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Comparative Study between Oral Nitroglycerine Spray and Intravenous Esmolol for Pressor Attenuation during Laryngoscopy and Intubation in Patients Undergoing General Anaesthesia

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Abstract

During laryngoscopy and endotracheal intubation haemodynamic changes like hypertension and tachycardia are observed due to the sympathetic stimulation. These changes are usually well tolerated by healthy individuals, but these may be fatal in patients with hypertension, coronary artery disease or intracranial aneurysm etc. Aim of this study was to compare the effects of Nitroglycerine Oral Spray and intravenous Esmolol on hemodynamic response following laryngoscopy and tracheal intubation in patients posted for elective surgical procedure under general anaesthesia and to study their safety and side effects if any. Total 100 patients were taken in the study and were randomly divided into two groups, 50 patients in each group. Group N(receiving NTG oral spray 2 puffs i.e. 800 micro gms) and Group E (receiving intravenous Esmolol 0.5 mg/kg)

Our study concludes that intravenous ESMOLOL in dose of 0.5 mg/kg is better drug for attenuating pressor response following laryngoscopy and intubation as compared to Nitroglycerine (NTG) oral spray.

Keywords: Intubation Response, Hypertension, I.V. Esmolol, Nitroglycerine Oral Spray

Introduction

Laryngoscopy and tracheal intubation cause sympathetic system stimulation leading to hypertension and tachycardia. This sympathetic stimulation leads to increase in plasma catecholamine concentration which is responsible for these effects. It leads to an average increase in blood pressure by 40-50%[1] and heart rate (HR) by 15-20%[2] from the baseline. These changes are usually well tolerated by healthy individuals, but these may be fatal in patients with hypertension, cardiac disease or intracranial aneurysm and may result in potentially deleterious effects like left ventricular failure, arrhythmias, myocardial infarction, cerebral haemorrhage and rupture of cerebral aneurysm.[3]

Intravenous anaesthetic induction agents alone do not adequately suppress the circulatory responses evoked by endotracheal intubation. Therefore prior to initiating laryngoscopy and endotracheal intubation additional pharmacological measures should be taken to avoid these responses. The present study was conducted to study the efficacy of oral Nitroglycerine spray and intravenous Esmolol in attenuating these responses.

Materials and methods

After institutional ethical committee approval, a prospective, randomized trial was done in Dept. of Anaesthesia on total 100 patients, ASA grade I and II, between 18 – 60 yrs of age, having weight between 40 - 90 kgs of either sex, admitted in Santokba Durlabhji Memorial Hospital Cum Medical Research Institute (Jaipur),scheduled for elective surgery under general anaesthesia to compare the efficacy of NTG oral spray and intravenous Esmolol on haemodynamic response to tracheal intubation. Patients suffering from uncontrolled hypertension, other cardiovascular diseases, severe obesity (body mass index >35 kg/m^2) were not included in the study.

Allocation of Groups

100 patients were taken in study and were randomly divided into two group –

1) Group N– 50 patients receiving NTG oral spray (2 puffs i.e. 800 micro gms)
2) Group-E – 50 patients receiving intravenous Esmolol 0.5 mg/kg

Anaesthetic Technique

All patients in this study were induced by standard general anaesthesia technique followed by endotracheal intubation. On the night before surgery tablet Alprazolam 0.25 mg, tablet Pantoprazole 40 mg were given to the patient. On arrival in operation room all standard monitors were attached and patient's Heart Rate, Systolic Blood Pressure, Diastolic Blood Pressure, Mean Arterial Pressure and peripheral oxygen saturation(SpO2) were recorded as baseline data.

Just after induction either Nitroglycerine (NTG) oral spray was sprayed as two metered sprays (800 mcg) in **group N** or intravenous Esmolol 0.5mg/kg in **group E**. Laryngoscopy was attempted 1 min. after induction of anaesthesia and NTG oral spray or i.v. esmolol. If laryngoscopy time exceeded 30 seconds or multiple attempts were required for intubation, patient was excluded from study. After confirmation of endotracheal tube position, anaesthesia was maintained using 50% nitrous oxide (N_20) and 50% Oxygen (O_2), isoflurane (1 MAC) and intermittent doses of atracurium .Heart rate was monitored continuously and Blood pressure(systolic blood pressure, diastolic blood pressure and mean arterial pressure were done) was recorded at predefined time intervals as per study protocol.

Haemodynamic parameters were recorded up to 10 min. after intubation which was sufficient to assess pressor response. No surgical intervention was allowed till this time, thereafter surgery was allowed to commence.

