecholamine have demonstrated an increase in noradrenaline following laryngoscopy and thus confirmed sympathetic mediation to this response. The increase in blood pressure is usually transitory, variable and unpredictable (Forbee and Dally, 1970) [6]. These changes are at their peak, 30 to 45 seconds

after laryngoscopy (Stoelting, 1977) [15]. Complications of the pressor response following laryngoscopy and tracheal intubation include left ventricular failure (Masson, 1964) [11], myocardial ischaemia, increase in intracranial pressure, intracranial haemorrhage and convulsions may be precipitated in pe-clamptic patients. These complications may be serious in hypertensive patients due to exaggerated response to laryngoscopy in them (Prys-Roberts, *et al*, 1971) [13]. Numerous techniques have been employed to modify the pressor response with varying success, for example, procaine chloride had been used to bring down the incidence of cardiac arrhythmias, diethylaminoethanol had been shown to reduce the occurrence of ECG abnormalities successfully, regional and topical analgesia have been used to block different impulses, intravenous lidocaine and deeper inhalational anaesthesia have been used to modify response at central nervous system level. Trimethaphan and phentolamine have been used for their peripheral effect. Other methods advocated are beta-adrenaline receptor blocker, intravenous nitroprusside, beta-receptor blockade and administration of droperidol and calcium blocker. None of these pharmacological approaches completely block the reflex and the method itself carries additional risks. Dich-Nielsen, J, *et al*, (1986) [4] showed that 2 mg of nitroglycerine intranasally, effectively controls the pressor response to laryngoscopy and intubation. Similarly Hood, *et al* (1985) has demonstrated nitroglycerine to attenuate the pressor response and Kamra, *et al*, (1986) [8] used topically 2% nitroglycerine for the same purpose. Similarly Fassoulaki and Kaniaris, (1983) [5] has demonstrated attenuation of pressor response to nitroglycerine intranasally. Nitroglycerine is well absorbed orally, sublingually, intranasally and via transdermal routes. When given intravenously it is predominantly venodilator. Kaplan, *et al*, (1976) [9] demonstrated that it reduces cardiac preload and afterload. It produces significant decrease in systolic, diastolic and mean arterial pressure, central venous pressure, left ventricular stroke work index, pulmonary capillary wedge pressure and systemic vascular resistance when used as infusion in 20 acutely hypertensive patients undergoing coronary artery surgery. The indices of myocardial oxygen demand were significantly reduced. Cohen, *et al*, (1973) [3] has shown that nitroglycerine has direct action on coronary vasculature and dilates coronary collaterals. Glyceral trinitrate is administered through oral, sublingual, intranasal, transdermal and intravenous route. The basic 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. The action of topically applied 2% nitroglycerine starts within 20 minutes and reached peak between 60-90 minutes, while intranasally its peak blood concentration are reached at 2 minutes and decrease rapidly within 15 minutes when given intravenously, its effect are seen within seconds and it has a plasma half-life of around 4 minutes.

Aim of the Study: The present series was undertaken to-
"Evaluate the efficacy of glycerol triturate in attenuating the pressor response secondary to laryngoscopy and tracheal intubation through various route viz. intranasally, Trans dermally and intravenously".

Material and Method
This study evaluated 100 adult patients of either sex belonging to ASA grade 1; aged 20 to 40 years, undergoing elective surgery needing endotracheal anaesthesia, were randomly allocated into 4 groups of 25 each.

Exclusion criteria
- Respiratory disorder
- Cardiovascular disorders
- Neurological disorders
- Marked anemia
- Bronchial asthma,
- Hypertension
- Increased intracranial pressure
- Increased intraocular tension
- Those who were sensitive to nitrate drugs were excluded from this study.

Drug used was nitroglycerine in the form of
1. Tablet, each tablet containing 0.5 mg of nitroglycerine.
2. Nitroglycerine. ointment of 2% concentration, giving 30 mg of nitroglycerine when applied on 2 inches of a specially designed dose measuring applicator provided with the tube (1"= 15 mg of nitroglycerine)
3. Injectable nitroglycerine contained in ampules, each ampule containing 10ml of the drug (1 ml + 1 mg of nitroglycerine).

Pre-anaesthetic preparation: Thorough pre- anaesthetic check-up including a detailed history, a thorough physical and systemic examination was conducted a day before the surgery. Special attention was given to any history relating to cardiovascular, respiratory and neurological disorders. All patients were normotensive and had a normal ECG, haemoglobin, BT, CT, urine examination, X-ray chest, blood sugar, and blood urea and serum creatinine.
The anaesthetic procedure was explained to the patient and informed consent was obtained from all the patients.