Data Recording

HR, SBP, DBP and MAP was recorded at—

T1 : Baseline (before premedication),
T2 : Just after premedication,
T3 : After injecting Propofol and succinylcholine, just before NTG spray or i.v. esmolol
T4 : 1 min. after NTG spray or i.v. esmolol, just before intubation
T5 : Just after intubation,
T6 : 1 min after intubation,
T7 : 2 min after intubation,
T8 : 5 min after intubation,
T9 : 10 min after intubation.

Any increase or decrease in haemodynamic parameter was calculated as compared to baseline value (T1). During the study period of 10 min, the occurrence of hypotension (fall in SBP >20% from baseline), hypertension (rise in SBP >20% from baseline), bradycardia (fall in HR >20% from baseline), tachycardia (rise in HR >20% of baseline),

arrhythmias, and ST-T changes was noted and treated. Inj. mephentermine 3 mg was given when SBP <90 mmHg. Inj.Atropine 0.6 mg was given if heart rate falls below 50 beats/min.

The data were analysed for inference using MS- Excel, Medcalc 16.4 software and SPSS – 18.0 trial versions. Two sample independent t test and ANOVA were used for comparison. The Tuckey's post hoc analysis was used for group testing in ANOVA. The differences in means were tested on 5% significance level. The P values <0.05 were considered as significant.

Results and Discussion

The two groups were comparable with respect to age, weight and gender.

Weight

Table 1

Comparison of weight								
	Medicine	**N**	**Mean**	**SD**	**Std. Error Mean**	**t**	**df**	**P value**
Weight	ESMOLOL	50	65.10	4.311	.610	-0.598	98	0.551
	NTG	50	65.62	4.389	.621			

Inference— it is observed that there is no significant difference in weight of patients in both the groups.

Comparison of Hemodynamic Parameters

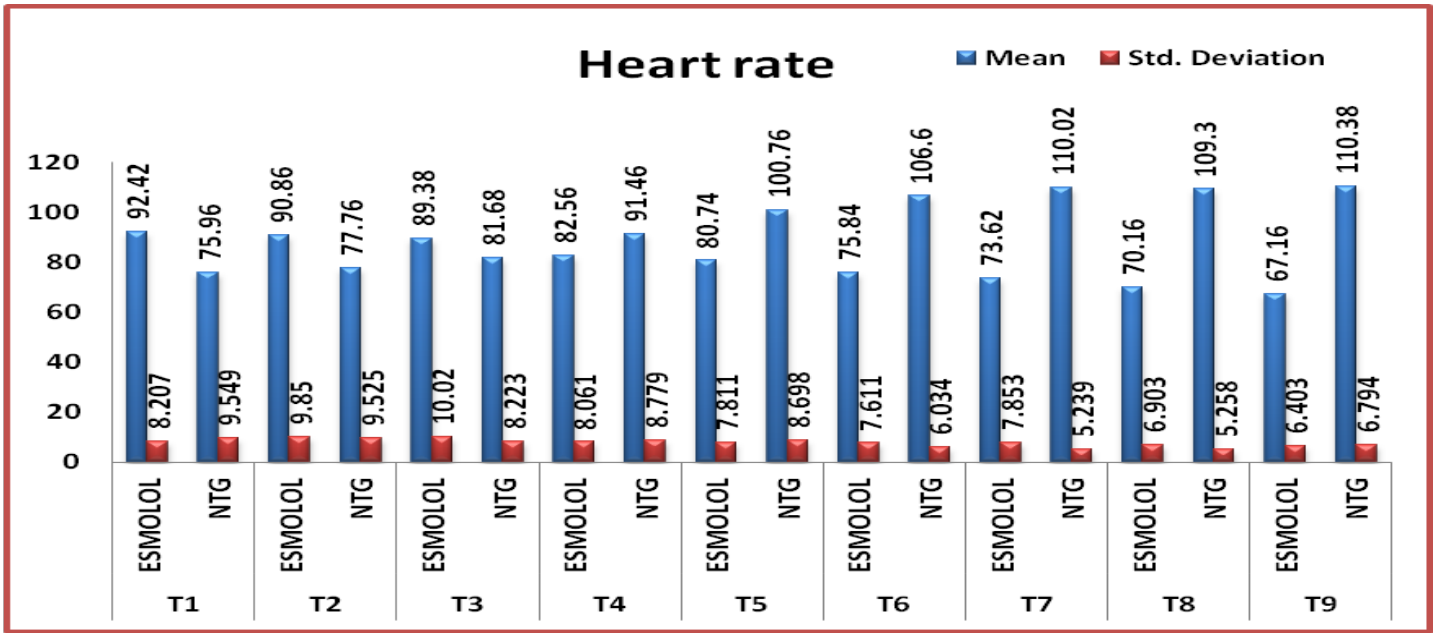
Comparison between Both The Drugs-

Table 2 Heart Rate

Comparison of Heart Rate in the both groups								
Phase	**Medicine**	**N**	**Mean**	**Std. Deviation**	**Std. Error Mean**	**t**	**df**	**P value**
T1_HEART RATE	ESMOLOL	50	92.42	8.207	1.161	9.244	98	.000
	NTG	50	75.96	9.549	1.350			
T2_HEART RATE	ESMOLOL	50	90.86	9.850	1.393	6.761	98	.000
	NTG	50	77.76	9.525	1.347			
T3_HEART RATE	ESMOLOL	50	89.38	10.020	1.417	4.201	98	.000
	NTG	50	81.68	8.223	1.163			
T4_HEART RATE	ESMOLOL	50	82.56	8.061	1.140	-5.280	98	.000
	NTG	50	91.46	8.779	1.242			
T5_HEART RATE	ESMOLOL	50	80.74	7.811	1.105	-12.109	98	.000
	NTG	50	100.76	8.698	1.230			
T6_HEART RATE	ESMOLOL	50	75.84	7.611	1.076	-22.393	98	.000
	NTG	50	106.60	6.034	.853			

T7_HEART RATE	ESMOLOL	50	73.62	7.853	1.111	-27.265	98	.000
	NTG	50	110.02	5.239	.741			
T8_HEART RATE	ESMOLOL	50	70.16	6.903	.976	-31.896	98	.000
	NTG	50	109.30	5.258	.744			
T9_HEART RATE	ESMOLOL	50	67.16	6.403	.905	-32.736	98	.000
	NTG	50	110.38	6.794	.961			

As observed from above table difference in means of Heart rate was found significant statistically (P>0.05) at all the Phases from T1 to T9 and it was found higher in Esmolol subjects at T1, T2 and T3 and then decreased subsequently but heart rate was higher in NTG subjects at phase T4 to T9, indicating that Esmolol is better drug in attenuating rise in heart rate following laryngoscopy and intubation as compared to oral NTG spray.



Graph 1: Comparison of Heart Rate in the Both Groups

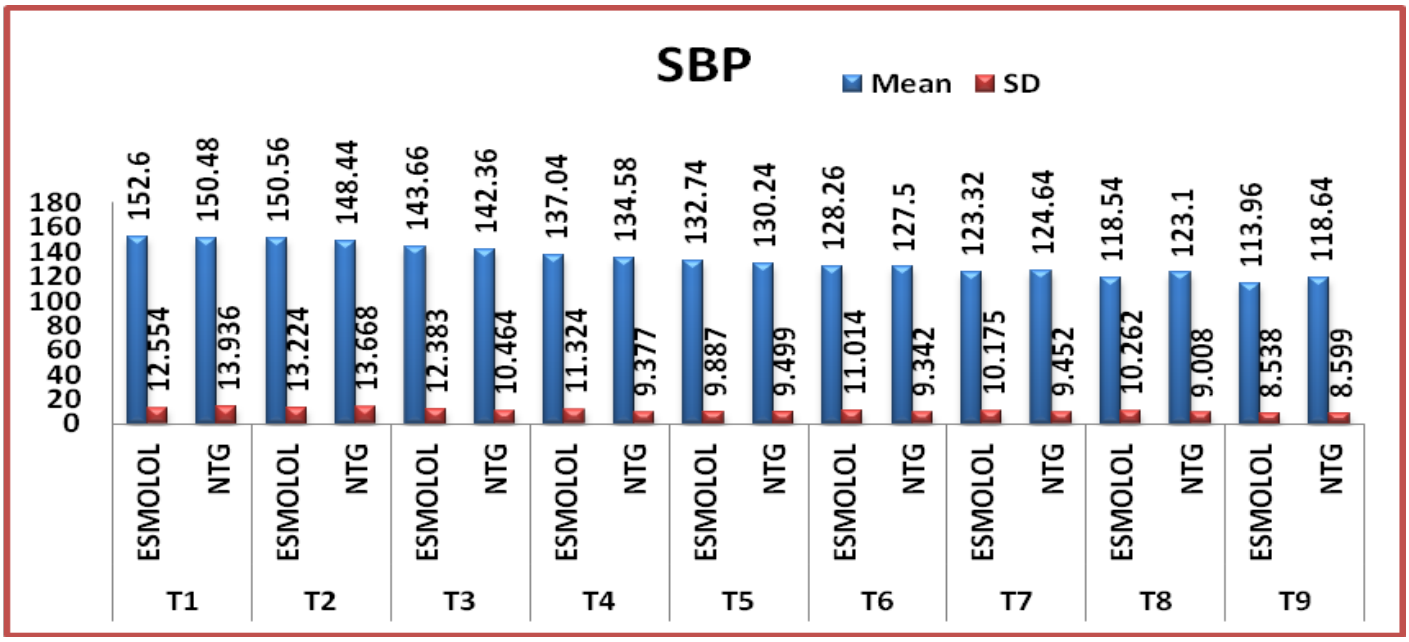
Comparison of Systolic Blood Pressure In Both The Groups