Pre-anaesthetic medication: All the patients were prepared by 12 hour preoperative fasting and overnight sedation with 10 mg diazepam orally at bedtime. Patients received 10 mg diazepam 2 hours before surgery. No atropine, glycopyrrolate or hyoscine was given to the patients. The patients were divided into four groups of 25 patients each as under:
- **Group 1- Acted as control group:** This group did not receive any pretreatment.
- **Group 2- Nitroglycerine intranasal group:** This group was pretreated with 2 ml solution 2mg nitroglycerine tablet dissolved in 2ml of distilled water (1 ml in each nostril using a syringe and 16 gauge medicate cannula) 3 minutes before induction of anesthesia.
- **Group 3- Nitroglycerine topical group:** This group was pretreated with 30 mg of 2% nitroglycerine ointment applied by spreading and rubbing on an area of 10 to 15 cm over the forehead using a specially designed dose measuring applicator provided with nitroglycerine ointment tube(1"= 15 mg of nitroglycerine) 20 minutes prior to induction of anesthesia.
- **Group 4- Nitroglycerine intravenous group:** This group was pretreated with slow intravenous nitroglycerine at the rate of 200mg per minute to be given till the systolic arterial blood pressure fell down by 20-30%.
- **Anaesthetic procedure:** On arrival of the patient of each group in the operation theatre, the blood pressure, ECG and heart rate were recorded after a resting period

of 3 minutes. This stage of recording was called the basal stage. After checking the basal recordings, pretreatment was started as designed for the four different groups. The anaesthetic procedure was started 3 minutes after pre-treatment in group 2, 20 minutes after pretreatment in group 3, and almost immediately in group 4.After pretreatment, patients were again checked for heart rate, blood pressure and ECG. This stage of recording was termed as pre-induction stage.

Induction of anaesthesia: Patients belonging to all the groups were anaesthetized by routine conventional method which is as under: 3 minutes of pre-oxygenation was followed by induction by 4 to 5 mg per kg body weight of sodium thiopentone intravenously followed by suxamethonium 1 to 1.5 mg per kg body weight intravenously to facilitate tracheal intubation. An appropriate size cuffed endotracheal tube was put using Macintosh laryngoscope. Without any undue delay endotracheal intubation was performed and patients with delayed intubation were discarded from the study. The drug in Group 3 was immediately removed with a gauze piece. During laryngoscopy and intubation, patients were again checked for heart rate, blood pressure and ECG. This stage of recording was termed intubation stage. For the next 15 minutes these recordings were again taken after every 5 minutes. Anaesthesia was maintained on nitrous oxide, oxygen, 0.5% isoflurane and a long acting muscle relaxant (atracurium besylate). Patients were put on intermittent positive pressure ventilation using semi-closed circuit with carbon dioxide absorber. Patients were observed for any skin rash or hypotension during intra operative period. 12 hour post-operative observation was done and the occurrence of nasal congestion, palpitation, hypotension, dizziness and nausea were recorded. The relative findings thus obtained were subjected to statistical evaluation at the end of the study.

- **Observations**

S.No.			Group 1	Group 2	Group 3	Group 4
1	Age		29.32 +/- 8.09	32.76 +/- 8.23	30.20 +/- 9.16	32.12 +/- 7.18
2	SEX	Male	68%	52%	56%	48%
		Female	32%	48%	44%	52%
3	Weight		50.80 +/- 8.80	54.16 +/- 9.15	54.72 +/- 10.56	52.84 +/-- 8.37

- **Changes in heart rate (beats per minute)**

S.No.	Stage		Group 1 Mean +/- S.D.		Group 2 Mean +/- S.D.		Group 3 Mean +/- S.D.		Group 4 Mean +/- S.D.	
1. a	**Basal**		82.12 +/- 4.80		81.76 +/- 3.90		82.68 +/- 4.78		82.08 +/- 4.30	
B	**T**	**p**	-	-	-	-	-	-	-	-
C	**Remarks**		-		-		-		-	
2. a	**During intubation**		116.80 +/- 11.39		115.56 +/-5.83		116.00 +/- 5.48		119.04 +/- 6.41	
B	T	P	14.16	<.001	2.44	<.02	0.28	>.20	24.16	<.001
C	Remarks		Highly significant		Significant		Not significant		Highly significant	
D	Variation percent	Increase	42.23		41.34		40.30		45.03	
		Fall	-		-		-		-	
3. a	5 minutes after intubation		104.00 +/- 7.26		102.92 +/- 5.37		103.60 +/- 3.87		104.32 +/- 6.10	
B	t	p	12.72	<.001	24.32	<.001	23.14	<.001	15.03	<.001
C	Remarks		Highly significant		Highly significant		Highly significant		Highly significant	
D	Variation percent	Increase	26.64		25.88		25.30		27.10	
		Fall	-		-		-		-	
4. a	10 minutes after intubation		84.17 +/- 3.21		93.12 +/- 3.84		89.20 +/- 3.38		91.68 +/- 8.32	
B	t	p	1.80	>.05	16.15	<.001	17.15	<.001	5.03	<.001
C	Remarks		Not significant		Highly significant		Highly significant		Highly significant	
D	Variation percent	Increase	2.50		13.89		7.89		11.70	
		Fall	-		-		-		-	
5. a	15 minutes after intubation		81.84 +/- 2.82		80.72 +/- 2.15		84.00 +/- 4.12		85.84 +/- 7.59	
B	t	p	0.25	>.20	1.18	>.20	1.06	>.20	2.17	<.05
C	Remarks		Not significant		Not significant		Not significant		significant	
D	Variation percent	Increase	-		-		1.60		4.58	
		Fall	0.34		1.27		-		-	