Table 3 SBP

Comparison of SBP in both the groups								
Phase	**Medicine**	**N**	**Mean**	**SD**	**Std. Error Mean**	**t**	**df**	**P value**
T1_SBP	ESMOLOL	50	152.60	12.554	1.775	.799	98	.426
	NTG	50	150.48	13.936	1.971			
T2_SBP	ESMOLOL	50	150.56	13.224	1.870	.788	98	.432
	NTG	50	148.44	13.668	1.933			
T3_SBP	ESMOLOL	50	143.66	12.383	1.751	.567	98	.572

	NTG	50	142.36	10.464	1.480			
T4_SBP	ESMOLOL	50	137.04	11.324	1.602	1.183	98	.240
	NTG	50	134.58	9.377	1.326			
T5_SBP	ESMOLOL	50	132.74	9.887	1.398	1.289	98	.200
	NTG	50	130.24	9.499	1.343			
T6_SBP	ESMOLOL	50	128.26	11.014	1.558	.372	98	.711
	NTG	50	127.50	9.342	1.321			
T7_SBP	ESMOLOL	50	123.32	10.175	1.439	-.672	98	.503
	NTG	50	124.64	9.452	1.337			
T8_SBP	ESMOLOL	50	118.54	10.262	1.451	-2.361	98	.020
	NTG	50	123.10	9.008	1.274			
T9_SBP	ESMOLOL	50	113.96	8.538	1.207	-2.731	98	.007
	NTG	50	118.64	8.599	1.216			

As observed from above table difference in means of SBP was not found significant statistically (P>0.05) at Phases from T1 to T 7. At T8 and T9 it was significant (P<0.05) and found higher in NTG group., since SBP is higher in NTG group patients, it implies that NTG is poor drug than Esmolol in controlling rise in SBP following laryngoscopy and intubation.



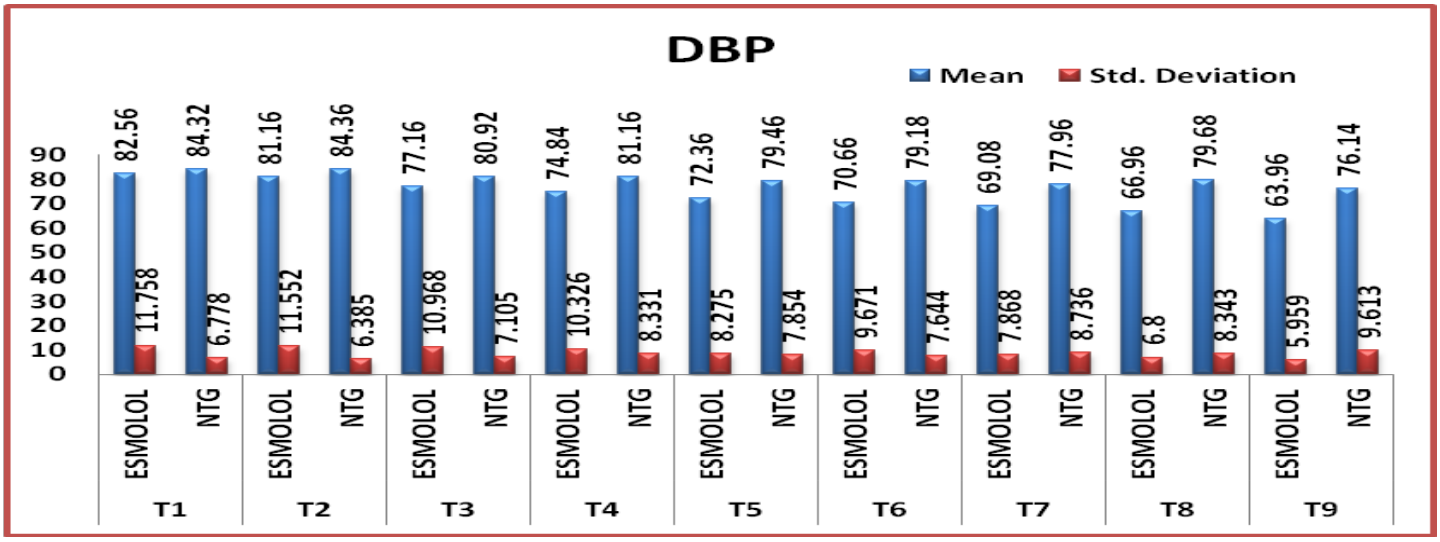
Graph 2: Comparison of SBP in Both the Groups

Comparison of Diastolic Blood Pressure in Both the Groups

Table 4 DBP

Comparison of DBP in both the groups								
Phase	**Medicine**	**N**	**Mean**	**Std. Deviation**	**Std. Error Mean**	**t**	**df**	**P value**
T1_DBP	ESMOLOL	50	82.56	11.758	1.663	-.917	98	.361
	NTG	50	84.32	6.778	.959			
T2_DBP	ESMOLOL	50	81.16	11.552	1.634	-1.714	98	.090
	NTG	50	84.36	6.385	.903			
T3_DBP	ESMOLOL	50	77.16	10.968	1.551	-2.034	98	.045
	NTG	50	80.92	7.105	1.005			
T4_DBP	ESMOLOL	50	74.84	10.326	1.460	-3.368	98	.001
	NTG	50	81.16	8.331	1.178			
T5_DBP	ESMOLOL	50	72.36	8.275	1.170	-4.400	98	.000
	NTG	50	79.46	7.854	1.111			
T6_DBP	ESMOLOL	50	70.66	9.671	1.368	-4.887	98	.000
	NTG	50	79.18	7.644	1.081			
T7_DBP	ESMOLOL	50	69.08	7.868	1.113	-5.341	98	.000
	NTG	50	77.96	8.736	1.236			
T8_DBP	ESMOLOL	50	66.96	6.800	.962	-8.356	98	.000
	NTG	50	79.68	8.343	1.180			
T9_DBP	ESMOLOL	50	63.96	5.959	.843	-7.615	98	.000
	NTG	50	76.14	9.613	1.359			

As observed from above table difference in means of DBP was not found significant statistically (P>0.05) at Phases T1 and T2. From T3 to T9 it was significant (P<0.05) and found higher in NTG group subjects indicating better haemodynamic stability in Esmolol.