- **Changes in systolic pressure (mm Hg)**

S.No.	Stage		Group 1 Mean +/- S.D.		Group 2 Mean +/- S.D.		Group 3 Mean +/- S.D.		Group 4 Mean +/- S.D.	
1. a	Basal		119.52 +/- 5.98		121.20 +/- 7.81		123.60 +/- 9.95		120.00 +/- 8.16	
B	t	P	-	-	-	-	-	-	-	-
C	Remarks		-		-		-		-	
2. a	During intubation		155 +/- 18.58		124.68 +/- 7.18		128.04 +/- 8.26		124.96 +/- 9.91	
B	t	P	9.41	<.001	1.66	>.10	1.73	>.05	1.95	>.05
C	Remarks		Highly significant		Not significant		Not significant		Not significant	
D	Variation percent	Increase	30.39		2.87		3.59		4.13	
		Fall	-		-		-		-	
3. a	5 minutes after intubation		13.081 +/- 9.78		121.52 +/- 6.84		124.32 +/-10.19		120.00 +/- 8.16	

B	t	P	5.09	<.001	0.16	>.20	0.26	>.20	0.27	>..20		
C	Remarks		Highly significant		Not significant		Not significant		Not significant			
D	Variation percent	Increase	9.67		0.26		0.58		0.63			
		Fall	-		-		-		-			
4. a	10 minutes after intubation		120.40 +/- 6.34		115.84 +/-7.23		123.36 +/- 9.52		116.72 +/- 11.73			
B	t	P	0.51	>.20	2.54	<.02	0.09	>.20	1.16	>.20		
C	Remarks		Not significant		Not significant		Not significant		Not significant			
D	Variation percent	Increase	0.74		-		-		-			
		Fall	-		4.42		0.19		2.73			
5. a	15 minutes after intubation		119.12 +/- 6.00		115.56 +/- 8.32		122.80 +/- 9.73		114.00 +/- 14.72			
B	t	P	0.24	>.24	2.52	<.02	0.29	>.20	1.80	>.05		
C	Remarks		Not significant		Significant		Not significant		Not significant			
D	Variation percent	Increase	-		-		-		-			
		Fall	0.33		4.65		0.65		5.00			

- **Changes in diastolic pressure (mm Hg)**

S. No.	Stage		Group 1 Mean +/- S.D.		Group 2 Mean +/- S.D.		Group 3 Mean +/- S.D.		Group 4 Mean +/- S.D.	
1. a	Basal		80.32 +/- 4.23		82.80 +/- 7.37		81.92 +/- 8.51		81.68 +/- 8.44	
b	t	P	-	-	-	-	-	-	-	-
c	Remarks		-		-		-		-	
2. a	During intubation		100.48 +/- 8.03		84.80 +/- 6.11		86.00 +/- 7.07		85.48 +/- 8.03	
b	t	p	11.20	<.001	1.05	>.20	1.86	>.05	1.65	>.10
c	Remarks		Highly significant		Not significant		Not significant		Not significant	
d	Variation percent	Increase	25.10		2.42		4.98		4.65	
		Fall	-		-		-		-	
3. a	5 minutes after intubation		88.80 +/- 5.57		80.64 +/- 5.31		82.80 +/- 8.41		79.76 +/- 8.45	
b	t	p	6.14	<.001	1.20	>.20	0.37	>.20	0.81	>.20
c	Remarks		Highly significant		Not significant		Not significant		Not significant	
d	Variation percent	Increase	10.56		-		1.07		-	
		Fall	-		2.61		-		2.35	
4. a	10 minutes after intubation		82.00 +/- 3.61		80.64 +/- 2.22		82.40 +/- 8.79		77.28 +/- 9.78	
b	t	p	1.53	>.10	1.42	>.10	0.20	>.20	1.72	>.05
c	Remarks		Highly significant		Not significant		Not significant		No significant	
d	Variation percent	Increase	2.09		-		0.58		-	
		Fall	-		2.61		-		5.39	
5. a	15 minutes after intubation		79.60 +/- 4..28		76.80 +/- 7.12		81.92 +/- 8.88		77.60 +/- 9.26	
b	t	p	0.61	>.20	2.96	<.01	No variation in averages		1.65	>.20
c	Remarks		Highly Significant		Significant				Not significant	
d	Variation percent	Increase	-		-		-		-	
		Fall	0.90		7.25		-		5.00	