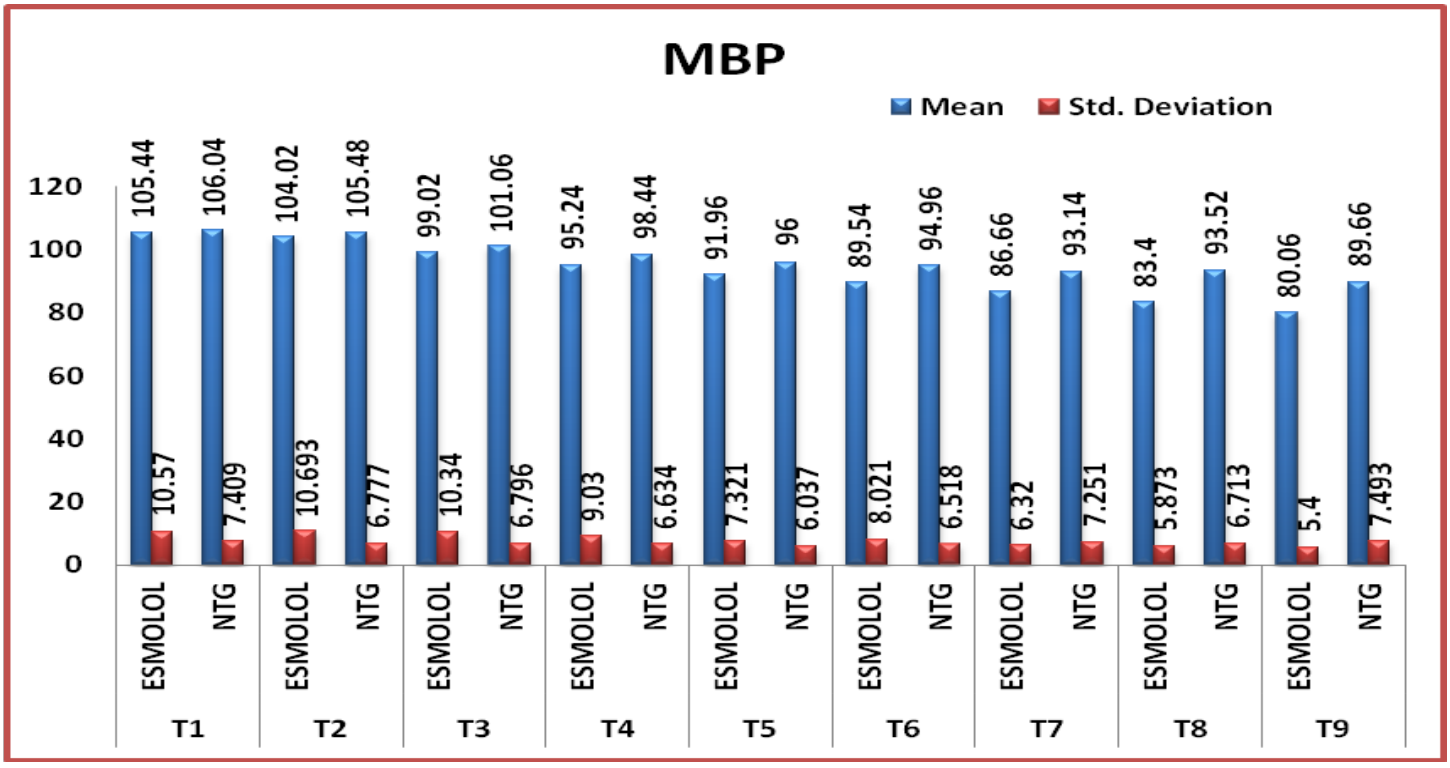
Graph 3: Comparison Of Dbp In Both The Groups

Comparison Of Mean Blood Pressure In Both The Groups

Table 5 Mean Bp

Comparison of MBP in both the groups								
Phase	**Medicine**	**N**	**Mean**	**Std. Deviation**	**Std. Error Mean**	**t**	**df**	**P value**
T1_MEAN BP	ESMOLOL	50	105.44	10.570	1.495	-.329	98	.743
	NTG	50	106.04	7.409	1.048			
T2_MEAN BP	ESMOLOL	50	104.02	10.693	1.512	-.815	98	.417
	NTG	50	105.48	6.777	.958			
T3_MEAN BP	ESMOLOL	50	99.02	10.340	1.462	-1.166	98	.247
	NTG	50	101.06	6.796	.961			
T4_MEAN BP	ESMOLOL	50	95.24	9.030	1.277	-2.020	98	.046
	NTG	50	98.44	6.634	.938			
T5_MEAN BP	ESMOLOL	50	91.96	7.321	1.035	-3.011	98	.003
	NTG	50	96.00	6.037	.854			
T6_MEAN BP	ESMOLOL	50	89.54	8.021	1.134	-3.708	98	.000
	NTG	50	94.96	6.518	.922			
T7_MEAN BP	ESMOLOL	50	86.66	6.320	.894	-4.764	98	.000
	NTG	50	93.14	7.251	1.025			
T8_MEAN BP	ESMOLOL	50	83.40	5.873	.831	-8.023	98	.000
	NTG	50	93.52	6.713	.949			
T9_MEAN BP	ESMOLOL	50	80.06	5.400	.764	-7.350	98	.000
	NTG	50	89.66	7.493	1.060			

As observed from above table difference in means of MBP was not found significant statistically (P>0.05) at Phases T1, T2 and T3. From T4 to T9 it was significant (P<0.05) and found higher in NTG group subjects indicating better haemodynamic stability of Esmolol as compared to NTG.



Graph 4: Comparison of Mbp in Both the Groups

Discussion

The induction of anaesthesia, laryngoscopy, endotracheal intubation and surgical stimulation often evoke cardiovascular responses like alterations in systemic blood pressure, heart rate, cardiac rhythm and blood sugar due to exaggerated sympathetic activity because of catecholamine release. The response following laryngoscopy and intubation peaks at 1-2 min and returns to baseline within 5-10 mins.

This response was first described by Reid and Brace in 1940[1] . These effects were usually well tolerated by healthy individuals, but these may be fatal in patients with hypertension, coronary artery disease or intracranial aneurysm. This sympathetic stimulation results in tachycardia and elevation of blood pressure[4,5,6]. Thus the attenuation of this response assumes a great significance especially in susceptible patients.

Several pharmacological agents used for the attenuation of the pressor response includes opioids[7], calcium channel blockers[8], beta-blockers like esmolol[9], nitroglycerine[10], alpha2 agonist like dexmedetomidine[11], gabapentin[12],magnesium sulphate[13], inhalational anaesthetic agents[14] etc.

In the present study esmolol and nitroglycerin oral spray were selected because of their similar pharmacokinetic profile i.e. rapid onset of action, short duration of action, rapid elimination. In this study we compared the effects, side effects, safety profile, haemodynamic responses of Nitroglycerine oral spray versus intravenous Esmolol following endotracheal intubation in the patients posted for elective surgical procedure.

Esmolol is an ultra short-acting cardioselective beta adrenoceptor antagonist with rapid onset, short duration of action and rapid elimination. The peak effect of esmolol occurs within 2 min. from the time of intravenous administration. It is metabolized by esterase in the cytosol of red blood cell, resulting in a short duration of action(8-9) min. These characteristics makes esmolol an ideal agent for suppressing acute increases in Blood Pressure and Heart Rate associated due to heightened catecholamine output[15] during laryngoscopy and intubation. Glyceryltrinitrate (NTG) is a vasodilator causing relaxation of vascular smooth muscles with venous dilation predominantly over arterial dilation. Due to venodilation it decreases the preload and blunts the hypertensive response of intubation. In the patients with low cardiac output and moderately elevated vascular resistance it seems to be the best choice[16]. However, vasodilation of NTG causes reflex tachycardia. Nitroglycerine lingual spray is a metered dose spray containing nitroglycerine. It delivers nitroglycerine (400 mcg per spray) in the form of spray droplets. NTG spray is easy to use and seems cost effective because there are approximately 70 metered sprays of NTG per pen spray, so can be used in many patients.

In our study Nitroglycerin oral spray prevented a rise in systolic blood pressure , diastolic blood pressure and mean blood pressure but it failed to attenuate rise in heart rate following laryngoscopy and intubation the reason for this could have been the tendency of Nitroglycerin (NTG) to cause reflex tachycardia , as seen in other studies also[10,17]. while Esmolol on the other hand effectively controlled increase in Systolic blood pressure, Diastolic blood pressure, Mean arterial pressure and Heart Rate following laryngoscopy and intubation. These findings are similar to those of other studies[18,19,20] where esmolol was used for Haemodynamic stability during laryngoscopy and intubation .

Dich-Nielsen et al (1986)[17] studied the effect of intranasally administered nitroglycerin (NTG) on the cardiovascular response to laryngoscopy and intubation and found that there was significant rise in heart rate in all the patients.

Gupta P et al (2009)[10] studied Attenuation of Haemodynamic Responses to Laryngoscopy & Intubation following Nitroglycerin and Esmolol infusion. At the end of study it was observed that nitroglycerin prevents rise in diastolic blood pressure and attenuates the rise in systolic blood pressure, but failed to attenuate increase in the heart rate, while esmolol effectively controlled the increase in systolic BP, diastolic BP and heart rate following intubation. So it was concluded that esmolol infusion is more effective in attenuating Haemodynamic responses to intubation as compared to nitroglycerin infusion. This finding is similar to that of Singh et al.[21]

and Vanden Berg et al.[19] who also reported failure of nitroglycerin to attenuate increase in heart rate following intubation.

Conclusion

With the above study we observed that intravenous Esmolol in dose of 0.5 mg/kg given 1 minute before laryngoscopy and intubation effectively attenuates rise in Blood pressure and Heart rate as compared to oral Nitroglycerine spray 2 puffs(800 mcg). NTG spray also controls rise in Blood Pressure, maintains cardiac stability, it but fails to attenuate increase in Heart Rate due to its tendency to produce reflex tachycardia.

So finally with our study we conclude that intravenous Esmolol in dose of 0.5 mg/kg is better drug for attenuating pressor response following laryngoscopy and intubation as compared to 800 mcg NTG oral spray.