Discussion

The hemodynamics changes occurring as a result of laryngoscopy and tracheal intubation stand out to be the matter of concern. In the present series efficacy of nitroglycerine in attenuating the pressor response as a result of laryngoscopy and tracheal intubation has been evaluated. Following parameters were observed:

- Heart rate
- Systolic blood pressure
- Diastolic blood pressure
- Electrocardiographic changes

These observations were recorded at basal level, pre intubation level, during intubation and every 5 minute after intubation up to 15 minutes.

Heart rate: In the present series the heart rate was found to be increased to almost an equal extent in control as well as the three study groups because of mechanical stimulation by laryngoscopy and intubation. In study groups heart rate remained increased for longer period than in control group. The tachycardia observed in all these studies maybe due to the fact that in patients with normal left ventricular end diastolic pressure, a decrease in blood pressure following glycerol triturate results in reflex tachycardia (Awan, *et al*, 1978) [1].

Systolic blood pressure: In control group the systolic arterial blood pressure increased during intubation and fifth minute after intubation. This observation is in agreement with the observation of King, *et al* (1951) [10], Wycof (1960) [18] and Prys-Roberts, *et al* (1971) [13]. In all the other groups a significant fall in arterial pressure following intubation as compared to basal level was noticed and is in agreement with the studies of Hood, *et al* (1985), Dich- Neilsen, J. *et al* (1986) [4], Mulay, *et al* (1988) [12].

Diastolic blood pressure: In control group there was a highly significant rise in diastolic arterial pressure during intubation which continued upto fifth minute after intubation. At tenth and fifteenth minute the variation were of insignificant nature. In other three groups there was insignificant rise in diastolic pressure which is in conformity with studies of Awan, *et al* (1978) [1].

The insignificant rise systemic blood pressure during intubation in nitroglycerine pretreated patients was because of the pharmacological effect of the drug, which by virtue of

its hypotensive property buffered the hypertensive response. The nitroglycerine has direct vasodilator effect, resulting in pooling of blood volume in the capacitance system and decreased venous return to the heart, leading to a fall in left ventricular filling of preload and therefore a fall in cardiac output. A fall in cardiac output without a compensatory increase in resistance results in decrease in systemic blood pressure. This phenomenon plus the mild arteriolar dilatory effect of the drug can result in further fall in systemic blood pressure (Awan, *et al*, 1978) [1]. The lower peak blood pressure lessens the risk of significant hypertensive morbidity following laryngoscopy and tracheal intubation (Hood, *et al*, 1988).

Electrocardiography: In the present series electrocardiography changes were seen in the form of sinus tachycardia and/or premature ventricular contractions, no other electrocardiographic abnormality was observed. Our observation is in conformity with the observations made by Burstein, *et al* (1950) [2] and Nicholas, *et al* (1961).Hypoxia, insufficient depth of anaesthesia, prolonged laryngoscopy with numerous attempts at intubation, respiratory obstruction before intubation and tracheal irritation after intubation (Burstein, *et al*, 1951 and Nicholas, *et al*, 1951) and pressure by the laryngoscopic blade on deep soft tissue adjacent to the epiglottis (Takeshima, *et al*, 1964) [16] were found to be important contributory factors in the development of these reflex genic electrocardiographic disturbances.

Conclusion

From this study the following conclusions were drawn:

- Nitroglycerine had no role in bringing down increased heart rate during intubation.
- Nitroglycerine as a pretreatment through various routes safely and effectively attenuates hypertensive response secondary to laryngoscopy and tracheal intubation.
- Nitroglycerine does not alter cardiac rhythm occurring in response to laryngoscopy and tracheal intubation.

It is thus concluded that nitroglycerine can be recommended in patients of cerebral and cardiovascular diseases, where major complications occurring as a result of significant Haemodynamic changes are apprehended.

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