References

1. Reid LC, Brace DE. Irritation of the respiratory tract and its reflex effect upon heart. Surg Gynaecol Obstet. 1940;70:157–62.
2. Bruder N, Ortega D, Granthil C. Consequences and prevention methods of hemodynamic changes during laryngoscopy and intratracheal intubation. Ann Fr Anesth Reanim. 1992;11:57–71.
3. Malade A, Sarode V. Attenuation of hemodynamic response to endotracheal intubation: Fentanyl v/s lignocaine. Internet J Anesthesiol. 2007;12:10954–64.
4. Forbes AM, Dally FG. Acute hypertension during induction of anaesthesia and endotracheal intubation in normotensive man. Br J Anaesth. 1970 ;42:618-24.
5. Nishikawa K, Kawana S, Namiki A. Comparison of the lightwand technique with direct laryngoscopy for awake endotracheal intubation in emergency cases. J Clin Anesth.2001;13:259–63.
6. Shribman AJ, Smith G, Achola KJ. Cardiovascular and catecholamine responses to laryngoscopy with and without tracheal intubation. Br J Anaesth. 1987;59:295–9.
7. Habib AS, Parker JL, Maguire AM, Rowbotham DJ. Effects of remifentanil and alfentanil on the cardiovascular responses to induction of anaesthesia and tracheal intubation in the elderly. Br J Anaesth. 2002;88:430–3
8. Kumar N, Batra YK, Bala I, Gopalan S. Nifedipine attenuates the hypertensive response to tracheal intubation in pregnancy-induced hypertension. Can J Anaesth. 1993;40:329–33
9. Kindler CH, Schumacher PG, Schneider MC, Urwyler A. Effects of intravenous lidocaine and/or esmolol on Haemodynamic responses to laryngoscopy and intubation: a double-blind, controlled clinical trial. Journal of clinical anaesthesia. 1996 1;8:491-6.
10. Gupta PK, Panda BK, Verma RK, Ranjan P. Attenuation of Haemodynamic responses to laryngoscopy and intubation following nitroglycerine and esmolol infusion. Internet J Anaesthesiol. 2010;22:5890-6110.
11. Yildiz M, Tavlan A, Tuncer S, Reisli R. Effect of Dexmedetomidine on Haemodynamic responses to laryngoscopy and intubation: perioperative haemodynamic and anesthetic requirements. Drugs RD 2006;7:43-52
12. Kumari I, Pathania VS. A prospective randomised double blind placebo controlled trial of oral Gabapentin in attenuation of haemodynamic responses during laryngoscopy & tracheal intubation. J Anaesth Clin Pharmacol 2009;25:439-43.
13. Ashton WB, James MF, Janicki P, Uys PC. Attenuation of the pressor response to tracheal intubation by magnesium sulphate with and without alfentanil in hypertensive proteinuric patients undergoing caesarean section. Br J Anaesth 1991;67:741-7.
14. Aouad MT, Sayyid SS, Zalaket MI, Baraka AS. Intravenous lidocaine as adjuvant to sevoflurane anaesthesia for endotracheal intubation in children. Anesth Analg 2003;96:1325–7.
15. Figueredo E, Garcia-fuentes EM. Assessment of the efficacy of esmolol on the haemodynamic changes induced by laryngoscopy and tracheal intubation: A meta-analysis. Acta Anaesthesiol Scand. 2001;1:1011–22.
16. Kaplan JA, Dunbar RW, Jones EL. Nitroglycerin infusion during coronary-artery surgery. Anesthesiology. 1976;45:14–21.

17. Dich-nielsen J, Hole P, Lang-Jensen T, Owen-falkenberg A. The effect of intranasal administered nitroglycerine on the blood pressure response to laryngoscopy and intubation in patients undergoing coronary artery by-pass surgery. Acta Anaesthesiol Scand 1986;30:23-7.
18. Hwang JJ, KoYP, Jen RK, Cheng CR. The Use of Intranasal Nitroglycerine to Prevent Pressor Responses during Intubation in General Anaesthesia: A Comparison of Various Doses. Acta Anaesthesiol Sin 1995,33: 205-10
19. Vanden Berg AA, Savva D, Honjol NM. Attenuation of the haemodynamic responses to noxious stimuli in patients undergoing cataract surgery. A comparison of magnesium sulphate, esmolol, lignocaine, nitroglycerine and placebo given i.v. with induction of anaesthesia. Euro J Anaesth. (1997), 14:2:134-147
20. Vucevic M. Purdy GM, Ellis FR. Esmolol hydrochloride for management of the cardiovascular stress responses to laryngoscopy and tracheal intubation. Br. J. Anaesth 1992;68: 529-30.
21. Singh H, Vichitvejpaisal P, Gaines GY et al. comparative effects of lidocaine, esmolol, and nitroglycerin in modifying the hemodynamic response to laryngoscopy and intubation. J. Clin. Anesth. 1995; 7: 5-8.